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Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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Abstract

Objectives: To summarize the range, strength, and validity of reported associations between environmental risk factors and non-Hodgkin lymphoma (NHL), and to evaluate the concordance between associations reported in meta-analyses (MAs) of summary level data and MAs of individual participant data (IPD).

Design: Umbrella review.

Data sources: MEDLINE, Embase, Scopus, Web of Science Core Collection, Cochrane Library, and Epistemonikos from inception to 23 July 2021.

Eligibility criteria: English language MAs of summary level data and MAs of IPD evaluating associations between environmental risk factors and incident NHL (overall and NHL subtypes).

Data extraction and synthesis: Summary effect estimates from MAs of summary level data were re-estimated using a random-effects model and classified as presenting non-significant, weak ($P<0.05$), suggestive ($P<10^{-3}$ and $>$1000 cases), highly suggestive ($P<10^{-6}$, $>$1000 cases, largest study reporting a significant association), or convincing ($P<10^{-6}$, $>$1000 cases, largest study reporting a significant association, $I^2 < 50\%$, 95\% prediction interval excluding the null value, and no evidence of small study effects and excess significance bias) evidence. When the same exposures, exposure contrast levels, and outcomes were evaluated in MAs of summary level data and MAs of IPD from the International Lymphoma Epidemiology (InterLymph) Consortium, concordance in terms of direction, level of significance, and overlap of 95\% confidence intervals (CI) was examined. We assessed the methodological quality of the MAs of summary level data using the A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2 tool.

Results: We identified 85 MAs of summary level data reporting 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. Most (225, 88\%) associations presented either non-significant or weak evidence. The 11 (4\%) associations presenting highly suggestive evidence were primarily for autoimmune or infectious disease-related risk factors. Only 1 association, history of celiac disease and risk of NHL, presented convincing evidence. Overall, 40 associations reported in MAs of summary level data were also evaluated in InterLymph MAs of IPD. Of these, 22 (55\%) pairs were in the same direction, had the same level of statistical significance, and had overlapping 95\% CIs. There were 28 (70\%) pairs where the summary effect sizes from the MAs of IPD were more conservative. Nearly all (79/85, 93\%) MAs of summary level data were classified as having critically low quality.
Conclusion: This umbrella review suggests that there is a mass production of low-quality MAs of summary level data, many of which report weak associations between environmental risk factors and NHL, and highlights the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.

Systematic review registration PROSPERO CRD42020178010.
What is already known on this topic

- Observational studies have suggested that environmental risk factors, including clinical, occupational, and lifestyle exposures, may be associated with the risk of developing non-Hodgkin lymphoma.
- As a result of the large number of observational studies evaluating the impact of environmental risk factors on non-Hodgkin lymphoma, dozens of systematic reviews and meta-analyses of summary and individual participant level data have focused on synthesizing evidence and identifying potential risk factors.
- Little is known about: (1) the range, strength, and validity of associations between environmental risk factors and non-Hodgkin lymphoma reported in meta-analyses or (2) the concordance between meta-analyses of summary level data and meta-analyses of individual participant data evaluating the same associations.

What this study adds

- This umbrella review suggests that although a large range of environmental risk factors for non-Hodgkin lymphoma have been evaluated in meta-analyses, the vast majority of meta-analyses of summary level data are low quality and present either non-significant or weak associations.
- Overall, only half of the associations that were evaluated in both meta-analyses of summary level data and meta-analyses of individual participant data were in the same direction, had the same level of statistical significance, and had overlapping 95% confidence intervals.
- Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, this umbrella review highlights the need for improving not only primary studies but also evidence synthesis in the field of non-Hodgkin lymphoma etiology.
Introduction

Non-Hodgkin lymphoma (NHL), a lymphoid cancer that originates in white blood cells called lymphocytes, is the 9th leading cause of cancer death among both men and women. NHL accounts for nearly 90% of all lymphomas and is the most common hematologic malignancy in the world. Although NHL can be broadly categorized into two major groups (i.e., B-cell, T-cell/natural killer-cell lymphomas), it represents a diverse group of malignant disorders with dozens of subtypes. Evidence suggests that NHL is more common among older adults, men, and people with a first degree relative with NHL. However, despite substantial effort to identify NHL causes and risk factors over the past few decades, the exact etiology of NHL is unknown.

Epidemiological studies have suggested that environmental risk factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors, may be associated with the risk of developing NHL. In particular, several prominent potential risk factors proposed in the literature include viruses (e.g., Epstein-Barr virus infection), autoimmune diseases (e.g., Sjogren’s syndrome, celiac disease, and rheumatoid arthritis), and immune dysregulation (i.e., patients with a history of organ transplantation, acquired immunodeficiency syndromes (HIV/AIDS), or immunosuppressive medication treatment). However, given that these exposures and conditions are relatively rare, a broad range of additional environmental risk factors, including exposure to insecticides, red and processed meat consumption, and hair dye, have been evaluated and proposed as potential risk factors.

As a result of the large number of observational studies evaluating the impact of environmental risk factors on NHL, dozens of systematic reviews and meta-analyses (MAs) of summary level data have focused on synthesizing evidence and identifying the most promising risk factors. Moreover, the International Lymphoma Epidemiology (InterLymph) Consortium, a group of investigators who pool data from their completed or ongoing NHL case-control studies, have published multiple MAs of individual participant data (IPD) evaluating associations between various environmental risk factors and NHL. Although these MAs of IPD contain thousands of NHL cases and are strengthened by their ability to utilize raw data that are harmonized across multiple studies, they do not include evidence from case-control and cohort studies conducted by investigators outside of the InterLymph Consortium. Therefore, MAs of summary level data and MAs of IPD evaluating the same associations between environmental risk factors and NHL may sometimes lead to discordant results and conclusions.
To provide an overview of the range, strength, and validity of reported associations between environmental risk factors and NHL, we conducted an umbrella review of the evidence across published systematic reviews and MAs. In addition to summarizing the results, determining hints of biases, and assessing the quality of reviews, we evaluated the consistency between all associations reported in both MAs of summary level data and InterLymph MAs of IPD.

Methods

We conducted an umbrella review on the reported associations between environmental risk factors and the risk of NHL. Umbrella reviews are used to systematically identify and evaluate evidence reported in published systematic reviews and MAs. Our study protocol was pre-registered on the International prospective register of systematic reviews (CRD42020178010) and posted on Open Science Framework (https://osf.io/6g2ev/). We did not involve patients or members of the public when designing the question and study, interpreting the results, and/or drafting the manuscript.

Database searches

Working with an experienced medical librarian (KN), we developed and performed a comprehensive search of multiple databases: MEDLINE (Ovid), Embase (Ovid), Scopus, Web of Science Core Collection (as licensed at Yale University), Cochrane Library, and Epistemonikos from inception to July 24th 2020 (eTable 1 in Supplement 1). In each database, we used three concepts: NHL, risk factors, and the study designs of interest (MAs, systematic reviews, and pooled analyses). The search strategy for NHL was based on the search strategy used in a published review. The study design search strategy used elements from a published search filter. Database limits were used to exclude conference papers and meeting abstracts. No language limits were used. Records were deduplicated in EndNote, the Yale Reference Deduplicator, and Covidence. No citation chaining was conducted.

On July 24th 2020, searches were run in each database and 14,753 references were identified. After deduplication in EndNote and Covidence, 8025 unique records were uploaded for screening. On July 23th 2021, all searches were rerun and deduplicated and 969 additional unique records were added to Covidence for manual screening. In total, our search retrieved 8994 unique records across all databases.

Eligibility criteria
We included English language systematic reviews, MAs of summary level data (i.e., MAs using effect estimates reported in individual studies), and MAs of IPD of observational studies evaluating associations between environmental risk factors and incident NHL (overall or any subtypes, eTable 2 in Supplement 1). We considered all non-genetic factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors that can affect a person’s health, as environmental risk factors. Systematic reviews and MAs were excluded if they primarily focused on genetic risk factors, evaluated risk factors for the treatment, relapse, remission, or prognosis of NHL patients, or examined NHL as a risk factor for other diseases (eText 1 in Supplement 1).

Two reviewers (XS and HZ) independently screened the titles and abstracts and then full-text versions of potentially eligible articles. Any disagreements or uncertainties were discussed with a third reviewer (JDW).

**Data extraction**

Data extraction was performed independently by two reviewers (XS and HZ), and a third reviewer (JDW) arbitrated all potential discrepancies. For each systematic review and MA, we recorded the first author, year of publication, article title, journal of publication, study design, population, examined exposures and their definitions, and examined outcomes and their definition (i.e., NHL or NHL subtypes). For all MAs of summary level data, we identified each unique exposure-outcome relationship and recorded the number of studies included, total sample size, number of cases, and study-specific adjusted relative risk estimates (e.g., relative risks, hazard ratios, or odds ratios) and corresponding 95% confidence intervals (CIs). For studies that considered multiple exposure contrast levels, control groups, and/or confounders, we prioritized the effect estimates comparing ever versus never exposure that were adjusted for the largest number of potential confounders. Whenever ever versus never exposures comparisons were not reported, we recorded the effect estimates comparing the highest versus lowest levels of exposures. When multiple MAs of summary level data were identified for the same environmental risk factor, we selected the effect estimates that were based on the largest number of component studies.

For systematic reviews with unique associations that were not investigated in MAs of summary level data, we recorded the number of studies identified, the reasons why MAs were not performed, and the main conclusions. Lastly, for all MAs of IPD, one author (JDW) identified the exposures, NHL subtypes, and number of NHL cases for: (1) all nominally statistically significant

(P<0.05) associations and (2) any associations that were also evaluated in MAs of summary level data.

**Statistical analysis**

First, we re-estimated all summary effect estimates and 95% CIs using a random-effects DerSimonian and Laird (DL) estimator. When summary effect estimates were reported without a corresponding P value, we used the 95% CIs to calculate the P value using a previously described method. Next, we categorized the strength of the reported associations across five levels (Table 1), following previously established methodology. All associations with P>0.05 were classified as non-significant. Associations with P<0.05 and fewer than 1000 cases were classified as weak. Associations with P<10^{-3} and at least 1000 cases were classified as suggestive. For associations with P<10^{-6}, at least 1000 cases, and P<0.05 for the largest component study, we sequentially evaluated 95% prediction intervals (PIs), presence of small study effects (Egger regression asymmetry test), and evidence of excess significance using the Ioannidis test. PIs provide a potential range of the true effect and incorporate the uncertainty of whether the observed effect will arise in future studies as well. P<0.1 for Egger’s test suggests the presence of small study effects (i.e. small studies are more prone to report larger or more significant results while larger studies tend to report more conservative results). The Ioannidis test estimates whether the observed number of studies with nominally statistically significant (P<0.05) results in a MA differs from the expected number of studies with nominally statistically significant studies. Associations with 95% PIs including the null, statistically significant Egger’s test (P<0.1), and/or evidence of excess significance were classified as highly suggestive. Associations with 95% prediction intervals excluding the null, non-statistically significant Egger’s test (P>0.1), and no evidence of excess significance were classified as convincing.

Statistical analysis was conducted using *metagen* package in R version 4.1.0. (eTable 3 in Supplement 1).

**Concordance between MAs of summary level data and InterLymph MAs of IPD**

When the same exposures, exposure contrast levels, and NHL subtypes were examined in MAs of summary level data and InterLymph MAs of IPD, two authors (XS and JDW) determined whether the effect estimates: (1) were in the same direction, (2) had overlapping 95% CIs, and/or (3) had the same level of statistical significance (P<0.05 or P≥0.05). Associations with all three criteria fulfilled were classified as fully concordant. Lastly, we determined how often MAs of summary
level data included at least one-third of the same component studies as the InterLymph MAs of IPD.

**Quality Assessment**

Four reviewers (XS, HZ, YD, and JDW) evaluated the quality of all MAs of summary level data using A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2. Any discrepancies were discussed and resolved by consensus. Based on the suggested rating scheme, the overall confidence in the results of the MAs of summary level data were classified as high, moderate, low, or critically low.

**Results**

**Literature search**

Among 16438 records identified through the literature search, 7444 were excluded as duplicates, leaving 8994 titles and abstracts for initial screening. 7970 records were excluded based on the title and abstract and 1024 were screened at the full text stage for inclusion. After excluding 904 records at the full text stage (Supplement 2), our searches identified 85 MAs of summary level data evaluating 134 unique environmental risk factors and 8 systematic reviews evaluating 8 unique risk factors (Figure 1, eText 2 in Supplement 1 and Supplement 3). In addition, we identified 27 MAs of IPD (Supplement 3), of which 24 (89%) were conducted by the InterLymph Consortium. More than one MA of summary level data was identified for 44 (44/134, 33%) risk factors (eTable 4 in Supplement 1). Among the MAs of summary level data selected based on the largest number of component studies, approximately half were also the most recently published (25/44, 57%) (eTable 4 in Supplement 1).

**MAs of summary level data**

Among the 257 associations reported in the MAs of summary level data, 124 and 133 evaluated the impact of environmental risk factors on the risk of NHL overall and NHL subtypes, respectively. NHL subtypes included follicular lymphoma (FL; 43, 17%), diffuse large B-cell lymphoma (DLBCL; 35, 14%), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL; 31, 12%), T-cell lymphoma (TCL; 12, 5%), B-cell lymphoma (BCL; 4, 2%), marginal zone lymphoma (MZL; 2, 1%), endemic Burkitt Lymphoma (eBL; 1, 0.4%), Burkitt lymphoma (BL; 1, 0.4%), primary cutaneous lymphoma (PCL; 1, 0.4%). The most common exposure
categories were dietary factors (90, 35%), medical histories and comorbidities (54, 21%), chemicals and pesticides (42, 16%), lifestyle factors (29, 11%), drugs, vaccinations, and medical procedures (30, 12%), and occupational (12, 5%). The median number of component studies per MA of summary level data was 5 (IQR 4-10). The median number of NHL cases, among the 64 (75%) MAs reporting this information, was 1533 (IQR, 482-5872).

**Credibility criteria**

After re-estimating the 257 associations using a random-effects DL estimator and applying the credibility criteria, 145 (56%) were classified as presenting non-significant evidence (Table 3). There were 80 (31%) nominally statistically significant ($P<0.05$) associations that were classified as presenting weak evidence. There were 20 (8%) statistically significant associations ($P<10^{-3}$), based on analyses with at least 1000 NHL cases, that were classified as presenting suggestive evidence. Only 12 (5%) associations were classified as presenting highly suggestive or convincing evidence, with a $P<10^{-6}$, at least 1000 cases, and a $P<0.05$ for the largest component study. The 11 highly suggestive associations were for history of renal transplantation and risk of NHL, rheumatoid arthritis and risk of NHL, primary Sjogren's syndrome and risk of NHL, systemic lupus erythematosus and risk of NHL, celiac disease and risk of TCL, tuberculosis and risk of NHL, hepatitis B virus (HBV) and risk of NHL and BCL, hepatitis C virus (HCV) and risk of NHL and DLBCL, and teaching as an occupation and risk of NHL (Table 2).

There was one association, between history of celiac disease and risk of NHL (OR 2.61, 95% CI 2.04 to 3.33; 110, 245 NHL cases from 8 individual studies), that was classified as presenting convincing evidence. Although the association had $P<10^{-6}$, at least 1000 cases, a nominally significant result for the largest component study, low heterogeneity ($I^2 <50\%$), a 95% PI excluding the null, and no evidence of small study effects, we were unable to conduct the Ioannidis test due to the incomplete information reported about the component studies. Across all the 112 nominally statistically significant associations, 63 (56%) had relative risk values that were between 0.67 and 1.50.

**Systematic reviews**

We identified 8 systematic reviews without quantitative synthesis with 8 unique associations that were not investigated by MAs of summary level data (eText 2 in Supplement 1).

**MAs of IPD**
We identified 27 MAs of IPD, of which 24 were from the InterLymph Consortium. The 24 InterLymph MAs of IPD reported 715 nominally statistically significant ($P<0.05$) associations. Of these, 116 and 21 associations were based on analyses with at least 1000 NHL cases and had $P<10^{-3}$ and $P<10^{-6}$, respectively (Table 4 and eTable 5 in Supplement 1). Overall, the unique suggestive exposures categories were alcohol consumption on risk of DLBCL, MZL and NHL, history of Sjogren’s syndrome on risk of DLBCL, MZL and NHL, recreational sun exposure on risk of DLBCL, FL and NHL, and history of HCV on risk of DLBCL, MZL and NHL. Although the 3 non-InterLymph MAs of IPD examined 5 associations not reported in systematic reviews and/or MAs of the summary level data, including fish eaters and risk of NHL, vegetarians and vegans and risk of NHL, maternal age at the time of the child’s birth and risk of NHL, paternal age at the time of the child’s birth and risk of NHL, and leisure-time physical activity and risk of NHL, none were nominally statistically significant.

Consistency between MAs of summary level data and InterLymph MAs of IPD

There were 40 associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD (Table 5 and eFigure 1 in Supplement 1). While 22 (55%) evaluated the impact of environmental risk factors on the risk of NHL overall, the other half (18, 45%) focused on various NHL subtypes (CLL/SLL, 5 (13%); DLBCL, 5 (13%); FL, 4 (10%); TCL, 3 (8%); MZL, 1 (3%)).

Overall, 22 of 40 (55%) of the associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. There were 10 (25%) pairs where the effect estimates were both statistically significantly increased, 3 (8%) where they were both statistically significantly decreased, 7 (18%) where they were both non-statistically significantly increased, and 2 (5%) where they were both non-statistically significantly decreased (Kappa=0.37, eTable 7 and eFigure 1 in Supplement 1). The 13 associations where the MAs of the summary level data and MAs of IPD effect estimates were both statistically significantly increased or decreased were for history of smoking and risk of TCL, history of drinking and risk of NHL, DLBCL, and FL, history of primary Sjogren's syndrome and risk of NHL, history of systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL, TCL and DLBCL, and history of HCV and risk of NHL, DLBCL, MZL and CLL/SLL. There were 28 (70%) pairs where the effect sizes...
from the MAs of IPD were more conservative than the effect sizes from the MAs of summary level data.

There were 4 suggestive associations reported in MAs of summary level data that were also evaluated in the InterLymph MAs of IPD. Of these, 3 associations from MAs of IPD had effect estimates in the same direction, had $P<10^{-3}$, and were based on analyses with at least 1000 NHL cases (i.e., history of psoriasis and risk of NHL, history of Herpes Zoster and risk of NHL, and history of farming as an occupation and risk of NHL). There were 8 highly suggestive associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD. Of these, 7 associations from the MAs of IPD had effect estimates in the same direction, had $P<10^{-6}$, and were based on analyses with at least 1000 NHL cases (i.e., history of rheumatoid arthritis and risk of NHL, history of primary Sjogren's syndrome and risk of NHL, history systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL and TCL, history of tuberculosis and risk of NHL, and history of HCV and risk of NHL).

There were 19 (48%) pairs where the MAs of summary level data included at least one-third of the same component studies as the InterLymph MAs of IPD. There was no difference in terms of concordance (direction, statistical significance of summary effect estimates and overlapping 95% CIs) between MAs of summary level data that included at least one-third versus fewer than one-third of the same component studies as the MAs of IPD (12/19 (63%) vs 10/21 (48%), $P=0.32$).

**Methodological quality**

The vast majority of the 85 MAs of summary level data had overall confidence ratings of low (3, 4%) or critically low (79, 93%) according to the AMSTAR 2 tool. There were 2 (2%) where the overall confidence in the results was classified as moderate. Only 1 (1%), evaluating the association between tuberculosis and risk of NHL, had an overall confidence rating of high (eTable 6 in Supplement 1). The most common unfulfilled critical domains of the AMSTAR 2 tool were incomplete justification of excluded studies (74, 87%) and missing or no information about preregistered protocols (72, 85%).

**Discussion**

In this umbrella review, we evaluated the range, strength, and validity of reported associations between environmental risk factors and NHL across 85 MAs of published observational studies.
Overall, we identified 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. The vast majority of the associations, including those evaluating various dietary, clinical, lifestyle, chemical, and occupational exposures, were classified as having either non-significant or weak evidence. More than half of the nominally significant associations were only marginally significant. Only 5% of the associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence. When the same associations were evaluated in MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Overall, effect sizes from MAs of IPD were more conservative. This umbrella review suggests that there is a mass production of low-quality MAs of summary level data reporting weak associations between environmental risk factors and NHL. These findings highlight the need for improving not only primary studies but also evidence synthesis in this field. Moreover, given that many of the assessed risk factors are correlated, simultaneous consideration of multiple risk factors will be useful to understand which ones have the strongest, independent effects on NHL risk.

Although a wide range of environmental exposures have been evaluated and proposed as potential risk factors for NHL, our evaluation suggests that the only highly suggestive or convincing exposures proposed in MAs of summary level data and MAs of IPD are related to autoimmune and infectious diseases. In particular, the prominent autoimmune disease-related risk factors include history of celiac disease, rheumatoid arthritis, primary Sjogren's syndrome, and systemic lupus erythematosus. Although the exact mechanisms behind these associations remains unclear, many autoimmune disorders are characterized by chronic inflammation, which may intensify B cell or T cell activation and promote the development of lymphoma. Previous studies have also suggested that the dysfunction of some protein families, such as FAS and tumor necrosis factor, and the interplay between various immune cells, could be potential mechanisms. However, there is uncertainty when it comes to the temporality of these associations, with studies reporting that autoimmune diseases can occur during lymphoma.

Associations between viral and bacterial infections and NHL risk have been suggested for several decades. Different hypotheses for HCV-related lymphomagenesis have been proposed. For instance, chromosomal aberrations, including chromosome t(14;18) translocation, have been found to be associated with mixed cryoglobulinemia, a disorder most commonly caused by HCV infection and that can evolve into lymphoproliferative disorders. Furthermore, genetic
variations, including Interleukin-10 polymorphisms, have also been proposed as a potential pathway between HCV infection and NHL susceptibility and development. Similar to autoimmune disease-related risk factors, it remains unclear whether these associations are driven by disease status, medication use, or disease-medication interactions. Considering how rare many of these autoimmune and infectious disease-related exposures are, future efforts are necessary to determine the impact of multiple environmental as well as non-environmental risk factors simultaneously.

Among 40 associations evaluated by both MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Unlike MAs of summary level data, MAs of IPD tend to focus on studies with more homogeneous designs and patient populations. Furthermore, MAs of IPD can allow for better harmonization of data across studies, more advanced one-stage meta-analytical approaches, and analyses accounting for many exposure categories and potential confounders. Although the InterLymph MAs of IPD are particularly robust due to the large number of NHL cases and subtypes considered, MAs of IPD without systematic reviews may exclude evidence from high-quality case-control or cohort studies. For instance, the InterLymph analyses only included evidence from completed and ongoing case-control studies from consortium members. Furthermore, the InterLymph findings may be difficult to disentangle, with at least 700 nominally statistically significant associations among thousands of analyses conducted across different subtypes of NHL and exposure levels (e.g., different type/ dosages of alcohol consumption). In the future, it will be necessary to monitor the consistency between MAs of summary level data and MAs of IPD, especially since approximately half of the MAs of summary level data had at least one-third of the same component studies as the MAs of IPD. In addition, authors of MAs should carefully evaluate whether any external studies can and should be included in their syntheses. Of interest, we observed that more than two thirds of the effect sizes were more conservative in the InterLymph MAs of IPD than in the MAs of summary level data. This may be a reflection of greater selective reporting bias in the corpus of studies available in the literature as compared with a set of studies participating in a consortium.

Our study suggests that nearly all MAs of summary level data evaluating associations between environmental risk factors and risk of NHL could be classified as having critically low quality according to the AMSTAR 2 tool. Previous umbrella reviews focused on the associations...
between environmental risk factors and health outcomes have noted similar concerns. However, the proportion of low or critically low-quality NHL reviews is higher than what has been observed among umbrella reviews for inflammatory bowel diseases, attention-deficit/hyperactivity disorder, eating disorders, early childhood caries, physical activity for academic achievement, and physical therapy for tendinopathy. These findings may not be surprising considering recent concerns about the mass production of systematic reviews. In the future, authors planning systematic reviews and MAs of summary level data of the associations between environmental exposures and NHL should adhere to reporting guidelines and critically evaluate how their studies relate to existing MAs of IPD.

**Limitations**

Our umbrella review has several limitations. First, we did not identify potential environmental risk factors that were only examined in individual observational studies. Our objective was to identify and summarize the associations that were reported by the MAs of summary level data, which already covered a wide space of diverse associations. Second, we did not evaluate the quality of individual studies included in the MAs of summary level data, the impact that individual studies have on the overall heterogeneity, or the potential role that residual/unmeasured confounding could have on associations. Individual risk of bias evaluations are outside the scope of umbrella reviews, and it is the expectation that MAs have already conducted these quality assessments. Third, we considered MAs that included cohort and case-control studies, and our assessments did not prioritize reviews of certain study designs or address differences across different study designs. Considering that certain NHL subtypes are rare, case-control studies may often be the most realistic study design to evaluate exposure histories. Fourth, although umbrella reviews provide a comprehensive summary of the associations reported in MAs, the validity of the summary effect estimates is dependent on the quality of the individual MAs. Although we attempted to standardize associations using a random-effects DL estimator, we did not evaluate or re-conduct the literature searches for all potential exposure-outcome relationships. Fifth, we did not calculate or conduct $I^2$, 95% PIs, Egger’s test, and excess significance test for non-significant and nominally statistically significant associations. Given the large number of associations identified, we prioritized these calculations for associations where these values were necessary to determine the strength of associations using the previously established classification system. Sixth, when
summary effect estimates of multiple exposure contrast levels were reported, we focused on the risk estimates comparing ever versus never exposure (or comparing the highest versus lowest levels of exposures). Although we did not consider all potential contrast levels and dose-response relationships, our objective was to provide a universal overview of the relationships between examined risk factors and NHL. Specific dose-response relationships may nevertheless exist for certain associations, and they would need to be examined on a case-by-case basis. Seventh, we only identified the nominally statistically significant associations among the thousands of associations reported in InterLymph MAs of IPD. Eighth, by excluding non-English language reviews, we may have missed additional potential associations. However, we utilized the same approach as previous umbrella reviews that focused on risk factors for health outcome(s). Ninth, MAs of IPD and MAs of summary level data can have different strengths and limitations, and our evaluation did not focus on comparing the potential quality of these types of studies. Lastly, when multiple MAs of summary level data evaluated the same exposures and outcomes, we selected the association based on the largest number of included studies. Although this approach does not ensure that the highest quality MAs are selected, this methodology has been utilized by previous umbrella reviews.

**Conclusion**

In this large-scale umbrella review, we identified dozens of MAs evaluating associations between environmental risk factors and NHL. However, the vast majority of MAs of summary level data were low quality and presented either non-significant or weak evidence. When the same associations were evaluated in MAs of summary level data and MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, these findings highlight the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.
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Transparency: The senior author (manuscripts guarantor) (JDW) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant registered) have been explained.

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# Tables and figures:

## Table 1. Grading criteria for evidence categories

| Strength of association | Descriptiona |
|-------------------------|--------------|
| Convincing (class I)    | Highly statistically significant association ($P < 10^{-6}$) |
|                         | At least 1000 NHL cases |
|                         | Low/moderate between study heterogeneity ($I^2 < 50\%$) |
|                         | 95% prediction interval excluding the null value |
|                         | Largest study reporting a nominally statistically significant ($P < 0.05$) |
|                         | No evidence of small-study effects |
|                         | No evidence of excess significance bias |
| Highly suggestive (class II) | Highly statistically significant association ($P < 10^{-6}$) |
|                         | At least 1000 NHL cases |
|                         | Largest study reporting a nominally statistically significant ($P < 0.05$) |
| Suggestive (class III)  | At least 1000 NHL cases |
|                         | Statistically significant association ($P < 10^{-3}$) |
| Weak (class IV)         | Nominally statistically significant association ($P < 0.05$) |
| Non-significant         | Non-statistically significant associations ($P > 0.05$) |

*aP value for the association that calculated by random effects model.

NHL=non-Hodgkin lymphoma.
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author or year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random<sup>a</sup> | Large study nominally significant (P<0.05) | I² (%) | 95% PI | Sma ll study effect<sup>b</sup> | Stren gth of reported association<sup>c</sup> |
|-----------------------|--------------------------|-------------------|---------|------------|----------------|-----------------------|--------------|--------------|---------------------------------------------|----------------|------------------------------------------|--------|------|----------------|------------------------------------------|
| Renal transplant      | Renal transplant         | Transplant recipients vs general population | NHL     | SRMA       | Wang 2018      | 6                     | 770          | SIR          | 10.66 (8.54, 13.31)                           | 3.44E-86 | Yes                                      | 80.2   | NA   | NA        | II                                      |
| Autoimmune diseases   | Rheumatoid arthritis     | Patients vs general population               | NHL     | SRMA       | Simon 2015     | 16                    | 1531         | SIR          | 2.26 (1.82, 2.81)                            | 8.42E-13 | Yes                                      | 96     | NA   | NA        | II                                      |
| Primary Sjogren's syndrome | Patients vs general population | NHL | SRMA       | Liang 2014 | 11                     | 1232 5               | RR             | 13.76 (8.53, 18.99)                           | 1.62E-34 | Yes                                      | 58.8   | NA   | NA        | II                                      |
| Systemic lupus erythematosus | Patients vs general population | NHL | MA         | Cao 2015   | 12                     | 166                   | RR             | 5.4 (3.75, 7.77)                             | 1.99E-18 | Yes                                      | 74.3   | NA   | NA        | II                                      |
| Celiac disease        | Patients vs general population | NHL | SRMA       | Tio 2012   | 8                      | 1102 45              | OR             | 2.61 (2.04, 3.33)                            | 9.32E-14 | Yes                                      | 23.4   | (1.57 , 4.33) | No        | I                                       |
| Celiac disease        | Patients vs general population | TCL | SRMA       | Tio 2012   | 5                      | 3535 8               | OR             | 15.84 (7.85, 31.94)                          | 6.90E-14 | Yes                                      | 55.5   | NA   | NA        | II                                      |
| Infectious diseases   | Tuberculosis             | Patients vs general population               | NHL     | SRMA       | Leung 2020      | 8                     | 2390         | RR             | 1.61 (1.34, 1.94)                           | 6.76E-07 | Yes                                      | 50.2   | NA   | NA        | II                                      |
| HBV                   | HBV infected vs non-infected | NHL | SRMA       | Li 2018    | 58                    | 5371 4               | OR             | 2.50 (2.2, 2.83)                            | 6.33E-42 | Yes                                      | 77.9   | NA   | NA        | II                                      |
| HBV                   | HBV infected vs non-infected | BCL | SRMA       | Li 2018    | 20                   | >100 0               | OR             | 2.46 (1.97, 3.07)                            | 1.24E-14 | Yes                                      | 62.9   | NA   | NA        | II                                      |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author/year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random<sup>a</sup> | Large study nominally significant (P<0.05) | I² (%) | 95% PI | Smallest study effect<sup>b</sup> | Strength of reported association<sup>c</sup> |
|-----------------------|----------------------------|---------------------|---------|------------|--------------|-----------------------|---------------|----------------|------------------------------------------|----------------|------------------------------------------|---------|--------|------------------------|-----------------------------|
| HCV                  | HCV infected vs non-infected | NHL                | SRMA    | Masaone 2019 | 27                   | 3307                  | 7            | OR             | 3.36 (2.4, 4.72)                           | 7.92E-12 | Yes                                      | 88      | NA     | NA                     | II                          |
| HCV                  | Patients vs general population | DLBL CL           | MA      | DalMaso 2006  | 8                    | 1020                  |              | RR             | 2.65 (1.88, 3.74)                           | 4.98E-08 | Yes                                      | 39      | (1.46, 5.81) | No                     | II                          |
| Occupation           | Teacher vs non-teachers     | NHL                | MA      | Boffetta 2007 | 19                   | >100                  | 0            | RR             | 1.47 (1.34, 1.61)                           | 1.60E-15 | Yes                                      | 76      | NA     | NA                     | II                          |

BCL=B cell lymphoma; CI=confidence interval; HBV=hepatitis B virus; HCV=hepatitis C virus; MA=meta-analysis; NA=not available; NHL=non-Hodgkin lymphoma; OR=odds ratio; PI=prediction interval; SIR=standardized incidence ratio; SRMA=systematic review and meta-analysis; RR=risk ratio; TCL=T-cell lymphoma.

<sup>a</sup> P value for summary effect estimates using a random-effects DerSimonian and Laird estimator.

<sup>b</sup> P<0.1 for Egger’s test suggests the presence of small study effects.

<sup>c</sup> Strength of association using the criteria listed in Table 1.
### Table 3. Environmental risk factors for NHL reported in MPL with suggestive (Class III), weak (Class IV) and non-significant evidence

| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|-----------------------------|---------------------|---------|------------|--------------|------------------------|--------------|---------------|-------------------------------------------|---------|-------------------------------|
| **Dietary factors**   |                             |                     |         |            |              |                        |              |               |                                           |         |                               |
| Meat                  | Red meat                    | Highest vs lowest   | NHL     | MA         | Yang 2015    | 18                     | 12579        | RR            | 1.32 (1.12, 1.55)                           | 8.52E-04| III                            |
|                       | Processed meat              | Highest vs lowest   | NHL     | MA         | Yang 2015    | 18                     | 14112        | RR            | 1.17 (1.07, 1.29)                           | 1.04E-03| IV                             |
|                       | Red meat                    | Highest vs lowest   | DLBCL   | MA         | Yang 2015    | 5                      | NA           | RR            | 1.34 (0.97, 1.86)                           | 7.80E-02| NS                             |
|                       | Processed meat              | Highest vs lowest   | DLBCL   | MA         | Yang 2015    | 5                      | NA           | RR            | 1.23 (1.03, 1.48)                           | 2.50E-02| IV                             |
|                       | Processed meat              | Highest vs lowest   | FL      | MA         | Yang 2015    | 5                      | NA           | RR            | 1.21 (0.98, 1.48)                           | 7.00E-02| NS                             |
|                       | Red meat                    | Highest vs lowest   | CLL/SL  | MA         | Yang 2015    | 5                      | NA           | RR            | 1.01 (0.84, 1.21)                           | 9.22E-01| NS                             |
|                       | Processed meat              | Highest vs lowest   | CLL/SL  | MA         | Yang 2015    | 5                      | NA           | RR            | 1.06 (0.85, 1.33)                           | 6.22E-01| NS                             |
|                       | White meat/poultry          | Highest vs lowest   | NHL     | MA         | Dong 2017    | 10                     | 10671        | RR            | 1.04 (0.86, 1.27)                           | 7.06E-01| NS                             |
|                       | White meat/poultry          | Highest vs lowest   | DLBCL   | SRMA       | Caini 2016   | 3                      | 1134         | RR            | 0.96 (0.63, 1.48)                           | 8.62E-01| NS                             |
|                       | White meat/poultry          | Highest vs lowest   | FL      | SRMA       | Caini 2016   | 3                      | 858          | RR            | 1.09 (0.51, 2.31)                           | 8.34E-01| NS                             |
|                       | White meat/poultry          | Highest vs lowest   | CLL/SL  | SRMA       | Caini 2016   | 3                      | 1337         | RR            | 1.05 (0.71, 1.54)                           | 8.17E-01| NS                             |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|-------------|---------------|----------------------------------------|----------|-------------------------------|
| Fish                  | Fish                      | Highest vs lowest   | NHL     | SRMA       | Caini 2016   | 11                     | 8839        | RR            | 0.93 (0.72, 1.19)                         | 5.83E-01 | NS                            |
| Fish                  | Highest vs lowest         | DLBCL               | SRMA    | Caini 2016 | 4            | 1228                   | RR          | 0.86 (0.48, 1.56) | 6.29E-01 | NS          |
| Fish                  | Highest vs lowest         | FL                  | SRMA    | Caini 2016 | 4            | 970                    | RR          | 0.86 (0.48, 1.56) | 6.29E-01 | NS          |
| Fish                  | Highest vs lowest         | CLL/SL              | SRMA    | Caini 2016 | 5            | 1703                   | RR          | 0.90 (0.72, 1.14) | 3.75E-01 | NS          |
| Fruits and vegetables | Fruit and vegetables      | Highest vs lowest   | NHL     | MA         | Chen 2013    | 4                      | 1747        | RR            | 0.78 (0.66, 0.92)                         | 3.00E-03 | IV                            |
| Fruit                 | Highest vs lowest         | NHL                 | MA      | Chen 2013  | 13           | 8476                   | RR          | 0.97 (0.87, 1.08) | 5.93E-01 | NS          |
| Vegetable             | Highest vs lowest         | NHL                 | MA      | Chen 2013  | 13           | 8332                   | RR          | 0.81 (0.71, 0.92) | 1.00E-03 | IV          |
| Fruit                 | Highest vs lowest         | DLBCL               | MA      | Chen 2013  | 8            | NA                     | RR          | 0.94 (0.79, 1.13) | 5.08E-01 | NS          |
| Vegetable             | Highest vs lowest         | DLBCL               | MA      | Chen 2013  | 7            | NA                     | RR          | 0.70 (0.54, 0.91) | 7.00E-03 | IV          |
| Fruit                 | Highest vs lowest         | FL                  | MA      | Chen 2013  | 8            | NA                     | RR          | 0.96 (0.72, 1.28) | 7.93E-01 | NS          |
| Vegetable             | Highest vs lowest         | FL                  | MA      | Chen 2013  | 7            | NA                     | RR          | 0.70 (0.53, 0.92) | 1.10E-02 | IV          |
| Eggs and dairy        | Eggs                      | Highest vs lowest   | NHL     | SRMA       | Caini 2016   | 10                     | 5775        | RR            | 1.17 (0.86, 1.60)                         | 3.26E-01 | NS                            |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|--------------------|---------|------------|--------------|------------------------|-------------|---------------|-----------------------------------|----------|-------------------------------------|
| Total dairy           | Highest vs lowest         | NHL                | MA      | Wang 2016  | 7            | 4207                   | RR          | 1.20          | (1.02, 1.42)                  | 3.00E-02 | IV                                  |
| Total dairy           | Highest vs lowest         | DLBCL              | MA      | Wang 2016  | 3            | 321                    | RR          | 1.73          | (1.22, 2.45)                  | 2.00E-03 | IV                                  |
| Total dairy           | Highest vs lowest         | FL                 | MA      | Wang 2016  | 3            | 355                    | RR          | 1.23          | (0.88, 1.72)                  | 2.28E-01 | NS                                  |
| Total dairy           | Highest vs lowest         | CLL/SL             | MA      | Wang 2016  | 3            | 390                    | RR          | 1.35          | (0.77, 2.39)                  | 3.03E-01 | NS                                  |
| Milk                  | Highest vs lowest         | NHL                | MA      | Wang 2016  | 16           | 7109                   | RR          | 1.41          | (1.08, 1.84)                  | 1.10E-02 | IV                                  |
| Milk                  | Highest vs lowest         | DLBCL              | MA      | Wang 2016  | 3            | 352                    | RR          | 1.49          | (1.08, 2.06)                  | 1.50E-02 | IV                                  |
| Milk                  | Highest vs lowest         | FL                 | MA      | Wang 2016  | 3            | 390                    | RR          | 0.99          | (0.47, 2.07)                  | 9.81E-01 | NS                                  |
| Milk                  | Highest vs lowest         | CLL/SL             | MA      | Wang 2016  | 3            | 477                    | RR          | 1.04          | (0.69, 1.55)                  | 8.60E-01 | NS                                  |
| Cheese                | Highest vs lowest         | NHL                | MA      | Wang 2016  | 10           | 5519                   | RR          | 1.14          | (0.96, 1.34)                  | 1.24E-01 | NS                                  |
| Cheese                | Highest vs lowest         | DLBCL              | MA      | Wang 2016  | 3            | 352                    | RR          | 0.93          | (0.63, 1.37)                  | 7.27E-01 | NS                                  |
| Cheese                | Highest vs lowest         | FL                 | MA      | Wang 2016  | 3            | 390                    | RR          | 1.04          | (0.74, 1.46)                  | 8.32E-01 | NS                                  |
| Cheese                | Highest vs lowest         | CLL/SL             | MA      | Wang 2016  | 3            | 477                    | RR          | 1.28          | (0.91, 1.81)                  | 1.60E-01 | NS                                  |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | P strength |
|-----------------------|----------------------------|---------------------|---------|------------|--------------|------------------------|-------------|--------------|----------------------------------------|-----------|-----------|
| Yogurt                | Highest vs lowest          | NHL                 | MA      | Wang 2016  | 4            | 2372                  | RR          | 0.78 (0.54, 1.12) | 1.83E-01                              | NS        |           |
| Yogurt                | Highest vs lowest          | DLBCL               | MA      | Wang 2016  | 3            | 352                   | RR          | 0.90 (0.67, 1.21) | 4.95E-01                              | NS        |           |
| Yogurt                | Highest vs lowest          | FL                  | MA      | Wang 2016  | 3            | 390                   | RR          | 0.89 (0.63, 1.25) | 5.15E-01                              | NS        |           |
| Yogurt                | Highest vs lowest          | CLL/SL              | MA      | Wang 2016  | 3            | 477                   | RR          | 0.97 (0.76, 1.23) | 8.16E-01                              | NS        |           |
| Butter                | Highest vs lowest          | NHL                 | MA      | Wang 2016  | 4            | 1534                  | RR          | 1.31 (1.04, 1.65) | 2.20E-02                              | IV        |           |
| Ice-cream             | Highest vs lowest          | NHL                 | MA      | Wang 2016  | 4            | 1598                  | RR          | 1.57 (1.11, 2.20) | 1.00E-02                              | IV        |           |
| Coffee and tea        | Coffee                     | Highest vs lowest   | NHL     | SRMA       | Mirtavoos-Mahyari 2019 | 11       | 4418                  | RR          | 1.21 (0.97, 1.50) | 8.60E-02                              | NS        |           |
| Black tea             | Highest vs lowest          | NHL                 | SRMA   | Mirtavoos-Mahyari 2019 | 5        | 1600                  | RR          | 1.01 (0.82, 1.24) | 9.40E-01                              | NS        |           |
| Green tea             | Highest vs lowest          | NHL                 | SRMA   | Mirtavoos-Mahyari 2019 | 3        | 637                   | RR          | 0.61 (0.38, 0.99) | 4.30E-02                              | IV        |           |
| Carotenoids           | Alpha-carotene             | Highest vs lowest   | NHL     | SRMA       | Chen 2017    | 8         | 2926                  | RR          | 0.87 (0.78, 0.97) | 1.20E-02                              | IV        |           |
| Carotenoids           | Alpha-carotene             | Highest vs lowest   | DLBCL   | SRMA       | Chen 2017    | 3         | NA                    | RR          | 0.75 (0.59, 0.97) | 2.30E-02                              | IV        |           |
| Carotenoids           | Alpha-carotene             | Highest vs lowest   | FL      | SRMA       | Chen 2017    | 4         | NA                    | RR          | 0.84 (0.60, 1.16) | 3.04E-01                              | NS        |           |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random a | Strength of reported association b |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|--------------|---------------|---------------------------------------------|------------|-------------------------------|
| Alpha-carotene        | Highest vs lowest         | CLL/SL              | SRMA    | Chen 2017  | 2            | NA                    | 2            | RR            | 1.41 (0.80, 2.50)                           | 2.40E-01   | NS                            |
| Beta-carotene         | Highest vs lowest         | NHL                 | SRMA    | Chen 2017  | 10           | 3946                  | RR           | 0.80 (0.68, 0.94)                              | 7.00E-03   | IV                            |
| Beta-carotene         | Highest vs lowest         | DLBCL               | SRMA    | Chen 2017  | 5            | NA                    | RR           | 0.65 (0.46, 0.91)                              | 1.30E-02   | IV                            |
| Beta-carotene         | Highest vs lowest         | FL                  | SRMA    | Chen 2017  | 6            | NA                    | RR           | 0.80 (0.55, 1.16)                              | 2.44E-01   | NS                            |
| Beta-carotene         | Highest vs lowest         | CLL/SL              | SRMA    | Chen 2017  | 4            | NA                    | RR           | 0.98 (0.76, 1.25)                              | 8.83E-01   | NS                            |
| Beta-cryptoxanthin    | Highest vs lowest         | NHL                 | SRMA    | Chen 2017  | 7            | 2325                  | RR           | 0.87 (0.75, 1.01)                              | 6.60E-02   | NS                            |
| Beta-cryptoxanthin    | Highest vs lowest         | DLBCL               | SRMA    | Chen 2017  | 4            | NA                    | RR           | 0.84 (0.67, 1.05)                              | 1.28E-01   | NS                            |
| Beta-cryptoxanthin    | Highest vs lowest         | FL                  | SRMA    | Chen 2017  | 4            | NA                    | RR           | 0.75 (0.50, 1.13)                              | 1.67E-01   | NS                            |
| Beta-cryptoxanthin    | Highest vs lowest         | CLL/SL              | SRMA    | Chen 2017  | 3            | NA                    | RR           | 0.51 (0.15, 1.72)                              | 2.83E-01   | NS                            |
| Lycopene              | Highest vs lowest         | NHL                 | SRMA    | Chen 2017  | 7            | 2325                  | RR           | 0.99 (0.88, 1.12)                              | 8.80E-01   | NS                            |
| Lycopene              | Highest vs lowest         | DLBCL               | SRMA    | Chen 2017  | 3            | NA                    | RR           | 1.04 (0.69, 1.57)                              | 8.62E-01   | NS                            |
| Lycopene              | Highest vs lowest         | FL                  | SRMA    | Chen 2017  | 3            | NA                    | RR           | 0.90 (0.54, 1.49)                              | 6.97E-01   | NS                            |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measurement | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|--------------------|---------|------------|--------------|------------------------|-------------|-------------------|------------------------------------------|----------|---------------------------------|
|                       | Lycopene                  | Highest vs lowest  | CLL/SL  | SRMA       | Chen 2017    | 2                      | NA          | RR                | 0.80 (0.60, 1.07)                          | 1.31E-01 | NS                              |
|                       | Andlutein/zeaxanthin      | Highest vs lowest  | NHL     | SRMA       | Chen 2017    | 7                      | 2325        | RR                | 0.82 (0.69, 0.97)                          | 2.20E-02 | IV                              |
|                       | Andlutein/zeaxanthin      | Highest vs lowest  | DLBCL   | SRMA       | Chen 2017    | 3                      | NA          | RR                | 0.87 (0.54, 1.40)                          | 5.78E-01 | NS                              |
|                       | Andlutein/zeaxanthin      | Highest vs lowest  | FL      | SRMA       | Chen 2017    | 3                      | NA          | RR                | 0.70 (0.48, 1.02)                          | 6.30E-02 | NS                              |
|                       | Andlutein/zeaxanthin      | Highest vs lowest  | CLL/SL  | SRMA       | Chen 2017    | 2                      | NA          | RR                | 0.93 (0.70, 1.23)                          | 6.26E-01 | NS                              |
| Micronutrient intake/| Vitamin A (retinol)       | Highest vs lowest  | NHL     | SRMA       | Psaltopoulou 2018 | 3                      | 3314        | RR                | 0.92 (0.80, 1.07)                          | 2.64E-01 | NS                              |
| supplements            | Vitamin C                 | Highest vs lowest  | NHL     | SRMA       | Psaltopoulou 2018 | 5                      | 3879        | RR                | 1.00 (0.90, 1.12)                          | 1.00E+00 | NS                              |
|                       | Vitamin D                 | Highest vs lowest  | NHL     | MA         | Lu 2014      | 6                      | 4400        | OR                | 1.07 (0.82, 1.40)                          | 6.33E-01 | NS                              |
|                       | Vitamin D                 | Highest vs lowest  | DLBCL   | MA         | Lu 2014      | 5                      | NA          | OR                | 1.05 (0.73, 1.52)                          | 8.06E-01 | NS                              |
|                       | Vitamin D                 | Highest vs lowest  | FL      | MA         | Lu 2014      | 5                      | NA          | OR                | 1.00 (0.63, 1.58)                          | 1.00E+00 | NS                              |
|                       | Vitamin D                 | Highest vs lowest  | CLL/SL  | MA         | Lu 2014      | 4                      | NA          | OR                | 1.10 (0.56, 2.14)                          | 7.93E-01 | NS                              |
|                       | Vitamin D                 | Highest vs lowest  | TCL     | MA         | Lu 2014      | 3                      | NA          | OR                | 1.69 (0.68, 4.20)                          | 2.62E-01 | NS                              |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|-------------|---------------|------------------------------------------|-----------|-------------------------------|
| Vitamin E             | Highest vs lowest         | NHL                 | SRMA    | Psaltopoulou 2018 | 5            | 3879                  | RR          | 0.98 (0.88, 1.10) | 7.36E-01 | NS                            |
| Dietary fat           | Total fat                 | Highest vs lowest   | NHL     | MA         | Han 2017     | 10         | 5042                 | RR          | 1.26 (1.12, 1.42) | 1.51E-04 | III                           |
| Total fat             | Highest vs lowest         | DLBCL               | MA      | Han 2017   | 5            | NA        | RR                   | 1.41 (1.08, 1.84) | 1.10E-02 | IV                            |
| Total fat             | Highest vs lowest         | FL                  | MA      | Han 2017   | 5            | NA        | RR                   | 1.21 (0.97, 1.52) | 9.60E-02 | NS                            |
| Total fat             | Highest vs lowest         | CLL/SL              | MA      | Han 2017   | 4            | NA        | RR                   | 0.91 (0.68, 1.23) | 5.44E-01 | NS                            |
| Total fat             | Highest vs lowest         | TCL                 | MA      | Han 2017   | 4            | NA        | RR                   | 1.12 (0.60, 2.09) | 7.35E-01 | NS                            |
| Animal fat            | Highest vs lowest         | NHL                 | MA      | Han 2017   | 5            | 1432      | RR                   | 1.31 (1.08, 1.58) | 5.00E-03 | IV                            |
| Vegetable fat         | Highest vs lowest         | NHL                 | MA      | Han 2017   | 5            | 1432      | RR                   | 1.00 (0.84, 1.20) | 1.00E+00 | NS                            |
| Dietary trans-fatty acid intake | Highest vs lowest | NHL | SRMA | Michels 2021 | 4          | 4701   | OR                   | 1.32 (0.99, 1.76) | 5.80E-02 | NS                            |
| Dietary nitrate and nitrite intake | Highest vs lowest | NHL | SRMA | Xie 2016 | 7          | 1703   | RR                   | 0.85 (0.68, 1.06) | 1.57E-01 | NS                            |
| Dietary nitrate       | Highest vs lowest         | NHL                 | SRMA    | Xie 2016  | 5            | 1547      | RR                   | 1.54 (0.98, 2.41) | 6.00E-02 | NS                            |
| Alcohol               | Ever vs never             | NHL                 | SRMA    | Tramacere 2012 | 29         | 18759     | RR                   | 0.85 (0.79, 0.91) | 8.50E-06 | III                           |
| Risk factors category       | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------------|-----------------------------|---------------------|---------|------------|--------------|----------------------|--------------|--------------|------------------------------------------|----------|------------------------------|
| Ever drinking               | Ever vs never               | TCL                | SRMA   | Tramacere  | 2012         | 8                    | NA           | RR           | 0.78 (0.58, 1.05)                           | 1.00E-01 | NS                           |
| Ever drinking               | Ever vs never               | BCL                | SRMA   | Tramacere  | 2012         | 15                   | NA           | RR           | 0.86 (0.76, 0.97)                           | 1.50E-02 | IV                           |
| Ever drinking               | Ever vs never               | DLBCL              | SRMA   | Tramacere  | 2012         | 14                   | NA           | RR           | 0.79 (0.68, 0.91)                           | 1.60E-03 | IV                           |
| Ever drinking               | Ever vs never               | FL                 | SRMA   | Tramacere  | 2012         | 14                   | NA           | RR           | 0.80 (0.69, 0.92)                           | 2.40E-03 | IV                           |
| Ever drinking               | Ever vs never               | CLL/SL             | SRMA   | Tramacere  | 2012         | 12                   | NA           | RR           | 1.00 (0.80, 1.26)                           | 1.00E+00 | NS                           |
| Heavy drinking              | Heavy vs never              | NHL                | SRMA   | Tramacere  | 2012         | 6                    | 1181         | RR           | 0.84 (0.70, 1.00)                           | 5.50E-02 | NS                           |
| Breastfeeding               | Breastfeeding               | Ever vs never      | childhood NHL | SRMA | Martin 2005 | 7                    | 477          | OR           | 1.00 (0.58, 1.73)                           | 1.00E+00 | NS                           |

**Drugs, vaccinations and procedures**

| Risk factors category       | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------------|-----------------------------|---------------------|---------|------------|--------------|----------------------|--------------|--------------|------------------------------------------|----------|------------------------------|
| Non-steroidal anti-inflammatory drugs | Aspirin | Users vs non-users | NHL | SRMA | Ye 2015 | 10 | 6818 | OR | 1.02 (0.89, 1.17) | 7.89E-01 | NS                           |
| Aspirin                     | Users vs non-users          | DLBCL              | SRMA   | Ye 2015   | 3            | NA                   | OR           | 1.06 (0.85, 1.33) | 6.22E-01 | NS                           |
| Aspirin                     | Users vs non-users          | FL                 | SRMA   | Ye 2015   | 3            | NA                   | OR           | 1.15 (0.83, 1.59) | 4.07E-01 | NS                           |
| Aspirin                     | Users vs non-users          | CLL/SL             | SRMA   | Ye 2015   | 4            | NA                   | OR           | 0.70 (0.54, 0.91) | 7.00E-03 | IV                           |
| NA-NSAIDS                   | Users vs non-users          | NHL                | SRMA   | Ye 2015   | 8            | 5427                 | OR           | 1.33 (1.11, 1.60) | 2.00E-03 | IV                           |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|-------------|--------------|------------------------------------------|----------|-------------------------------|
| NA-NSAIDS             | Users vs non-users        | CLL/SL             | SRMA    | Ye 2015    | 3            | NA                     | OR          | 1.26         | (0.86, 1.85)                            | 2.39E-01 | NS                            |
| NSAIDS                | Users vs non-users        | NHL                | SRMA    | Ye 2015    | 13           | 9896                   | OR          | 1.05         | (0.90, 1.22)                            | 5.41E-01 | NS                            |
| NSAIDS                | Users vs non-users        | DLBCL              | SRMA    | Ye 2015    | 3            | NA                     | OR          | 0.99         | (0.81, 1.21)                            | 9.28E-01 | NS                            |
| NSAIDS                | Users vs non-users        | FL                 | SRMA    | Ye 2015    | 3            | NA                     | OR          | 1.07         | (0.69, 1.68)                            | 7.78E-01 | NS                            |
| NSAIDS                | Users vs non-users        | CLL/SL             | SRMA    | Ye 2015    | 4            | NA                     | OR          | 0.77         | (0.51, 1.15)                            | 2.09E-01 | NS                            |
| NSAIDS                | Users vs non-users        | TCL                | SRMA    | Ye 2015    | 3            | NA                     | OR          | 1.04         | (0.52, 2.07)                            | 9.19E-01 | NS                            |
| NSAIDS                | Users vs non-users        | BCL                | SRMA    | Ye 2015    | 5            | NA                     | OR          | 1.01         | (0.75, 1.36)                            | 9.52E-01 | NS                            |
| Corticosteroids       | Corticosteroids           | NHL                | MA       | Bernatsky 2007 | 8            | 6897                   | OR          | 1.13         | (0.99, 1.29)                            | 7.00E-02 | NS                            |
| Statin use            | Statin                    | Users vs non-users | NHL     | SRMA       | Ye 2017      | 9          | 7825                    | OR          | 0.82         | (0.69, 0.99)                            | 3.10E-02 | IV                            |
| Statin                | Users vs non-users        | DLBCL              | SRMA    | Ye 2017      | 4            | 897                     | OR          | 0.78         | (0.55, 1.11)                            | 1.66E-01 | NS                            |
| Statin                | Users vs non-users        | FL                 | SRMA    | Ye 2017      | 4            | 495                     | OR          | 0.89         | (0.62, 1.27)                            | 5.35E-01 | NS                            |
| Statin                | Users vs non-users        | MZL                | SRMA    | Ye 2017      | 3            | 215                     | OR          | 0.54         | (0.31, 0.94)                            | 2.90E-02 | IV                            |

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| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|--------------|----------------|------------------------------------------|----------|-------------------------------|
|                       | Statin                    | Users vs non-users  | TCL     | SRMA       | Ye 2017      | 4                      | 227          | OR             | 0.70 (0.41, 1.19) | 1.91E-01 | NS                            |
|                       | Paracetamol               | Users vs non-users  | NHL     | SRMA       | Preg-Dominguez 2021 | 3                      | 3022         | RR             | 1.20 (0.96, 1.51) | 1.10E-01 | NS                            |
|                       | Bacillus calmette-guerin vaccination | Yes vs no          | NHL     | SRMA       | Salmon 2020   | 11                     | 4350         | RR             | 1.20 (1.01, 1.43) | 4.00E-02 | IV                            |
|                       | Insulin                   | Yes vs no           | NHL     | SRMA       | Karlstad 2013 | 4                      | NA           | RR             | 1.16 (0.83, 1.62) | 3.91E-01 | NS                            |
|                       | Inflammatory bowel disease treatment | Yes vs no         | NHL     | SRMA       | Yang 2018     | 3                      | 35           | RR             | 1.34 (0.62, 2.89) | 4.70E-01 | NS                            |
|                       | Azathioprine and 6-mercaptopurine | Patients vs general population | NHL | MA | Kandiel 2005 | 3                      | 9            | SIR            | 3.92 (1.78, 7.47) | 2.10E-04 | IV                            |
|                       | HAART among patients with HIV/AIDS | Pre vs post-HAART eras | NHL     | SRMA       | Cobucci 2015 | 6                      | 7701         | SIR            | 0.42 (0.26, 0.67) | 3.00E-04 | III                           |
|                       | Red blood cell transfusions | Yes vs no          | NHL     | MA | Castillo 2010 | 14                     | 5904         | RR             | 1.2 (1.07, 1.35) | 2.00E-03 | IV                            |
|                       | Red blood cell transfusion | Yes vs no          | Cll/sl   | MA | Castillo 2010 | 5                      | 3450         | RR             | 1.66 (1.08, 2.56) | 2.10E-02 | IV                            |
|                       | Red blood cell transfusion | Yes vs no          | FL       | MA | Castillo 2010 | 6                      | NA           | RR             | 1.02 (0.67, 1.55) | 9.32E-01 | NS                            |
|                       | Red blood cell transfusion | Yes vs no          | Dlbcl    | MA | Castillo 2010 | 5                      | NA           | RR             | 1.06 (0.86, 1.3)  | 5.92E-01 | NS                            |

**Non-dietary lifestyle factors**

| Risk factors category         | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-------------------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|--------------|----------------|------------------------------------------|----------|-------------------------------|
| Physical activity             | Physical activity        | Highest vs lowest   | NHL     | SRMA       | Davies 2020   | 17                     | 13425        | RR             | 0.92 (0.84, 1.00) | 6.00E-02 | NS                            |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|-----------------------|--------------|---------------|-------------------------------------------|---------|-------------------------------|
| Physical activity     | Highest vs lowest         | DLBCL               | SRMA    | Davies 2020| 10           | 1957                  | RR           | 0.95          | (0.83, 1.09)                              | 4.70E-01| NS                            |
| Physical activity     | Highest vs lowest         | FL                  | SRMA    | Davies 2020| 10           | 1467                  | RR           | 0.95          | (0.80, 1.12)                              | 5.60E-01| NS                            |
| Physical activity     | Highest vs lowest         | CLL/SL              | SRMA    | Davies 2020| 8            | 1452                  | RR           | 0.95          | (0.76, 1.20)                              | 6.70E-01| NS                            |
| Hair dye              | Highest vs lowest         | NHL                 | MA      | Qin 2019   | 16           | 10967                 | OR           | 1.14          | (1.01, 1.29)                              | 3.60E-02| IV                            |
| Hair dye              | User before 1980 vs never user | FL               | SRMA    | Odotula 2020| 4            | 439                   | OR           | 1.66          | (1.22, 2.25)                              | 1.20E-03| IV                            |
| Night shift work      | Shift workers vs non shift workers | NHL               | SRMA    | Dun 2020   | 5            | >1000                 | OR           | 1.05          | (0.99, 1.10)                              | 6.91E-01| NS                            |
| Indoor tanning        | Ever vs never             | NHL                 | SRMA    | O'Sullivan 2018| 10          | 14018                | RR           | 0.95          | (0.83, 1.08)                              | 4.54E-01| NS                            |
| Indoor tanning        | Ever vs never             | BCL                 | SRMA    | O'Sullivan 2018| 4            | NA                   | RR           | 0.82          | (0.70, 0.95)                              | 1.10E-02| IV                            |
| Indoor tanning        | Ever vs never             | TCL                 | SRMA    | O'Sullivan 2018| 3            | NA                   | RR           | 1.23          | (0.95, 1.59)                              | 1.15E-01| NS                            |
| Residential exposure to petrochemical activity | Living near vs far | NHL | SRMA | Jephcote 2020 | 9 | 1078 | RR | 1.06 | (0.97, 1.17) | 2.25E-01 | NS |
| Smoking               | Ever vs never childhoo d NHL | MA             | Boffetta 2000 | 4 | 204 | RR | 2.08 | (1.08, 3.98) | 2.80E-02 | IV |
| Maternal smoking      | Ever vs never childhoo d NHL | MA             | Antonopoulos 2011 | 7 | 1072 | OR | 1.22 | (1.02, 1.46) | 2.57E-02 | IV |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|----------------------------|---------------------|---------|------------|--------------|------------------------|-------------|--------------|------------------------------------------|----------|-----------------------------|
| Ever smoking          | Ever vs never              | NHL                 | MA      | Sergentanis | 2013         | 33                     | 25891       | RR           | 1.05 (1.00, 1.09)                          | 2.60E-02 | IV             |
| Ever smoking          | Ever vs never              | DLBCL               | MA      | Sergentanis | 2013         | 12                     | NA          | RR           | 1.01 (0.95, 1.07)                          | 7.60E-01 | NS             |
| Ever smoking          | Ever vs never              | FL                  | MA      | Sergentanis | 2013         | 11                     | NA          | RR           | 1.05 (0.88, 1.25)                          | 6.00E-01 | NS             |
| Ever smoking          | Ever vs never              | CLL/SL              | MA      | Sergentanis | 2013         | 9                      | NA          | RR           | 0.96 (0.89, 1.04)                          | 3.10E-01 | NS             |
| Sun exposure          | Personal sunlight exposure | Highest vs lowest   | NHL     | MA         | Kim 2021     | 15                     | 11272       | OR           | 0.81 (0.71, 0.92)                          | 1.50E-02 | IV             |
| Sun exposure          | Personal sunlight exposure | Highest vs lowest   | CLL/SL  | MA         | Kim 2021     | 4                      | 1564        | OR           | 0.80 (0.63, 1.00)                          | 5.80E-02 | NS             |
| Sun exposure          | Personal sunlight exposure | Highest vs lowest   | DLBCL   | MA         | Kim 2021     | 5                      | 1843        | OR           | 0.76 (0.66, 0.87)                          | 1.10E-04 | III            |
| Sun exposure          | Personal sunlight exposure | Highest vs lowest   | FL      | MA         | Kim 2021     | 5                      | 1348        | OR           | 0.81 (0.67, 0.99)                          | 3.40E-02 | IV             |
| Sun exposure          | Personal sunlight exposure | Highest vs lowest   | TCL     | MA         | Kim 2021     | 4                      | 413         | OR           | 1.00 (0.68, 1.46)                          | 1.00E+00 | NS             |
| Ambient sunlight exposure during lifetime | Highest vs lowest | NHL     | MA         | Kim 2021     | 7                      | 196272      | OR           | 0.84 (0.73, 0.96)                          | 1.30E-02 | IV             |
| Ambient sunlight exposure during lifetime | Highest vs lowest | CLL/SL  | MA         | Kim 2021     | 4                      | NA          | OR           | 0.93 (0.73, 1.19)                          | 5.70E-01 | NS             |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|----------------|------------------------------------------|----------|-------------------------------|
|                       | Ambient sunlight exposure during lifetime | Highest vs lowest | DLBCL   | MA         | Kim 2021     | 4                     | NA          | OR             | 0.80 (0.69, 0.92) | 2.40E-03 | IV                            |
|                       | Ambient sunlight exposure during lifetime | Highest vs lowest | FL      | MA         | Kim 2021     | 4                     | NA          | OR             | 0.82 (0.72, 0.93) | 2.40E-03 | IV                            |
|                       | Occupational ultraviolet exposure | Occupation vs general population | NHL    | MA         | Lu 2017      | 11                    | 8829        | OR             | 1.15 (0.99, 1.32) | 5.60E-02 | NS                            |
|                       | Occupational ultraviolet exposure | Occupation vs general population | TCL    | MA         | Lu 2017      | 4                     | NA          | OR             | 1.16 (0.90, 1.50) | 2.60E-01 | NS                            |
| Medical history and comorbid diseases | B-cell activating diseases |
| Autoimmune diseases | Pernicious anemia | Patients vs general population | NHL    | SRMA       | Lahner 2018  | 3                     | 70          | RR             | 1.16 (0.79, 1.71) | 4.60E-01 | NS                            |
| T-cell activating diseases |
| Psoriasis | Patients vs general population | NHL    | SRMA       | Vaengebjerg 2020 | 8                   | 7626       | RR             | 1.48 (1.30, 1.69) | 9.49E-09 | III                           |
| Type 1 diabetes | Patients vs general population | NHL    | MA         | Wang 2020   | 3                     | 1155       | RR             | 1.55 (1.15, 2.08) | 4.00E-03 | IV                            |
| celiac disease | Patients vs general population | DLBCL  | MA         | Tio 2012    | 3                     | 13990      | RR             | 2.25 (1.32, 3.85) | 3.03E-03 | IV                            |
| celiac disease | Patients vs general population | CLL     | MA         | Tio 2012    | 3                     | 51984      | RR             | 0.80 (0.46, 1.38) | 4.34E-01 | NS                            |
| Dermatitis herpetiformis | Patients vs general population | NHL    | MA         | Kane 2011   | 6                     | <1000      | RR             | 6.48 (2.32, 18.1) | 3.91E-04 | IV                            |
| Systemic sclerosis | Patients vs general population | NHL    | SRMA       | Zhang 2013  | 4                     | 23         | SIR            | 2.75 (1.42, 5.33) | 2.60E-03 | IV                            |

Medical history and comorbid diseases
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|--------------|---------------|------------------------------------------|-----------|-----------|-----------------------------|
| Behcet's disease      | Patients vs general population | NHL | SRMA | Wang 2019 | 3 | 4 | RR | 7.79 (3.76, 16.11) | 3.16E-08 | IV |
| Ankylosing spondylitis | Patients vs general population | NHL | SRMA | Deng 2016 | 5 | >1000 | RR | 1.03 (0.83, 1.28) | 8.00E-01 | NS |
| Inflammatory bowel disease | Crohn's disease | Patients vs general population | NHL | SRMA | Lo 2021 | 6 | 30 | IRR | 1.81 (0.94, 3.49) | 7.60E-02 | NS |
| Ulcerative colitis    | Patients vs general population | NHL | SRMA | Lo 2021 | 8 | 79 | IRR | 1.34 (0.95, 1.88) | 9.30E-02 | NS |
| Allergy/Atopic diseases | Asthma | Patients vs general population | NHL | SRMA | Yang 2017 | 15 | 36903 | OR | 0.92 (0.86, 0.99) | 3.00E-02 | IV |
| Hay fever             | Patients vs general population | NHL | SRMA | Yang 2017 | 8 | 4528 | OR | 0.73 (0.62, 0.84) | 5.67E-05 | III |
| Food allergy          | Patients vs general population | NHL | SRMA | Yang 2017 | 6 | 6191 | OR | 0.71 (0.51, 0.98) | 3.90E-02 | IV |
| Eczema                | Patients vs general population | NHL | SRMA | Yang 2017 | 15 | NA | OR | 0.99 (0.81, 1.21) | 9.28E-01 | NS |
| Type 2 diabetes       | Type 2 diabetes | Patients vs general population | NHL | SRMA | Castillo 2012 | 21 | 17282 | OR/RR, Not specified | 1.22 (1.07, 1.39) | 2.94E-03 | IV |
| Parkinson's disease   | Parkinson's disease | Patients vs general population | NHL | SRMA | Zhang 2019 | 5 | 620 | OR/RR, Not specified | 0.80 (0.74, 0.87) | 1.10E-07 | IV |
| Sarcoidosis           | Sarcoidosis | Patients vs general population | NHL | SRMA | Bonifazi 2015 | 8 | 150 | RR | 1.43 (1.03, 1.99) | 3.30E-02 | IV |
| Biliary cirrhosis     | Biliary cirrhosis | Patients vs general population | NHL | SRMA | Liang 2012 | 3 | 2860 | SIR | 1.15 (0.36, 1.94) | 7.58E-01 | NS |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|--------------------------|---------|---------------------------------|
| Overweight and obesity | Overweight | Overweight vs normal weight | NHL | SRMA | Larsson 2007 | 16 | 21720 | RR | 1.07 (1.01, 1.14) | 2.80E-02 | IV |
| Overweight | Overweight vs normal weight | DLBCL | MA | Castillo 2014 | 16 | 7349 | RR | 1.14 (1.04, 1.24) | 3.50E-03 | IV |
| Overweight | Overweight vs normal weight | CLL | MA | Castillo 2012 | 9 | 2142 | RR | 1.10 (1.03, 1.17) | 3.40E-03 | IV |
| Overweight | Overweight vs normal weight | FL | SRMA | Odutola 2020 | 14 | 1798 | RR | 0.99 (0.92, 1.07) | 8.10E-01 | NS |
| Obesity | Obesity vs normal weight | NHL | SRMA | Larsson 2007 | 16 | 21720 | RR | 1.20 (1.07, 1.34) | 1.50E-03 | IV |
| Obesity | Obesity vs normal weight | DLBCL | MA | Castillo 2014 | 16 | 7349 | RR | 1.29 (1.16, 1.43) | 2.50E-06 | III |
| Obesity | Obesity vs normal weight | CLL | MA | Castillo 2012 | 10 | 912 | RR | 1.17 (1.08, 1.27) | 1.60E-04 | IV |
| Obesity | Obesity vs normal weight | FL | SRMA | Odutola 2020 | 13 | 903 | RR | 1.08 (0.99, 1.17) | 7.10E-02 | NS |
| Infection | Herpes zoster | Yes vs no | NHL | SRMA | Schmidt 2017 | 7 | 52134 | RR | 1.72 (1.27, 2.32) | 4.49E-04 | III |
| Herpes zoster | Yes vs no | CLL | SRMA | Schmidt 2017 | 4 | >1000 | RR | 1.65 (1.20, 2.25) | 2.00E-03 | IV |
| HPgV | Yes vs no | DLBCL | SRMA | Fama 2019 | 3 | 54 | OR | 3.29 (1.63, 6.62) | 1.00E-03 | IV |
| HPgV | Yes vs no | FL | SRMA | Fama 2019 | 3 | 75 | OR | 3.01 (1.95, 4.63) | 8.64E-07 | IV |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|-----------|--------------|-----------------------|-------------|---------------|---------------------------------------------|----------|-------------------------------|
| Epstein–Barr virus    | Early antigen             | High (75th percentile) vs low (<25th percentile) | NHL     | MA        | Teras 2015   | 8                     | 1421        | RR            | 1.52 (1.16, 1.99)                           | 2.40E-03 | IV                            |
| Epstein–Barr virus    | Viral capsid antigen      | High (75th percentile) vs low (<25th percentile) | NHL     | MA        | Teras 2015   | 9                     | 1764        | RR            | 1.20 (1.00, 1.44)                           | 5.00E-02 | NS                            |
| Borrelia burgdorferi | Yes vs no                 | PCL                 | SRMA    | Travaglino 2020 | 10                   | 410         | OR            | 10.88 (3.84, 30.81)                        | 8.98E-06 | IV                            |
| Borrelia burgdorferi | Yes vs no                 | DLBCL               | SRMA    | Travaglino 2020 | 3                     | 53          | OR            | 8.15 (1.25, 53.06)                          | 2.80E-02 | IV                            |
| HBV                   | Yes vs no                 | TCL                 | SRMA    | Li 2018    | 12                     | NA          | OR            | 1.59 (1.11, 2.26)                           | 1.07E-02 | IV                            |
| HBV                   | Yes vs no                 | DLBCL               | SRMA    | Li 2018    | 10                     | 11943       | OR            | 2.06 (1.48, 2.88)                           | 2.53E-05 | III                           |
| HBV                   | Yes vs no                 | FL                  | SRMA    | Li 2018    | 9                      | 5124        | OR            | 1.60 (1.24, 2.07)                           | 3.50E-04 | III                           |
| HBV                   | Yes vs no                 | CLL/SL             | SRMA    | Li 2018    | 8                      | 10738       | OR            | 1.87 (1.34, 2.61)                           | 2.60E-04 | III                           |
| HBV                   | Yes vs no                 | BL                  | SRMA    | Li 2018    | 3                      | 264         | OR            | 2.12 (0.97, 4.65)                           | 6.00E-02 | NS                            |
| HCV                   | Patients vs general       | FL                  | MA      | DalMaso 2006 | 7                     | 193         | RR            | 2.73 (2.20, 3.38)                           | 9.12E-19 | IV                            |
| HCV                   | Patients vs general       | MZL                 | MA      | DalMaso 2006 | 5                     | 134         | RR            | 3.41 (2.39, 4.87)                           | 4.48E-11 | IV                            |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|----------------------------|---------------------|---------|------------|--------------|------------------------|-------------|---------------|------------------------------------------|----------|-------------------------------|
| HCV                   | Patients vs general population | TCL/MA DalMa No. of primary studies = 4 | 122 | RR 1.52 (1.13, 2.05) 5.90E-03 IV | |
| HCV                   | Patients vs general population | MA DalMa No. of primary studies = 5 | 88 | RR 1.65 (1.35, 2.02) 1.57E-06 IV | |
| Malaria infection     | Yes vs no eBL SRMa Kotepui No. of primary studies = 5 | 6055 | OR 0.87 (0.54, 1.39) 5.80E-01 NS | |
| Chemicals and pesticides | Solvent | Formaldehyde Ever vs never FL SRMa Odutola 21 No. of primary studies = 3 | 292 | RR 1.03 (0.83, 1.28) 8.00E-01 NS | |
| Chlorinated solvents | Ever vs never FL SRMa Odutola 21 No. of primary studies = 3 | 143 | RR 1.35 (1.09, 1.68) 6.60E-03 IV | |
| Any solvent | Ever vs never FL SRMa Odutola 21 No. of primary studies = 3 | 669 | IRR 1.16 (1.00, 1.34) 4.60E-02 IV | |
| Aromatic hydrocarbons | Styrene Highest vs lowest NHL SRMa Collins 2018 No. of primary studies = 16 | 553 | RR 1.14 (0.91, 1.43) 2.59E-01 NS | |
| Benzene | Ever vs never NHL SRMa Kane 2010 No. of primary studies = 24 | 1420 | OR/OR, Not specified 1.11 (0.94, 1.30) 2.10E-01 NS | |
| Benzene | Ever vs never FL SRMa Odutola 21 No. of primary studies = 3 | 333 | OR 1.30 (0.86, 1.97) 2.20E-01 NS | |
| Aromatic hydrocarbons | Ever vs never FL SRMa Odutola 21 No. of primary studies = 3 | 7262 | OR 1.24 (0.88, 1.75) 2.20E-01 NS | |
| Polychlorinated biphenyls | PCBs Highest vs lowest NHL SRMa Catalani 2019 No. of primary studies = 30 | 1439 | RR 0.96 (0.85, 1.07) 4.97E-01 NS | |
| PCBs | Highest vs lowest DLBCL SRMa Catalani 2019 No. of primary studies = 6 | NA | RR 0.68 (0.24, 1.12) 3.31E-01 NS | |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|-------------|--------------|----------------------------------------|----------|----------------------------------|
| PCBs                 | Highest vs lowest FL     | SRMA                | Catalani 2019 | 5          | NA          | RR                     | 1.21 (0.79, 1.64) | 3.11E-01 | NS                                      |
| PCBs                 | Highest vs lowest CLL    | SRMA                | Catalani 2019 | 4          | 573         | RR                     | 0.63 (0.39, 0.87) | 2.40E-02 | IV                                      |
| Dioxin               | Highest vs lowest FL     | SRMA                | Xu 2016     | 4          | 4263        | RR                     | 1.09 (0.92, 1.30) | 3.34E-01 | NS                                      |
| Trichloroethylene    | Highest vs lowest NHL    | SRMA                | Scott 2011  | 17         | >1000       | RR                     | 1.23 (1.07, 1.42) | 7.70E-03 | IV                                      |
| Occupational exposure to methylene chloride | Highest vs lowest NHL MA | Liu 2013 | 6          | 3001       | OR          | 1.28 (0.96, 1.70) | 9.00E-02 | NS                                      |
| Occupational exposure to gasoline | Highest vs lowest NHL MA | Kane 2010 | 35         | 1042       | RR          | 1.02 (0.94, 1.12) | 6.71E-01 | NS                                      |
| Carbamate/thiocarbamate pesticides | Highest vs lowest NHL SRMA | Schinasi 2014 | 3          | 1621       | RR          | 1.40 (1.10, 2.00) | 2.70E-02 | IV                                      |
| Carbamate insecticides | Highest vs lowest NHL SRMA | Schinasi 2014 | 3          | 1621       | RR          | 1.70 (1.30, 2.30) | 2.90E-04 | III                                     |
| Organophosphate pesticides | Highest vs lowest NHL SRMA | Boffetta 2021 | 6          | 1297       | RR          | 1.05 (0.90, 1.24) | 5.60E-01 | NS                                      |
| Glycosate            | Highest vs lowest DLBCL  | SRMA                | Boffetta 2021 | 4          | 1285       | RR                     | 1.29 (1.02, 1.63) | 3.30E-02 | IV                                      |
| Glycosate            | Ever vs never FL         | SRMA                | Odutola 2021 | 4          | 897         | RR                     | 0.90 (0.60, 1.34) | 6.20E-01 | NS                                      |
| Malathion            | Yes vs no                | NHL MA               | Hu 2017     | 7          | NA          | OR                     | 1.17 (0.82, 1.67) | 3.94E-01 | NS                                      |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|---------------|------------------------------------------|----------|-------------------------------|
| Diazinon             | Yes vs no                 | NHL                 | MA      | Hu 2017    | 7            | NA                   | OR          | 1.39 (1.11, 1.73) | 4.00E-03 IV |          |                               |
| Terbufos             | Yes vs no                 | NHL                 | MA      | Hu 2017    | 5            | NA                   | OR          | 1.07 (0.85, 1.36) | 5.84E-01 NS |          |                               |
| Organophosphate pesticides | Yes vs no       | NHL                 | MA      | Hu 2017    | 10           | NA                   | OR          | 1.22 (1.04, 1.43) | 1.40E-02 IV |          |                               |
| Organophosphate pesticidesc | Ever vs never  | FL                  | SRMA   | Odutola 2021 | 3            | 545                  | OR          | 1.75 (0.46, 6.72) | 4.20E-01 NS |          |                               |
| Organochlorine pesticides | Highest vs lowest  | NHL                 | MA      | Luo 2016    | 5            | 1010                  | OR         | 1.02 (0.81, 1.28) | 8.73E-01 NS |          |                               |
| DDTc                 | Highest vs lowest          | FL                  | SRMA   | Odutola 2021 | 3            | 741                  | RR          | 1.25 (0.75, 2.07) | 4.00E-01 NS |          |                               |
| DDEc                 | Highest vs lowest          | NHL                 | MA      | Luo 2016    | 11           | 1905                  | OR          | 1.38 (1.14, 1.66) | 8.00E-04 III |          |                               |
| DDEc                 | Highest vs lowest          | FL                  | SRMA   | Odutola 2021 | 4            | 255                  | RR          | 1.51 (0.99, 2.31) | 5.60E-02 NS |          |                               |
| HCH                  | Highest vs lowest          | NHL                 | MA      | Luo 2016    | 6            | 1184                  | OR          | 1.36 (0.95, 1.95) | 9.18E-02 NS |          |                               |
| HCB                  | Highest vs lowest          | NHL                 | MA      | Luo 2016    | 7            | 1265                  | OR          | 1.54 (1.20, 1.99) | 8.00E-04 III |          |                               |
| Chlordane            | Highest vs lowest          | NHL                 | MA      | Luo 2016    | 8            | 1218                  | OR          | 1.89 (1.42, 2.50) | 1.29E-05 III |          |                               |
| Organochlorine pesticides | Highest vs lowest  | NHL                 | MA      | Luo 2016    | 13           | 6582                  | OR          | 1.42 (1.27, 1.59) | 2.16E-09 III |          |                               |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|----------------------|---------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|--------------|---------------------------------|----------|----------------------------------|
| Pentachlorophenol<sup>c</sup> | Highest vs lowest | NHL | SRMA | Zheng 2015 | 5 | 419 | OR | 2.65 (1.33, 5.27) | 6.00E-03 | IV |
| Phenoxy herbicides | 2,4-D | Highest vs lowest | NHL | SRMA | Smith 2017 | 11 | <1000 | OR | 1.82 (1.14, 2.92) | 1.30E-02 | IV |
| MCPA | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 5 | 3986 | RR | 1.50 (0.90, 2.50) | 1.20E-01 | NS |
| Phenoxy herbicides | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 12 | 6493 | RR | 1.40 (1.20, 1.60) | 6.00E-06 | III |
| Other pesticides | Amide herbicides | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 4 | 1155 | RR | 1.30 (0.80, 1.90) | 2.40E-01 | NS |
| Benzoic acid herbicides | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 4 | 1155 | RR | 1.30 (0.90, 1.90) | 1.70E-01 | NS |
| Triazine herbicides | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 4 | 1155 | RR | 1.50 (1.00, 2.10) | 3.20E-02 | IV |
| Trifluralin | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 4 | 1346 | RR | 0.90 (0.60, 1.30) | 6.10E-01 | NS |
| Pyrethroid/pyrethrin<sup>c</sup> | Ever vs never | FL | SRMA | Odutola 2021 | 4 | 697 | RR | 1.45 (0.91, 2.32) | 1.20E-01 | NS |

**Occupation**

| Occupation | Attendants vs general population | Attendants vs general population | Attendants vs general population | Attendants vs general population | Attendants vs general population | Attendants vs general population | Attendants vs general population | Attendants vs general population | Attendants vs general population | Attendants vs general population |
|-----------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| Flight attendant | Female flight attendant<sup>c</sup> | NHL | MA | Buja 2006 | 3 | NA | SIR | 1.19 (0.52, 2.15) | 6.44E-01 | NS |
| Farmer | Farmer | NA | NHL | MA | Boffetta 2007 | 50 | >1000 | RR | 1.11 (1.05, 1.17) | 1.74E-04 | III |
| Firefighter | Firefighter vs general population | NHL | SRMA | Jalilian 2019 | 14 | NA | SIR | 1.07 (0.96, 1.20) | 2.37E-01 | NS |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome Study type | Author, year | No. of primary studies | No. of cases | Effect measure (95% CI) | P random a | Random effects summary effect size (95% CI) | Strength of reported association b |
|-----------------------|---------------------------|---------------------|-------------------|--------------|-----------------------|-------------|-------------------------|-----------|----------------------------------------|-------------------------------|
| Firefighter | Ever vs never | FL SRMA | Odutola 2021 | 3 5 | RR | 1.16 (0.38, 3.52) | 8.10E-01 | NS | | |
| Hairdresser | Hairdresser | NA | NHL MA | Takkouche 2009 | 13 22425 | RR | 1.11 (0.94, 1.32) | 2.30E-01 | NS | |
| Petroleum refinery worker | Petroleum refinery worker | Worker vs general population | NHL SRMA | Schnatter 2018 | 16 NA | RR | 0.98 (0.89, 1.09) | 7.09E-01 | NS | |
| Meat worker | Meat worker | Worker vs general population | NHL MA | Boffetta 2007 | 9 NA | RR | 0.99 (0.77, 1.29) | 9.40E-01 | NS | |
| Printer | Printer | Worker vs general population | NHL MA | Boffetta 2007 | 6 >1000 | RR | 1.86 (1.38, 2.50) | 5.00E-05 | III | |
| Wood worker | Wood worker | Worker vs general population | NHL MA | Boffetta 2007 | 11 NA | RR | 1.04 (0.79, 1.37) | 7.90E-01 | NS | |
| Occupational exposure to polycyclic aromatic hydrocarbons | Aluminum plant workers | Worker vs general population | NHL SRMA | Alicandro 2016 | 8 167 | RR | 1.19 (0.98, 1.44) | 7.60E-02 | NS | |
| Iron and steel foundry workers | Worker vs general population | NHL SRMA | Alicandro 2016 | 8 57 | RR | 0.94 (0.73, 1.22) | 6.50E-01 | NS | |

2,4-D=2,4-Dichlorophenoxyacetic acid; ALC=anaplastic large cell lymphoma; BL=Burkitt Lymphoma; CI=confidence interval; CLL/SLL=chronic lymphocytic leukemia/small lymphocytic lymphoma; DDE=dichlorodiphenyldichloroethylene; DDT=dichlorodiphenyltrichloroethane; DLBCL=diffuse large B-cell lymphoma; eBL=endemic Burkitt Lymphoma; FL=follicular lymphoma; HAART=Highly Active Antiretroviral Therapy; HBV=hepatitis B virus; HCB=hexachlorobenzene; HCH=hexachlorocyclohexane; HCV=hepatitis C virus; HIV/AIDS=human immunodeficiency virus, acquired immunodeficiency syndrome; HPgV=human Papillomavirus; IRR=incidence rate ratio; MA=meta-analysis; MZL=marginal zone lymphoma; MCPA=2-methyl-4-chlorophenoxyacetic acid; NA-NSAIDS=non-aspirin non-steroidal anti-inflammatory drugs; NSAIDS=non-steroidal anti-inflammatory drugs; NA=not available; NHL=non-Hodgkin lymphoma; OR=odds ratio; PCBs=polychlorinated biphenyls; PI=prediction interval; SIR=standardized incidence ratio; SRMA=systematic review and meta-analysis; RR=risk ratio; TCL=T-cell lymphoma.

a P value for summary effect estimates using a random-effects DerSimonian and Laird estimator.
b Strength of association using the criteria listed in Table 1.
c These studies considered NHL incidence and mortality.
d Summary effect estimates were calculated using a fixed effect estimator.
e Not using inverse variance weighting. WHAT DOES THIS MEAN XS: They used Bayesian hierarchical models, i remember at some point Josh mentioned that we should make notes for this! but I'm okay with removing this footnote.
| NHL subtype       | At least 1000 cases and $P<10^{-3}$                                                                 | At least 1000 cases and $P<10^{-6}$                                                                 |
|-------------------|--------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| CLL/SLL          | Years since quitting cigarette smoking; printing pressmen                                        | None                                                                                             |
| CLL/SLL/PLL/MCL  | Adult infectious mononucleosis                                                                    | None                                                                                             |
| DLBCL            | Alcohol; Any atopic disorder; Allergy; B and T-cell activating autoimmune diseases; HCV; Hay fever; Recreational sun exposure; Socioeconomic status (high vs low); BMI as young adult (25-30 kg/m²); Rheumatoid arthritis; Blood transfusion; Weight | History of B-cell activating autoimmune disease; Sjogren’s syndrome; HCV; Young adult BMI (%25 kg/m²); Years since quit cigarette smoking; Age first alcohol consumption (20-29 years vs. nondrinker); Current alcohol consumption status as of ~2 years prior to diagnosis/interview. |
| FL               | Blood transfusions; Young adult BMI (%25 kg/m²); Recreational sun exposure; History of cigarette smoking (females); Current cigarette smoking; University and higher education teachers; Male height (100% vs. 60%); Any atopic disorder | None                                                                                             |
| MZL              | Systemic lupus erythematosus; HCV, Peptic ulcer; Wine                                            | History of B-cell activating autoimmune disease; Sjogren’s syndrome                               |
| HCL              | Current cigarette smoking                                                                         | None                                                                                             |
| NHL              | Hormone replacement therapy; Systemic lupus erythematosus; HCV; Allergy; Food allergy; Hay fever; Blood transfusion; Height; Alcohol exposures; Recreational hair dye use; Socioeconomic status (high vs low); Secondary Sjogren’s syndrome; Childhood measles | Sjogren’s syndrome; History of B-cell activating autoimmune disease; Hay fever; Young adult BMI (%25 kg/m²); Recreational sun exposure (%Q3-Q4 hours/week); Recreational hair dye use (%Q3-Q4 hours/week); Beer, wine, and liquor |

BMI=body mass index; CI=confidence interval; CLL=chronic lymphocytic leukemia; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; HCL=hairy cell leukemia; HCV=hepatitis C virus; MCL=mantle cell lymphoma; MZL=marginal zone lymphoma; NHL=non-Hodgkin lymphoma; SLL=small lymphocytic lymphoma; PLL=prolymphocytic leukemia.

* These were protective risk factors.
| Exposure [NHL subtype] | Effect estimate (95% CI) | Streng th of reported association | Exposure [NHL subtype] | Effect estimate (95% CI) | Effect estimates in the same direction | Overlapping 95% confidence intervals | Same level of statistical significance (P<0.05) | At least one-third of studies overlapping evidence |
|------------------------|--------------------------|----------------------------------|------------------------|--------------------------|---------------------------------------|--------------------------------------|-----------------------------------------------|--------------------------------------------------|
| Red blood cell transfusion [NHL] | RR 1.20 (1.07, 1.35) | IV | History of blood transfusion [NHL] | OR 0.83 (0.77, 0.91) | No | No | Both | Yes |
| Red blood cell transfusion [CLL/SLL] | RR 1.66 (1.08, 2.56) | IV | History of blood transfusion [CLL/SLL] | OR 0.79 (0.66, 0.94) | No | No | Both | Yes |
| Red blood cell transfusion [FL] | RR 1.02 (0.67, 1.55) | NS | History of blood transfusion [FL] | OR 0.78 (0.68, 0.89) | No | Yes | MA of IPD only | Yes |
| Red blood cell transfusion [DLBCL] | RR 1.06 (0.86, 1.30) | NS | History of blood transfusion [DLBCL] | OR 0.84 (0.75, 0.95) | No | Yes | MA of IPD only | Yes |
| Ever smoking [NHL] | RR 1.05 (1.00, 1.09) | IV | Any smoking [NHL] | OR 1.02 (0.97, 1.07) | Yes | Yes | Neither | No |
| Ever smoking [DLBCL] | RR 1.01 (0.95, 1.07) | NS | Any smoking [DLBCL] | OR 1.01 (0.94, 1.08) | Yes | Yes | Neither | No |
| Ever smoking [FL] | RR 1.05 (0.88, 1.25) | NS | Any smoking [FL] | OR 1.09 (1.00, 1.18) | Yes | Yes | Neither | Yes |
| Ever smoking [CLL/SLL] | RR 0.96 (0.89, 1.04) | NS | Any smoking [CLL/SLL] | OR 0.90 (0.81, 0.99) | Yes | Yes | MA of IPD only | Yes |
| Ever smoking [TCL] | RR 1.23 (1.06, 1.43) | IV | Any smoking [TCL] | OR 1.32 (1.09, 1.59) | Yes | Yes | Both | No |
| Ever drinking [NHL] | RR 0.85 (0.79, 0.91) | III | Any alcohol [NHL] | OR 0.87 (0.81, 0.93) | Yes | Yes | Both | Yes |
| Ever drinking [TCL] | RR 0.78 (0.58, 1.05) | NS | Any alcohol [TCL] | OR 0.68 (0.53, 0.87) | Yes | Yes | MA of IPD only | Yes |
| Ever drinking [DLBCL] | RR 0.79 (0.68, 0.91) | IV | Any alcohol [DLBCL] | OR 0.81 (0.73, 0.89) | Yes | Yes | Both | Yes |
| Ever drinking [FL] | RR 0.80 (0.69, 0.92) | IV | Any alcohol [FL] | OR 0.86 (0.77, 0.96) | Yes | Yes | Both | Yes |
| Exposure [NHL subtype] | Effect estimate (95% CI) | Strength of reported association | Exposure [NHL subtype] | Effect estimate (95% CI) | Effect estimates in the same direction | Overlapping 95% confidence intervals | Same level of statistical significance \( (P<0.05) \) | At least one-third of studies overlapping |
|-----------------------|--------------------------|----------------------------------|------------------------|--------------------------|----------------------------------------|-------------------------------------|-------------------------------------------|-------------------------------|
| Ever drinking [CLL/SLL] | RR 1.00 (0.80, 1.26) | NS | Any alcohol [CLL/SLL] | OR 1.04 (0.90, 1.19) | Yes | Yes | Neither | Yes |
| Pernicious anemia [NHL] | RR 1.16 (0.79, 1.71) | NS | Pernicious anemia [NHL] | OR 1.37 (0.62, 3.03) | Yes | Yes | Neither | No |
| Rheumatoid arthritis [NHL] | SIR 2.26 (1.82, 2.81) | II | Rheumatoid Arthritis [NHL] | OR 1.32 (0.99, 1.77) | Yes | No | MA of summary level data only | No |
| Primary Sjogren's syndrome [NHL] | RR 13.76 (8.53, 18.99) | II | Sjogren's syndrome [NHL] | OR 7.52 (3.68, 15.36) | Yes | Yes | Both | No |
| Systemic lupus erythematosus [NHL] | RR 5.40 (3.75, 7.77) | II | Systemic Lupus Erythematosus [NHL] | OR 2.83 (1.81, 4.11) | Yes | Yes | Both | No |
| Psoriasis [NHL] | RR 1.48 (1.3, 1.69) | III | Psoriasis [NHL] | OR 1.08 (0.90, 1.29) | Yes | No | MA of summary level data only | No |
| Type 1 diabetes [NHL] | RR 1.55 (1.15, 2.08) | IV | Type 1 diabetes [NHL] | OR 1.15 (0.80, 1.66) | Yes | Yes | MA of summary level data only | No |
| Celiac disease [NHL] | OR 2.61 (2.04, 3.33) | II | Celiac disease [NHL] | OR 1.77 (1.05, 2.99) | Yes | Yes | Both | Yes |
| Celiac disease [TCL] | OR 15.84 (7.85, 31.94) | II | Celiac disease [TCL] | OR 14.82 (7.27, 30.19) | Yes | Yes | Both | Yes |
| Celiac disease [DLBCL] | OR 2.25 (1.32, 3.85) | IV | Celiac disease [DLBCL] | OR 2.09 (1.04, 4.18) | Yes | Yes | Both | Yes |
| Celiac disease [CLL] | OR 0.80 (0.46, 1.38) | NS | Celiac disease [CLL/SLL] | OR 0.60 (0.14, 2.61) | Yes | Yes | Neither | Yes |
| Sarcoidosis [NHL] | RR 1.43 (1.03, 1.99) | IV | Sarcoidosis [NHL] | OR 0.71 (0.39, 1.29) | No | Yes | Neither | No |
| Exposure [NHL subtype] | Effect estimate (95% CI) | Strength of reported association | Exposure [NHL subtype] | Effect estimate (95% CI) | Effect estimates in the same direction | Overlapping 95% confidence intervals | Same level of statistical significance (P<0.05) | At least one-third of studies overlapping |
|------------------------|--------------------------|---------------------------------|------------------------|--------------------------|----------------------------------------|--------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Tuberculosis [NHL]     | RR 1.61 (1.34, 1.94)     | II                               | Adult Tuberculosis infection [NHL] | OR 1.16 (0.96, 1.39)     | Yes                                    | Yes                                  | MA of summary level data only                | No                                            |
| Herpes Zoster [NHL]    | RR 1.72 (1.27, 2.32)     | III                              | Adult shingles [NHL]        | OR 1.05 (0.93, 1.19)     | Yes                                    | No                                   | MA of summary level data only                | No                                            |
| Hepatitis C virus [NHL]| OR 3.36 (2.40, 4.72)     | II                               | Hepatitis C virus [NHL]      | OR 1.81 (1.39, 2.37)     | Yes                                    | No                                   | Both                                          | No                                            |
| Hepatitis C virus [DLBCL]| OR 2.65 (1.88, 3.74)   | II                               | hepatitis C virus [DLBCL]    | OR 2.33 (1.71, 3.19)     | Yes                                    | Yes                                  | Both                                          | Yes                                           |
| Hepatitis C virus [FL] | OR 2.73 (2.20, 3.38)     | IV                               | Hepatitis C virus [FL]       | OR 0.57 (0.30, 1.10)     | No                                     | No                                   | MA of summary level data only                | Yes                                           |
| Hepatitis C virus [MZL]| OR 3.41 (2.39, 4.87)     | IV                               | Hepatitis C virus [MZL]      | OR 3.04 (1.65, 5.60)     | Yes                                    | Yes                                  | Both                                          | Yes                                           |
| Hepatitis C virus [CLL/SLL]| OR 1.65 (1.35, 2.02) | IV                               | Hepatitis C virus [CLL/SLL]  | OR 2.08 (1.23, 3.49)     | Yes                                    | Yes                                  | Both                                          | Yes                                           |
| Farmer [NHL]           | RR 1.11 (1.05, 1.17)     | III                              | Farmer [NHL]                | OR 1.03 (0.95, 1.13)     | Yes                                    | Yes                                  | Neither                                       | No                                            |
| Firefighter [NHL]      | SIR 1.07 (0.96, 1.20)    | NS                               | Firefighter [NHL]           | OR 0.76 (0.53, 1.09)     | No                                     | Yes                                  | Neither                                       | No                                            |
| Hairdresser [NHL]      | RR 1.11 (0.94, 1.32)     | NS                               | Hairdresser [NHL]           | OR 1.21 (0.96, 1.52)     | Yes                                    | Yes                                  | Both                                          | No                                            |
| Petroleum refinery worker [NHL] | RR 0.98 (0.89, 1.09) | NS                               | Petroleum workers [NHL]     | OR 0.79 (0.38, 1.67)     | Yes                                    | Yes                                  | Neither                                       | No                                            |
| Teacher [NHL]          | RR 1.47 (1.34, 1.61)     | II                               | Teacher [NHL]               | OR 0.89 (0.81, 0.98)     | No                                     | No                                   | Both                                          | No                                            |
| Meat worker [NHL]      | RR 0.99 (0.77, 1.29)     | NS                               | Meat worker [NHL]           | OR 1.08 (0.81, 1.42)     | No                                     | Yes                                  | Neither                                       | No                                            |
| Printer [NHL]          | RR 1.86 (1.38, 2.50)     | III                              | Printers [NHL]              | OR 0.95 (0.78, 1.17)     | No                                     | No                                   | MA of summary level data only                | No                                            |
| Exposure [NHL subtype] | Effect estimate (95% CI) | Strength of reported association | Exposure [NHL subtype] | Effect estimate (95% CI) | Effect estimates in the same direction | Overlapping 95% confidence intervals | Same level of statistical significance ($P<0.05$) | At least one-third of studies overlapping |
|------------------------|--------------------------|---------------------------------|------------------------|--------------------------|----------------------------------------|--------------------------------------|--------------------------------|-------------------------------|
| Wood worker [NHL]      | RR 1.04 (0.79, 1.37)     | IV                              | Wood workers [NHL]     | OR 1.04 (0.89, 1.22)     | Yes                                    | Yes                                  | Neither                         | No                            |

CI=confidence interval; CLL/SLL=chronic lymphocytic leukemia/small lymphocytic lymphoma; DLBCL=diffuse large B-cell lymphoma; NA=not available; NHL= non-Hodgkin lymphoma; OR=odds ratio; SIR=standardized incidence ratio; RR=risk ratio; TCL=T-cell lymphoma.
Identification of studies in six electronic databases

Records identified from:
- MEDLINE (n = 5543)
- Embase (n = 4336)
- Scopus (n = 3173)
- Web of Science Core Collection* (n = 2417)
- Cochrane Library (n = 167)
- Epistemonikos (n = 802)
- Total (n = 16438)

Records removed before screening: Duplicate records removed (n = 7444)

Records screened (n = 8994)

Records excluded (n = 7970)

Full-text reports assessed for eligibility (n = 1024)

Reports excluded (n = 904)**:
- Non-English (n = 20)
- Duplicate (n = 8)
- Wrong study design (n = 240)
- Wrong topic (n = 442)
- Wrong exposure (n = 22)
- Wrong study focus (n = 14)
- Wrong component study design (n = 10)
- Insufficient data for analyses (n = 40)
- Overlapping review (n = 102)
- inability to retrieve full text (n = 6)

Studies included (n = 120)

MAAs of summary level data (n = 85)
MAAs of IPD (n = 27)
Systematic reviews (n = 8)

Figure 1: Study selection flowchart

* Web of Science Core Collection as licensed at Yale: Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years

** Wrong study design: the examined study was not a systematic review, meta-analysis or pooled analysis
Wrong topic: the examined review did not examine non-Hodgkin lymphoma or its subtypes as an outcome OR the study did not examine the impact of an environmental exposure on the risk of non-Hodgkin lymphoma development
Wrong exposure: the examined risk factor does not meet the definition of environmental risk factor in our study
Wrong study focus: the review did not examine the impact of an exposure on the risk of developing NHL
Wrong component study design: the review did not synthesize observational study data
Insufficient data for analyses: the review included fewer than 3 component studies
Overlapping review: a larger review was identified for the same association
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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eTable 1: Search strategy

Database searches, 2021-07-23
Searches on the Ovid platform can be rerun at https://tools.ovid.com/ovidtools/launcher.html

| Ovid MEDLIN E(R) ALL <1946 to July 22, 2021> |     |
|--------------------------------------------|-----|
| 1  [Xiaoting Shi]                         | 0   |
| 2  [concept two: SRs]                     | 0   |
| 3  (systematic adj4 review).ti.            | 1604|
| 4  systematic review.pt.                   | 1621|
| 5  Cochrane Database of Systematic Reviews.jn. and review.pt. | 1365|
| 6  [approach c: based on Lee 2012]        | 8   |
| 7  medline.tw. or systematic review.ti. or meta-analysis.pt. or pubmed.tw. | 3574|
| 8  [from our previous searches]           | 0   |
| 9  (pooled analysis or pooled analyses).mp.| 1173|
| 10 (metaanalysis or meta-analysis).af.     | 2201|
| 11 [NHL concept]                          | 0   |
| 12 neoplasms/ or lymphoma/ or exp lymphoma, non-hodgkin/ | 5895|
| 13 [alternative based on https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004024.pub2/appendices#CD004024-sec1-0011] | 0   |
| 14 *Lymphoma/                             | 3602|
| 15 *hematologic neoplasms/                | 1082|
| 16 lymphom*.mp.                           | 2585|
| 17 non-hodgkin*.mp.                       | 5802|
| 18 nonhodgkin*.mp.                        | 136 |
| 19 (non adj1 hodgkin*).mp.                | 5802|
| 20 nhl.mp.                                | 1393|
| 21 (hemato* adj1 malign*).mp.             | 2696|
| 22 (haemato* adj1 malign*).mp.            | 5497|
| 23 (hemato* adj1 neoplas*).mp.            | 1661|
| 24 (haemato* adj1 neoplas*).mp.          | 415 |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

|   |   |   |
|---|---|---|
|25| 11 | 7217 |
|26| 94 | 9999 |
|27| 716 | 2899 |
|28| 716 | 2899 |
|29| 79 | 4231 |
|30| 79 | 5543 |

**Embase**

|   |   |   |
|---|---|---|
|1| 0 | 7217 |
|2| 31 | 6726 |
|3| 1 | 4582 |
|4| 5 | 3598 |
|5| 80 | 3504 |
|6| 8 | 6054 |
|7| 7 | 6219 |
|8| 1 | 6055 |
|9| 0 | 2544 |
|10| 5 | 6301 |
|11| 5 | 9491 |
|12| 84 | 4590 |
|13| 584 | 689 |
|14| 14 | 8218 |
|15| 5 | 2714 |
|16| 584 | 4327 |
|17| 125 | 4368 |
|18| 0 | 0 |
|19| 26 | 1918 |
|20| 7 | 1124 |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

|   |   |
|---|---|
| 21 | medline.tw. or systematic review.ti. or pubmed.tw. |
| 22 | (pooled analysis or pooled analyses).mp. |
| 23 | (metaanalysis or meta-analysis).af. |
| 24 | or/19-23 |
| 25 | 14 and 17 |
| 26 | limit 25 to meta analysis |
| 27 | limit 25 to systematic review |
| 28 | 25 and 24 |
| 29 | 26 or 27 or 28 |
| 30 | limit 29 to conference abstract status |
| 31 | 29 not 30 |

Scopus

TS=(lymphom* OR non-hodgkin* OR (non NEAR/1 hodgkin*) OR nhl OR ((hemato* OR haemato*) NEAR/1 (malign* OR neoplas*))) AND (TITLE-ABS-KEY (risk* OR protective-factor*)) AND (TITLE-ABS-KEY ((systematic W/4 review) OR medline OR pubmed OR "pooled analysis" OR "pooled analyses" OR metaanalysis OR meta-analysis) ) AND (EXCLUDE (DOCTYPE, "cp"))

Web of Science Core Collection

TS=(lymphom* OR non-hodgkin* OR (non NEAR/1 hodgkin*) OR nhl OR ((hemato* OR haemato*) NEAR/1 (malign* OR neoplas*))) AND (TITLE-ABS-KEY ((systematic W/4 review) OR medline OR pubmed OR "pooled analysis" OR "pooled analyses" OR metaanalysis OR meta-analysis) ) AND (EXCLUDE (DOCTYPE, "cp"))

Refined by excluding the Web of Science document types proceedings papers and meeting abstracts

Cochrane Library

#1 ((systematic NEAR/4 review):ti OR (systematic review):pt OR (medline or pubmed or "pooled analysis" OR "pooled analyses" OR metaanalysis OR meta-analysis):ti,ab,kw (Word variations have been searched) 2939 6

#2 MeSH descriptor: [Neoplasms] this term only 6376

#3 MeSH descriptor: [Lymphoma] this term only 1369

#4 MeSH descriptor: [Lymphoma, Non-Hodgkin] explode all trees 2056

#5 MeSH descriptor: [Hematologic Neoplasms] this term only 466

#6 (lymphom* or non-hodgkin* or nonhodgkin* or (non NEAR/1 hodgkin*) or nhl or (hemato* NEAR/1 malign*) or (haemato* NEAR/1 malign*) or (hemato* NEAR/1 neoplas*) or (haemato* NEAR/1 neoplas*) ):ti,ab,kw 1414 4

#7 2019 2

#8 (risk* or (protective NEAR/1 factor*)):ti,ab,kw 2539 10

#9 MeSH descriptor: [Risk] this term only 3322

#10 MeSH descriptor: [Protective Factors] this term only 135
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

|   |   | MeSH descriptor: [Risk Factors] this term only |   |
|---|---|---------------------------------------------|---|
| #11 |   | 2495                                       | 5 |
| #12 |   | #8 or #9 or #10 or #11                     | 2539 |
| #13 |   | #1 and #7 and #12                          | 10 |
|     |   | Limited to reviews (not trials)            | 273 |

**Epistemionkos**

| Filter Type       | Query                                                                 |   |
|-------------------|----------------------------------------------------------------------|---|
| SR filter         | (title:(lymphoma*) OR abstract:(lymphoma*)) AND (title:(risk* OR protective) OR abstract:(risk* OR protective)) | 736 |
| Broad synthesis filter | (title:(lymphoma*) OR abstract:(lymphoma*)) AND (title:(risk* OR protective) OR abstract:(risk* OR protective)) | 24 |
| No filter         | (title:(lymphoma*) OR abstract:(lymphoma*)) AND (title:(risk* OR protective) OR abstract:(risk* OR protective)) AND (title:"pooled analysis" OR "pooled analyses") OR abstract:("pooled analysis" OR "pooled analyses") | 42 |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

### eTable 2: NHL subtypes

| Category                  | Subtypes                                                                 | Eligibility as NHL |
|----------------------------|--------------------------------------------------------------------------|--------------------|
| Chronic lymphocytic leukemia/small lymphocytic lymphoma | Yes                                                                 |
| Monoclonal B-cell lymphocytosis* | No                                                                   |
| B-cell prolymphocytic leukemia | Yes                                                                  |
| Splenic marginal zone lymphoma   | Yes                                                                  |
| Hairy cell leukemia            | Yes                                                                  |
| Splenic B-cell lymphoma/leukemia, unclassifiable | Yes                                                                  |
| Splenic diffuse red pulp small B-cell lymphoma | Yes                                                                  |
| Hairy cell leukemia-variant   | Yes                                                                  |
| Lymphoplasmacytic lymphoma     | Yes                                                                  |
| Waldenström macroglobulinemia | Yes                                                                  |
| Monoclonal gammopathy of undetermined significance (MGUS), IgM* | No                                                                  |
| μ heavy-chain disease          | No                                                                   |
| γ heavy-chain disease          | No                                                                   |
| α heavy-chain disease          | No                                                                   |
| Monoclonal gammopathy of undetermined significance (MGUS), IgG/A* | No                                                                  |
| Plasma cell myeloma            | No                                                                   |
| Solitary plasmacytoma of bone  | No                                                                   |
| Extrasosseous plasmacytoma     | No                                                                   |
| Monoclonal immunoglobulin deposition diseases* | No                                                                  |
| Extrannodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) | Yes                                                                  |
| Nodal marginal zone lymphoma   | Yes                                                                  |
| Pediatric nodal marginal zone lymphoma | Yes                                                                  |
| Follicular lymphoma            | Yes                                                                  |
| In situ follicular neoplasia*  | Yes                                                                  |
| Duodenal-type follicular lymphoma* | Yes                                                                  |
| Pediatric-type follicular lymphoma* | Yes                                                                  |
| Large B-cell lymphoma with IRF4 rearrangement* | Yes                                                                  |
| Primary cutaneous follicle center lymphoma | Yes                                                                  |
| Mantle cell lymphoma           | Yes                                                                  |
| In situ mantle cell neoplasia* | Yes                                                                  |
| Diffuse large B-cell lymphoma (DLBCL), NOS | Yes                                                                  |
| Germinal center B-cell type*   | Yes                                                                  |
| Activated B-cell type*         | Yes                                                                  |
| T-cell/histiocyte-rich large B-cell lymphoma | Yes                                                                  |
| Primary DLBCL of the central nervous system (CNS) | Yes                                                                  |
| Primary cutaneous DLBCL, leg type | Yes                                                                  |
| EBV+ DLBCL, NOS*               | Yes                                                                  |
| EBV+mucocutaneous ulcer*       | No                                                                   |
| DLBCL associated with chronic inflammation | Yes                                                                  |
| Lymphomatoïd granulomatosis    | Yes                                                                   |
| Primary mediastinal (thymic) large B-cell lymphoma | Yes                                                                  |
| Intravascular large B-cell lymphoma | Yes                                                                  |
| ALK+ large B-cell lymphoma     | Yes                                                                  |
## Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Category                        | Subtypes                                                                 | Eligibility as NHL |
|---------------------------------|--------------------------------------------------------------------------|--------------------|
|                                 | Plasmablastic lymphoma                                                   | Yes                |
|                                 | Primary effusion lymphoma                                                | Yes                |
|                                 | HHV8+DLBCL, NOS*                                                         | Yes                |
|                                 | Burkitt lymphoma                                                         | Yes                |
|                                 | Burkitt-like lymphoma with 11q aberration*                               | Yes                |
|                                 | High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements* | Yes                |
|                                 | High-grade B-cell lymphoma, NOS*                                         | Yes                |
|                                 | B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma | Yes                |
|                                 | Double hit/triple hit lymphoma                                           | Yes                |
|                                 | T-cell prolymphocytic leukemia                                           | Yes                |
|                                 | T-cell large granular lymphocytic leukemia                                | Yes                |
|                                 | Chronic lymphoproliferative disorder of NK cells                         | Yes                |
|                                 | Aggressive NK-cell leukemia                                              | Yes                |
|                                 | Systemic EBV+ T-cell lymphoma of childhood*                              | Yes                |
|                                 | Hydroa vacciniforme–like lymphoproliferative disorder*                   | Yes                |
|                                 | Adult T-cell leukemia/lymphoma                                           | Yes                |
|                                 | Extranodal NK-/T-cell lymphoma, nasal type                               | Yes                |
|                                 | Enteropathy-associated T-cell lymphoma                                   | Yes                |
|                                 | Monomorphic epitheliotropic intestinal T-cell lymphoma*                  | Yes                |
|                                 | Indolent T-cell lymphoproliferative disorder of the GI tract*            | No                 |
|                                 | Hepatosplenic T-cell lymphoma                                            | Yes                |
|                                 | Subcutaneous panniculitis-like T-cell lymphoma                           | Yes                |
|                                 | Mycosis fungoides                                                       | Yes                |
|                                 | Sézary syndrome                                                         | Yes                |
|                                 | Primary cutaneous CD30+ T-cell lymphoproliferative disorders             | Yes                |
|                                 | Lymphomatoid papulosi                                                    | No                 |
|                                 | Primary cutaneous anaplastic large cell lymphoma                         | Yes                |
|                                 | Primary cutaneous γδ T-cell lymphoma                                      | Yes                |
|                                 | Primary cutaneous CD8+aggressive epidermotropic cytotoxic T-cell lymphoma| Yes                |
|                                 | Primary cutaneous acral CD8+T-cell lymphoma*                            | Yes                |
|                                 | Primary cutaneous CD4+small/medium T-cell lymphoproliferative disorder*  | No                 |
|                                 | Peripheral T-cell lymphoma, NOS                                           | Yes                |
|                                 | Angioimmunoblastic T-cell lymphoma                                       | Yes                |
|                                 | Follicular T-cell lymphoma*                                              | Yes                |
|                                 | Nodal peripheral T-cell lymphoma with TFH phenotype*                     | Yes                |
|                                 | Anaplastic large-cell lymphoma, ALK+                                     | Yes                |
|                                 | Anaplastic large-cell lymphoma, ALK−*                                    | Yes                |
|                                 | Breast implant–associated anaplastic large-cell lymphoma*                | Yes                |
|                                 | Acute lymphoblastic leukaemia (ALL)                                      | No                 |

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| Category | Subtypes | Eligibility as NHL |
|----------|----------|--------------------|

Footnotes:
* Changes from the 2008 classification.
NOS: not otherwise specified
Information source: 2016 WHO classification of mature lymphoid neoplasms (https://pubmed.ncbi.nlm.nih.gov/26980727/)
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**eTable 3: R code**

| Below is the R code example for the association between Behcet disease and NHL |
|---|
| # read in data_Behcet Disease |
| meta1 = read_excel("RR_effect_sizes_Behcet Disease #4206.xlsx") |
| head(meta1) |
| # conduct main analysis |
| meta2<-metagen(meta1$LNRR,meta1$SE, |
| sm="R",studlab=paste(lastname,publication_year) |
| ,data=meta1,method.bias="Egger",prediction = TRUE, |
| level.predict =0.95) |
| summary(meta2) |
| # create forest plot, funnel plot |
| forest(meta2) |
| funnel(meta2) |
| meta2$pval.random |
| # conduct egger's test |
| metabias(meta2,method.bias="Egger",plotit=TRUE, correct= TRUE, k=3) |
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**eTable 4: Overlapping meta-analyses of summary level data**

| Environmental risk factors                          | Largest review (First author, year) | Number of overlapping meta-analyses | Number of primary studies in the largest meta-analyses | Most recent (Y/N) | Highest impact factor one (Y/N) |
|-----------------------------------------------------|-------------------------------------|-------------------------------------|------------------------------------------------------|------------------|--------------------------------|
| **Dietary factors**                                 |                                     |                                     |                                                      |                  |                                |
| Red meat                                            | Yang 2015                           | 4                                   | 18                                                   | N                | N                              |
| Processed meat                                      | Yang 2015                           | 4                                   | 18                                                   | N                | N                              |
| White meat/poultry                                  | Dong 2017                           | 3                                   | 10                                                   | N                | N                              |
| Fish                                                | Cai 2016                            | 3                                   | 11                                                   | N                | N                              |
| Fruit and vegetable                                 | Chen 2013                           | 2                                   | 4                                                    | N                | Y                              |
| Fruit                                               | Chen 2013                           | 2                                   | 13                                                   | N                | Y                              |
| Vegetable                                           | Chen 2013                           | 2                                   | 13                                                   | N                | Y                              |
| Eggs                                                | Cai 2016                            | 2                                   | 10                                                   | N                | N                              |
| Total dairy products                                | Wang 2016                           | 2                                   | 7                                                    | Y                | Y                              |
| Milk                                                | Wang 2016                           | 3                                   | 16                                                   | N                | Y                              |
| Cheese                                              | Wang 2016                           | 2                                   | 10                                                   | Y                | Y                              |
| Vitamin D                                           | Lu 2014                             | 2                                   | 6                                                    | N                | N                              |
| **Drugs, vaccinations and procedures**              |                                     |                                     |                                                      |                  |                                |
| Aspirin                                             | Ye 2015                             | 2                                   | 10                                                   | Y                | Y                              |
| Non-steroidal anti-inflammatory drugs               | Ye 2015                             | 2                                   | 13                                                   | Y                | N                              |
| Statin                                              | Ye 2017                             | 3                                   | 9                                                    | Y                | Y                              |
| **Non-dietary lifestyle factors**                   |                                     |                                     |                                                      |                  |                                |
| Physical activity                                   | Davies 2020                         | 3                                   | 17                                                   | Y                | Y                              |
| Hair dye                                            | Qin 2019                            | 2                                   | 16                                                   | Y                | N                              |
| Petrochemical exposure                              | Jephcote 2020                       | 2                                   | 9                                                    | Y                | Y                              |
| Maternal smoking                                    | Antonopoulos 2011                   | 2                                   | 7                                                    | N                | Y                              |
| Ever smoking                                        | Sergentanis 2013                    | 2                                   | 33                                                   | Y                | N                              |
| Ever drinking                                       | Tramacere 2012                      | 3                                   | 29                                                   | N                | Y                              |
| Heavy drinking                                      | Tramacere 2012                      | 2                                   | 6                                                    | N                | Y                              |
| **Medical history and comorbid diseases**           |                                     |                                     |                                                      |                  |                                |
| Rheumatoid arthritis                                | Simon 2015                          | 2                                   | 17                                                   | Y                | N                              |
| Primary Sjogren's syndrome                           | Liang 2014                          | 2                                   | 11                                                   | Y                | Y                              |
| Systemic lupus erythematosus                        | Cao 2015                            | 3                                   | 12                                                   | N                | N                              |
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| Environmental risk factors | Largest review (First author, year) | Number of overlapping meta-analyses | Number of primary studies in the largest meta-analyses | Most recent (Y/N) | Highest impact factor one (Y/N) |
|---------------------------|------------------------------------|-------------------------------------|-------------------------------------------------------|-------------------|-------------------------------|
| Psoriasis                 | Vaengebjerg 2020                   | 3                                   | 8                                                      | Y                 | Y                             |
| Type 1 diabetes           | Wang 2020                          | 2                                   | 3                                                      | Y                 | N                             |
| Celiac disease            | Tio 2012                           | 2                                   | 8                                                      | Y                 | Y                             |
| Systemic sclerosis        | Zhang 2013                         | 2                                   | 4                                                      | Y                 | N                             |
| Asthma                    | Yang 2017                          | 2                                   | 15                                                     | Y                 | Y                             |
| Type 2 diabetes           | Castillo 2012                      | 8                                   | 21                                                     | N                 | N                             |
| Overweight                | Larsson 2007                       | 11                                  | 16                                                     | N                 | Y                             |
| Obesity                   | Larsson 2007                       | 11                                  | 16                                                     | N                 | Y                             |
| Hepatitis B virus         | Li 2018                            | 5                                   | 58                                                     | N                 | N                             |
| Hepatitis C virus         | Masarone 2019                      | 4                                   | 27                                                     | Y                 | Y                             |
| **Chemicals and pesticides** |                                    |                                     |                                                        |                   |                               |
| Benzene                   | Kane 2010                          | 4                                   | 24                                                     | Y                 | N                             |
| Polychlorinated biphenyls | Catalani 2019                      | 3                                   | 30                                                     | Y                 | N                             |
| Trichloroethylene         | Scott 2011                         | 3                                   | 17                                                     | N                 | N                             |
| Glyphosate                | Boffetta 2021                      | 4                                   | 6                                                      | Y                 | N                             |
| 2,4-Dichlorophenoxyacetic acid | Smith 2017                | 3                                   | 11                                                     | Y                 | Y                             |
| **Occupation**            |                                    |                                     |                                                        |                   |                               |
| Female flight attendant   | Buja 2006                          | 4                                   | 3                                                      | Y                 | N                             |
| Farmer                    | Boffetta 2007                      | 4                                   | 50                                                     | Y                 | N                             |
| Firefighter               | Jalilian 2019                      | 3                                   | 14                                                     | Y                 | Y                             |
| Petroleum refinery worker | Schnatter 2018                     | 2                                   | 16                                                     | Y                 | N                             |

Y=Yes; N=No.
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**eTable 5: Nominally significant associations from meta-analysis of individual participant data**

| Study     | Outcome | Exposure                                                                 | Numb er of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-----------|---------|---------------------------------------------------------------------------|------------------|--------------------------|----------------------------|-------|
| Kane 2013 | NHL     | Hormone therapy (ever vs. never)                                          | 2094             | 0.79 (0.69-0.90)          | Suggestive                 | NA    |
| Kane 2013 | NHL     | Hormone therapy age first used (50-54 years vs. never used)               | 1987             | 0.74 (0.61-0.91)          | Weak                       | NA    |
| Kane 2013 | NHL     | Hormone therapy age first used (55+ years vs. never used)                 | 1987             | 0.78 (0.62-0.98)          | Weak                       | NA    |
| Kane 2013 | NHL     | Hormone therapy years used (<2 years vs. never used)                      | 2094             | 0.78 (0.62-0.98)          | Weak                       | NA    |
| Kane 2013 | NHL     | Hormone therapy years used (5 to <10 years vs. never used)                | 2094             | 0.72 (0.57-0.91)          | Weak                       | NA    |
| Kane 2013 | NHL     | Hormone therapy years since last used (current vs. never used)            | 2035             | 0.70 (0.54-0.90)          | Weak                       | NA    |
| Kane 2013 | DLBCL   | Hormone therapy (ever vs. never)                                          | 675              | 0.66 (0.54-0.80)          | Weak                       | NA    |
| Kane 2013 | DLBCL   | Hormone therapy age first used (50-54 years vs. never used)               | 637              | 0.58 (0.42-0.80)          | Weak                       | NA    |
| Kane 2013 | DLBCL   | Hormone therapy years used (5 to <10 years vs. never used)                | 675              | 0.59 (0.40-0.86)          | Weak                       | NA    |
| Kane 2013 | DLBCL   | Hormone therapy years since last used (current vs. never used)            | 552              | 0.57 (0.44-0.74)          | Weak                       | NA    |
| Kane 2013 | FL      | Hormone therapy years since last used (current vs. never used)            | 418              | 0.76 (0.58-0.99)          | Weak                       | NA    |
| Cocco 2013| DLBCL   | Duration trichloroethylene exposure (30-39)                               | 1251             | 0.4 (0.2-1.0)             | Weak                       | NA    |
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| Study     | Outcome | Exposure                                                                 | Numb. of cases | Effect estimate (95% CI) | Classificat. of evidence | Model |
|-----------|---------|--------------------------------------------------------------------------|----------------|--------------------------|--------------------------|-------|
| Cocco 2013 | DLBCL   | Frequency trichloroethylene exposure (<=5% work time vs. unexposed)      | 1251           | 0.6 (0.4-1.0)            | Weak                     | NA    |
| Cocco 2013 | FL      | Frequency trichloroethylene exposure (31%+ work time vs. unexposed)     | 639            | 1.8 (1.1-2.9)            | Weak                     | NA    |
| Cocco 2013 | FL      | Intensity of trichloroethylene exposure (>150 ppm vs. unexposed)        | 639            | 2.2 (1.1-4.2)            | Weak                     | NA    |
| Willet 2008 | NHL     | Male height (100% vs. 60%)                                               | 5731           | 1.19 (1.06-1.34)         | Weak                     | NA    |
| Willet 2008 | FL      | Male height (100% vs. 60%)                                               | 1047           | 1.47 (1.18-1.84)         | Weak                     | NA    |
| Willet 2008 | CLL/SLL | Female height (20% vs. 60%)                                              | 625            | 0.72 (0.56-0.93)         | Weak                     | NA    |
| Willet 2008 | Other BCL | Male height (100% vs. 60%)                                              | 228            | 1.71 (1.14-2.58)         | Weak                     | NA    |
| Willet 2008 | Other BCL | Female height (80% vs. 60%)                                              | 174            | 1.87 (1.14-3.05)         | Weak                     | NA    |
| Willet 2008 | DLBCL   | Weight (Grade 3 obese vs. normal weight)                                 | 6285           | 1.80 (1.23-2.62)         | Weak                     | NA    |
| Willet 2008 | BL      | Weight (Underweight vs. normal weight)                                   | 90             | 3.13 (1.19-8.25)         | Weak                     | NA    |
| Slager 2014 | CLL/SLL | Any atopic disease (yes vs. no)                                          | 2345           | 0.86 (0.78-0.95)         | Weak                     | Basic |
| Slager 2014 | CLL/SLL | Allergy (yes vs. no)                                                     | 2182           | 0.87 (0.77-0.98)         | Weak                     | Basic |
| Slager 2014 | CLL/SLL | Blood transfusion (yes vs. no)                                           | 1168           | 0.79 (0.66-0.94)         | Weak                     | Basic |
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| Study     | Outcome      | Exposure                                                                 | Number of cases | Effect estimate (95% CI)          | Classification of evidence | Model |
|-----------|--------------|---------------------------------------------------------------------------|-----------------|-----------------------------------|----------------------------|-------|
| Slager 2014 | CLL/SLL      | Total number of transfusions (1 vs none)                                  | 1168            | 0.81 (0.66-0.99)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | Number of years from first transfusion to date of diagnosis (<20 years vs. no transfusion) | 1168            | 0.71 (0.55-0.92)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | Transfusion before 1990 (Transfusion 1990+ vs. No transfusion)            | 1168            | 0.68 (0.49-0.94)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | Adult height (Q4 vs Q1)                                                   | 1794            | 1.23 (1.05-1.44)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | Adult height (continuous, 10 cm)                                          | 1794            | 1.10 (1.02-1.19)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | HCV                                                                       | 994             | 1.99 (1.16-3.41)                  | Weak                       | Full  |
| Slager 2014 | CLL/SLL      | Ever lived or worked on a farm (yes vs. no)                              | 1595            | 1.21 (1.07-1.36)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | Farmer (yes vs. no)                                                       | 1042            | 1.20 (1.06-1.35)                  | Weak                       | Full  |
| Slager 2014 | CLL/SLL      | Animal farmer (yes vs. no)                                                | 1042            | 0.64 (0.43-0.96)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | Mixed animal and crop farmer (yes vs. no)                                 | 1013            | 1.32 (1.08-1.61)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | Hairdresser (yes vs. no)                                                  | 1042            | 1.77 (1.05-3.01)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | Total sun exposure (quartile 4 (high) vs. 1 (low))                        | 685             | 0.75 (0.59-0.96)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | Recreational sun exposure (Quartile 4 (high) vs 1 (low))                  | 1301            | 0.80 (0.69-0.94)                  | Weak                       | Basic |
| Slager 2014 | CLL/SLL      | Recreational sun exposure (Quartile 2 vs. 1)                              | 1301            | 0.81 (0.68-0.96)                  | Weak                       | Basic |
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| Study  | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|--------|---------|---------------------------------------------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Slager 2014 | CLL/SLL | History of cigarette smoking (yes vs. no)                               | 2191            | 0.90 (0.81-0.99)         | Weak                        | Basic |
| Slager 2014 | CLL/SLL | Smoking status as of ~1 year before diagnosis/interview (current vs.nonsmoker) | 2191            | 0.82 (0.71-0.94)         | Weak                        | Basic |
| Slager 2014 | CLL/SLL | Age started smoking cigarettes (14-<18 years)                           | 2191            | 0.87 (0.76-0.99)         | Weak                        | Basic |
| Slager 2014 | CLL/SLL | Age started smoking cigarettes (18-<20 years)                           | 2191            | 0.83 (0.71-0.98)         | Weak                        | Basic |
| Slager 2014 | CLL/SLL | Frequency of cigarette smoking (30+ cigarettes/day vs. nonsmoker)         | 2191            | 0.72 (0.57-0.90)         | Weak                        | Basic |
| Slager 2014 | CLL/SLL | Duration of cigarette smoking (30-39 years vs. nonsmoker)                | 2191            | 0.82 (0.71-0.96)         | Weak                        | Basic |
| Slager 2014 | CLL/SLL | Years since quitting cigarette smoking (former smoker unknown when quit vs.nonsmoker) | 1714            | 2.54 (1.53-4.21)         | Suggestive                  | Basic |
| Slager 2014 | CLL/SLL | Lifetime cigarette exposure (>20-35 plack-years vs. nonsmoker)           | 2191            | 0.84 (0.72-0.98)         | Weak                        | Basic |
| Slager 2014 | CLL/SLL | Lifetime cigarette exposure (>35 plack-years vs. nonsmoker)              | 2191            | 0.82 (0.70-0.95)         | Weak                        | Basic |
| Slager 2014 | CLL/SLL | Frequency of hair dye use (12+ times/year vs. never hair dye)            | 404             | 1.51 (1.09-2.10)         | Weak                        | Basic |
| Morton 2014 | NHL    | History of B-cell activating autoimmune disease (any vs. none)           | 17471           | 1.96 (1.60-2.40)         | Highly suggestive            | NA    |
| Morton 2014 | MZL    | History of B-cell activating autoimmune disease (any vs. none)           | 1052            | 5.46 (3.81-7.83)         | Highly suggestive            | NA    |
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| Study     | Outcome | Exposure                                                      | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-----------|---------|---------------------------------------------------------------|-----------------|--------------------------|----------------------------|-------|
| Morton 2014 | LPL/WM  | History of B-cell activating autoimmune disease (any vs. none) | 374             | 2.61 (1.34-5.08)         | Weak                       | NA    |
| Morton 2014 | DLBCL   | History of B-cell activating autoimmune disease (any vs. none) | 4667            | 2.45 (1.91-3.16)         | Highly suggestive           | NA    |
| Morton 2014 | NHL     | Hemolytic anemia (any vs. non)                                | 17471           | 2.24 (1.03-4.87)         | Weak                       | NA    |
| Morton 2014 | DLBCL   | Hemolytic anemia (any vs. non)                                | 4667            | 2.72 (1.13-6.57)         | Weak                       | NA    |
| Morton 2014 | MZL     | Pernicious anemia                                             | 1052            | 3.45 (1.07-11.15)        | Weak                       | NA    |
| Morton 2014 | DLBCL   | Rheumatoid arthritis (any vs. none)                          | 4667            | 1.94 (1.35-2.79)         | Suggestive                 | NA    |
| Morton 2014 | NHL     | Sjogren's syndrome (any vs. none)                             | 17471           | 7.52 (3.68-15.36)        | Highly suggestive           | NA    |
| Morton 2014 | MZL     | Sjogren's syndrome (any vs. none)                             | 1052            | 38.07 (16.94-85.55)      | Highly suggestive           | NA    |
| Morton 2014 | LPL/WM  | Sjogren's syndrome (any vs. none)                             | 374             | 12.14 (3.16-46.58)       | Weak                       | NA    |
| Morton 2014 | DLBCL   | Sjogren's syndrome (any vs. none)                             | 4667            | 8.77 (3.94-19.54)        | Highly suggestive           | NA    |
| Morton 2014 | FL      | Sjogren's syndrome (any vs. none)                             | 3530            | 3.23 (1.19-8.80)         | Weak                       | NA    |
| Morton 2014 | NHL     | Systemic lupus erythematous (any vs. none)                   | 17471           | 2.83 (1.82-4.41)         | Suggestive                 | NA    |
| Morton 2014 | MF/SS   | Systemic lupus erythematous (any vs. none)                   | 324             | 5.03 (1.16-21.57)        | Weak                       | NA    |
| Morton 2014 | PTCL    | Systemic lupus erythematous (any vs. none)                   | 584             | 3.90 (1.24-12.30)        | Weak                       | NA    |
| Morton 2014 | MZL     | Systemic lupus erythematous (any vs. none)                   | 1052            | 6.54 (3.10-13.82)        | Suggestive                 | NA    |
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| Study       | Outcome | Exposure                                      | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------------|---------|-----------------------------------------------|-----------------|--------------------------|------------------------------|-------|
| Morton 2014 | LPL/WM  | Systemic lupus erythematosus (any vs. none)   | 374             | 8.41 (2.81-25.20)        | Weak                         | NA    |
| Morton 2014 | DLBCL   | Systemic lupus erythematosus (any vs. none)   | 4667            | 2.49 (1.42-4.37)         | Weak                         | NA    |
| Morton 2014 | MF/SS   | History of T-cell activating autoimmune disease | 324             | 1.66 (1.00-2.75)         | Weak                         | NA    |
| Morton 2014 | PTCL    | History of T-cell activating autoimmune disease | 584             | 1.95 (1.37-2.77)         | Weak                         | NA    |
| Morton 2014 | NHL     | Celiac disease (any vs. none)                 | 17471           | 1.77 (1.05-2.99)         | Weak                         | NA    |
| Morton 2014 | PTCL    | Celiac disease (any vs. none)                 | 584             | 14.82 (7.27-30.19)       | Weak                         | NA    |
| Morton 2014 | DLBCL   | Celiac disease (any vs. none)                 | 4667            | 2.09 (1.04-4.18)         | Weak                         | NA    |
| Morton 2014 | PTCL    | Psoriasis (any vs. none)                      | 584             | 2.05 (1.23-3.42)         | Weak                         | NA    |
| Morton 2014 | MF/SS   | Systemic sclerosis/scleroderma                | 324             | 8.87 (1.11-71.25)        | Weak                         | NA    |
| Morton 2014 | HCL     | Systemic sclerosis/scleroderma                | 154             | 12.74 (1.49-108.84)      | Weak                         | NA    |
| Morton 2014 | NHL     | Hepatitis C virus seropositivity              | 17471           | 1.81 (1.39-2.37)         | Suggestive                   | NA    |
| Morton 2014 | MZL     | Hepatitis C virus seropositivity              | 1052            | 3.04 (1.65-5.60)         | Suggestive                   | NA    |
| Morton 2014 | LPL/WM  | HCV                                           | 374             | 2.70 (1.11-6.56)         | Weak                         | NA    |
| Morton 2014 | DLBCL   | HCV                                           | 4667            | 2.33 (1.71-3.19)         | Highly suggestive            | NA    |
| Morton 2014 | CLL/SLL | HCV                                           | 2440            | 2.08 (1.23-3.49)         | Weak                         | NA    |
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| Study     | Outcome | Exposure       | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-----------|---------|----------------|-----------------|--------------------------|-----------------------------|-------|
| Morton 2014 | MZL     | Peptic ulcer   | 1052            | 1.56 (1.21-2.03)         | Suggestive                  | NA    |
| Morton 2014 | NHL     | Allergy        | 17471           | 0.86 (0.81-0.92)         | Suggestive                  | NA    |
| Morton 2014 | DLBCL   | Allergy        | 4667            | 0.82 (0.74-0.90)         | Suggestive                  | NA    |
| Morton 2014 | CLL/SLL | Allergy        | 2440            | 0.87 (0.77-0.98)         | Weak                        | NA    |
| Morton 2014 | FL      | Allergy        | 3530            | 0.88 (0.79-0.98)         | Weak                        | NA    |
| Morton 2014 | MCL     | Hay fever      | 557             | 0.63 (0.48-0.82)         | Weak                        | NA    |
| Morton 2014 | MCL     | Allergy        | 557             | 0.79 (0.63-0.98)         | Weak                        | NA    |
| Morton 2014 | NHL     | Food allergy   | 17471           | 0.83 (0.74-0.92)         | Suggestive                  | NA    |
| Morton 2014 | DLBCL   | Asthma         | 4667            | 0.87 (0.77-0.98)         | Weak                        | NA    |
| Morton 2014 | DLBCL   | Food allergy   | 4667            | 0.77 (0.65-0.91)         | Weak                        | NA    |
| Morton 2014 | FL      | Food allergy   | 3530            | 0.79 (0.67-0.94)         | Weak                        | NA    |
| Morton 2014 | NHL     | Hay fever      | 17471           | 0.82 (0.77-0.88)         | Suggestive                  | NA    |
| Morton 2014 | BL      | Systemic       | 295             | 20.16 (2.44-166.28)      | Weak                        | NA    |
| Morton 2014 | BL      | Hay fever      | 295             | 0.64 (0.44-0.95)         | Weak                        | NA    |
| Morton 2014 | LPL/WM  | Hay fever      | 374             | 0.70 (0.52-0.96)         | Weak                        | NA    |
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| Study   | Outcome | Exposure                                           | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|---------|---------|----------------------------------------------------|-----------------|--------------------------|----------------------------|-------|
| Morton 2014 | DLBCL   | Hay fever                                         | 4667            | 0.78 (0.70-0.86)         | Suggestive                 | NA    |
| Morton 2014 | FL      | Asthma                                             | 3530            | 0.85 (0.74-0.97)         | Weak                       | NA    |
| Morton 2014 | FL      | Hay fever                                         | 3530            | 0.82 (0.73-0.91)         | Weak                       | NA    |
| Morton 2014 | NHL     | History of blood transfusion (any vs. none)       | 17471           | 0.83 (0.77-0.91)         | Suggestive                 | NA    |
| Morton 2014 | DLBCL   | History of blood transfusion (any vs. none)       | 4667            | 0.84 (0.75-0.95)         | Weak                       | NA    |
| Morton 2014 | CLL/SLL | History of blood transfusion (any vs. none)       | 2440            | 0.79 (0.66-0.94)         | Weak                       | NA    |
| Morton 2014 | FL      | History of blood transfusion (any vs. none)       | 3530            | 0.78 (0.68-0.89)         | Weak                       | NA    |
| Morton 2014 | HCL     | History of blood transfusion (any vs. none)       | 154             | 0.21 (0.05-0.86)         | Weak                       | NA    |
| Morton 2014 | NHL     | Age at least transfusion (%>40 years)             | 17471           | 0.80 (0.71-0.90)         | Suggestive                 | NA    |
| Morton 2014 | DLBCL   | Age at least transfusion (%>40 years)             | 4667            | 0.83 (0.70-0.97)         | Weak                       | NA    |
| Morton 2014 | CLL/SLL | Age at least transfusion (%>40 years)             | 2440            | 0.73 (0.56-0.96)         | Weak                       | NA    |
| Morton 2014 | FL      | Age at least transfusion (%>40 years)             | 3530            | 0.76 (0.63-0.92)         | Weak                       | NA    |
| Morton 2014 | HCL     | Age at least transfusion (%>40 years)             | 154             | 0.10 (0.01-0.93)         | Weak                       | NA    |
| Morton 2014 | NHL     | No. transfusions (% 2+)                           | 17471           | 0.72 (0.61-0.85)         | Suggestive                 | NA    |
| Morton 2014 | DLBCL   | No. transfusions (% 2+)                           | 4667            | 0.70 (0.56-0.88)         | Weak                       | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study          | Outcome | Exposure                          | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|----------------|---------|-----------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Morton 2014    | CLL/SLL | No. transfusions (% 2+)           | 2440            | 0.64 (0.45-0.92)         | Weak                        | NA    |
| Morton 2014    | FL      | No. transfusions (% 2+)           | 3530            | 0.61 (0.47-0.79)         | Suggestive                  | NA    |
| Morton 2014    | NHL     | Blood transfusion <1990           | 17471           | 0.76 (0.67-0.87)         | Suggestive                  | NA    |
| Morton 2014    | DLBCL   | Blood transfusion <1991           | 4667            | 0.78 (0.65-0.94)         | Weak                        | NA    |
| Morton 2014    | CLL/SLL | Blood transfusion <1992           | 2440            | 0.68 (0.52-0.88)         | Weak                        | NA    |
| Morton 2014    | FL      | Blood transfusion <1993           | 3530            | 0.66 (0.52-0.82)         | Suggestive                  | NA    |
| Morton 2014    | HCL     | Blood transfusion <1994           | 154             | 0.06 (0.00-0.82)         | Weak                        | NA    |
| Morton 2014    | DLBCL   | Year first Ocs use (%<1970)       | 4667            | 0.74 (0.59-0.93)         | Weak                        | NA    |
| Morton 2014    | DLBCL   | Ever used HRT                     | 4667            | 0.78 (0.65-0.94)         | Weak                        | NA    |
| Morton 2014    | MF/SS   | Usual adult BMI (% 25 kg/m^2+)    | 324             | 1.95 (1.10-3.46)         | Weak                        | NA    |
| Morton 2014    | LPL/WM  | Usual adult BMI (% 25 kg/m^2+)    | 374             | 0.40 (0.23-0.69)         | Weak                        | NA    |
| Morton 2014    | DLBCL   | Usual adult BMI (% 25 kg/m^2+)    | 4667            | 1.32 (1.11-1.57)         | Weak                        | NA    |
| Morton 2014    | DLBCL   | Young adult BMI (% 25 kg/m^2+)    | 4667            | 3.02 (2.13-4.37)         | Highly suggestive            | NA    |
| Morton 2014    | FL      | Young adult BMI (% 25 kg/m^2+)    | 3530            | 2.13 (1.44-3.14)         | Suggestive                  | NA    |
| Morton 2014    | BL      | Height (% Q3-Q4)                  | 295             | 2.43 (1.37-4.31)         | Weak                        | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study        | Outcome | Exposure                          | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|--------------|---------|-----------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Morton 2014  | DLBCL   | Height (% Q3-Q4)                  | 4667            | 1.16                     | (1.01-1.33)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | CLL/SLL | Physical activity (%>=moderate)   | 2440            | 0.80                     | (0.65-0.99)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | CLL/SLL | Height (% Q3-Q4)                  | 2440            | 1.29                     | (1.06-1.57)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | FL      | Height (% Q3-Q4)                  | 3530            | 1.20                     | (1.02-1.40)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | HCL     | Height (% Q3-Q4)                  | 154             | 3.46                     | (1.62-7.39)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | MF/SS   | Physical activity (%>=moderate)   | 324             | 0.53                     | (0.30-0.93)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | MF/SS   | Weight (% Q3-Q4)                  | 324             | 1.68                     | (1.06-2.67)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | MZL     | Weight (% Q3-Q4)                  | 1052            | 0.74                     | (0.58-0.95)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | LPL/WM  | Weight (% Q3-Q4)                  | 374             | 0.55                     | (0.36-0.82)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | DLBCL   | Weight (% Q3-Q4)                  | 4667            | 1.26                     | (1.10-1.44)                 | Suggestive |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | MCL     | Physical activity (%>=moderate)   | 557             | 2.09                     | (1.24-3.51)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | NHL     | Ever used HRT                     | 17471           | 0.84                     | (0.73-0.96)                 | Weak  |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | NHL     | Young adult BMI (% 25 kg/m^2+)    | 17471           | 1.95                     | (1.51-2.53)                 | Highly suggestive |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | NHL     | Height (% Q3-Q4)                  | 17471           | 1.20                     | (1.08-1.32)                 | Suggestive |
|              |         |                                   |                 |                          | NA                          |       |
| Morton 2014  | NHL     | Any alcohol                       | 17471           | 0.87                     | (0.81-0.93)                 | Suggestive |
|              |         |                                   |                 |                          | NA                          |       |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study         | Outcome | Exposure  | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|---------------|---------|-----------|-----------------|--------------------------|----------------------------|-------|
| Morton 2014   | PTCL    | Any alcohol | 584            | 0.68 (0.53-0.87)         | Weak                       | NA    |
| Morton 2014   | MZL     | Any alcohol | 1052           | 0.75 (0.62-0.91)         | Weak                       | NA    |
| Morton 2014   | DLBCL   | Any alcohol | 4667           | 0.81 (0.73-0.89)         | Suggestive                 | NA    |
| Morton 2014   | FL      | Any alcohol | 3530           | 0.86 (0.77-0.96)         | Weak                       | NA    |
| Morton 2014   | NHL     | Status (% current) | 17471 | 0.86 (0.78-0.94) | Weak                       | NA    |
| Morton 2014   | MZL     | Status (% current) | 1052 | 0.73 (0.55-0.98) | Weak                       | NA    |
| Morton 2014   | BL      | Any alcohol | 295            | 0.64 (0.48-0.87)         | Weak                       | NA    |
| Morton 2014   | BL      | Status (% current) alcohol | 295 | 0.53 (0.31-0.91) | Weak                       | NA    |
| Morton 2014   | DLBCL   | Status (% current) alcohol | 4667 | 0.70 (0.62-0.80) | Suggestive                 | NA    |
| Morton 2014   | NHL     | Age at initiation (% <20 years) | 17471 | 0.85 (0.75-0.97) | Weak                       | NA    |
| Morton 2014   | BL      | Age at initiation (% <20 years) alcohol | 295 | 0.44 (0.21-0.92) | Weak                       | NA    |
| Morton 2014   | DLBCL   | Age at initiation (% <20 years) | 4667 | 0.73 (0.62-0.86) | Suggestive                 | NA    |
| Morton 2014   | NHL     | Frequency (%>14 servings/week) alcohol | 17471 | 0.82 (0.75-0.91) | Suggestive                 | NA    |
| Morton 2014   | MZL     | Frequency (%>14 servings/week) | 1052 | 0.61 (0.45-0.84) | Weak                       | NA    |
| Morton 2014   | BL      | Frequency (%>14 servings/week) alcohol | 295 | 0.49 (0.31-0.76) | Weak                       | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study       | Outcome | Exposure                                | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------------|---------|-----------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Morton 2014 | DLBCL   | Frequency (%>14 servings/week) alcohol  | 4667            | 0.73 (0.64-0.83)         | Suggestive                  | NA    |
| Morton 2014 | FL      | Frequency (%>14 servings/week) alcohol  | 3530            | 0.82 (0.69-0.96)         | Weak                        | NA    |
| Morton 2014 | BL      | Duration (%>30 years) alcohol           | 295             | 0.44 (0.21-0.93)         | Weak                        | NA    |
| Morton 2014 | DLBCL   | Duration (%>30 years) alcohol           | 4667            | 0.73 (0.62-0.86)         | Suggestive                  | NA    |
| Morton 2014 | BL      | Lifetime (%>200 kg) alcohol             | 295             | 0.28 (0.12-0.70)         | Weak                        | NA    |
| Morton 2014 | DLBCL   | Lifetime (%>200 kg) alcohol             | 4667            | 0.64 (0.52-0.79)         | Suggestive                  | NA    |
| Morton 2014 | NHL     | Any beer                                | 17471           | 0.90 (0.84-0.97)         | Weak                        | NA    |
| Morton 2014 | PTCL    | Any beer                                | 584             | 0.61 (0.46-0.80)         | Weak                        | NA    |
| Morton 2014 | DLBCL   | Any beer                                | 4667            | 0.84 (0.76-0.93)         | Weak                        | NA    |
| Morton 2014 | NHL     | Frequency (%>14 servings/week) beer     | 17471           | 0.83 (0.71-0.96)         | Weak                        | NA    |
| Morton 2014 | PTCL    | Frequency (%>14 servings/week) beer     | 584             | 0.49 (0.27-0.88)         | Weak                        | NA    |
| Morton 2014 | DLBCL   | Lifetime (%>200 kg) beer                | 4667            | 0.64 (0.46-0.87)         | Weak                        | NA    |
| Morton 2014 | DLBCL   | Frequency (%>14 servings/week) beer     | 4667            | 0.67 (0.55-0.83)         | Suggestive                  | NA    |
| Morton 2014 | FL      | Frequency (%>14 servings/week) beer     | 3530            | 0.78 (0.61-0.99)         | Weak                        | NA    |
| Morton 2014 | NHL     | Lifetime (%>200 kg) beer                | 17471           | 0.74 (0.58-0.94)         | Suggestive                  | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study     | Outcome | Exposure            | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-----------|---------|---------------------|-----------------|--------------------------|-----------------------------|-------|
| Morton 2014 | NHL     | Any liquor          | 17471           | 0.84 (0.78-0.91)         | Suggestive                  | NA    |
| Morton 2014 | MF/SS   | Eczema              | 324             | 2.31 (1.68-3.17)         | Weak                        | NA    |
| Morton 2014 | MF/SS   | Any liquor          | 324             | 0.66 (0.47-0.92)         | Weak                        | NA    |
| Morton 2014 | MZL     | Any liquor          | 1052            | 0.71 (0.58-0.88)         | Weak                        | NA    |
| Morton 2014 | DLBCL   | Any liquor          | 4667            | 0.81 (0.73-0.90)         | Suggestive                  | NA    |
| Morton 2014 | FL      | Any liquor          | 3530            | 0.86 (0.76-0.97)         | Weak                        | NA    |
| Morton 2014 | NHL     | Frequency (%>=14 servings/week) any liquor | 17471 | 0.77 (0.64-0.93) | Weak                        | NA    |
| Morton 2014 | MZL     | Frequency (%>=14 servings/week) any liquor | 1052 | 0.37 (0.19-0.70) | Weak                        | NA    |
| Morton 2014 | BL      | Frequency (%>=14 servings/week) any liquor | 295 | 0.33 (0.15-0.74) | Weak                        | NA    |
| Morton 2014 | DLBCL   | Frequency (%>=14 servings/week) any liquor | 4667 | 0.65 (0.50-0.84) | Weak                        | NA    |
| Morton 2014 | FL      | Frequency (%>=23 servings/week) any liquor | 3530 | 1.70 (1.15-2.52) | Weak                        | NA    |
| Morton 2014 | BL      | Lifetime (%>200 kg) any liquor | 295 | 0.15 (0.03-0.84) | Weak                        | NA    |
| Morton 2014 | DLBCL   | Lifetime (%>200 kg) any liquor | 4667 | 0.57 (0.41-0.79) | Suggestive                  | NA    |
| Morton 2014 | NHL     | Any wine            | 17471           | 0.85 (0.79-0.91)         | Suggestive                  | NA    |
| Morton 2014 | PTCL    | Any wine            | 584             | 0.67 (0.52-0.86)         | Weak                        | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study       | Outcome | Exposure                              | Number of cases | Effect estimate (95% CI)             | Classification of evidence | Model |
|-------------|---------|---------------------------------------|-----------------|--------------------------------------|----------------------------|-------|
| Morton 2014 | MZL     | Any wine                              | 1052            | 0.64 (0.53-0.78)                      | Suggestive                | NA    |
| Morton 2014 | BL      | Any wine                              | 295             | 0.69 (0.51-0.95)                      | Weak                      | NA    |
| Morton 2014 | DLBCL   | Any wine                              | 4667            | 0.81 (0.73-0.89)                      | Suggestive                | NA    |
| Morton 2014 | FL      | Any wine                              | 3530            | 0.85 (0.76-0.95)                      | Weak                      | NA    |
| Morton 2014 | NHL     | Frequency (%>=14 servings/week) wine  | 17471           | 0.81 (0.72-0.92)                      | Suggestive                | NA    |
| Morton 2014 | PTCL    | Frequency (%>=14 servings/week) wine  | 584             | 0.61 (0.39-0.95)                      | Weak                      | NA    |
| Morton 2014 | MZL     | Frequency (%>=14 servings/week) wine  | 1052            | 0.45 (0.30-0.69)                      | Suggestive                | NA    |
| Morton 2014 | BL      | Frequency (%>=14 servings/week) wine  | 295             | 0.41 (0.23-0.73)                      | Weak                      | NA    |
| Morton 2014 | DLBCL   | Frequency (%>=14 servings/week) wine  | 4667            | 0.67 (0.57-0.80)                      | Suggestive                | NA    |
| Morton 2014 | BL      | Lifetime (%>200 kg) any wine          | 295             | 0.17 (0.05-0.65)                      | Weak                      | NA    |
| Morton 2014 | DLBCL   | Lifetime (%>200 kg) any wine          | 4667            | 0.52 (0.39-0.70)                      | Suggestive                | NA    |
| Morton 2014 | PTCL    | History of cigarette smoking (any vs. none) | 584   | 1.32 (1.09-1.59)                      | Weak                      | NA    |
| Morton 2014 | CLL/SLL | History of cigarette smoking (any vs. none) | 2440 | 0.90 (0.81-0.99)                      | Weak                      | NA    |
| Morton 2014 | FL      | History of cigarette smoking (any vs. none) | 3530 | 1.09 (1.00-1.18)                      | Weak                      | NA    |
| Morton 2014 | HCL     | History of cigarette smoking (any vs. none) | 154  | 0.51 (0.37-0.71)                      | Weak                      | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study          | Outcome | Exposure                                               | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|---------------|---------|--------------------------------------------------------|-----------------|--------------------------|----------------------------|-------|
| Morton 2014   | PTCL    | Status (% current) cigarette smoking                   | 584             | 1.46 (1.16-1.84)         | Weak                       | NA    |
| Morton 2014   | CLL/SLL | Status (% current) cigarette smoking                   | 2440            | 0.83 (0.73-0.94)         | Weak                       | NA    |
| Morton 2014   | FL      | Status (% current) cigarette smoking                   | 3530            | 1.18 (1.06-1.31)         | Weak                       | NA    |
| Morton 2014   | HCL     | Years since quitting (%>15 years) cigarette smoking   | 154             | 0.40 (0.26-0.61)         | Weak                       | NA    |
| Morton 2014   | HCL     | Age at initiation (%<20 years) cigarette smoking       | 154             | 0.49 (0.30-0.81)         | Weak                       | NA    |
| Morton 2014   | HCL     | Frequency (%>20 years) cigarette smoking               | 154             | 0.23 (0.12-0.44)         | Weak                       | NA    |
| Morton 2014   | HCL     | Duration (%>=20 years) cigarette smoking               | 154             | 0.37 (0.22-0.62)         | Weak                       | NA    |
| Morton 2014   | HCL     | Packyears (%>20) cigarette smoking                     | 154             | 0.30 (0.18-0.51)         | Weak                       | NA    |
| Morton 2014   | HCL     | Status (% current) cigarette smoking                   | 154             | 0.37 (0.23-0.57)         | Weak                       | NA    |
| Morton 2014   | PTCL    | Years since quitting (%>15 years)                     | 584             | 1.54 (1.23-1.94)         | Weak                       | NA    |
| Morton 2014   | LPL/WM  | Years since quitting (%>15 years) cigarette smoking   | 374             | 1.37 (1.01-1.85)         | Weak                       | NA    |
| Morton 2014   | CLL/SLL | Years since quitting (%>15 years)                     | 2440            | 0.82 (0.72-0.94)         | Weak                       | NA    |
| Morton 2014   | FL      | Years since quitting (%>15 years)                     | 3530            | 1.17 (1.06-1.29)         | Weak                       | NA    |
| Morton 2014   | PTCL    | Age since initiation (% <20 years) cigarette smoking   | 584             | 1.29 (1.00-1.66)         | Weak                       | NA    |
| Morton 2014   | LPL/WM  | Age since initiation (% <20 years) cigarette smoking   | 374             | 1.38 (1.02-1.86)         | Weak                       | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study   | Outcome | Exposure                                           | Numb of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|---------|---------|----------------------------------------------------|---------------|--------------------------|-----------------------------|-------|
| Morton 2014 | FL      | Age since initiation (% <20 years) cigarette smoking | 3530          | 1.13 (1.02-1.26)         | Weak                        | NA    |
| Morton 2014 | PTCL    | Frequencey (%>20) cigarette smoking                | 584           | 1.60 (1.16-2.19)         | Weak                        | NA    |
| Morton 2014 | CLL/SLL | Frequencey (%>20) cigarette smoking                | 2440          | 0.78 (0.66-0.93)         | Weak                        | NA    |
| Morton 2014 | PTCL    | Duration (%>=20 years) cigarette smoking           | 584           | 1.75 (1.33-2.30)         | Weak                        | NA    |
| Morton 2014 | MZL     | Duration (%>=20 years) cigarette smoking           | 1052          | 1.27 (1.03-1.57)         | Weak                        | NA    |
| Morton 2014 | LPL/WM  | Forestry worker                                    | 374           | 3.17 (1.08-9.31)         | Weak                        | NA    |
| Morton 2014 | LPL/WM  | Duration (%>=20 years) cigarette smoking           | 374           | 1.50 (1.10-2.04)         | Weak                        | NA    |
| Morton 2014 | CLL/SLL | Duration (%>=20 years) cigarette smoking           | 2440          | 0.84 (0.74-0.96)         | Weak                        | NA    |
| Morton 2014 | FL      | Duration (%>=20 years) cigarette smoking           | 3530          | 1.19 (1.06-1.33)         | Weak                        | NA    |
| Morton 2014 | PTCL    | Packyears (%>20) cigarette smoking                 | 584           | 1.67 (1.28-2.18)         | Weak                        | NA    |
| Morton 2014 | CLL/SLL | Packyears (%>20) cigarette smoking                 | 2440          | 0.80 (0.70-0.91)         | Weak                        | NA    |
| Morton 2014 | FL      | Packyears (%>20) cigarette smoking                 | 3530          | 1.13 (1.01-1.27)         | Weak                        | NA    |
| Morton 2014 | NHL     | Frequency (%->12 times/year) personal hairdye use  | 17471         | 1.16 (1.00-1.35)         | Weak                        | NA    |
| Morton 2014 | MZL     | Frequency (%->12 times/year) personal hairdye use  | 1052          | 1.55 (1.05-2.29)         | Weak                        | NA    |
| Morton 2014 | NHL     | Duration of hairdye use (%>=20 years)              | 17471         | 1.18 (1.02-1.35)         | Weak                        | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study          | Outcome | Exposure                                      | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|----------------|---------|-----------------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Morton 2014    | NHL     | Any hairdye use <1980                         | 17471           | 1.23 (1.06-1.42)         | Weak                        | NA    |
| Morton 2014    | FL      | Any hairdye use <1980                         | 3530            | 1.32 (1.05-1.65)         | Weak                        | NA    |
| Morton 2014    | NHL     | Recreational hairdye use (%Q3-Q4 hours/week)  | 17471           | 0.74 (0.66-0.83)         | Suggestive                  | NA    |
| Morton 2014    | NHL     | Sun exposure (%Q3-Q4 hours/week)              | 17471           | 0.79 (0.68-0.91)         | Weak                        | NA    |
| Morton 2014    | DLBCL   | Sun exposure (%Q3-Q4 hours/week)              | 4667            | 0.79 (0.64-0.98)         | Weak                        | NA    |
| Morton 2014    | NHL     | Recreational sun exposure (%Q3-Q4 hours/week) | 17471           | 0.74 (0.66-0.83)         | Highly suggestive            | NA    |
| Morton 2014    | DLBCL   | Recreational sun exposure (%Q3-Q4 hours/week) | 4667            | 0.75 (0.64-0.88)         | Suggestive                  | NA    |
| Morton 2014    | FL      | General unspecified laborer                   | 3530            | 1.28 (1.06-1.55)         | Weak                        | NA    |
| Morton 2014    | FL      | Baker/miller                                  | 3530            | 0.51 (0.28-0.93)         | Weak                        | NA    |
| Morton 2014    | FL      | Recreational sun exposure (%Q3-Q4 hours/week) | 3530            | 0.70 (0.58-0.84)         | Suggestive                  | NA    |
| Morton 2014    | NHL     | Socioeconomic status (% low)                  | 17471           | 0.88 (0.83-0.93)         | Suggestive                  | NA    |
| Morton 2014    | DLBCL   | Socioeconomic status (% low)                  | 4667            | 0.82 (0.76-0.90)         | Suggestive                  | NA    |
| Morton 2014    | HCL     | Socioeconomic status (% low)                  | 154             | 1.72 (1.13-2.63)         | Weak                        | NA    |
| Morton 2014    | PTCL    | History of living or working on a farm        | 584             | 0.73 (0.55-0.95)         | Weak                        | NA    |
| Morton 2014    | CLL/SLL | History of living or working on a farm        | 2440            | 1.21 (1.07-1.36)         | Weak                        | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study       | Outcome | Exposure                               | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------------|---------|----------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Morton 2014 | HCL     | History of living or working on a farm | 154             | 1.68 (1.04-2.71)         | Weak                        | NA    |
| Morton 2014 | MCL     | Ever lived on a farm                   | 557             | 1.40 (1.03-1.90)         | Weak                        | NA    |
| Morton 2014 | PTCL    | Mixed/unspecified farmer               | 584             | 0.56 (0.31-0.98)         | Weak                        | NA    |
| Morton 2014 | PTCL    | Ever worked on a farm                  | 584             | 0.68 (0.47-0.99)         | Weak                        | NA    |
| Morton 2014 | MCL     | Electonical/electronics worker          | 557             | 1.63 (1.09-2.44)         | Weak                        | NA    |
| Morton 2014 | CLL/SLL | Farmer any type                         | 2440            | 1.23 (1.04-1.45)         | Weak                        | NA    |
| Morton 2014 | NHL     | Animal farmer                           | 17471           | 0.77 (0.63-0.94)         | Weak                        | NA    |
| Morton 2014 | NHL     | Field crop/vegetable farmer             | 17471           | 1.32 (1.06-1.61)         | Weak                        | NA    |
| Morton 2014 | MF/SS   | Lifetime liquor (>200 kg)               | 324             | 3.18 (1.44-7.05)         | Weak                        | NA    |
| Morton 2014 | MF/SS   | Field crop/vegetable farmer             | 324             | 2.80 (1.38-5.68)         | Weak                        | NA    |
| Morton 2014 | DLBCL   | Field crop/vegetable farmer             | 4667            | 1.48 (1.14-1.93)         | Weak                        | NA    |
| Morton 2014 | CLL/SLL | Mixed/unspecified farmer                | 2440            | 1.31 (1.07-1.60)         | Weak                        | NA    |
| Morton 2014 | HCL     | Mixed/unspecified farmer                | 154             | 2.34 (1.36-4.01)         | Weak                        | NA    |
| Morton 2014 | NHL     | General farmer worked                   | 17471           | 1.28 (1.10-1.50)         | Weak                        | NA    |
| Morton 2014 | MF/SS   | General farmer worked                   | 324             | 2.07 (1.06-4.07)         | Weak                        | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study            | Outcome   | Exposure              | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|------------------|-----------|-----------------------|-----------------|--------------------------|-----------------------------|-------|
| Morton 2014      | CLL/SLL   | General farm worker   | 2440            | 1.46 (1.15-1.85)         | Weak                        | NA    |
| Morton 2014      | NHL       | Hairdresser           | 17471           | 1.34 (1.05-1.72)         | Weak                        | NA    |
| Morton 2014      | DLBCL     | Hairdresser           | 4667            | 1.49 (1.10-2.03)         | Weak                        | NA    |
| Morton 2014      | CLL/SLL   | Hairdresser           | 2440            | 1.77 (1.05-2.98)         | Weak                        | NA    |
| Morton 2014      | NHL       | Women’s hairdresser   | 17471           | 1.42 (1.07-1.89)         | Weak                        | NA    |
| Morton 2014      | DLBCL     | Women’s hairdresser   | 4667            | 1.63 (1.15-2.31)         | Weak                        | NA    |
| Morton 2014      | CLL/SLL   | Women’s hairdresser   | 2440            | 2.46 (1.31-4.62)         | Weak                        | NA    |
| Morton 2014      | ALL       | Leather worker        | 152             | 3.89 (1.34-11.33)        | Weak                        | NA    |
| Morton 2014      | MF/SS     | Painter               | 324             | 3.42 (1.81-6.47)         | Weak                        | NA    |
| Morton 2014      | PTCL      | Textile worker        | 584             | 1.55 (1.03-2.33)         | Weak                        | NA    |
| Morton 2014      | DLBCL     | Textile worker        | 4667            | 1.20 (1.02-1.41)         | Weak                        | NA    |
| Morton 2014      | DLBCL     | Welder/flamecutter    | 4667            | 1.33 (1.00-1.77)         | Weak                        | NA    |
| Morton 2005      | NHL       | Wine and beer         | 6492            | 0.85 (0.75-0.96)         | Weak                        | NA    |
| Morton 2005      | NHL       | Ever drinker vs. never drinker | 6492 | 0.83 (0.76-0.89) | Suggestive | NA |
| Morton 2005      | NHL       | Wine and liquor       | 6492            | 0.79 (0.70-0.90)         | Suggestive | NA |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study         | Outcome      | Exposure                                      | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|---------------|--------------|-----------------------------------------------|-----------------|--------------------------|-----------------------------|--------|
| Morton 2005   | NHL          | Beer, wine, and liquor                        | 6492            | 0.76 (0.68-0.84)         | Highly suggestive            | NA     |
| Morton 2005   | NHL          | Frequency (1-6 servings per week vs. none) alcohol | 6492            | 0.81 (0.74-0.88)         | Suggestive                  | NA     |
| Morton 2005   | NHL          | Frequency (7-13 servings per week vs. none) alcohol | 6492            | 0.83 (0.74-0.92)         | Suggestive                  | NA     |
| Morton 2005   | NHL          | Frequency (14-27 servings per week vs. none)   | 6492            | 0.85 (0.76-0.95)         | Weak                        | NA     |
| Morton 2005   | NHL          | Frequency (>=28 servings per week vs. none)    | 6492            | 0.87 (0.76-0.99)         | Weak                        | NA     |
| Morton 2005   | NHL          | Beer                                          | 6492            | 0.85 (0.76-0.95)         | Weak                        | NA     |
| Morton 2005   | NHL          | Wine                                          | 6492            | 0.85 (0.74-0.99)         | Weak                        | NA     |
| Morton 2005   | BL           | Ever vs. non-drinker                          | 111             | 0.51 (0.33-0.77)         | Weak                        | NA     |
| Morton 2005   | BL           | Current vs. non-drinker                       | 111             | 0.29 (0.13-0.64)         | Weak                        | NA     |
| Morton 2005   | DLBCL        | Ever vs. non-drinker                          | 2126            | 0.75 (0.66-0.84)         | Suggestive                  | NA     |
| Morton 2005   | DLBCL        | Current vs. non-drinker                       | 2126            | 0.64 (0.53-0.77)         | Suggestive                  | NA     |
| Morton 2005   | FL           | Ever vs. non-drinker                          | 1307            | 0.84 (0.73-0.97)         | Weak                        | NA     |
| Morton 2005   | Other T-cell NHL | Ever vs. non-drinker                         | 148             | 0.66 (0.45-0.98)         | Weak                        | NA     |
| Morton 2005   | BL           | Frequency (1-6 servings per week vs. none)     | 111             | 0.60 (0.37-0.96)         | Weak                        | NA     |
| Morton 2005   | BL           | Frequency (7-13 servings per week vs. none)    | 111             | 0.42 (0.21-0.85)         | Weak                        | NA     |
| Study          | Outcome | Exposure                                                                 | Numb of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|---------------|---------|--------------------------------------------------------------------------|---------------|--------------------------|----------------------------|-------|
| Morton 2005   | BL      | Frequency (14-27 servings per week vs. none) drinking                     | 111           | 0.41 (0.19-0.92)         | Weak                       | NA    |
| Morton 2005   | BL      | Frequency (>=28 servings per week vs. none) drinking                      | 111           | 0.36 (0.14-0.89)         | Weak                       | NA    |
| Morton 2005   | CLL/SLL | Frequency (1-6 servings per week vs. none) drinking                       | 991           | 0.80 (0.65-0.99)         | Weak                       | NA    |
| Morton 2005   | DLBCL   | Frequency (1-6 servings per week vs. none) drinking                       | 2126          | 0.76 (0.67-0.87)         | Suggestive                 | NA    |
| Morton 2005   | DLBCL   | Frequency (7-13 servings per week vs. none) drinking                      | 2126          | 0.73 (0.62-0.85)         | Suggestive                 | NA    |
| Morton 2005   | DLBCL   | Frequency (14-27 servings per week vs. none) drinking                     | 2126          | 0.73 (0.61-0.86)         | Suggestive                 | NA    |
| Morton 2005   | DLBCL   | Frequency (>=28 servings per week vs. none) drinking                      | 2126          | 0.73 (0.60-0.90)         | Weak                       | NA    |
| Morton 2005   | FL      | Frequency (1-6 servings per week vs. none) drinking                       | 1307          | 0.82 (0.70-0.96)         | Weak                       | NA    |
| Morton 2005   | FL      | Frequency (7-13 servings per week vs. none) drinking                      | 1307          | 0.80 (0.65-0.98)         | Weak                       | NA    |
| Morton 2005   | BL      | Duration (21-30 years) drinking                                           | 111           | 0.24 (0.08-0.76)         | Weak                       | NA    |
| Morton 2005   | BL      | Duration (31-40 years) drinking                                           | 111           | 0.27 (0.07-0.99)         | Weak                       | NA    |
| Morton 2005   | DLBCL   | Duration (1-20 years) drinking                                            | 2126          | 0.72 (0.56-0.92)         | Weak                       | NA    |
| Morton 2005   | DLBCL   | Duration (21-30 years) drinking                                           | 2126          | 0.74 (0.57-0.94)         | Weak                       | NA    |
| Morton 2005   | DLBCL   | Duration (31-40 years) drinking                                           | 2126          | 0.72 (0.57-0.93)         | Weak                       | NA    |
| Morton 2005   | DLBCL   | Duration (>=41 years) drinking                                            | 2126          | 0.67 (0.53-0.85)         | Suggestive                 | NA    |
### Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study          | Outcome       | Exposure                                      | Number of cases | Effect estimate (95% CI)           | Classification of evidence | Model |
|---------------|---------------|-----------------------------------------------|-----------------|------------------------------------|----------------------------|-------|
| Morton 2005   | NHL           | Hemolytic anemia (any vs. non)                | 12091           | 2.69 (1.68-4.30)                   | Weak                       | NA    |
| Ekstrom 2008  | NHL           | Systemic lupus erythematosus (any vs. none)   | 3263            | 2.57 (1.27-5.21)                   | Weak                       | NA    |
| Ekstrom 2008  | NHL           | Hemolytic anemia (any vs. non)                | 8230            | 6.56 (3.10-13.9)                   | Suggestive                 | NA    |
| Ekstrom 2008  | NHL           | Primary sjogren's syndrom                     | 8199            | 4.75 (1.79-12.6)                   | Weak                       | NA    |
| Ekstrom 2008  | NHL           | Secondary sjogren's syndrome                  | 8207            | 9.57 (2.90-31.6)                   | Suggestive                 | NA    |
| Ekstrom 2008  | DLBCL         | Hemolytic anemia (any vs. non)                | 3364            | 2.74 (1.47-5.11)                   | Weak                       | NA    |
| Ekstrom 2008  | DLBCL         | Systemic lupus erythematosus (any vs. none)   | 3364            | 2.74 (1.47-5.11)                   | Weak                       | NA    |
| Ekstrom 2008  | DLBCL         | Sjogren's syndrome (any vs. none)             | 2368            | 8.92 (3.82-20.7)                   | Highly suggestive           | NA    |
| Ekstrom 2008  | DLBCL         | Primary sjogren's syndrom                     | 2356            | 6.57 (2.12-20.3)                   | Weak                       | NA    |
| Ekstrom 2008  | DLBCL         | Secondary sjogren's syndrome                  | 2360            | 6.57 (2.12-20.3)                   | Weak                       | NA    |
| Ekstrom 2008  | FL            | Sjogren's syndrome (any vs. none)             | 1801            | 3.91 (1.39-11.0)                   | Weak                       | NA    |
| Ekstrom 2008  | FL            | Secondary sjogren's syndrome                  | 1799            | 7.55 (1.75-32.7)                   | Weak                       | NA    |
| Ekstrom 2008  | CLL/SLL/PLL/MCL | Type 1 diabetes                        | 1813            | 1.97 (1.00-3.88)                   | Weak                       | NA    |
| Ekstrom 2008  | MZL           | Sjogren's syndrome (any vs. none)             | 411             | 30.6 (12.3-76.1)                   | Weak                       | NA    |
### Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study      | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|------------|---------|--------------------------------------------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Ekstrom 2008 | MZL     | Systemic lupus erythematosus (any vs. none)                             | 593             | 7.52 (3.39-16.7)         | Weak                        | NA    |
| Ekstrom 2008 | MZL     | Primary sjorgen’s syndrome                                              | 404             | 23.1 (7.16-74.5)         | Weak                        | NA    |
| Ekstrom 2008 | MZL     | Secondary sjorgen’s syndrome                                            | 403             | 44.6 (10.6-187)          | Weak                        | NA    |
| Cerhan 2019 | NHL     | History of blood transfusion (any vs. none) white men                   | 4599            | 0.74 (0.65-0.83)         | Suggestive                  | NA    |
| Cerhan 2019 | NHL     | Number of blood transfusions (One vs none) white men                   | 4571            | 0.70 (0.60-0.81)         | Suggestive                  | NA    |
| Cerhan 2019 | NHL     | Age of 1st transfusion (21-30 years vs. none) white men                | 4599            | 0.61 (0.45-0.82)         | Weak                        | NA    |
| Cerhan 2019 | NHL     | Age of 1st transfusion (31-40 years vs. none) white men                | 4599            | 0.71 (0.51-0.97)         | Weak                        | NA    |
| Cerhan 2019 | NHL     | Age of 1st transfusion (41-50 years vs. none) white men                | 4599            | 0.68 (0.50-0.92)         | Weak                        | NA    |
| Cerhan 2019 | NHL     | Era first transfusion (<1970) white men                                 | 4501            | 0.77 (0.61-0.98)         | Weak                        | NA    |
| Cerhan 2019 | NHL     | Era first transfusion (1970s) white men                                 | 4501            | 0.58 (0.42-0.79)         | Suggestive                  | NA    |
| Cerhan 2019 | NHL     | Era first transfusion (1990+) white men                                 | 4501            | 0.66 (0.52-0.84)         | Suggestive                  | NA    |
| Cerhan 2019 | NHL     | Number of blood transfusions (two vs none) white women                 | 4047            | 0.76 (0.63-0.92)         | Weak                        | NA    |
| Cerhan 2019 | NHL     | Age of 1st transfusion (31-40 years vs. none) white women              | 4061            | 0.78 (0.63-0.97)         | Weak                        | NA    |
| Cerhan 2019 | NHL     | Age of 1st transfusion (51-60 years vs. none) white women              | 4061            | 0.70 (0.50-0.97)         | Weak                        | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study       | Outcome | Exposure                                           | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------------|---------|----------------------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Cerhan 2019 | FL      | History of blood transfusion (any vs. none) white men | 987             | 0.70 (0.56-0.88)         | Weak                         | NA    |
| Cerhan 2019 | DLBCL   | History of blood transfusion (any vs. none) white men | 1395            | 0.72 (0.59-0.87)         | Weak                         | NA    |
| Cerhan 2019 | CLL/SLL | History of blood transfusion (any vs. none) white men | 684             | 0.67 (0.52-0.87)         | Weak                         | NA    |
| Cerhan 2019 | FL      | History of blood transfusion (any vs. none) white women | 1094            | 0.77 (0.64-0.92)         | Weak                         | NA    |
| Morton 2005 (Cigarette smoking) | NHL | Status (% current) cigarette smoking | 10351           | 1.10 (1.00-1.20)         | Weak                         | NA    |
| Morton 2005 (Cigarette smoking) | NHL | Intensity (11-20 cigarettes/d) | 6393            | 1.12 (1.02-1.22)         | Weak                         | NA    |
| Morton 2005 (Cigarette smoking) | NHL | Intensity (21-30 cigarettes/d) | 6393            | 1.19 (1.04-1.36)         | Weak                         | NA    |
| Morton 2005 (Cigarette smoking) | NHL | Duration (21-35 years) cigarette smoking | 6570            | 1.12 (1.02-1.23)         | Weak                         | NA    |
| Morton 2005 (Cigarette smoking) | NHL | Duration (>=36 years) cigarette smoking | 6570            | 1.16 (1.05-1.28)         | Weak                         | NA    |
| Morton 2005 (Cigarette smoking) | NHL | Pack-years (21-35) cigarette smoking | 6373            | 1.14 (1.02-1.27)         | Weak                         | NA    |
| Morton 2005 (Cigarette smoking) | NHL | Pack-years (>=36) cigarette smoking | 6373            | 1.21 (1.09-1.34)         | Weak                         | NA    |
| Morton 2005 (Cigarette smoking) | FL | Ever vs. never smoker | 1452            | 1.15 (1.12-1.52)         | Weak                         | NA    |
| Morton 2005 | FL      | Status (% current) cigarette smoking | 1452            | 1.31 (1.12-1.52)         | Suggestive                   | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study                          | Outcome   | Exposure                                      | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|--------------------------------|-----------|-----------------------------------------------|-----------------|--------------------------|----------------------------|-------|
| (Cigarette smoking)            |           |                                               |                 |                          |                            |       |
| Morton 2005 (Cigarette smoking) | FL        | Age at initiation (% >-20 years) cigarette smoking | 1452            | 1.24 (1.05-1.46)         | Weak                        | NA    |
| Morton 2005 (Cigarette smoking) | DLBCL     | Intensity (21-30 cigarettes/d)                | 2211            | 1.27 (1.05-1.53)         | Weak                        | NA    |
| Morton 2005 (Cigarette smoking) | DLBCL     | Pack-years (>=36) cigarette smoking           | 2211            | 1.24 (1.06-1.44)         | Weak                        | NA    |
| Morton 2005 (Cigarette smoking) | PTCL      | Age at initiation (18-19 years vs. nonsmoker) | 89              | 0.34 (0.12-0.96)         | Weak                        | NA    |
| Morton 2005 (Cigarette smoking) | PTCL      | Pack-years (>=36) cigarette smoking           | 89              | 0.38 (0.15-0.97)         | Weak                        | NA    |
| Morton 2005 (Cigarette smoking) | MCL       | Intensity (11-20 cigarettes/d)                | 185             | 0.63 (0.40-0.98)         | Weak                        | NA    |
| Morton 2005 (Cigarette smoking) | Other T-cell NHL | Years since quit cigarette smoking (>=31 vs. nonsmoker) | 163 | 2.04 (1.14-3.65) | Weak                        | NA    |
| Morton 2005 (Cigarette smoking) | FL        | Intensity (11-20 cigarettes/d)                | 1452            | 1.25 (1.08-1.46)         | Weak                        | NA    |
| Morton 2005 (Cigarette smoking) | FL        | Intensity (21-30 cigarettes/d)                | 1452            | 1.33 (1.06-1.67)         | Weak                        | NA    |
| Morton 2005 (Cigarette smoking) | FL        | Duration (21-35 years) cigarette smoking      | 1452            | 1.21 (1.03-1.42)         | Weak                        | NA    |
| Morton 2005 (Cigarette smoking) | FL        | Duration (>=36 years) cigarette smoking       | 1452            | 1.28 (1.08-1.53)         | Weak                        | NA    |
### Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study                        | Outcome                  | Exposure                                                                 | Number of cases | Effect estimate (95% CI)  | Classification of evidence | Model |
|------------------------------|--------------------------|--------------------------------------------------------------------------|-----------------|---------------------------|------------------------------|-------|
| Morton 2005 (Cigarette smoking) | FL                       | Pack-years (>=36) cigarette smoking                                       | 1452            | 1.30 (1.08-1.56)          | Weak                         | NA    |
| De Sanjose 2008              | NHL                      | HCV                                                                      | 4784            | 1.78 (1.40-2.25)          | Suggestive                   | NA    |
| De Sanjose 2008              | DLBCL                    | HCV                                                                      | 1494            | 2.24 (1.68-2.99)          | Highly suggestive            | NA    |
| De Sanjose 2008              | LPL                      | HCV                                                                      | 144             | 2.57 (1.14-5.79)          | Weak                        | NA    |
| De Sanjose 2008              | MZL                      | HCV                                                                      | 383             | 2.47 (1.44-4.23)          | Weak                        | NA    |
| De Sanjose 2008              | Other B-cell lymphoma (small B-lymphocytic NOS, mediastinal large B-cell lymphoma, large B-cell immunoblastic, B-cell NOS, precursor B NHL, other B NHL, precursor B-lymphoblastic leukemia or lymphoma, hairy cell leukemia, and lymphoblastic lymphoma) | HCV                                                            | 244             | 2.36 (1.11-5.01)          | Weak                        | NA    |
| Becker 2012                  | NHL                      | Childhood measles                                                       | 5486            | 0.84 (0.76-0.93)          | Suggestive                  | NA    |
| Becker 2012                  | MZL                      | Childhood whooping cough/pertussis                                       | 4131            | 0.85 (0.78-0.93)          | Suggestive                  | NA    |
| Becker 2012                  | NHL                      | Adult infectious mononucleosis                                           | 12585           | 1.26 (1.01-1.57)          | Weak                        | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study       | Outcome | Exposure                                      | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------------|---------|-----------------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Becker 2012 | CLL/SLL/PLL/MCL | Adult infectious mononucleosis | 2142 | 1.71 (1.30-2.25) | Suggestive | NA |
| Becker 2012 | T-cell | Adult infectious mononucleosis | 703 | 1.41 (1.01-1.97) | Weak | NA |
| Becker 2012 | PTCL | Adult infectious mononucleosis | 361 | 1.72 (1.14-2.59) | Weak | NA |
| Mbulaiteye 2014 | BL | Asthma (<50 years age) | 113 | 0.35 (0.13-0.95) | Weak | Basic |
| Mbulaiteye 2014 | BL | Number of blood transfusions (>=3 vs. no transfusion), <50 years age | 79 | 6.46 (1.75-23.81) | Weak | Basic |
| Mbulaiteye 2014 | BL | Lifetime alcohol consumed (>400 kg vs. nondrinker), >=50 years age | 130 | 0.22 (0.06-0.86) | Weak | Basic |
| Mbulaiteye 2014 | BL | Lifetime alcohol consumed (drinker, consumption unknown), >=50 years age | 130 | 0.63 (0.40-0.98) | Weak | Basic |
| Mbulaiteye 2014 | BL | Duration of employment as cleaner (1-10 years vs. never) | 64 | 3.27 (1.24-8.60) | Weak | Basic |
| Mbulaiteye 2014 | BL | Eczema with no other atopic conditions (<50 years age) | 103 | 2.54 (1.20-5.40) | Weak | Final |
| Mbulaiteye 2014 | BL | Usual adult height (Q4 vs. Q1, <50 years age) | 94 | 2.17 (1.08-4.36) | Weak | Final |
| Mbulaiteye 2014 | BL | Charworker cleaner or related work (<50 years age) | 64 | 3.49 (1.13-10.7) | Weak | Final |
| Mbulaiteye 2014 | BL | HCV (>=50 years) | 31 | 4.19 (1.05-16.61) | Weak | Final |
| Mbulaiteye 2014 | BL | Usual adult body mass index (25<30 Kg/m^2) (>=50 years age) | 94 | 0.27 (0.08-0.98) | Weak | Final |
## Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study          | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI)    | Classification of evidence | Model |
|----------------|---------|---------------------------------------------------------------------------|-----------------|------------------------------|-----------------------------|-------|
| Mbulaiteye 2014 | BL      | Drinker (at least 1 drink per month vs. non-drinker)                      | 94              | 0.63 (0.40-0.98)             | Weak                        | Final |
| Wang 2014      | PTCL    | Celiac disease (any vs. none)                                            | 398             | 17.80 (8.61-36.79)           | Weak                        | Full  |
| Wang 2014      | PTCL    | Allergy                                                                   | 495             | 0.69 (0.54-0.87)             | Weak                        | Full  |
| Wang 2014      | PTCL    | Eczema                                                                    | 537             | 1.41 (1.07-1.85)             | Weak                        | Full  |
| Wang 2014      | PTCL    | Psoriasis (any vs. none)                                                 | 301             | 1.97 (1.17-3.32)             | Weak                        | Full  |
| Wang 2014      | PTCL    | Duration of cigarette smoking (40+ years)                                 | 505             | 1.92 (1.41-2.62)             | Weak                        | Full  |
| Wang 2014      | PTCL    | Smoker, duration unknown                                                 | 505             | 4.44 (2.14-9.25)             | Weak                        | Full  |
| Wang 2014      | PTCL    | Drinker (at least 1 drink per month vs. non-drinker)                      | 368             | 0.64 (0.49-0.82)             | Weak                        | Full  |
| Wang 2014      | PTCL    | Electrical fitters                                                        | 334             | 2.89 (1.41-5.95)             | Weak                        | Full  |
| Wang 2014      | PTCL    | Textile worker                                                            | 328             | 1.58 (1.05-2.38)             | Weak                        | Full  |
| Wang 2014      | PTCL    | Ever lived or worked on a farm                                            | 363             | 0.72 (0.55-0.95)             | Weak                        | Full  |
| Wang 2014      | PTCL-NOS | Celiac disease (any vs. none)                                           | 161             | 8.66 (1.97-38.1)             | Weak                        | Full  |
| Wang 2014      | PTCL-NOS | Allergy                                                                   | 194             | 0.67 (0.46-0.98)             | Weak                        | Full  |
| Wang 2014      | PTCL-NOS | Psoriasis (any vs. none)                                                 | 139             | 2.41 (1.15-5.04)             | Weak                        | Full  |
| Wang 2014      | PTCL-NOS | Duration of cigarette smoking (40+ years)                                 | 205             | 1.76 (1.14-2.72)             | Weak                        | Full  |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study       | Outcome                  | Exposure                                                                 | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------------|--------------------------|--------------------------------------------------------------------------|-----------------|--------------------------|----------------------------|-------|
| Wang 2014   | PTCL-NOS                 | Smoker, duration unknown                                                 | 205             | 3.61 (1.26-10.4)         | Weak                       | Full  |
| Wang 2014   | PTCL-NOS                 | Drinker (at least 1 drink per month vs. non-drinker)                     | 161             | 0.65 (0.45-0.93)         | Weak                       | Full  |
| Wang 2014   | ALCL                     | Celiac disease (any vs. none)                                            | 110             | 16.59 (3.27-84.3)        | Weak                       | Full  |
| Wang 2014   | ALCL                     | Duration of cigarette smoking (40+ years)                               | 149             | 2.46 (1.30-4.65)         | Weak                       | Full  |
| Wang 2014   | ALCL                     | Smoker, duration unknown                                                | 149             | 5.26 (1.31-21.1)         | Weak                       | Full  |
| Wang 2014   | ALCL                     | Recreation sun exposure (Q4 (high) vs. Q1)                              | 107             | 0.48 (0.26-0.88)         | Weak                       | Full  |
| Wang 2014   | ALCL                     | Electrical fitters                                                      | 68              | 4.08 (1.36-12.2)         | Weak                       | Full  |
| Wang 2014   | ALCL                     | Textile worker                                                          | 82              | 2.60 (1.21-5.58)         | Weak                       | Full  |
| Wang 2014   | Angioimmunoblastic lymphoma | Electrical fitters                                                  | 49              | 5.45 (1.20-24.7)         | Weak                       | Full  |
| Wang 2014   | Primary cutaneous ALCL   | Hay fever                                                               | 29              | 6.38 (1.77-23.0)         | Weak                       | Full  |
| Wang 2014   | Primary cutaneous ALCL   | Celiac disease (any vs. none)                                           | 28              | 39.91 (3.15-506.4)       | Weak                       | Full  |
| Wang 2014   | Primary cutaneous ALCL   | Duration of cigarette smoking (1-19 years)                            | 33              | 3.62 (1.13-11.55)        | Weak                       | Full  |
| Wang 2014   | Primary cutaneous ALCL   | Duration of cigarette smoking (40+ years)                             | 33              | 5.82 (1.63-20.80)        | Weak                       | Full  |
| Wang 2014   | Primary cutaneous ALCL   | Smoker, duration unknown                                               | 33              | 16.37 (1.49-183.4)       | Weak                       | Full  |
| Wang 2014   | PTCL-Cutaneous NOS       | Asthma with allergy, hay fever, and/or eczema                          | 17              | 10.2 (2.90-35.5)         | Weak                       | Full  |
### Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study          | Outcome                                | Exposure                                      | Number of cases | Effect estimate (95% CI)      | Classification of evidence | Model |
|----------------|----------------------------------------|-----------------------------------------------|-----------------|--------------------------------|-----------------------------|-------|
| Wang 2014      | PTCL-Cutaneous NOS                     | Fire fighter                                  | 22              | 15.2 (2.69-85.7)               | Weak                        | Full  |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome | Duration (> =40 years) cigarette smoking   | 324             | 1.55 (1.04-2.31)              | Weak                        | Full  |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome | Usual adult body mass index (30-50 kg/m^2)   | 324             | 1.57 (1.03-2.40)              | Weak                        | Full  |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome  | B and T-cell activation                       | 324             | 9.45 (1.80-49.60)             | Weak                        | Full  |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome | History of eczema                             | 324             | 2.38 (1.73-3.29)              | Weak                        | Full  |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome | Multiple myeloma                              | 324             | 6.17 (2.39-15.91)             | Weak                        | Basic |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome | Crop and vegetable farm workers               | 324             | 2.37 (1.14-4.92)              | Weak                        | Full  |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome | Painter                                       | 324             | 3.71 (1.94-7.07)              | Weak                        | Full  |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome | Woodworkers                                   | 324             | 2.20 (1.18-4.08)              | Weak                        | Full  |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome | General carpenter                             | 324             | 4.07 (1.54-10.75)             | Weak                        | Full  |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome | Physical activity (%>=vigorous)               | 324             | 0.50 (0.28-0.90)              | Weak                        | Basic |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides and Sézary syndrome | Physical activity (%>=moderate)               | 324             | 0.46 (0.22-0.97)              | Weak                        | Full  |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study     | Outcome | Exposure                                      | Number of cases | Effect estimate (95% CI)                       | Classification of evidence | Model |
|-----------|---------|-----------------------------------------------|-----------------|-----------------------------------------------|----------------------------|-------|
| Bracci 2014 | MZL     | Sjogren's syndrome (any vs. none)             | 606             | 38.38 (17.04-86.48)                          | Weak                       | NA    |
| Bracci 2014 | MZL     | Systemic lupus erythematosus (any vs. none)   | 884             | 6.57 (3.11-13.86)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | B-cell activation                             | 1017            | 5.74 (3.97-8.33)                           | Highly suggestive           | NA    |
| Bracci 2014 | MZL     | HCV                                           | 368             | 3.04 (1.65-5.60)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Ulcer                                         | 810             | 1.56 (1.21-2.03)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Asthma with out other atopy                   | 852             | 1.42 (1.03-1.97)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Recreational sun exposure (Q2 vs Q1 hours/week) | 627          | 0.66 (0.52-0.84)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Recreational sun exposure (Q3 vs Q1 hours/week) | 627          | 0.78 (0.62-0.97)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Recreational sun exposure (Q4 vs Q1 hours/week) | 627          | 0.68 (0.54-0.85)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Years since quit cigarette smoking (Former <5 years vs. nonsmoker) | 863          | 1.62 (1.17-2.24)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Years since quit cigarette smoking (Former unknown years) | 863          | 3.24 (1.49-7.05)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Any type of alcohol (Q1 vs nondrinker g/wk)   | 669             | 0.76 (0.59-0.98)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Any type of alcohol (Q3 vs nondrinker g/wk)   | 669             | 0.60 (0.44-0.82)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Any type of alcohol (Q4 vs nondrinker g/wk)   | 669             | 0.61 (0.42-0.88)                           | Weak                       | NA    |
| Bracci 2014 | MZL     | Wine (Q2 vs. nondrinker g/wk)                 | 669             | 0.62 (0.46-0.84)                           | Weak                       | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study       | Outcome | Exposure                                      | Number of cases | Effect estimate (95% CI)  | Classification of evidence | Model |
|-------------|---------|-----------------------------------------------|-----------------|---------------------------|----------------------------|-------|
| Bracci 2014 | MZL     | Wine (Q3 vs. nondrinker g/wk)                 | 669             | 0.60 (0.44-0.80)          | Weak                       | NA    |
| Bracci 2014 | MZL     | Wine (Q4 vs. nondrinker g/wk)                 | 669             | 0.59 (0.37-0.95)          | Weak                       | NA    |
| Bracci 2014 | MZL     | Teacher                                       | 639             | 0.50 (0.35-0.70)          | Weak                       | NA    |
| Bracci 2014 | MZL     | General carpenter                             | 599             | 2.34 (1.23-4.45)          | Weak                       | NA    |
| Bracci 2014 | EMZL    | Sjogren's syndrome (any vs. none)             | 377             | 40.25 (17.5-92.6)         | Weak                       | NA    |
| Bracci 2014 | EMZL    | Systemic lupus erythematosus (any vs. none)   | 553             | 8.44 (3.58-19.91)         | Weak                       | NA    |
| Bracci 2014 | EMZL    | B-cell activation                             | 633             | 6.40 (4.24-9.68)          | Weak                       | NA    |
| Bracci 2014 | EMZL    | HCV                                           | 221             | 5.29 (2.48-11.28)         | Weak                       | NA    |
| Bracci 2014 | EMZL    | Ulcer                                         | 473             | 1.83 (1.35-2.49)          | Weak                       | NA    |
| Bracci 2014 | EMZL    | Years since quit cigarette smoking (Former <5 years vs. nonsmoker) | 507 | 1.55 (1.03-2.33) | Weak | NA |
| Bracci 2014 | EMZL    | Years since quit cigarette smoking (Former unknown years) | 507 | 3.58 (1.65-7.78) | Weak | NA |
| Bracci 2014 | EMZL    | Any type of alcohol (Q3 vs nondrinker g/wk)   | 379             | 0.55 (0.36-0.84)          | Weak                       | NA    |
| Bracci 2014 | EMZL    | Any type of alcohol (Q4 vs nondrinker g/wk)   | 379             | 0.48 (0.28-0.82)          | Weak                       | NA    |
| Bracci 2014 | EMZL    | Wine (Q2 vs. nondrinker g/wk)                 | 344             | 0.61 (0.41-0.92)          | Weak                       | NA    |
| Bracci 2014 | NMZL    | Wine (Q3 vs. nondrinker g/wk)                 | 89              | 0.65 (0.43-0.98)          | Weak                       | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study   | Outcome | Exposure                                                                 | Numb of cases | Effect estimate (95% CI)     | Classification of evidence | Model |
|---------|---------|---------------------------------------------------------------------------|---------------|------------------------------|----------------------------|-------|
| Bracci 2014 | NMZL    | Any type of alcohol (Q1 vs nondrinker g/wk)                             | 104           | 0.50 (0.29-0.88)             | Weak                       | NA    |
| Bracci 2014 | NMZL    | Any type of alcohol (Q2 vs nondrinker g/wk)                             | 104           | 0.41 (0.21-0.83)             | Weak                       | NA    |
| Bracci 2014 | NMZL    | Wine (Q1 vs. nondrinker g/wk)                                           | 89            | 0.38 (0.20-0.72)             | Weak                       | NA    |
| Bracci 2014 | NMZL    | Wine (Q2 vs. nondrinker g/wk)                                           | 89            | 0.37 (0.17-0.78)             | Weak                       | NA    |
| Bracci 2014 | NMZL    | Wine (Q3 vs. nondrinker g/wk)                                           | 89            | 0.45 (0.22-0.90)             | Weak                       | NA    |
| Bracci 2014 | NMZL    | Sjogren's syndrome (any vs. none)                                       | 89            | 141 (25.01-800)              | Weak                       | NA    |
| Bracci 2014 | NMZL    | Systemic lupus erythematosus (any vs. none)                             | 65            | 9.24 (1.95-43.74)            | Weak                       | NA    |
| Bracci 2014 | NMZL    | B and T-cell activation                                                 | 157           | 11.67 (1.33-103)             | Weak                       | NA    |
| Bracci 2014 | NMZL    | Metal worker                                                             | 80            | 3.56 (1.67-7.58)             | Weak                       | NA    |
| Bracci 2014 | SMZL    | B-cell activation                                                        | 140           | 4.25 (1.49-12.14)            | Weak                       | NA    |
| Bracci 2014 | SMZL    | Asthma no other atopy                                                    | 130           | 2.28 (1.23-4.23)             | Weak                       | NA    |
| Bracci 2014 | SMZL    | General unspecified laborer                                              | 116           | 2.10 (1.15-3.84)             | Weak                       | NA    |
| Bracci 2014 | SMZL    | Teacher                                                                  | 116           | 0.33 (0.12-0.91)             | Weak                       | NA    |
| Bracci 2014 | SMZL    | Use hair dyes before 1980                                                | 32            | 14.85 (1.94-114)             | Weak                       | NA    |
| Bracci 2014 | SMZL    | Color of hairdye used (women only; light vs. never)                      | 32            | 9.69 (2.12-44.34)            | Weak                       | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study       | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------------|---------|---------------------------------------------------------------------------|-----------------|--------------------------|----------------------------|-------|
| Bracci 2014 | SMZL    | Color of hairdye used (women only; dark vs. never)                        | 32              | 5.30 (1.19-23.66)        | Weak                       | NA    |
| Bracci 2014 | SMZL    | Type of hairdye used (women only; permanent vs. never)                    | 32              | 6.59 (1.54-28.17)        | Weak                       | NA    |
| Bracci 2014 | SMZL    | Physical activity (%>=vigor)                                              | 56              | 0.44 (0.22-0.90)         | Weak                       | NA    |
| Bracci 2014 | SMZL    | Ever used hairdye                                                         | 32              | 6.54 (1.53-27.85)        | Weak                       | NA    |
| Smedby 2014 | MCL     | Any atopic disorder                                                       | 540             | 0.74 (0.61-0.89)         | Weak                       | NA    |
| Smedby 2014 | MCL     | Allergy                                                                  | 486             | 0.79 (0.63-0.98)         | Weak                       | NA    |
| Smedby 2014 | MCL     | Allergy and asthma, hay fever, or eczema                                 | 486             | 0.68 (0.52-0.88)         | Weak                       | NA    |
| Smedby 2014 | MCL     | Hay fever                                                                | 431             | 0.63 (0.48-0.82)         | Weak                       | NA    |
| Smedby 2014 | MCL     | Hay fever but no other atopic conditions                                  | 431             | 0.55 (0.33-0.93)         | Weak                       | NA    |
| Smedby 2014 | MCL     | Hay fever and asthma, allergy, or eczema                                  | 431             | 0.66 (0.49-0.89)         | Weak                       | NA    |
| Smedby 2014 | MCL     | Ever lived on a farm                                                      | 201             | 1.40 (1.03-1.90)         | Weak                       | NA    |
| Smedby 2014 | MCL     | Divers: material handling equipment operators                             | 286             | 3.05 (1.47-6.31)         | Weak                       | NA    |
| Smedby 2014 | MCL     | Electrical and electronics workers                                        | 286             | 1.63 (1.09-2.44)         | Weak                       | NA    |
| Vajdic 2014 | LPL/WM  | Sjogren's syndrome (any vs. none)                                         | 177             | 14.0 (3.60-54.5)         | Weak                       | Full  |
| Vajdic 2014 | LPL/WM  | Systemic lupus erythematous (any vs. none)                                | 274             | 8.23 (2.69-25.2)         | Weak                       | Full  |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study | Outcome | Exposure | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------|---------|----------|----------------|--------------------------|----------------------------|-------|
| Vajdic 2014 | LPL/WM | HCV | 207 | 2.51 (1.03-6.17) | Weak | Full |
| Vajdic 2014 | LPL/WM | B-cell activation | 374 | 2.78 (1.43-5.43) | Weak | Basic |
| Vajdic 2014 | LPL/WM | Hay fever | 282 | 0.73 (0.44-0.99) | Weak | Full |
| Vajdic 2014 | LPL/WM | Usual adult weight (Q2 vs Q1) | 324 | 0.71 (0.51-0.99) | Weak | Full |
| Vajdic 2014 | LPL/WM | Usual adult weight (Q3 vs Q1) | 324 | 0.72 (0.53-0.98) | Weak | Full |
| Vajdic 2014 | LPL/WM | Usual adult weight (Q4 vs Q1) | 324 | 0.61 (0.44-0.85) | Weak | Full |
| Vajdic 2014 | LPL/WM | Duration (>=40 years) cigarette smoking | 306 | 1.46 (1.04-2.05) | Weak | Full |
| Vajdic 2014 | LPL/WM | Age started smoking cigarettes (>=20 years vs. nonsmoker) | 306 | 1.45 (1.05-2.00) | Weak | Basic |
| Vajdic 2014 | LPL/WM | Medical doctor | 183 | 5.54 (2.19-14.0) | Weak | Full |
| Linet 2014 | FL | Sjogren's syndrome (any vs. none) | 1494 | 3.37 (1.23-9.19) | Weak | NA |
| Linet 2014 | FL | Any atopic disorder | 3452 | 0.87 (0.80-0.94) | Suggestive | NA |
| Linet 2014 | FL | Allergy | 2493 | 0.88 (0.79-0.98) | Weak | NA |
| Linet 2014 | FL | Food allergy | 2351 | 0.79 (0.67-0.94) | Weak | NA |
| Linet 2014 | FL | Astma | 3154 | 0.85 (0.74-0.97) | Weak | NA |
| Linet 2014 | FL | Hay fever | 2607 | 0.82 (0.73-0.91) | Weak | NA |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study | Outcome | Exposure | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------|---------|----------|----------------|--------------------------|-----------------------------|-------|
| Linet 2014 | FL | Blood transfusion, Male | 1097 | 0.74 (0.59-0.92) | Weak | NA |
| Linet 2014 | FL | Blood transfusion, Female | 1216 | 0.80 (0.68-0.95) | Weak | NA |
| Linet 2014 | FL | BMI as young adult (kg/m^2) continuous, Female | 1745 | 1.25 (1.09-1.44) | Weak | NA |
| Linet 2014 | FL | Physical activity (Mild), Female | 594 | 1.53 (1.02-2.30) | Weak | NA |
| Linet 2014 | FL | Recreational sun exposure (Q2 vs Q1 hours/week), Male | 825 | 0.77 (0.61-0.96) | Weak | NA |
| Linet 2014 | FL | Recreational sun exposure (Q3 vs Q1 hours/week), Male | 825 | 0.74 (0.58-0.93) | Weak | NA |
| Linet 2014 | FL | Recreational sun exposure (Q4 vs Q1 hours/week), Male | 825 | 0.77 (0.62-0.95) | Weak | NA |
| Linet 2014 | FL | Spray-painter (except construction), Male | 803 | 3.83 (1.87-7.84) | Weak | NA |
| Linet 2014 | FL | University and higher education teachers, Male | 972 | 0.53 (0.31-0.90) | Weak | NA |
| Linet 2014 | FL | History of cigarettte smoking (any vs. none), Female | 1506 | 1.22 (1.09-1.37) | Suggestive | NA |
| Linet 2014 | FL | Drinker (at least 1 drink per month vs. non-drinker), Female | 1034 | 0.79 (0.68-0.91) | Weak | NA |
| Linet 2014 | FL | Recreational sun exposure (Q2 vs Q1 hours/week), Female | 1016 | 0.77 (0.64-0.93) | Weak | NA |
| Linet 2014 | FL | Recreational sun exposure (Q3 vs Q1 hours/week), Female | 1016 | 0.78 (0.64-0.95) | Weak | NA |
| Linet 2014 | FL | Recreational sun exposure (Q4 vs Q1 hours/week), Female | 1016 | 0.70 (0.58-0.85) | Suggestive | NA |
| Linet 2014 | FL | Blood transfusion | 2313 | 0.78 (0.68-0.89) | Suggestive | NA |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study   | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|---------|---------|--------------------------------------------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Linet 2014 | FL      | Blood transfusion 1 vs none                                              | 2313            | 0.83 (0.71-0.97)         | Weak                         | NA    |
| Linet 2014 | FL      | Blood transfusion 2 vs none                                              | 2313            | 0.63 (0.46-0.86)         | Weak                         | NA    |
| Linet 2014 | FL      | Number of years from 1st blood transfusion to date of diagnosis/interview (<20 years) | 2313            | 0.77 (0.63-0.94)         | Weak                         | NA    |
| Linet 2014 | FL      | Number of years from 1st blood transfusion to date of diagnosis/interview (20-39 years) | 2313            | 0.76 (0.62-0.93)         | Weak                         | NA    |
| Linet 2014 | FL      | Blood transfusion <1990                                                  | 2313            | 0.83 (0.71-0.96)         | Weak                         | NA    |
| Linet 2014 | FL      | Blood transfusion after 1990                                             | 2313            | 0.62 (0.45-0.86)         | Weak                         | NA    |
| Linet 2014 | FL      | BMI as young adult (25-<30 kg/m^2)                                       | 929             | 1.49 (1.21-1.83)         | Suggestive                  | NA    |
| Linet 2014 | FL      | BMI as young adult (kg/m^2) continuous (5 kg/m^2 increase)                | 929             | 1.21 (1.09-1.35)         | Weak                         | NA    |
| Linet 2014 | FL      | Usual adult height (Q4 vs. Q1)                                           | 2662            | 1.15 (1.02-1.30)         | Weak                         | NA    |
| Linet 2014 | FL      | Physical activity (mild vs. no)                                          | 1026            | 1.41 (1.04-1.91)         | Weak                         | NA    |
| Linet 2014 | FL      | Status (% current) cigarette smoking                                      | 3013            | 1.19 (1.07-1.32)         | Weak                         | NA    |
| Linet 2014 | FL      | Age started smoking cigarettes regularly (14-17 years)                   | 3013            | 1.12 (1.01-1.25)         | Weak                         | NA    |
| Linet 2014 | FL      | Frequency of cigarette smoking (11-20 per day)                           | 3013            | 1.13 (1.02-1.25)         | Weak                         | NA    |
| Linet 2014 | FL      | Duration (>=40 years) cigarette smoking                                  | 3013            | 1.18 (1.04-1.35)         | Weak                         | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study   | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|---------|---------|--------------------------------------------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| Linet 2014 | FL      | Pack-years (21-35) cigarette smoking                                     | 3013            | 1.18 (1.04-1.34)         | Weak                         | NA    |
| Linet 2014 | FL      | Drinker (at least 1 drink per month vs. non-drinker)                    | 2106            | 0.86 (0.77-0.96)         | Weak                         | NA    |
| Linet 2014 | FL      | Alcohol consumption status (Drinker status unknown vs. nondrinker)       | 2106            | 0.81 (0.69-0.95)         | Weak                         | NA    |
| Linet 2014 | FL      | Duration of alcohol consumption (Drinker duration unknown vs. nondrinker) | 2106            | 0.80 (0.69-0.93)         | Weak                         | NA    |
| Linet 2014 | FL      | Servings of alcohol per week as an adult (1-6 drinks/week vs. nondrinker) | 2106            | 0.85 (0.75-0.97)         | Weak                         | NA    |
| Linet 2014 | FL      | Servings of alcohol per week as an adult (7-13 drinks/week vs. nondrinker) | 2106            | 0.84 (0.72-0.99)         | Weak                         | NA    |
| Linet 2014 | FL      | Servings of alcohol per week as an adult (>=28 drinks/week vs. nondrinker) | 2106            | 0.78 (0.64-0.96)         | Weak                         | NA    |
| Linet 2014 | FL      | Servings of alcohol per week as an adult (Drinker drinks/week unknown vs. nondrinker) | 2106            | 3.00 (1.25-7.23)         | Weak                         | NA    |
| Linet 2014 | FL      | Grams of ethanol per week as adult (Q1 vs nondrinker)                   | 2106            | 0.79 (0.68-0.92)         | Weak                         | NA    |
| Linet 2014 | FL      | Grams of ethanol per week as adult (Q2 vs nondrinker)                   | 2106            | 0.83 (0.71-0.97)         | Weak                         | NA    |
| Linet 2014 | FL      | Grams of ethanol per week as adult (Q4 vs nondrinker)                   | 2106            | 0.79 (0.66-0.94)         | Weak                         | NA    |
| Linet 2014 | FL      | Lifetime alcohol consumption (1-100 kg vs nondrinker)                    | 2106            | 0.75 (0.60-0.93)         | Weak                         | NA    |
| Linet 2014 | FL      | Lifetime alcohol consumption (101- | 2106            | 0.68 (0.51-0.91)         | Weak                         | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study       | Outcome | Exposure                                      | Number of cases | Effect estimate (95% CI) | Classificat ion of evidence | Model |
|-------------|---------|-----------------------------------------------|-----------------|--------------------------|----------------------------|-------|
| Linet 2014  | FL      | 200 kg vs nondrinker                          | 1235            | 0.83 (0.69-0.99)         | Weak                       | NA    |
| Linet 2014  | FL      | Total sun exposure (Q2 vs Q1 hours/week)      | 1235            | 0.82 (0.69-0.99)         | Weak                       | NA    |
| Linet 2014  | FL      | Total sun exposure (Q4 vs Q1 hours/week)      | 1841            | 0.77 (0.67-0.90)         | Suggestive                 | NA    |
| Linet 2014  | FL      | Total sun exposure (Q3 vs Q1 hours/week)      | 1841            | 0.74 (0.65-0.89)         | Suggestive                 | NA    |
| Linet 2014  | FL      | Recreational sun exposure (Q2 vs Q1 hours/week) | 1841          | 0.77 (0.66-0.89)         | Suggestive                 | NA    |
| Linet 2014  | FL      | Recreational sun exposure (Q4 vs Q1 hours/week) | 1841          | 0.74 (0.65-0.86)         | Suggestive                 | NA    |
| Linet 2014  | FL      | Recreational sun exposure (Q3 vs Q1 hours/week) | 1841          | 0.74 (0.65-0.89)         | Suggestive                 | NA    |
| Linet 2014  | FL      | Bakers and millers                            | 2144            | 0.51 (0.28-0.93)         | Weak                       | NA    |
| Linet 2014  | FL      | Spray-painter (except construction)           | 1790            | 2.66 (1.36-5.34)         | Weak                       | NA    |
| Linet 2014  | FL      | University and higher education teachers      | 2141            | 0.58 (0.41-0.83)         | Suggestive                 | NA    |
| Cerhan 2014 | DLBCL   | Sjogren's syndrome (any vs. none)             | 2299            | 9.35 (4.20-20.86)        | Highly suggestive           | Basic |
| Cerhan 2014 | DLBCL   | Systemic lupus erythematosus (any vs. none)   | 3905            | 2.53 (1.44-4.43)         | Weak                       | Basic |
| Cerhan 2014 | DLBCL   | Hemolytic anemia (any vs. non)                | 1390            | 2.72 (1.13-6.57)         | Weak                       | Basic |
| Cerhan 2014 | DLBCL   | Celiac disease (any vs. none)                 | 2331            | 2.14 (1.07-4.28)         | Weak                       | Basic |
| Cerhan 2014 | DLBCL   | Rheumatoid arthritis (any vs. none)           | 2642            | 1.94 (1.35-2.79)         | Suggestive                 | Basic |
| Cerhan 2014 | DLBCL   | Allergy                                       | 3215            | 0.82 (0.74-0.90)         | Suggestive                 | Basic |
| Cerhan 2014 | DLBCL   | Asthma                                        | 4224            | 0.87 (0.77-0.98)         | Weak                       | Basic |
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| Study    | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI)          | Classification of evidence | Model |
|----------|---------|--------------------------------------------------------------------------|-----------------|----------------------------------|---------------------------|-------|
| Cerhan   | DLBCL   | Hay fever                                                                | 3355            | 0.78 (0.70-0.86)                 | Suggestive               | Basic |
| Cerhan   | DLBCL   | Age at first blood transfusion                                            | 3065            | 0.69 (0.54-0.88)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Total number of blood transfusions (2+ vs none)                          | 3065            | 0.70 (0.53-0.92)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Total number of blood transfusions unknown                               | 3065            | 0.44 (0.20-0.96)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Number of years from 1st blood transfusion to date of diagnosis/interview (<20 years) | 3065            | 0.83 (0.70-0.98)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Transfusions before 1990                                                 | 3065            | 0.87 (0.76-0.99)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Usual adult height (Q4 vs Q1)                                             | 3509            | 1.12 (1.01-1.25)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Usual adult weight (Q4 vs Q1)                                             | 3509            | 1.20 (1.07-1.33)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Usual adult body mass index (15-<18.5 vs. 18.5-<22.5)                     | 3509            | 0.60 (0.41-0.88)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Usual adult body mass index (35-50 vs. 18.5-<22.5)                        | 3509            | 1.26 (1.04-1.53)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Smoking status as of ~1 year before diagnosis/interview (status unknown vs. nonsmoker) | 4139            | 1.26 (1.01-1.57)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Frequency of cigarette smoking (21-30 cigarettes/day vs. nonsmoker)       | 4139            | 1.17 (1.01-1.35)                 | Weak                      | Basic |
| Cerhan   | DLBCL   | Smoker, duration unknown                                                 | 4139            | 1.42 (1.04-1.95)                 | Weak                      | Basic |
## Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study | Outcome | Exposure | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------|---------|----------|-----------------|------------------------|---------------------------|-------|
| Cerhan 2014 | DLBCL | Years since quit cigarette smoking (Former unknown years) | 3993 | 2.20 (1.65-2.95) | Highly suggestive | Basic |
| Cerhan 2014 | DLBCL | History of alcohol consumption (>=1 drink/month v. nondrinker) | 3034 | 0.81 (0.73-0.89) | Suggestive | Basic |
| Cerhan 2014 | DLBCL | Alcohol consumption status as of ~2 years prior to diagnosis/interview (current drinker vs. nondrinker) | 3034 | 0.71 (0.63-0.80) | Highly suggestive | Basic |
| Cerhan 2014 | DLBCL | Age first alcohol consumption (20-29 years vs. nondrinker) | 3034 | 0.71 (0.62-0.82) | Highly suggestive | Basic |
| Cerhan 2014 | DLBCL | Duration of alcohol consumption (1-20 years vs. nondrinker) | 3034 | 0.79 (0.65-0.95) | Weak | Basic |
| Cerhan 2014 | DLBCL | Duration of alcohol consumption (21-30 years vs. nondrinker) | 3034 | 0.60 (0.60-0.91) | Weak | Basic |
| Cerhan 2014 | DLBCL | Duration of alcohol consumption (30-39 years vs. nondrinker) | 3034 | 0.82 (0.68-0.99) | Weak | Basic |
| Cerhan 2014 | DLBCL | Duration of alcohol consumption (40+ years vs. nondrinker) | 3034 | 0.71 (0.60-0.85) | Suggestive | Basic |
| Cerhan 2014 | DLBCL | Duration of alcohol consumption (Drinker duration unknown vs. nondrinker) | 3034 | 0.86 (0.75-0.98) | Weak | Basic |
| Cerhan 2014 | DLBCL | Servings of alcohol per week as an adult (1-6 drinks/week vs. nondrinker) | 3034 | 0.81 (0.73-0.91) | Weak | Basic |
| Cerhan 2014 | DLBCL | Servings of alcohol per week as an adult (7-13 drinks/week vs. nondrinker) | 3034 | 0.76 (0.67-0.87) | Suggestive | Basic |
| Cerhan 2014 | DLBCL | Servings of alcohol per week as an adult (14-27 drinks/week vs. nondrinker) | 3034 | 0.77 (0.67-0.89) | Suggestive | Basic |
### Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study          | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI)       | Classification of evidence | Model |
|----------------|---------|--------------------------------------------------------------------------|-----------------|-------------------------------|----------------------------|-------|
| Cerhan 2014    | DLBCL   | Servings of alcohol per week as an adult (>=28 drinks/week vs. nondrinker) | 3034            | 0.77 (0.66-0.90)              | Suggestive                 | Basic |
| Cerhan 2014    | DLBCL   | Servings of beer per week as an adult (<1 drinks/week vs. nondrinker)    | 3034            | 0.80 (0.69-0.92)              | Weak                       | Basic |
| Cerhan 2014    | DLBCL   | Servings of beer per week as an adult (1-6 drinks/week vs. nondrinker)   | 3034            | 0.82 (0.72-0.94)              | Weak                       | Basic |
| Cerhan 2014    | DLBCL   | Servings of beer per week as an adult (7-13 drinks/week vs. nondrinker)  | 3034            | 0.75 (0.62-0.92)              | Weak                       | Basic |
| Cerhan 2014    | DLBCL   | Servings of liquor per week as an adult (<1 drinks/week vs. nondrinker)  | 3034            | 0.71 (0.62-0.82)              | Suggestive                 | Basic |
| Cerhan 2014    | DLBCL   | Servings of liquor per week as an adult (1-6 drinks/week vs. nondrinker) | 3034            | 0.78 (0.67-0.90)              | Weak                       | Basic |
| Cerhan 2014    | DLBCL   | Servings of wine per week as an adult (1-6 drinks/week vs. nondrinker)   | 3034            | 0.75 (0.66-0.85)              | Suggestive                 | Basic |
| Cerhan 2014    | DLBCL   | Servings of wine per week as an adult (7-13 drinks/week vs. nondrinker)  | 3034            | 0.70 (0.58-0.83)              | Suggestive                 | Basic |
| Cerhan 2014    | DLBCL   | Servings of wine per week as an adult (14-27 drinks/week vs. nondrinker) | 3034            | 0.78 (0.65-0.93)              | Weak                       | Basic |
| Cerhan 2014    | DLBCL   | Servings of wine per week as an adult (>=28 drinks/week vs. nondrinker)  | 3034            | 0.75 (0.61-0.92)              | Weak                       | Basic |
| Cerhan 2014    | DLBCL   | Grams of ethanol per week as adult (Q1 vs nondrinker)                     | 3034            | 0.84 (0.75-0.96)              | Weak                       | Basic |
| Cerhan 2014    | DLBCL   | Grams of ethanol per week as adult (Q2 vs nondrinker)                     | 3034            | 0.79 (0.70-0.90)              | Suggestive                 | Basic |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study     | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-----------|---------|--------------------------------------------------------------------------|-----------------|---------------------------|-----------------------------|-------|
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult (Q3 vs nondrinker)                     | 3034            | 0.77 (0.68-0.88)          | Suggestive                   | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult (Q4 vs nondrinker)                     | 3034            | 0.78 (0.67-0.90)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult , Beer (Q1 vs nondrinker)              | 3034            | 0.80 (0.69-0.92)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult, beer (Q2 vs nondrinker)               | 3034            | 0.78 (0.66-0.91)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult, beer (Q4 vs nondrinker)               | 3034            | 0.75 (0.63-0.88)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Drinker, wine & liquor (no beer)                                          | 3034            | 0.81 (0.72-0.91)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult , wine (Q1 vs nondrinker)              | 3034            | 0.78 (0.68-0.90)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult, wine (Q2 vs nondrinker)               | 3034            | 0.78 (0.68-0.90)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult, wine (Q3 vs nondrinker)               | 3034            | 0.75 (0.65-0.86)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult, wine (Q4 vs nondrinker)               | 3034            | 0.78 (0.66-0.91)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult, liquoe (Q1 vs nondrinker)             | 3034            | 0.70 (0.59-0.83)          | Suggestive                   | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult, liquor (Q2 vs nondrinker)             | 3034            | 0.79 (0.67-0.93)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult, liquor (Q3 vs nondrinker)             | 3034            | 0.74 (0.62-0.89)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Grams of ethanol per week as adult, liquor (Q4 vs nondrinker)             | 3034            | 0.81 (0.68-0.98)          | Weak                         | Basi c |
| Cerhan 2014 | DLBCL   | Drinker, wine & beer (no liquor)                                          | 3034            | 0.84 (0.76-0.94)          | Weak                         | Basi c |
## Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study       | Outcome | Exposure                                           | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-------------|---------|----------------------------------------------------|-----------------|---------------------------|-----------------------------|-------|
| Cerhan 2014 | DLBCL   | Lifetime beer consumption (1-100 kg vs. nondrinker) | 3034            | 0.78 (0.66-0.92)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Lifetime wine consumption (201-400 kg vs. nondrinker) | 3034            | 0.63 (0.44-0.91)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Lifetime wine consumption (unknown vs. nondrinker)  | 3034            | 0.82 (0.72-0.93)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Drinker, wine, & liquor (no beer)                   | 3034            | 0.81 (0.72-0.93)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Lifetime liquor consumption (1-100 kg vs. nondrinker) | 3034            | 0.74 (0.62-0.89)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Lifetime liquor consumption (201-400 kg vs. nondrinker) | 3034            | 0.67 (0.47-0.94)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Lifetime liquor consumption (unknown vs. nondrinker)  | 3034            | 0.79 (0.69-0.89)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Lifetime wine consumption (1-100 kg vs. nondrinker)  | 3034            | 0.74 (0.53-0.86)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Lifetime wine consumption (101-200 kg vs. nondrinker) | 3034            | 0.70 (0.53-0.92)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Lifetime wine consumption (201-400 kg vs. nondrinker) | 3034            | 0.71 (0.52-0.98)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Lifetime wine consumption (400+ kg vs. nondrinker)   | 3034            | 0.56 (0.40-0.79)          | Suggestive                  | Basic |
| Cerhan 2014 | DLBCL   | Lifetime wine consumption (unknown vs. nondrinker)   | 3034            | 0.83 (0.74-0.94)          | Weak                        | Basic |
| Cerhan 2014 | DLBCL   | Color of hair dye used (unknown vs. never)           | 1155            | 1.41 (1.07-1.87)          | Weak                        | Basic |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study  | Outcome | Exposure                                      | Number of cases | Effect estimate (95% CI)                     | Classification of evidence | Model |
|--------|---------|-----------------------------------------------|-----------------|---------------------------------------------|----------------------------|-------|
| Cerhan 2014 | DLBCL | Drivers: material handling equipment | 3064            | 1.56 (1.03-2.37)                          | Weak                       | Basic |
| Cerhan 2014 | DLBCL | Cleaners and related workers                  | 3064            | 1.27 (1.03-1.57)                          | Weak                       | Basic |
| Cerhan 2014 | DLBCL | Hairdresser                                   | 3066            | 1.49 (1.10-2.03)                          | Weak                       | Basic |
| Cerhan 2014 | DLBCL | Textile worker                                | 3066            | 1.20 (1.02-1.41)                          | Weak                       | Basic |
| Cerhan 2014 | DLBCL | Fiber preparers                              | 1645            | 2.21 (1.21-4.03)                          | Weak                       | Basic |
| Cerhan 2014 | DLBCL | Socioeconomic status (medium vs. low)         | 4667            | 0.88 (0.81-0.95)                          | Weak                       | Final |
| Cerhan 2014 | DLBCL | Socioeconomic status (high vs. low)           | 4667            | 0.86 (0.79-0.94)                          | Suggestive                 | Final |
| Cerhan 2014 | DLBCL | B-cell activation                            | 4546            | 2.36 (1.80-3.09)                          | Highly suggestive          | Final |
| Cerhan 2014 | DLBCL | B and T-cell activation                       | 4546            | 4.86 (2.31-10.25)                         | Suggestive                 | Final |
| Cerhan 2014 | DLBCL | Any atopic disorder                          | 4577            | 0.82 (0.76-0.89)                          | Suggestive                 | Final |
| Cerhan 2014 | DLBCL | HCV                                           | 2382            | 2.02 (1.47-2.76)                          | Suggestive                 | Final |
| Cerhan 2014 | DLBCL | Blood transfusion                            | 3264            | 0.81 (0.72-0.91)                          | Suggestive                 | Final |
| Cerhan 2014 | DLBCL | BMI as young adult (25-<30 kg/m^2)            | 3645            | 1.47 (1.22-1.77)                          | Suggestive                 | Final |
| Cerhan 2014 | DLBCL | BMI as young adult (30-50 kg/m^2)             | 3645            | 1.58 (1.12-2.23)                          | Weak                       | Final |
| Cerhan 2014 | DLBCL | Lifetime alcohol consumption (1-100 kg vs nondrinker) | 4124 | 0.80 (0.68-0.95)                          | Weak                       | Final |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study          | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI)  | Classification of evidence | Model |
|----------------|---------|---------------------------------------------------------------------------|-----------------|---------------------------|----------------------------|-------|
| Cerhan 2014    | DLBCL   | Lifetime alcohol consumption (101-200 kg vs nondrinker)                   | 4124            | 0.79 (0.63-0.98)          | Weak                       | Final |
| Cerhan 2014    | DLBCL   | Lifetime alcohol consumption (201-400 kg vs nondrinker)                   | 4124            | 0.66 (0.53-0.83)          | Suggestive                 | Final |
| Cerhan 2014    | DLBCL   | Lifetime alcohol consumption (unknown)                                    | 4124            | 0.87 (0.77-0.97)          | Weak                       | Final |
| Cerhan 2014    | DLBCL   | Recreational sun exposure (Q3 vs Q1 hours/week)                           | 2863            | 0.79 (0.69-0.90)          | Suggestive                 | Final |
| Cerhan 2014    | DLBCL   | Recreational sun exposure (Q4 vs Q1 hours/week)                           | 2863            | 0.78 (0.69-0.89)          | Suggestive                 | Final |
| Cerhan 2014    | DLBCL   | Field crop/vegetable farmer                                               | 2765            | 1.49 (1.14-1.95)          | Weak                       | Final |
| Cerhan 2014    | DLBCL   | Sewer and embroiderer                                                    | 3086            | 1.43 (1.10-1.87)          | Weak                       | Final |
| Cerhan 2014    | DLBCL   | Women's hairdresser                                                       | 2983            | 1.61 (1.13-2.31)          | Weak                       | Final |
| Monnere au 2014| HCL     | Lifetime cigarette exposure (11-20 pack-years vs. nonsmoker)              | 120             | 0.56 (0.34-0.95)          | Weak                       | Final |
| Monnere au 2014| HCL     | Lifetime cigarette exposure (21-35 pack-years vs. nonsmoker)              | 120             | 0.48 (0.28-0.83)          | Weak                       | Final |
| Monnere au 2014| HCL     | Lifetime cigarette exposure (>35 pack-years)                              | 120             | 0.29 (0.14-0.58)          | Weak                       | Final |
| Monnere au 2014| HCL     | Ever lived on a farm                                                      | 46              | 1.70 (1.02-2.82)          | Weak                       | Final |
| Monnere au 2014| HCL     | Height (Q3 vs. Q1)                                                        | 110             | 2.40 (1.23-4.70)          | Weak                       | Final |
| Monnere au 2014| HCL     | Height (Q4 vs. Q1)                                                        | 110             | 2.59 (1.32-5.07)          | Weak                       | Final |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study         | Outcome | Exposure                                                                 | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|---------------|---------|--------------------------------------------------------------------------|-----------------|--------------------------|----------------------------|-------|
| Monnere au 2014 | HCL     | History of cigarette smoking (any vs. none)                              | 154             | 0.51 (0.37-0.71)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Status (% current) cigarette smoking                                     | 154             | 0.34 (0.21-0.55)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Age started smoking cigarettes regularly (14-17 years)                   | 148             | 0.46 (0.30-0.72)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Age started smoking cigarettes regularly (18-19 years)                   | 148             | 0.48 (0.25-0.91)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Frequency of cigarette smoking (11-20 per day)                           | 154             | 0.49 (0.32-0.75)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Frequency of cigarette smoking (21-30 per day)                           | 154             | 0.34 (0.13-0.85)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Frequency of cigarette smoking (>30 per day)                            | 154             | 0.22 (0.07-0.71)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Duration of cigarette smoking (21-30 years)                             | 154             | 0.39 (0.22-0.69)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Duration of cigarette smoking (30-39 years)                             | 154             | 0.44 (0.25-0.78)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Duration of cigarette smoking (40+ years)                               | 154             | 0.49 (0.27-0.91)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Lifetime cigarette exposure (continuous)                                | 154             | 0.98 (0.96-0.99)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Ever worked as a mixed animal and crop farmer                           | 91              | 2.34 (1.36-4.01)         | Weak                       | Basic |
| Monnere au 2014 | HCL     | Duration as mixed animal and crop farmer (10 years+ vs. never)           | 91              | 2.98 (1.50-5.93)         | Weak                       | Basic |
| Kane 2012      | FL      | Years since last child (<10 years)                                      | 4901            | 1.87 (1.02-3.40)         | Weak                       | NA    |
| Kane 2012      | FL      | Contraception among women born in 1925 or later                          | 5138            | 1.30 (1.04-1.63)         | Weak                       | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study          | Outcome | Exposure                                         | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|----------------|---------|--------------------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| tMannetje 2016 | NHL     | Charworkers, cleaners and related                | 10046           | 1.17 (1.01-1.36)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Railway-engine drivers and firemen              | 10046           | 0.45 (0.22-0.94)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Vehicle electrician                              | 10046           | 2.58 (1.20-5.55)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Other motor-vehicle drivers                     | 10046           | 0.65 (0.46-0.92)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Field crop/vegetable farmer                     | 10046           | 1.26 (1.05-1.51)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Field crop farm worker general                   | 10046           | 1.38 (1.07-1.77)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | General farmer worked                           | 10046           | 1.19 (1.03-1.37)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Women’s hairdresser                              | 10046           | 1.34 (1.02-1.74)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Medical assistants                               | 10046           | 0.69 (0.50-0.95)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Spray-painter (except construction)             | 10046           | 2.07 (1.30-3.29)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Teachers                                         | 10046           | 0.89 (0.81-0.98)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | University and higher education teachers         | 10046           | 0.75 (0.61-0.90)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Secondary education teachers                     | 10046           | 0.82 (0.69-0.98)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Head teacher                                     | 10046           | 2.16 (1.15-4.06)         | Weak                        | NA    |
| tMannetje 2016 | NHL     | Other teachers                                   | 10046           | 0.63 (0.40-0.98)         | Weak                        | NA    |
| Study         | Outcome | Exposure                                      | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|---------------|---------|-----------------------------------------------|-----------------|--------------------------|----------------------------|-------|
| tMannetje 2016 | NHL     | Milliners and hatmakers                       | 10046           | 2.46 (1.28-4.74)         | Weak                       | NA    |
| tMannetje 2016 | NHL     | Carpenter, general                            | 10046           | 1.42 (1.04-1.93)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Charworkers, cleaners and related              |                 | 1.27 (1.03-1.58)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Field crop/vegetable farmer                   |                 | 1.50 (1.15-1.97)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Field crop farm worker general                 |                 | 1.48 (1.01-2.17)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Hairdresser                                   |                 | 1.47 (1.08-2.00)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Women's hairdresser                           |                 | 1.60 (1.13-2.27)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Medical workers                               |                 | 0.85 (0.72-0.99)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Metal melters and reheaters                   |                 | 2.31 (1.01-5.26)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Special education teachers                    |                 | 1.94 (1.01-3.71)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Textile worker                                |                 | 1.19 (1.01-1.41)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Milliners and hatmakers                       |                 | 2.90 (1.30-6.45)         | Weak                       | NA    |
| tMannetje 2016 | DLBCL   | Sewer and embroiderer                         |                 | 1.51 (1.16-1.96)         | Weak                       | NA    |
| tMannetje 2016 | FL      | Bakers and millers                            | 2140            | 0.54 (0.30-0.99)         | Weak                       | NA    |
| tMannetje 2016 | FL      | Spray-painter (except construction)           | 2140            | 2.67 (1.36-5.25)         | Weak                       | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study           | Outcome | Exposure                                      | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|-----------------|---------|-----------------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| tMannetje 2016 | FL      | University and higher education teachers      | 2140            | 0.62 (0.44-0.89)         | Weak                        | NA    |
| tMannetje 2016 | CLL/SLL | Farmer-animal                                 | 1014            | 0.63 (0.42-0.96)         | Weak                        | NA    |
| tMannetje 2016 | CLL/SLL | Farmers-mix and unspecified                   | 1014            | 1.30 (1.06-1.60)         | Weak                        | NA    |
| tMannetje 2016 | CLL/SLL | General farm worker                           | 1014            | 1.44 (1.13-1.84)         | Weak                        | NA    |
| tMannetje 2016 | CLL/SLL | Hairdresser                                   | 1014            | 1.79 (1.06-3.03)         | Weak                        | NA    |
| tMannetje 2016 | CLL/SLL | Women's hairdresser                           | 1014            | 2.69 (1.43-5.06)         | Weak                        | NA    |
| tMannetje 2016 | CLL/SLL | Printing pressmen                             | 1014            | 6.52 (2.79-15.21)        | Suggestive                  | NA    |
| tMannetje 2016 | CLL/SLL | Preprimary education teachers                  | 1014            | 2.00 (1.04-3.87)         | Weak                        | NA    |
| tMannetje 2016 | CLL/SLL | Carpenter, general                            | 1014            | 2.10 (1.08-4.09)         | Weak                        | NA    |
| tMannetje 2016 | PTCL    | Electric fitters                              | 652             | 2.02 (1.03-3.97)         | Weak                        | NA    |
| tMannetje 2016 | PTCL    | Metal workers                                 | 652             | 0.66 (0.45-0.99)         | Weak                        | NA    |
| tMannetje 2016 | PTCL    | Painters                                      | 652             | 1.80 (1.14-2.84)         | Weak                        | NA    |
| tMannetje 2016 | PTCL    | Textile worker                                | 652             | 1.60 (1.18-2.17)         | Weak                        | NA    |
| tMannetje 2016 | PTCL    | Spinners, weavers, knitters, dyers, and related workers | 652 | 1.85 (1.21-2.83) | Weak | NA |
| tMannetje 2016 | PTCL    | Wood workers                                  | 652             | 1.54 (1.04-2.27)         | Weak                        | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Study          | Outcome | Exposure                                  | Number of cases | Effect estimate (95% CI) | Classification of evidence | Model |
|----------------|---------|-------------------------------------------|-----------------|--------------------------|-----------------------------|-------|
| tMannetje 2016 | PTCL    | Cabinetmakers                             | 652             | 2.41 (1.22-4.74)         | Weak                        | NA    |
| Kricker 2008   | NHL     | Recreational sun exposure (Q4 vs Q1 hours/week) | 7284             | 0.76 (0.63-0.91)         | Weak                        | NA    |
| Kricker 2008   | FL      | Recreational sun exposure (Q2 vs Q1 hours/week) | 1642             | 0.83 (0.71-0.96)         | Weak                        | NA    |
| Kricker 2008   | FL      | Recreational sun exposure (Q4 vs Q1 hours/week) | 1642             | 0.73 (0.62-0.86)         | Suggestive                  | NA    |
| Kricker 2008   | DLBCL   | Recreational sun exposure (Q3 vs Q1 hours/week) | 2176             | 0.75 (0.61-0.93)         | Weak                        | NA    |
| Kricker 2008   | DLBCL   | Recreational sun exposure (Q4 vs Q1 hours/week) | 2176             | 0.69 (0.55-0.87)         | Weak                        | NA    |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

eTable 6: AMSTAR 2 evaluation

| Rating  | Title                                                                 | Author year | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|---------|-----------------------------------------------------------------------|-------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Criticall y low  | Benzene and the risk of non-Hodgkin lymphoma: a review and meta-analysis of the literature. | Kane 2010   | No     | No     | NA     | No     | No     | No     | Yes    | No     | No     | No     | No     | No     | No     | Yes    | No     | Yes    |
| Criticall y low  | Maternal smoking during pregnancy and childhood lymphoma: a meta-analysis. | Antonopoulous 2011 | Yes    | No     | NA     | Yes    | No     | Yes    | Partial Yes | No     | No     | Yes    | No     | Yes    | No     | Yes    | Yes    | Yes    |
| Criticall y low  | Lifestyle and risk of follicular lymphoma: a systematic review and meta-analysis of observational studies | Odutola 2020 | No     | Partial Yes | NA     | No     | Yes    | Yes    | No     | No     | Yes    | No     | Yes    | Yes    | Yes    | No     | Yes    | Yes    |
| Criticall y low  | Dietary trans-fatty acid intake in relation to cancer risk: a systematic review and meta-analysis | Michels 2021 | Yes    | Partial Yes | NA     | Partial Yes | Yes    | No     | No     | Partial Yes | Yes    | No     | Yes    | No     | No     | No     | No     | Yes    | Yes    |
| Criticall y low  | Sunlight exposure in association with risk of lymphoid malignancy: a meta-analysis of | Kim 2021    | Yes    | No     | NA     | Partial Yes | No     | Yes    | No     | Partial Yes | Yes    | No     | Yes    | No     | Yes    | No     | No     | Yes    | Yes    |
# Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Rating    | Title                                                                 | Author year | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|-----------|-----------------------------------------------------------------------|-------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Low       | Observational studies                                                |             |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |
| Low       | Non-Hodgkin lymphoma and gluten-sensitive enteropathy: estimate of risk using meta-analyses. | Kane 2011   | Yes    | No     | NA     | No     | No     | No     | No     | No     | No     | No     | No     | No     | No     | No     | Yes    | Yes    | Yes    |
| Low       | Trichloroethylene and cancer: systematic and quantitative review of epidemiologic evidence for identifying hazards. | Scott 2011  | No     | No     | NA     | Partial Yes | No     | No     | No     | No     | No     | No     | No     | No     | No     | Yes    | Yes    | Yes    |
| Low       | The relationship between physical activity and lymphoma: a systematic review and meta analysis | Davies 2020 | Yes    | Partial Yes | No     | Partial Yes | Yes    | No     | No     | No     | No     | Yes    | No     | No     | No     | Yes    | Yes    | Yes    |
| Low       | Association between red blood cell transfusions and development of non-Hodgkin lymphoma: a meta-analysis of | Castillo 2010 | No     | No     | NA     | No     | Yes    | Ye s   | No     | No     | Yes    | No     | No     | No     | No     | No     | No     | Yes    |

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Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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|-------------|-----------------------------------------------------------------------|-------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Criticall   | A systematic review and meta-analysis of occupational exposures and risk of follicular lymphoma | Odutola 2021      | No     | Parial| NA     | No     | Ye     | Ye     | No     | Yes    | Yes    | No     | Ye     | Ye     | Ye     | Ye     | Yes    | Ye     |
| low         |                                                                      |                   |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |
| Criticall   | Malaria Infection and Risk for Endemic Burkitt Lymphoma: A Systematic Review and Meta-Analysis | Kotepui 2021      | Yes    | No     | NA     | Parial| Yes    | Ye     | No     | Parial| Yes    | No     | No     | No     | No     | Yes    | No     | Yes    |
| low         |                                                                      |                   |        |        |        |        |        |        |        |       |        |        |        |        |        |        |        |        |
| Criticall   | Meta-analysis: coeliac disease and the risk of all-cause mortality, any malignancy and lymphoid malignancy. | Tio 2012          | No     | No     | NA     | Parial| No     | No     | No     | Parial| No     | No     | Ye     | No     | No     | Ye     | Yes    | Yes    |
| low         |                                                                      |                   |        |        |        |        |        |        |        |       |        |        |        |        |        |        |        |        |
| Criticall   | The Risk of Extraintestinal Cancer in Inflammatory Bowel Disease: A Systematic Review and Meta-analysis of Population-based Cohort Studies | Lo 2021           | Yes    | Parial| NA     | Parial| Yes    | No     | No     | Ye     | Yes    | No     | No     | No     | No     | No     | No     | Yes    |
| low         |                                                                      |                   |        |        |        |        |        |        |        |       |        |        |        |        |        |        |        |        |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Rating            | Title                                                                 | Author year          | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|-------------------|----------------------------------------------------------------------|----------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low    | Primary biliary cirrhosis and cancer risk: a systematic review and meta-analysis. | Liang 2012          | Yes    | No     | NA     | No     | No     | Yes    | Yes    | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    |
| Low               | Paracetamol Intake and Hematologic Malignancies: A Meta-Analysis of Observational Studies | Pregoz Dominguez 2021 | Yes    | Partial Yes | No     | Partial Yes | No     | No     | Yes    | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Yes    |
| Critically low    | Non-Hodgkin's lymphoma--meta-analyses of the effects of corticosteroids and non-steroidal anti-inflammatories. | Bernatsky 2007      | No     | No     | No     | No     | No     | Yes    | No     | No     | No     | Yes    | No     | Yes    | No     | Yes    | Ye     |
| Critically low    | Cigarette smoking and risk of lymphoma in adults: a comprehensive meta-analysis on Hodgkin and non-Hodgkin disease. | Sergentani 2013     | No     | No     | NA     | Partial Yes | No     | Yes    | No     | Yes    | No     | Yes    | No     | Yes    | Yes    | Ye     |
| Critically low    | Exposure to glyphosate and risk of non-Hodgkin | Boffetta 2021       | No     | No     | NA     | No     | Yes    | No     | No     | No     | No     | Yes    | No     | No     | Yes    | Ye     | Yes    |
### Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Rating | Title                                                                 | Author          | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|--------|----------------------------------------------------------------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        | Fruits and vegetables consumption and risk of non-Hodgkin's lymphoma: a meta-analysis of observational studies.      | Chen 2013       | No     | No     | NA     | No     | No     | Yes    | No     | No     | No     | Yes    | No     | No     | No     | No     | Yes    | Yes    |
|        | Occupation and the risk of non-Hodgkin lymphoma.                   | Boffetta 2007   | No     | No     | No     | No     | No     | No     | No     | No     | No     | Yes    | No     | No     | No     | No     | Yes    | No     |
|        | Breast-feeding and childhood cancer: A systematic review with metanalysis.                                           | Martin 2005     | Yes    | No     | NA     | No     | No     | No     | No     | No     | No     | Yes    | Yes    | Yes    | No     | Yes    | Yes    | Yes    |
|        | The risk of cancer development in systemic sclerosis: a meta-analysis.                                               | Zhang 2013      | No     | No     | NA     | No     | No     | Yes    | No     | No     | No     | Yes    | No     | No     | No     | Yes    | No     | No     |
|        | Occupational exposure to methylene chloride and risk of cancer: a meta-analysis.                                      | Liu 2013        | No     | No     | NA     | Partial Yes | No     | No     | No     | Yes    | No     | Yes    | No     | No     | No     | Yes    | No     | No     |

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|-----------------|-----------------------------------------------------------------------|---------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low  | Primary Sjogren’s syndrome and malignancy risk: a systematic review and meta-analysis. | Liang 2014    | Yes    | No     | NA     | No     | Ye     | No     | Ye     | No     | Yes    | No     | No     | Yes    | No     | Yes    | Yes    |
| Critically low  | Increased risk of lymphoma among inflammatory bowel disease patients treated with azathioprine and 6-mercaptopurine. | Kandiel 2005  | Yes    | No     | No     | No     | Ye     | No     | No     | Yes    | No     | No     | Yes    | No     | Yes    | Yes    |
| Critically low  | Occupational exposure to pentachlorophenol causing lymphoma and hematopoietic malignancy for two generations. | Zheng 2015    | No     | No     | NA     | No     | Ye     | No     | No     | Partial Yes | No     | No     | Yes    | No     | Yes    | Yes    |
| Critically low  | Epstein-Barr virus and risk of non-Hodgkin lymphoma in the cancer prevention study-II and a meta-analysis of serologic studies. | Teras 2015    | No     | No     | NA     | No     | No     | No     | No     | No     | No     | No     | Yes    | No     | Yes    | Yes    |
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|--------------|-----------------------------------------------------------------------|-------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low | Assessing the impact of HAART on the incidence of defining and non-defining AIDS cancers among patients with HIV/AIDS: a systematic review. | Cobucci 2015 | Yes    | No     | NA     | Partial | Yes    | No     | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    | No     | No     | Yes    |
| Critically low | Use of non-steroidal anti-inflammatory drugs and risk of non-Hodgkin lymphoma: a systematic review and meta-analysis. | Ye 2015     | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Partial | Yes    | No     | Yes    | No     | No     | Yes    | Yes    | Yes    | Yes    |
| Critically low | Incidence of malignancy in adult patients with rheumatoid arthritis: a meta-analysis. | Simon 2015  | Yes    | No     | NA     | No     | No     | No     | No     | No     | No     | No     | No     | Yes    | Yes    | Yes    | Yes    | Yes    |
| Critically low | Vitamin D status and risk of non-Hodgkin lymphoma: a meta-analysis. | Lu 2014     | No     | No     | No     | Partial | Yes    | No     | No     | No     | No     | Yes    | No     | No     | Yes    | Yes    | No     | No     |
| Critically low | Red and Processed Meat Consumption | Yang 2015   | No     | No     | NA     | No     | Yes    | Yes    | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    |
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|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Low    | Increases Risk for Non-Hodgkin Lymphoma: A PRISMA-Compliant Meta-Analysis of Observational Studies. Catalani 2019 | Yes | No | NA | Partial Yes | Yes | Yes | No | No | No | No | No | No | Yes | Yes | Yes |
| Critically low | Allergic conditions are not associated with the risk of non-Hodgkin's lymphoma or Hodgkin's lymphoma: a systematic review and meta-analysis. Yang 2017 | No | No | NA | Partial Yes | Yes | Yes | No | No | No | No | No | No | Yes | Yes | Yes |
| Critically low | Occupational ultraviolet exposure and risk of non-Hodgkin's lymphomas: a meta-analysis. Lu 2017 | No | No | NA | Partial Yes | No | Yes | No | No | No | No | Yes | No | Yes | Yes | Yes |
| Critically low | Cancer risks in recipients of renal transplants: a meta-analysis of cohort studies. Wang 2017 | Yes | No | NA | Partial Yes | No | Yes | No | Yes | No | Yes | Yes | No | Yes | Yes | Yes |
| Low    | Occupational and environmental exposure to... Catalani 2019 | Yes | Partial Yes | NA | Partial Yes | Yes | No | No | Partial Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes |
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| Rating | Title                                                                                                                                 | Author          | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|--------|----------------------------------------------------------------------------------------------------------------------------------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low | polychlorinated biphenyls and risk of non-Hodgkin lymphoma: a systematic review and meta-analysis of epidemiology studies. | Masarone 2019   | Yes    | No     | NA     | Partial Yes | Yes    | No     | Partial Yes | Partial Yes | No     | No     | Yes    | No     | No     | No     | Yes    | Ye s    |
| Critically low | Hepatitis C virus infection and non-hepatocellular malignancies in the DAA era: A systematic review and meta-analysis. | Mirtavos-Mahyari 2019 | Yes    | No     | NA     | No     | Yes    | No     | Yes    | No     | Yes    | No     | Yes    | No     | No     | Yes    | Yes    |
| Critically low | Effects of Coffee, Black Tea and Green Tea Consumption on the Risk of Non-Hodgkin's Lymphoma: A Systematic Review and Dose-Response Meta-Analysis of Observational Studies. | Mirtavos-Mahyari 2019 | Yes    | No     | NA     | No     | Yes    | No     | Yes    | No     | Yes    | No     | Yes    | No     | No     | Yes    | Yes    |
## Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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|---------------|----------------------------------------------------------------------|---------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low| Systemic lupus erythematous and malignancy risk: a meta-analysis.    | Cao 2015      | Yes    | No     | NA     | Partial Yes | No    | Yes    | No     | Yes    | No     | Yes    | No     | Yes    | Yes    | Yes    |
| Critically low| Food of animal origin and risk of non-Hodgkin lymphoma and multiple myeloma: A review of the literature and meta-analysis. | Caini 2016    | No     | No     | No     | Partial Yes | Yes   | No     | No     | No     | No     | No     | No     | No     | No     | Yes    | Yes    |
| Critically low| Dairy Product Consumption and Risk of Non-Hodgkin Lymphoma: A Meta-Analysis. | Wang 2016     | No     | No     | NA     | No     | Yes    | Yes    | No     | No     | No     | No     | No     | Yes    | Yes    | Yes    | Yes    |
| Critically low| Exposure to organochlorine pesticides and non-Hodgkin lymphoma: a meta-analysis of observational studies. | Luo 2016      | No     | No     | NA     | Partial Yes | No    | Yes    | No     | No     | No     | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    |
| Critically low| Association between dietary nitrate and nitrite intake and sitespecific | Xie 2016      | No     | No     | NA     | No     | No     | No     | No     | No     | No     | No     | No     | No     | Yes    | Yes    | Yes    | Yes    |
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|----------|------------------------------------------------------------------------|----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Low      | Association between dioxin and cancer incidence and mortality: a meta-analysis. | Xu 2016        | Yes    | No     | NA     | No     | No     | Yes    | No     | Yes    | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Yes    |
| Low      | Associations between statin use and non-Hodgkin lymphoma (NHL) risk and survival: a meta-analysis. | Ye 2017        | No     | No     | Ye     | No     | Ye     | Yes    | No     | No     | No     | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    |
| Low      | Lack of association of poultry and eggs intake with risk of non-Hodgkin lymphoma: a meta-analysis of observational studies. | Dong 2017      | No     | No     | NA     | Partial Yes | Yes | Yes    | No     | No     | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Yes    |
| Low      | Herpes zoster as a marker of occult cancer: A systematic review and meta-analysis. | Schmidt 2017   | Yes    | Yes    | NA     | No     | Ye     | Yes    | No     | Ye     | Ye     | Ye     | Ye     | Ye     | Ye     | Ye     | Ye     | Ye     |
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|--------------|-----------------------------------------------------------------------|-------------|--------|--------|--------|----------|----------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low | Carotenoid intake and risk of non-Hodgkin lymphoma: a systematic review and dose-response meta-analysis of observational studies. | Chen 2017   | No     | No     | NA     | Partial Yes | No       | Yes    | No     | No     | No     | Yes    | No     | No     | Yes    | No     | Yes    | Yes    |
| Critically low | Dietary Fat Consumption and Non-Hodgkin's Lymphoma Risk: A Meta-analysis. | Han 2017    | No     | No     | No     | No       | Yes      | Yes    | No     | No     | No     | Yes    | No     | No     | Yes    | No     | Yes    | Yes    |
| Critically low | Occupational exposure to polycyclic aromatic hydrocarbons and lymphatic and hematopoietic neoplasms: a systematic review and meta-analysis of cohort studies. | Alicandro 2016 | Yes    | No     | NA     | Partial Yes | No       | No     | Yes    | Yes    | No     | No     | No     | Yes    | Yes    | Yes    | Yes    |
| Critically low | Risk of malignancy in ankylosing spondylitis: a systematic review | Deng 2016    | Yes    | No     | No     | No       | Yes      | Yes    | No     | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    |
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|--------------|------------------------------------------------------------------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Criticall y low | The association between non-Hodgkin lymphoma and organophosphate pesticides exposure: A meta-analysis. | Hu 2017         | No     | No     | NA     | No     | No     | Ye     | No     | Yes    | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Yes    |
| Criticall y low | Incidence of cancer (other than gastric cancer) in pernicious anaemia: A systematic review with meta-analysis. | Lahner 2018     | No     | No     | NA     | Partial Yes | Yes    | Yes    | No     | Yes    | Yes    | No     | No     | No     | No     | No     | No     | Yes    |
| Criticall y low | 2,4-dichlorophenoxy acetic acid (2,4-D) and risk of non-Hodgkin lymphoma: a meta-analysis accounting for exposure levels. | Smith 2017      | No     | No     | NA     | Partial Yes | No     | No     | No     | Partial Yes | Yes    | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    |
| Criticall y low | Systematic Review and Meta-Analysis of Selected Cancers in Petroleum | Schnatter 2018  | Ye     | No     | Ye     | Partial Yes | Ye     | No     | No     | No     | No     | Ye     | Yes    | No     | No     | Yes    | Yes    | Yes    |
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|--------|-----------------------------------------------------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Low    | Indoor tanning and the risk of developing non-cutaneous cancers: a systematic review and meta-analysis. | O'Sullivan 2018 | No | No | No | No | Yes | Yes | No | No | No | No | Yes | No | No | Yes | Yes |
| Low    | Micronutrient Intake and Risk of Hematological Malignancies in Adults: A Systematic Review and Meta-analysis of Cohort Studies. | Psaltopoulou 2018 | Yes | Partial Yes | Yes | No | Yes | Yes | No | Yes | Yes | No | Yes | No | No | No | Yes | Yes |
| Low    | Risk of childhood cancer and adult lung cancer after childhood exposure to passive smoke: A meta-analysis. | Boffetta 2000 | No | No | NA | No | No | No | Yes | No | No | Yes | No | No | No | Yes | No | No |
| Low    | Hepatitis B virus and risk of non-Hodgkin lymphoma: An updated meta-analysis of 58 studies. | Li 2018 | Yes | No | NA | No | Yes | Yes | No | No | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes |
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|-------------------|-----------------------------------------------------------------------|-------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low    | A systematic review of epidemiologic studies of styrene and cancer. | Collins 2018            | Yes    | No     | NA     | No     | Yes    | Ye     | No     | Parti  | Yes    | No     | No     | No     | No     | Ye     | Yes    | Ye     |
| Critically low    | Risk of malignancy in Behcet disease: A meta-analysis with systematic review. | Wang 2019               | Yes    | No     | NA     | Ye     | Ye     | No     | Ye     | No     | Yes    | No     | No     | No     | No     | Ye     | Yes    | Ye     |
| Critically low    | Alcohol drinking and non-Hodgkin lymphoma risk: a systematic review and a meta-analysis. | Tramacere 2012          | No     | No     | NA     | Ye     | Ye     | No     | Ye     | No     | Yes    | No     | No     | No     | No     | Yes    | Yes    | Ye     |
| Critically low    | Cancer incidence and mortality among firefighters.                  | Jalilian 2019           | Yes    | No     | NA     | Ye     | Ye     | No     | Ye     | No     | Yes    | No     | No     | No     | No     | Yes    | Yes    | No     |
| Critically low    | Risk of Lymphoma in Patients With Inflammatory Bowel Disease Treated With Anti-tumour Necrosis Factor Alpha Agents: A Systematic Review and Meta-analysis. | Yang 2018               | Yes    | No     | Ye     | Ye     | Ye     | Yes    | No     | Yes    | No     | No     | No     | No     | No     | Ye     | Yes    | Yes    |
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|-----------------|-----------------------------------------------------------------------|-------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low  | A Meta-Analysis on the Relationship Between Hair Dye and the Incidence of Non-Hodgkin's Lymphoma. | Qin 2019    | No     | No     | NA     | Partial Yes | Yes     | Yes     | No     | Yes     | No     | Yes     | No     | Yes     | Yes     | No     | Yes     | Yes     |
| Critically low  | Association between Parkinson's Disease and Risk of Cancer: A PRISMA-compliant Meta-analysis. | Zhang 2019  | Yes    | No     | NA     | Partial Yes | No     | No     | No     | Partial Yes | No     | No     | Yes     | No     | Yes     | Yes     | Yes     | Yes     |
| Critically low  | Association between type 1 and type 2 diabetes and risk of non-Hodgkin's lymphoma: A meta-analysis of cohort studies. | Wang 2020   | No     | No     | NA     | No     | Yes     | Yes     | No     | Yes     | No     | Yes     | No     | Yes     | Yes     | Yes     | Yes     | Yes     |
| Moderate        | Association between Bacillus Calmette-Guerin (BCG) vaccination and lymphoma risk: A systematic review and meta-analysis. | Salmon 2020 | No     | Partial Yes | Ye s     | Partial Yes | No     | Ye s     | Yes     | Ye s     | Yes     | Ye s     | Yes     | Ye s     | Yes     | Ye s     | Yes     | Yes     |
### Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Rating          | Title                                                                 | Author                      | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|-----------------|----------------------------------------------------------------------|-----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low  | Prevalence, Incidence, and Risk of Cancer in Patients With Psoriasis and Psoriatic Arthritis: A Systematic Review and Meta-analysis. | Vaengebjerg 2020            | Yes    | Partial Yes | NA    | No     | Yes    | No     | No     | Yes    | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    |
| Critically low  | Human Pegivirus Infection and Lymphoma Risk: A Systematic Review and Meta-analysis. | Fama 2020                   | Yes    | No     | NA     | No     | Yes    | No     | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    |
| Critically low  | Sarcoidosis and Cancer Risk Systematic Review and Meta-analysis of Observational Studies | Bonifazi 2015               | No     | No     | NA     | No     | Yes    | No     | Yes    | No     | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    |
| High            | Cancer incidence attributable to tuberculosis in 2015: global, regional, and national estimates | Leung 2020                  | Yes    | Partial Yes | NA    | Partial Yes | Yes    | Yes    | Yes    | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    |
| Critically low  | Non-hodgkin lymphoma and occupational exposure to | Schinasi 2014               | No     | No     | NA     | No     | No     | No     | Yes    | No     | No     | No     | Yes    | No     | No     | Yes    | No     | Yes    |

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| Rating     | Title                                                                 | Author        | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|------------|-----------------------------------------------------------------------|---------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low | Agricultural pesticide chemical groups and active ingredients: A systematic review and meta-analysis | Buja 2006 | No     | No     | No     | Partial Yes | No     | No     | No     | No     | No     | No     | Yes     | No     | No     | Yes     | No     | No     |
| Low        | Cancer incidence among female flight attendants: a meta-analysis of published data. | Jephcote 2020 | Yes    | Partial Yes | NA    | Partial Yes | Yes    | Yes    | No     | Partial Yes | Yes | No     | Yes     | Yes     | Yes     | Yes     | Yes     |
| Critically low | Association Between Night-Shift Work and Cancer Risk: Updated Systematic Review and Meta-Analysis | Dun 2020 | Yes    | No     | NA    | No     | Yes    | Yes    | No     | No     | No     | Yes     | Yes     | Yes     | Yes     | Yes     | Yes     | Yes     |
| Critically low | Risk of cancer among hairdressers and | Takkouche 2009 | Yes    | No     | NA    | Yes    | Yes    | No     | No     | No     | Yes     | No     | Yes     | Yes     | Yes     | Yes     | Yes     | Yes     | Yes     |
## Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Rating         | Title                                                                 | Author                | Year      | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|----------------|----------------------------------------------------------------------|-----------------------|-----------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low | Occupational exposure to gasoline and the risk of non-Hodgkin lymphoma: a review and meta-analysis | Kane 2010             | Yes       | No     | NA     | No     | No     | No     | No     | No     | No     | No     | No     | Yes    | Yes    | Yes    | Yes    | Yes    |
| Critically low | Borrelia burgdorferi in primary cutaneous lymphomas: a systematic review and meta-analysis | Travaglino 2020       | No        | No     | NA     | Partial | Yes    | No     | Yes    | Partial | Yes    | Yes    | No     | Yes    | No     | Yes    | No     | Yes    |
| Moderate       | Use of insulin and insulin analogs and risk of cancer - systematic review and meta-analysis of observational studies | Karlstad 2013         | Yes       | Partial | Yes    | Partial | Yes    | Yes    | Partial | Yes    | Yes    | No     | Yes    | No     | Yes    | No     | Yes    | Yes    |
| Critically low | Obesity and risk of non-Hodgkin's lymphoma: a meta-analysis          | Larsson 2007          | Yes       | No     | NA     | No     | No     | No     | Partial | Yes    | Partial | Yes    | No     | No     | Yes    | No     | Yes    | No     | No     |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Rating          | Title                                                                 | Author year | Item 1 | Item 2 | Item 3 | Item 4  | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|-----------------|-----------------------------------------------------------------------|-------------|--------|--------|--------|---------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Critically low  | Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies | Castillo 2014 | Yes    | No     | NA     | Partial Yes | No     | No     | No     | Yes    | No     | Yes    | No     | No     | No     | Yes    | Yes    |
| Critically low  | Obesity but not overweight increases the incidence and mortality of leukemia in adults: A meta-analysis of prospective cohort studies | Castillo 2012 | Yes    | No     | NA     | Partial Yes | Yes    | Yes    | No     | Yes    | No     | Yes    | No     | Yes    | No     | Yes    | Yes    |
| Critically low  | Increased incidence of non-Hodgkin lymphoma, leukemia, and myeloma in patients with diabetes mellitus type 2: a meta-analysis of observational studies | Castillo 2012 | Yes    | No     | NA     | Partial Yes | No     | No     | No     | Yes    | No     | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    |
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| Rating       | Title                                                                 | Author     | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8  | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|--------------|----------------------------------------------------------------------|------------|--------|--------|--------|--------|--------|--------|--------|---------|--------|---------|---------|---------|---------|---------|---------|---------|
| Critically low | Hepatitis C virus and risk of lymphoma and other lymphoid neoplasms: a meta-analysis of epidemiologic studies | DalMaso 2006 | Yes    | No     | NA     | No     | No     | No     | No     | Partial Yes | No     | Yes     | No      | No      | Yes     | No      | No      | No      |

Note:
Question 2, 4, 7, 9, 11, 13, 15 are critical domains as suggested in the guidance document of AMSTAR 2
### eTable 7: Consistency between meta-analyses of summary level data and meta-analyses of individual participant data

| Exposure [NHL subtype] | Effect estimate (95% CI) | Exposure [NHL subtype] in pooled analyses | Pooled analysis effect estimates (95% CI) | Same direction | Overlapping confidence interval | Level of statistical significance (P<0.05) | Class of association | At least one-third of studies overlapping across both meta-analyses |
|------------------------|-------------------------|------------------------------------------|------------------------------------------|----------------|-------------------------------|---------------------------------|-------------------|---------------------------------------------------------------|
| Red blood cell transfusion [NHL] | RR 1.2 (1.07, 1.35) | History of blood transfusion [NHL] | OR 0.83 (0.77, 0.91) | No | No | Both | IV | Yes |
| Red blood cell transfusion [CLL/SLL] | RR 1.66 (1.08, 2.56) | History of blood transfusion [CLL/SLL] | OR 0.79 (0.66, 0.94) | No | No | Both | IV | Yes |
| Red blood cell transfusion [FL] | RR 1.02 (0.67, 1.55) | History of blood transfusion [FL] | OR 0.79 (0.66, 0.94) | No | Yes | Pooled analysis only | NS | Yes |
| Red blood cell transfusion [DLBCL] | RR 1.06 (0.86, 1.3) | History of blood transfusion [DLBCL] | OR 0.84 (0.75, 0.95) | No | Yes | Pooled analysis only | NS | Yes |
| Ever smoking [NHL] | RR 1.05 (1.00, 1.09) | Any smoking [NHL] | OR 1.02 (0.97, 1.07) | Yes | Yes | Neither | IV | No |
| Ever smoking [DLBCL] | RR 1.01 (0.95, 1.07) | Any smoking [DLBCL] | OR 1.01 (0.94, 1.08) | Yes | Yes | Neither | NS | No |
| Ever smoking [FL] | RR 1.05 (0.88, 1.25) | Any smoking [FL] | OR 1.09 (1.00, 1.18) | Yes | Yes | Neither | NS | Yes |
| Ever smoking [CLL/SLL] | RR 0.96 (0.89, 1.04) | Any smoking [CLL/SLL] | OR 0.9 (0.81, 0.99) | Yes | Yes | Pooled analysis only | NS | Yes |
| Ever smoking [TCL] | RR 1.23 (1.06, 1.43) | Any smoking [TCL] | OR 1.32 (1.09, 1.59) | Yes | Yes | Both | IV | No |
### Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Exposure [NHL subtype] | Effect estimate (95% CI) | Exposure [NHL subtype] in pooled analyses | Pooled analysis effect estimates (95% CI) | Concordance | Class of association | At least one-third of studies overlapping across both meta-analyses |
|------------------------|--------------------------|------------------------------------------|------------------------------------------|-------------|---------------------|------------------------------------------------------------------|
| Ever drinking [NHL]    | RR 0.85 (0.79, 0.91)     | Any alcohol [NHL]                        | OR 0.87 (0.81, 0.93)                    | Yes         | Both                | Yes                                                              |
| Ever drinking [TCL]    | RR 0.78 (0.58, 1.05)     | Any alcohol [TCL]                        | OR 0.68 (0.53, 0.87)                    | Yes         | Pooled analysis only | Yes                                                              |
| Ever drinking [DLBCL]  | RR 0.79 (0.68, 0.91)     | Any alcohol [DLBCL]                      | OR 0.81 (0.73, 0.89)                    | Yes         | Both                | IV                                                               |
| Ever drinking [FL]     | RR 0.8 (0.69, 0.92)      | Any alcohol [FL]                         | OR 0.86 (0.77, 0.96)                    | Yes         | Both                | IV                                                               |
| Ever drinking [CLL/SLL]| RR 1 (0.8, 1.26)         | Any alcohol [CLL/SLL]                    | OR 1.04 (0.9, 1.19)                     | Yes         | Neither             | NS                                                               |
| Pernicious Anaemia [NHL]| RR 1.16 (0.79, 1.71)     | Pernicious anaemia [NHL]                | OR 1.37 (0.62, 3.03)                    | Yes         | Neither             | NS                                                               |
| Rheumatoid Arthritis [NHL]| SIR 2.26 (1.82, 2.81)    | Rheumatoid Arthritis [NHL]              | OR 1.32 (0.99, 1.77)                    | Yes         | Meta-analysis only  | II                                                               |
| Primary Sjogren's Syndrome [NHL]| RR 13.76 (8.53, 18.99) | Sjogren's syndrome [NHL]                | OR 7.52 (3.68, 15.36)                   | Yes         | Both                | II                                                               |
| Systemic Lupus Erythematosus [NHL]| RR 5.4 (3.75, 7.77) | Systemic Lupus Erythematosus [NHL] | OR 2.83 (1.81, 4.11)                    | Yes         | Both                | II                                                               |
| Psoriasis [NHL]        | RR 1.48 (1.3, 1.69)      | Psoriasis [NHL]                         | OR 1.08 (0.9, 1.29)                     | Yes         | Meta-analysis only  | III                                                              |

Note: The table continues with similar entries for other exposures.
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Exposure [NHL subtype] | Effect estimate (95% CI) | Exposure [NHL subtype] in pooled analyses | Pooled analysis effect estimates (95% CI) | Concordance | Overlapping confidence interval | Level of statistical significance (P<0.05) | Class of association | At least one-third of studies overlapping across both meta-analyses |
|-------------------------|--------------------------|------------------------------------------|------------------------------------------|-------------|--------------------------------|-------------------------------------------|---------------------|-----------------------------------------------|
| Type 1 diabetes [NHL]   | RR 1.55 (1.15, 2.08)     | Type 1 diabetes [NHL]                    | OR 1.15 (0.8, 1.66)                      | Yes         | Yes                            | Meta-analysis only                       | IV                  | No                                            |
| Celiac disease [NHL]    | OR 2.61 (2.04, 3.33)     | Celiac disease [NHL]                     | OR 1.77 (1.05, 2.99)                     | Yes         | Yes                            | Both                                      | II                  | Yes                                           |
| Celiac disease [TCL]    | OR 15.84 (7.85, 31.94)   | Celiac disease [TCL]                     | OR 14.82 (7.27, 30.19)                   | Yes         | Yes                            | Both                                      | II                  | Yes                                           |
| Celiac disease [DLBCL]  | OR 2.25 (1.32, 3.85)     | Celiac disease [DLBCL]                    | OR 2.09 (1.04, 4.18)                     | Yes         | Yes                            | Both                                      | IV                  | Yes                                           |
| Celiac Disease [CLL]    | OR 0.80 (0.46, 1.38)     | Celiac disease [CLL/SLL]                  | OR 0.6 (0.14, 2.61)                      | Yes         | Yes                            | Neither                                   | NS                  | Yes                                           |
| Sarcoidosis [NHL]       | RR 1.43 (1.03, 1.99)     | Sarcoidosis [NHL]                        | OR 0.71 (0.39, 1.29)                     | No          | Yes                            | Neither                                   | IV                  | No                                            |
| Tuberculosis [NHL]      | RR 1.61 (1.34, 1.94)     | Adult Tuberculosis infection [NHL]        | OR 1.16 (0.96, 1.39)                     | Yes         | Yes                            | Meta-analysis only                        | II                  | No                                            |
| Herpes Zoster [NHL]     | RR 1.72 (1.27, 2.32)     | Adult shingles [NHL]                      | OR 1.05 (0.93, 1.19)                     | Yes         | No                             | Meta-analysis only                        | III                 | No                                            |
| Hepatitis C virus [NHL] | OR 3.36 (2.4, 4.72)      | Hepatitis C virus [NHL]                   | OR 1.81 (1.39, 2.37)                     | Yes         | No                             | Both                                      | II                  | No                                            |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Exposure [NHL subtype] | Effect estimate (95% CI) | Exposure [NHL subtype] in pooled analyses | Pooled analysis effect estimates (95% CI) | Same direction | Overlapping confidence interval | Level of statistical significance (P<0.05) | Class of association | At least one-third of studies overlapping across both meta-analyses |
|-----------------------|--------------------------|------------------------------------------|------------------------------------------|---------------|---------------------------------|------------------------------------------|---------------------|---------------------------------------------------------------|
| Hepatitis C virus [DLBCL] | OR 2.65 (1.88, 3.74) | hepatitis C virus [DLBCL] | OR 2.33 (1.71, 3.19) | Yes | Yes | Both | IV | Yes |
| Hepatitis C virus [FL] | OR 2.73 (2.2, 3.38) | Hepatitis C virus [FL] | OR 0.57 (0.3, 1.1) | No | No | Metanalysis only | IV | Yes |
| Hepatitis C virus [MZL] | OR 3.41 (2.39, 4.87) | Hepatitis C virus [MZL] | OR 3.04 (1.65, 5.6) | Yes | Yes | Both | IV | Yes |
| Hepatitis C virus [CLL/SLL] | OR 1.65 (1.35, 2.02) | Hepatitis C virus [CLL/SLL] | OR 2.08 (1.23, 3.49) | Yes | Yes | Both | IV | Yes |
| Farmer [NHL] | RR 1.11 (1.05, 1.17) | Farmer [NHL] | OR 1.03 (0.95, 1.13) | Yes | Yes | Neither | III | No |
| Firefighter [NHL] | SIR 1.07 (0.96, 1.20) | Firefighter [NHL] | OR 0.76 (0.53, 1.09) | No | Yes | Neither | NS | No |
| Hairdresser [NHL] | RR 1.11 (0.94, 1.32) | Hairdressers [NHL] | OR 1.21 (0.96, 1.52) | Yes | Yes | Both | NS | No |
| Petroleum Refinery Worker [NHL] | RR 0.98 (0.89, 1.09) | Petroleum workers [NHL] | OR 0.79 (0.38, 1.67) | Yes | Yes | Neither | NS | No |
| Teacher [NHL] | RR 1.47 (1.34, 1.61) | Teacher [NHL] | OR 0.89 (0.81, 0.98) | No | No | Both | II | No |
| Meat worker [NHL] | RR 0.99 (0.77, 1.29) | Meat worker [NHL] | OR 1.08 (0.81, 1.42) | No | Yes | Neither | NS | No |
| Printer [NHL] | RR 1.86 (1.38, 2.50) | Printers [NHL] | OR 0.95 (0.78, 1.17) | No | No | Metanalysis only | III | No |
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| Exposure [NHL subtype] | Effect estimate (95% CI) | Exposure [NHL subtype] in pooled analyses | Pooled analysis effect estimates (95% CI) | Same direction | Overlapping confidence interval | Level of statistical significance (P<0.05) | Class of association | At least one-third of studies overlapping across both meta-analyses |
|------------------------|--------------------------|------------------------------------------|------------------------------------------|----------------|-------------------------------|------------------------------------------|---------------------|---------------------------------------------------------------|
| Wood worker [NHL]      | RR 1.04 (0.79, 1.37)     | Wood workers [NHL]                       | OR 1.04 (0.89, 1.22)                     | Yes            | Yes                           | Neither                                  | IV                  | No                                                            |
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eFigure 1

Supplement Figure 1: Scatterplot of summary effect estimates in meta-analyses of summary level data and meta-analyses of IPD (pooled analyses) reporting the same associations between environmental risk factors and non-Hodgkin lymphoma

CI=confidence interval.
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eText 1: eligibility criteria
Supplements of Eligibility criteria for systematic reviews and (or) meta-analyses

**General inclusion criteria**

Language: English only.

Study types: Systematic review and (or) meta-analysis (referred as ‘Review studies’ in the following contents).

Study designs included in review studies: Observational epidemiological studies¹.

Study subjects: Human only².

**General exclusion criteria**

Review studies that:

1. Focus on **genetic risk factors**³ for non-Hodgkin lymphoma (NHL)
2. Focus on **biomarkers**⁴ for NHL
3. Focus on risk factors for **treatment, relapse, remission, or prognosis** on NHL patients
4. Examine NHL as a risk factor for other diseases
5. Focus on cancer, hematological cancers, lymphoma, or any broader spectrum of diseases, but fail to provide specific data for NHL⁵
6. Only include experimental studies
7. Focus on NHL as a **metastasis/secondary cancer** of other primary cancers
8. Focus on NHL in a particular population but fail to provide detailed information on environmental risk factors⁶
9. Investigate the prevalence/incidence of NHL

Besides the aforementioned eligibility criteria, based on our definition of environmental risk factors, personal medical history and comorbidities (excluding metastasis of tumors) will be considered eligible in our study. In addition to the 8th General exclusion criteria,³⁹

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¹ Cohort studies or case control studies only
² Review studies mixed with human and animal subjects will be checked in details at full text screening stage
³ Including genetic polymorphisms, family history/familial aggregation
⁴ Any substance, structure, or process that can be measured in the body or its products that can influence or predict the incidence of outcome or disease. Ref: http://www.inchem.org/documents/ehc/ehc/ehc222.htm (accessed 24th April, 2020)
⁵ This may be unclear at the title-abstract screening, therefore when in doubt, two researchers will send it on to the full text screening
⁶ For example, NHL in indigenous population, or men who have sex with men (MSM)
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studies focus on NHL on a particular occupational population would be included since occupation can act as proxy for certain environmental exposures.

Study types, exposures and outcome definition

Systematic reviews and (or) Meta-analyses of summary level data and individual participant data:

The eligible study types in our study are systematic reviews (SRs), meta-analyses (MAs), systematic reviews and meta-analyses (SRMAs) or pooled analyses. To be eligible, SRs and SRMAs must have performed a systematic search in at least one bibliographic database. SRs, MAs and SRMAs should clearly define themselves as systematic reviews and/or meta-analyses. For SRs in particular, we will only include exposure-outcome relationships (i.e., associations) that have not been investigated in MAs or SRMAs.

In terms of pooled analyses, the primary goal for including pooled analyses in our study is to incorporate the valuable pooled information of individual level data from scientific institutes on NHL and its subtypes, such as The International Lymphoma Epidemiology Consortium (InterLymph) and to add to the evidence for meta-analyses on certain risk factors.

Environmental risk factors:

We define environmental risk factors as a broad concept of non-genetic factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors that can affect a person’s health, as environmental risk factors.

Outcome of interest:

Our study outcome is non-Hodgkin lymphoma, including its subtypes (eTable 2 in Supplement 1). The classification of NHL subtypes was consulted and confirmed by an epidemiologist on NHL from InterLymph consortia.

We will identify with the definition/diagnostic criteria of NHL from the original review studies.

References

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An open scientific forum for epidemiologic research in non-Hodgkin's lymphoma and a group of international investigators who have completed or have ongoing case-control studies and who discuss and undertake research projects that pool data across studies or otherwise undertake collaborative research. Ref: https://epi.grants.cancer.gov/interlymph/ (accessed 24th April, 2020)
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4. Prüss-Ustün A, van Deventer E, Mudu P, et al. Environmental risks and non-communicable diseases. *BMJ*. 2019;364:l265.

**eText 2**

**Systematic reviews**

We identified 8 systematic reviews without quantitative synthesis with 8 unique associations that were not investigated by meta-analyses of the published literature (Supplement). Among them, 6 (75.0%) concluded that there were weak or non-statistically significant associations between the examined risk factors (Omega-3 fatty acids, sugar intake, artificial sweetener consumption, hazardous waste, preterm birth, and prenatal/postnatal Diagnostic X-rays and childhood) and NHL risk. Two (25%) additional systematic reviews suggested possible associations between Gaucher disease and NHL risk and breast implants and anaplastic large cell lymphoma risk. Half (4, 50.0%) of the systematic reviews outlined that quantitative analyses were not conducted due to high levels of heterogeneity and/or a small number of eligible studies. The remaining 4 (50.0%) systematic reviews did not provide any reasons for not conducting quantitative analyses.

**Exclusion reasons**

Among the 1024 records screened at the full text level, 904 were excluded, mostly because they were for the wrong topic (442, 48.9%), they had the wrong study design (240, 26.5%), or they were not the largest meta-analysis of the published literature for a specific association (102, 11.3%).

**References**

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7. Arends M, van Dussen L, Biegstraaten M, Hollak CE. Malignancies and monoclonal gammopathy in Gaucher disease; a systematic review of the literature. British journal of haematology. 2013 Jun;161(6):832-42.

8. Kim B, Roth C, Chung KC, Young VL, van Busum K, Schnyer C, Mattke S. Anaplastic large cell lymphoma and breast implants: a systematic review. Plastic and reconstructive surgery. 2011 Jun 1;127(6):2141-50.
| Title                                                                 | Authors                                                                 | Published Year | Journal                                      | Volume | Issue | Pages       |
|----------------------------------------------------------------------|------------------------------------------------------------------------|----------------|----------------------------------------------|--------|-------|-------------|
| Body mass inuncio, Kai; Li, Fe                                        |                                                                        | 2017           | European journal                          | 26     | 1     | 94-105      |
| Do polychlorirZani, Claudia;                                          |                                                                        | 2017           | Chemosphere                                 | 183    | b4d   | 0320657 97-106 |
| CARING (CAncStarup-Linde);                                            |                                                                        | 2013           | Current drug issues                        | 8      |       | 296-332    |
| Effect of hepaMatsoo, Keita;                                          |                                                                        | 2004           | Cancer science                             | 95     |       | 745-52     |
| Diabetes and iMitr, Joanna;                                           |                                                                        | 2008           | Diabetes care                              | 31     |       | 12 2391-7  |
| A meta-analyseSmitten, Allic;                                         |                                                                        | 2008           | Arthritis resea                            | 10     |       | 2 R45      |
| Consumption Sergenanis, T                                            |                                                                        | 2018           | Leukemia & ly                              | 59     |       | 2 434-447  |
| Alcohol consuPsaltopoulou,                                            |                                                                        | 2018           | International j                            | 143    |       | 3 486-495  |
| Association beYi, Hai-zhen; C                                        |                                                                        | 2014           | Medical oncol                              | 31     |       | 8 84        |
| Agricultural us:Baris, D; Zahm                                        |                                                                        | 1998           | Occupational :                              | 55     |       | 8 522-7    |
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http://dx.doi.org/10.1016/s0001-4079(19)30406-6
Lepre 2019
Exclusion reason: Non-English;
10.1684/ERS.2020.1495
Lefranc 2020
Exclusion reason: Non-English;
10.1007/s10269-013-2261-2 Ancellin 2013 Exclusion reason: Non-English;
http://dx.doi.org/Lemogne 2011 Exclusion reason: Non-English;
Title
Postmenopausal hormone therapy and non-Hodgkin lymphoma: a pooled analysis from the InterLymph Non-Hodgkin Lymphoma Subtypes Project.

Occupational exposure to trichloroethylene and the risk of non-Hodgkin lymphoma: a pooled analysis from the InterLymph Non-Hodgkin Lymphoma Subtypes Project.

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Medical history, lifestyle, family history, and occupational risk factors for mycosis fungoides and Sézary syndrome: the InterLymph Non-Hodgkin Lymphoma Subtypes Project.

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Occupational exposure to trichloroethylene and risk of non-Hodgkin lymphoma and its major subtypes: a pooled InterLymph analysis.

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Cancer in British vegetarians: updated analyses of 4998 incident cases in a cohort of 32,491 meat eaters, 8612 fish eaters, 18,298 vegetarians, and 2246 vegans.

Parental age and risk of childhood cancer: a pooled analysis from the International Lymphoma Epidemiology Consortium (InterLymph).

Lifestyle and risk of follicular lymphoma: a systematic review.

Dietary trans-fatty acid intake in relation to cancer risk: a systematic review.

Sunlight exposure in association with risk of lymphoid malignancy: a meta-analysis of observational studies.

Dietary trans-fatty acid intake in relation to cancer risk: a systematic review.

Lifestyle and risk of follicular lymphoma: a systematic review.

Cigarette smoking and risk of non-Hodgkin lymphoma: a pooled analysis from the InterLymph Non-Hodgkin Lymphoma Subtypes Project.

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| Slager 2014    |
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| Monnereau 2014 |
| de Sanjose 2008|
| Kane 2012      |
| Becker 2012    |
| Kricker 2008   |
| t Mannetje 2016|
| Mbulaiteye 2014|
| Wang 2014      |
| Aschebrook-Kilfoy 2014 |
| Bracci 2014    |
| Smedby 2014    |
| Vajdic 2014    |
| Linet 2014     |
| Cerhan 2014    |
| Morton 2005    |
| Cerhan 2019    |
| Ekstrom 2008   |
| Vajdic 2009    |
| Morton 2005    |
| Key 2014       |
| Johnson 2009   |
| Moore 2016     |
| Kane 2010      |
| Antonopoulos 2011 |
| Odutola 2020   |
| Michels 2021   |
| Kim 2021       |
| Kane 2011      |
| Scott 2011     |
| Davies 2020    |
| Castillo 2010  |
| Odutola 2021   |
| Kotei 2021     |
| Tio 2012       |
| Lo 2021        |
| Liang 2012     |
| Prego-Dominguez 2021 |
| Year       | Author                      |
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| 2007       | Bernatsky                   |
| 2013       | Sergentanis                 |
| 2021       | Boffetta                    |
| 2013       | Chen                        |
| 2007       | Boffetta                    |
| 2005       | Martin                      |
| 2013       | Zhang                       |
| 2013       | Liu                         |
| 2014       | Liang                       |
| 2005       | Kandiel                     |
| 2015       | Zheng                       |
| 2015       | Teras                       |
| 2015       | Cobucci                     |
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| 2015       | Simon                       |
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| 2015       | Yang                        |
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| 2017       | Wang                        |
| 2019       | Catalani                    |
| 2019       | Masarone                    |
| 2019       | Mirtavoos-Mahyari           |
| 2015       | Cao                         |
| 2016       | Caini                       |
| 2016       | Wang                        |
| 2016       | Luo                         |
| 2016       | Xie                         |
| 2016       | Xu                          |
| 2017       | Ye                          |
| 2017       | Dong                        |
| 2017       | Schmidt                     |
| 2017       | Chen                        |
| 2017       | Han                         |
| 2016       | Alicandro                   |
| 2016       | Deng                        |
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| 2018       | Lahner                      |
| 2017       | Smith                       |
| 2018       | Schnatter                   |
| 2018       | O'Sullivan                  |
| 2018       | Psaltopoulou                |

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Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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Abstract

Objectives: To summarize the range, strength, and validity of reported associations between environmental risk factors and non-Hodgkin lymphoma (NHL), and to evaluate the concordance between associations reported in meta-analyses (MAs) of summary level data and MAs of individual participant data (IPD).

Design: Umbrella review.

Data sources: MEDLINE, Embase, Scopus, Web of Science Core Collection, Cochrane Library, and Epistemonikos from inception to 23 July 2021.

Eligibility criteria: English language MAs of summary level data and MAs of IPD evaluating associations between environmental risk factors and incident NHL (overall and NHL subtypes).

Data extraction and synthesis: Summary effect estimates from MAs of summary level data were re-estimated using a random-effects model and classified as presenting non-significant, weak ($P<0.05$), suggestive ($P<10^{-3}$ and >1000 cases), highly suggestive ($P<10^{-6}$, >1000 cases, largest study reporting a significant association), or convincing ($P<10^{-6}$, >1000 cases, largest study reporting a significant association, $P^2<50\%$, 95% prediction interval excluding the null value, and no evidence of small study effects and excess significance bias) evidence. When the same exposures, exposure contrast levels, and outcomes were evaluated in MAs of summary level data and MAs of IPD from the International Lymphoma Epidemiology (InterLymph) Consortium, concordance in terms of direction, level of significance, and overlap of 95% confidence intervals (CI) was examined. We assessed the methodological quality of the MAs of summary level data using the A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2 tool.

Results: We identified 85 MAs of summary level data reporting 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. Most (225, 88.7%) associations presented either non-significant or weak evidence. The 11 (4.3%) associations presenting highly suggestive evidence were primarily for autoimmune or infectious disease-related risk factors. Only 1 association, history of celiac disease and risk of NHL, presented convincing evidence. Overall, 40 associations reported in MAs of summary level data were also evaluated in InterLymph MAs of IPD. Of these, 22 (55.6%) pairs were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. There were 28 (70.6%) pairs where the summary effect sizes from the MAs of IPD were more conservative. Nearly all (79/85, 92.9%) MAs of summary level data were classified as having critically low quality.
Conclusion: This umbrella review suggests that there is a mass production of low-quality MAs of summary level data, many of which report weak associations between environmental risk factors and NHL, and highlights the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.

Systematic review registration PROSPERO CRD42020178010.
What is already known on this topic

- Observational studies have suggested that environmental risk factors, including clinical, occupational, and lifestyle exposures, may be associated with the risk of developing non-Hodgkin lymphoma.
- As a result of the large number of observational studies evaluating the impact of environmental risk factors on non-Hodgkin lymphoma, dozens of systematic reviews and meta-analyses of summary and individual participant level data have focused on synthesizing evidence and identifying potential risk factors.
- Little is known about: (1) the range, strength, and validity of associations between environmental risk factors and non-Hodgkin lymphoma reported in meta-analyses or (2) the concordance between meta-analyses of summary level data and meta-analyses of individual participant data evaluating the same associations.

What this study adds

- This umbrella review suggests that although a large range of environmental risk factors for non-Hodgkin lymphoma have been evaluated in meta-analyses, the vast majority of meta-analyses of summary level data are low quality and present either non-significant or weak associations.
- Overall, only half of the associations that were evaluated in both meta-analyses of summary level data and meta-analyses of individual participant data were in the same direction, had the same level of statistical significance, and had overlapping 95% confidence intervals.
- Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, this umbrella review highlights the need for improving not only primary studies but also evidence synthesis in the field of non-Hodgkin lymphoma etiology.
Introduction

Non-Hodgkin lymphoma (NHL), a lymphoid cancer that originates in white blood cells called lymphocytes, is the 9th leading cause of cancer death among both men and women.\(^1\) NHL accounts for nearly 90% of all lymphomas\(^2\) and is the most common hematologic malignancy in the world.\(^3\)

Although NHL can be broadly categorized into two major groups (i.e., B-cell, T-cell/natural killer-cell lymphomas), it represents a diverse group of malignant disorders with dozens of subtypes.\(^4\)

Evidence suggests that NHL is more common among older adults, men, and people with a first degree relative with NHL.\(^5,6\) However, despite substantial effort to identify NHL causes and risk factors over the past few decades, the exact etiology of NHL is unknown.\(^5\)

Epidemiological studies have suggested that environmental risk factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors, may be associated with the risk of developing NHL. In particular, several prominent potential risk factors proposed in the literature include viruses (e.g., Epstein-Barr virus infection),\(^7\) autoimmune diseases (e.g., Sjogren’s syndrome, celiac disease, and rheumatoid arthritis),\(^8-10\) and immune dysregulation (i.e., patients with a history of organ transplantation, acquired immunodeficiency syndromes (HIV/AIDS), or immunosuppressive medication treatment).\(^5,6,11\) However, given that these exposures and conditions are relatively rare,\(^11\) a broad range of additional environmental risk factors, including exposure to insecticides,\(^12\) red and processed meat consumption,\(^13\) and hair dye,\(^14\) have been evaluated and proposed as potential risk factors.

As a result of the large number of observational studies evaluating the impact of environmental risk factors on NHL, dozens of systematic reviews and meta-analyses (MAs) of summary level data have focused on synthesizing evidence and identifying the most promising risk factors. Moreover, the International Lymphoma Epidemiology (InterLymph) Consortium,\(^15\) a group of investigators who pool data from their completed or ongoing NHL case-control studies, have published multiple MAs of individual participant data (IPD) evaluating associations between various environmental risk factors and NHL.\(^16-18\) Although these MAs of IPD contain thousands of NHL cases and are strengthened by their ability to utilize raw data that are harmonized across multiple studies, they do not include evidence from case-control and cohort studies conducted by investigators outside of the InterLymph Consortium. Therefore, MAs of summary level data and MAs of IPD evaluating the same associations between environmental risk factors and NHL may sometimes lead to discordant results and conclusions.
To provide an overview of the range, strength, and validity of reported associations between environmental risk factors and NHL, we conducted an umbrella review of the evidence across published systematic reviews and MAs. In addition to summarizing the results, determining hints of biases, and assessing the quality of reviews, we evaluated the consistency between all associations reported in both MAs of summary level data and InterLymph MAs of IPD.

**Methods**

We conducted an umbrella review on the reported associations between environmental risk factors and the risk of NHL. Umbrella reviews are used to systematically identify and evaluate evidence reported in published systematic reviews and MAs.\(^\text{19,20}\) Our study protocol was pre-registered on the International prospective register of systematic reviews (CRD42020178010) and posted on Open Science Framework (https://osf.io/6g2ev/). We did not involve patients or members of the public when designing the question and study, interpreting the results, and/or drafting the manuscript.

**Database searches**

Working with an experienced medical librarian (KN), we developed and performed a comprehensive search of multiple databases: MEDLINE (Ovid), Embase (Ovid), Scopus, Web of Science Core Collection (as licensed at Yale University), Cochrane Library, and Epistemonikos from inception to July 24th, 2020 (eTable 1 in Supplement 1). In each database, we used three concepts: NHL, risk factors, and the study designs of interest (MAs, systematic reviews, and pooled analyses). The search strategy for NHL was based on the search strategy used in a published review.\(^\text{21}\) The study design search strategy used elements from a published search filter.\(^\text{22}\) Database limits were used to exclude conference papers and meeting abstracts. No language limits were used. Records were deduplicated in EndNote, the Yale Reference Deduplicator, and Covidence.

No citation chaining was conducted.

On July 24th, 2020, searches were run in each database and 14,753 references were identified. After deduplication in EndNote and Covidence, 8025 unique records were uploaded for screening. On July 23rd, 2021, all searches were rerun and deduplicated and 969 additional unique records were added to Covidence for manual screening. In total, our search retrieved 8994 unique records across all databases.

**Eligibility criteria**
We included English language systematic reviews, MAs of summary level data (i.e., MAs using effect estimates reported in individual studies), and MAs of IPD of observational studies evaluating associations between environmental risk factors and incident NHL (overall or any subtypes, eTable 2 in Supplement 1). We considered all non-genetic factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors that can affect a person’s health, as environmental risk factors. Systematic reviews and MAs were excluded if they primarily focused on genetic risk factors, evaluated risk factors for the treatment, relapse, remission, or prognosis of NHL patients, or examined NHL as a risk factor for other diseases (eText Table 3 in Supplement 1).

Two reviewers (XS and HZ) independently screened the titles and abstracts and then full-text versions of potentially eligible articles. Any disagreements or uncertainties were discussed with a third reviewer (JDW).

Data extraction

Data extraction was performed independently by two reviewers (XS and HZ), and a third reviewer (JDW) arbitrated all potential discrepancies. For each systematic review and MA, we recorded the first author, year of publication, article title, journal of publication, study design, population, examined exposures and their definitions, and examined outcomes and their definition (i.e., NHL or NHL subtypes). For all MAs of summary level data, we identified each unique exposure-outcome relationship and recorded the number of studies included, total sample size, number of cases, and study-specific adjusted relative risk estimates (e.g., relative risks, hazard ratios, or odds ratios) and corresponding 95% confidence intervals (CIs). For studies that considered multiple exposure contrast levels, control groups, and/or confounders, we prioritized the effect estimates comparing ever versus never exposure that were adjusted for the largest number of potential confounders. Whenever ever versus never exposures comparisons were not reported, we recorded the effect estimates comparing the highest versus lowest levels of exposures. When multiple MAs of summary level data were identified for the same environmental risk factor, we selected the effect estimates that were based on the largest number of component studies.

For systematic reviews with unique associations that were not investigated in MAs of summary level data, we recorded the number of studies identified, the reasons why MAs were not performed, and the main conclusions. Lastly, for all MAs of IPD, one author (JDW) identified the exposures, NHL subtypes, and number of NHL cases for: (1) all nominally statistically significant
(P<0.05) associations and (2) any associations that were also evaluated in MAs of summary level data.

**Statistical analysis**

First, we re-estimated all summary effect estimates and 95% CIs using a random-effects DerSimonian and Laird (DL) estimator. When summary effect estimates were reported without a corresponding P value, we used the 95% CIs to calculate the P value using a previously described method. Next, we categorized the strength of the reported associations across five levels (Table 1), following previously established methodology. All associations with P>0.05 were classified as non-significant. Associations with P<0.05 and fewer than 1000 cases were classified as weak. Associations with P<10^{-3} and at least 1000 cases were classified as suggestive. For associations with P<10^{-6}, at least 1000 cases, and P<0.05 for the largest component study, we sequentially evaluated 95% prediction intervals (PIs), presence of small study effects (Egger regression asymmetry test), and evidence of excess significance using the Ioannidis test. PIs provide a potential range of the true effect and incorporate the uncertainty of whether the observed effect will arise in future studies as well. P<0.1 for Egger’s test suggests the presence of small study effects (i.e. small studies are more prone to report larger or more significant results while larger studies tend to report more conservative results). The Ioannidis test estimates whether the observed number of studies with nominally statistically significant (P<0.05) results in a MA differs from the expected number of studies with nominally statistically significant studies. Associations with 95% PIs including the null, statistically significant Egger’s test (P<0.1), and/or evidence of excess significance were classified as highly suggestive. Associations with 95% prediction intervals excluding the null, non-statistically significant Egger’s test (P>0.1), and no evidence of excess significance were classified as convincing.

Statistical analysis was conducted using metagen package in R version 4.1.0. (eTable 34 in Supplement 1).

**Concordance between MAs of summary level data and InterLymph MAs of IPD**

When the same exposures, exposure contrast levels, and NHL subtypes were examined in MAs of summary level data and InterLymph MAs of IPD, two authors (XS and JDW) determined whether the effect estimates: (1) were in the same direction, (2) had overlapping 95% CIs, and/or (3) had the same level of statistical significance (P<0.05 or P≥0.05). Associations with all three criteria fulfilled were classified as fully concordant. Lastly, we determined how often MAs of summary
level data included at least one-third of the same component studies as the InterLymph MAs of IPD.

Quality Assessment

Four reviewers (XS, HZ, YD, and JDW) evaluated the quality of all MAs of summary level data using A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2. Any discrepancies were discussed and resolved by consensus. Based on the suggested rating scheme, the overall confidence in the results of the MAs of summary level data were classified as high, moderate, low, or critically low.

Results

Literature search

Among 16438 records identified through the literature search, 7444 were excluded as duplicates, leaving 8994 titles and abstract for initial screening. 7970 records were excluded based on the title and abstract, and 1024 records were screened at full text stage for inclusion (Figure 1 and eText 1 in Supplement 1). Overall, our searches identified 85 MAs of summary level data evaluating 134 unique environmental risk factors and 8 systematic reviews evaluating 8 unique risk factors (Figure 1, eText 2 in Supplement 1 and Supplement 23). In addition, we identified 27 MAs of IPD (eXXXX in Supplement 23), of which 24 (89.2%) were conducted by the InterLymph Consortium. More than one MA of summary level data was identified for 44 (44/134, 33.2%) risk factors (eTable 45 in Supplement 1). Among the MAs of summary level data selected based on the largest number of component studies, approximately half were also the most recently published (25/44, 57.6%) (eTable 45 in Supplement 1).

MAs of summary level data

Among the 257 associations reported in the MAs of summary level data, 124 and 133 evaluated the impact of environmental risk factors on the risk of NHL overall and NHL subtypes, respectively. NHL subtypes included follicular lymphoma (FL; 43, 17.6%), diffuse large B-cell lymphoma (DLBCL; 35, 14.2%), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL; 31, 12.4%), T-cell lymphoma (TCL; 12, 5.4%), B-cell lymphoma (BCL; 4, 24.6%), marginal zone lymphoma (MZL; 2, 10.8%), endemic Burkitt Lymphoma (eBL; 1, 0.4%), Burkitt
lymphoma (BL; 1, 0.4%), primary cutaneous lymphoma (PCL; 1, 0.4%). The most common
exposure categories were dietary factors (90, 35.0%), medical histories and comorbidities (54,
31.4%), chemicals and pesticides (42, 16.3%), lifestyle factors (29, 11.3%), drugs, vaccinations,
and medical procedures (30, 12.1%), and occupational (12, 5.4%). The median number of
component studies per MA of summary level data was 5 (IQR 4-10). The median number of NHL
cases, among the 64 (75.3%) MAs reporting this information, was 1533 (IQR, 482-5872).

Credibility criteria
After re-estimating the 257 associations using a random-effects DL estimator and applying the
credibility criteria, 145 (56.4%) were classified as presenting non-significant evidence (Table 3).
There were 80 (31.4%) nominally statistically significant ($P<0.05$) associations that were
classified as presenting weak evidence. There were 20 (7.8%) statistically significant associations
($P<10^{-3}$), based on analyses with at least 1000 NHL cases, that were classified as presenting
suggestive evidence. Only 12 (54.2%) associations were classified as presenting highly suggestive
or convincing evidence, with a $P<10^{-6}$, at least 1000 cases, and a $P<0.05$ for the largest component
study. The 11 highly suggestive associations were for history of renal transplantation and risk of
NHL, rheumatoid arthritis and risk of NHL, primary Sjogren's syndrome and risk of NHL,
systemic lupus erythematosus and risk of NHL, celiac disease and risk of TCL, tuberculosis and
risk of NHL, hepatitis B virus (HBV) and risk of NHL and BCL, hepatitis C virus (HCV) and risk
of NHL and DLBCL, and teaching as an occupation and risk of NHL (Table 2).

There was one association, between history of celiac disease and risk of NHL (OR 2.61,
95% CI 2.04 to 3.33; 110, 245 NHL cases from 8 individual studies), that was classified as
presenting convincing evidence. Although the association had $P<10^{-6}$, at least 1000 cases, a
nominally significant result for the largest component study, low heterogeneity ($I^2<50\%$), a 95%
PI excluding the null, and no evidence of small study effects, we were unable to conduct the
Ioannidis test due to the incomplete information reported about the component studies.

Among across all the 112 nominally statistically significant associations, we found 63 (56\%) of
them were marginally had relative risk values that were between 0.67 and 1.50 significant (e.g.,
$1<\text{effect estimate}<1.50$ or $0.67<\text{effect estimate}<1$).

Systematic reviews
We identified 8 systematic reviews without quantitative synthesis with 8 unique associations that were not investigated by MAs of summary level data (eText 24 in Supplement 1).

**MAs of IPD**

We identified 27 MAs of IPD, of which 24 were from the InterLymph Consortium. The 24 InterLymph MAs of IPD reported 715 nominally statistically significant ($P<0.05$) associations. Of these, 116 and 21 associations were based on analyses with at least 1000 NHL cases and had $P<10^{-3}$ and $P<10^{-6}$, respectively (Table 4 and eTable 56 in Supplement 1). Overall, the unique suggestive exposures categories were alcohol consumption on risk of DLBCL, MZL and NHL, history of Sjogren’s syndrome on risk of DLBCL, MZL and NHL, recreational sun exposure on risk of DLBCL, FL and NHL, and history of HCV on risk of DLBCL, MZL and NHL. Although the 3 non-InterLymph MAs of IPD examined 5 associations not reported in systematic reviews and/or MAs of the summary level data, including fish eaters and risk of NHL, vegetarians and vegans and risk of NHL, maternal age at the time of the child’s birth and risk of NHL, paternal age at the time of the child’s birth and risk of NHL, and leisure-time physical activity and risk of NHL, none were nominally statistically significant.

**Consistency between MAs of summary level data and InterLymph MAs of IPD**

There were 40 associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD (Table 5 and eFigure 1 in Supplement 1). While 22 (55.0%) evaluated the impact of environmental risk factors on the risk of NHL overall, the other half (18, 45.0%) focused on various NHL subtypes (CLL/SLL, 5 (12.5%); DLBCL, 5 (12.5%); FL, 4 (10.0%); TCL, 3 (7.5%); MZL, 1 (2.5%)).

Overall, 22 of 40 (55.0%) of the associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. There were 10 (25.0%) pairs where the effect estimates were both statistically significantly increased, 3 (7.5%) where they were both statistically significantly decreased, 7 (17.5%) where they were both non-statistically significantly increased, and 2 (5.0%) where they were both non-statistically significantly decreased (Kappa=0.37, eTable 87 and eFigure 1 in Supplement 1). The 13 associations where the MAs of the summary level data and MAs of IPD effect estimates were both statistically significantly increased or decreased were for history of smoking and risk of TCL, history of drinking and risk of NHL, DLBCL, and FL, history of primary Sjogren’s syndrome and risk of NHL, history of
systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL, TCL and DLBCL, and history of HCV and risk of NHL, DLBCL, MZL and CLL/SLL. There were 28 (70.0%) pairs where the effect sizes from the MAs of IPD were more conservative than the effect sizes from the MAs of summary level data.

There were 4 suggestive associations reported in MAs of summary level data that were also evaluated in the InterLymph MAs of IPD. Of these, 3 associations from MAs of IPD had effect estimates in the same direction, had \( P < 10^{-3} \), and were based on analyses with at least 1000 NHL cases (i.e., history of psoriasis and risk of NHL, history of Herpes Zoster and risk of NHL, and history of farming as an occupation and risk of NHL). There were 8 highly suggestive associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD. Of these, 7 associations from the MAs of IPD had effect estimates in the same direction, had \( P < 10^{-6} \), and were based on analyses with at least 1000 NHL cases (i.e., history of rheumatoid arthritis and risk of NHL, history of primary Sjogren's syndrome and risk of NHL, history systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL and TCL, history of tuberculosis and risk of NHL, and history of HCV and risk of NHL).

There were 19 (48.7%) pairs where the MAs of summary level data included at least one-third of the same component studies as the InterLymph MAs of IPD. There was no difference in terms of concordance (direction, statistical significance of summary effect estimates and overlapping 95% CIs) between MAs of summary level data that included at least one-third versus fewer than one-third of the same component studies as the MAs of IPD (12/19 (63.2%) vs 10/21 (48.7%), \( P = 0.32 \)).

**Methodological quality**

The vast majority of the 85 MAs of summary level data had overall confidence ratings of low (3, 43.5%) or critically low (79, 93.2%) according to the AMSTAR 2 tool. There were 2 (2.4%) where the overall confidence in the results was classified as moderate. Only 1 (1.2%), evaluating the association between tuberculosis and risk of NHL, had an overall confidence rating of high (eTable 62 in Supplement 1). The most common unfulfilled critical domains of the AMSTAR 2 tool were incomplete justification of excluded studies (74, 87.4%) and missing or no information about preregistered protocols (72, 84.4%).

**Discussion**
In this umbrella review, we evaluated the range, strength, and validity of reported associations between environmental risk factors and NHL across 85 MAs of published observational studies. Overall, we identified 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. The vast majority of the associations, including those evaluating various dietary, clinical, lifestyle, chemical, and occupational exposures, were classified as having either non-significant or weak evidence. **More than half of the nominally significant associations were only marginally significant.** Only 5% of the associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence. When the same associations were evaluated in MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Overall, effect sizes from MAs of IPD were more conservative. This umbrella review suggests that there is a mass production of low-quality MAs of summary level data reporting weak associations between environmental risk factors and NHL. These findings highlight the need for improving not only primary studies but also evidence synthesis in this field. Moreover, given that many of the assessed risk factors are correlated, simultaneous consideration of multiple risk factors will be useful to understand which ones have the strongest, independent effects on NHL risk.

Although a wide range of environmental exposures have been evaluated and proposed as potential risk factors for NHL, our evaluation suggests that the only highly suggestive or convincing exposures proposed in MAs of summary level data and MAs of IPD are related to autoimmune and infectious diseases. In particular, the prominent autoimmune disease-related risk factors include history of celiac disease, rheumatoid arthritis, primary Sjogren's syndrome, and systemic lupus erythematosus. Although the exact mechanisms behind these associations remains unclear, many autoimmune disorders are characterized by chronic inflammation, which may intensify B cell or T cell activation and promote the development of lymphoma. Previous studies have also suggested that the dysfunction of some protein families, such as FAS and tumor necrosis factor, and the interplay between various immune cells, could be potential mechanisms. However, there is uncertainty when it comes to the temporality of these associations, with studies reporting that autoimmune diseases can occur during lymphoma.

Associations between viral and bacterial infections and NHL risk have been suggested for several decades. Different hypotheses for HCV-related lymphomagenesis have been proposed. For instance, chromosomal aberrations, including chromosome t(14;18) translocation,
have been found to be associated with mixed cryoglobulinemia, a disorder most commonly caused by HCV infection and that can evolve into lymphoproliferative disorders.\textsuperscript{50-52} Furthermore, genetic variations, including Interleukin-10 polymorphisms, have also been proposed as a potential pathway between HCV infection and NHL susceptibility and development.\textsuperscript{53} Similar to autoimmune disease-related risk factors, it remains unclear whether these associations are driven by disease status, medication use, or disease-medication interactions.\textsuperscript{54-58} Considering how rare many of these autoimmune and infectious disease-related exposures are, future efforts are necessary to determine the impact of multiple environmental as well as non-environmental risk factors simultaneously.\textsuperscript{5,6}

Among 40 associations evaluated by both MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Unlike MAs of summary level data, MAs of IPD tend to focus on studies with more homogeneous designs and patient populations. Furthermore, MAs of IPD can allow for better harmonization of data across studies, more advanced one-stage meta-analytical approaches, and analyses accounting for many exposure categories and potential confounders.\textsuperscript{59,60} Although the InterLymph MAs of IPD are particularly robust due to the large number of NHL cases and subtypes considered, MAs of IPD without systematic reviews may exclude evidence from high-quality case-control or cohort studies. For instance, the InterLymph analyses only included evidence from completed and ongoing case-control studies from consortium members. Furthermore, the InterLymph findings may be difficult to disentangle, with at least 700 nominally statistically significant associations among thousands of analyses conducted across different subtypes of NHL, and different levels of exposures, and exposure levels (e.g., different type/dosage of alcohol consumption). In the future, it will be necessary to monitor the consistency between MAs of summary level data and MAs of IPD, especially since approximately half of the MAs of summary level data had at least one-third of the same component studies as the MAs of IPD. In addition, authors of MAs should carefully evaluate whether any external studies can and should be included in their syntheses. Of interest, we observed that more than two thirds of the effect sizes were more conservative in the InterLymph MAs of IPD than in the MAs of summary level data. This may be a reflection of greater selective reporting bias in the corpus of studies available in the literature as compared with a set of studies participating in a consortium.
Our study suggests that nearly all MAs of summary level data evaluating associations between environmental risk factors and risk of NHL could be classified as having critically low quality according to the AMSTAR 2 tool. Previous umbrella reviews focused on the associations between environmental risk factors and health outcomes have noted similar concerns. However, the proportion of low or critically low-quality NHL reviews is higher than what has been observed among umbrella reviews for inflammatory bowel diseases, attention-deficit/hyperactivity disorder, eating disorders, early childhood caries, physical activity for academic achievement, and physical therapy for tendinopathy. These findings may not be surprising considering recent concerns about the mass production of systematic reviews. In the future, authors planning systematic reviews and MAs of summary level data of the associations between environmental exposures and NHL should adhere to reporting guidelines and critically evaluate how their studies relate to existing MAs of IPD.

Limitations

Our umbrella review has several limitations. First, we did not identify potential environmental risk factors that were only examined in individual observational studies. Our objective was to identify and summarize the associations that were reported by the MAs of summary level data, which already covered a wide space of diverse associations. Furthermore, we did not evaluate the quality of individual studies included in the MAs of summary level data, the impact that individual studies have on the overall heterogeneity, or the potential role that residual/unmeasured confounding could have on associations. Individual risk of bias evaluations are outside the scope of umbrella reviews, and it is the expectation that MAs have already conducted these quality assessments. Second, we considered included reviews MAs of both cohort and case-control studies, and our assessments did not prioritize reviews of certain study designs or address differences across different study designs. Considering the fact that NHL subtypes are rare, case-control studies may often be the most realistic study design to evaluate exposure histories, and a group of chronic diseases, including reviews of different study designs are of importance to better understand its etiology. Third, although umbrella reviews provide a comprehensive summary of the associations reported in MAs, the validity of the summary effect estimates is dependent on the quality of the individual MAs. Although we attempted to standardize associations using a random-effects DL
estimator, we did not evaluate or re-conduct the literature searches for all potential exposure-outcome relationships. Fifth, we did not calculate or conduct $I^2$, 95% PIs, Egger’s test, and excess significance test for non-significant and nominally statistically significant associations. Given the large number of associations identified, we prioritized these calculations for associations where these values were necessary to determine the strength of associations using the previously established classification system. Sixth, as in previous umbrella reviews, when summary effect estimates of multiple exposure contrast levels were reported, we focused on the risk estimates comparing ever versus never exposure (or comparing the highest versus lowest levels of exposures). Although we did not consider all potential contrast levels and dose-response relationships, our objective was to provide a universal overview of the relationships between examined risk factors and NHL. Specific dose-response relationships may nevertheless exist for certain associations, and they would need to be examined on a case-by-case basis. Seventh, we only identified the nominally statistically significant associations among the thousands of associations reported in InterLymph MAs of IPD. Eighth, we only focused on systematic reviews written in English by excluding non-English language reviews, we may have missed additional potential associations. However, we utilized the same approach as previous umbrella reviews that focused on risk factors for health outcome(s). Ninth, MAs of IPD and MAs of summary level data can have different strengths and limitations, and our evaluation did not focus on comparing the potential quality of these types of studies. Lastly, when multiple MAs of summary level data evaluated the same exposures and outcomes, we selected the association based on the largest number of included studies. Although this approach does not ensure that the highest quality MAs are selected, this methodology has been utilized by previous umbrella reviews.

Conclusion

In this large-scale umbrella review, we identified dozens of MAs evaluating associations between environmental risk factors and NHL. However, the vast majority of MAs of summary level data were low quality and presented either non-significant or weak evidence. When the same associations were evaluated in MAs of summary level data and MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Although several associations, primarily those for autoimmune and infectious disease-related risk
factors, presented either highly suggestive or convincing evidence, these findings highlight the
need for improving not only primary studies but also evidence synthesis in the field of NHL
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analysis. XS and JDW and drafted the manuscript. XS, JPAI, and JDW participated in the
interpretation of the data. All authors and critically revised the manuscript for important
intellectual content. XS and JDW had full access to all the data in the study and take
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**Data sharing:** The dataset will be made available via a publicly accessible repository on
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**Transparency:** The senior author (manuscripts guarantor) (JDW) affirms that the manuscript is
an honest, accurate, and transparent account of the study being reported; that no important
aspects of the study have been omitted; and that any discrepancies from the study as planned
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### Table 1. Grading criteria for evidence categories

| Strength of association | Description* |
|-------------------------|--------------|
| Highly statistically significant association ($P < 10^{-6}$) | At least 1000 NHL cases |
Low/moderate between study heterogeneity ($I^2 < 50\%$)
95% prediction interval excluding the null value
Largest study reporting a nominally statistically significant ($P < 0.05$)
No evidence of small-study effects
No evidence of excess significance bias

| Highly suggestive (class II) | Highly statistically significant association ($P < 10^{-6}$) |
|------------------------------|-------------------------------------------------------------|
|                              | At least 1000 NHL cases                                     |
|                              | Largest study reporting a nominally statistically significant ($P < 0.05$) |
| Suggestive (class III)       | At least 1000 NHL cases                                     |
|                              | Statistically significant association ($P < 10^{-3}$)       |
| Weak (class IV)              | Nominally statistically significant association ($P < 0.05$) |
| Non-significant              | Non-statistically significant associations ($P > 0.05$)     |

* $P$ value for the association that calculated by random effects model.
NHL = non-Hodgkin lymphoma.
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author or year | No. of primary studies | No. of cases | Efficacy measure | Random effects summary effect size (95% CI) | P randoma | I² (%) | 95% PI | Small study effect size | Strength of reported association |
|-----------------------|-----------------------------|--------------------|---------|------------|----------------|----------------------|---------------|----------------|-------------------------------------------|-----------|--------|--------|------------------|-----------------------------|
| Renal transplant      | Renal transplant recipients vs general population | NHL | SRMA | Wang 2018 | 6 | 770 | SIR | 10.66 (8.54, 13.31) | 3.44E-86 | Yes | 80.2 | NA | NA | II |
| Autoimmune diseases   | Rheumatoid arthritis | NHL | SRMA | Simon 2015 | 16 | 1531 | SIR | 2.26 (1.82, 2.81) | 8.42E-13 | Yes | 96 | NA | NA | II |
| Primary Sjogren's syndrome | Patients vs general population | NHL | SRMA | Liang 2014 | 11 | 1232 | RR | 13.76 (8.53, 18.99) | 1.62E-34 | Yes | 58.8 | NA | NA | II |
| Systemic lupus erythematosus | Patients vs general population | NHL | MA | Cao 2015 | 12 | 166 | RR | 5.4 (3.75, 7.77) | 1.99E-18 | Yes | 74.3 | NA | NA | II |
| Celiac disease        | Patients vs general population | NHL | SRMA | Tio 2012 | 8 | 1102 | OR | 2.61 (2.04, 3.33) | 9.32E-14 | Yes | 23.4 | (1.57, 4.33) | No | I |
| Celiac disease        | Patients vs general population | TCL | SRMA | Tio 2012 | 5 | 3535 | OR | 15.84 (7.85, 31.94) | 6.90E-14 | Yes | 55.5 | NA | NA | II |
| Infectious diseases   | Tuberculosis | NHL | SRMA | Leung 2020 | 8 | 2390 | RR | 1.61 (1.34, 1.94) | 6.76E-07 | Yes | 50.2 | NA | NA | II |
| HBV                   | HBV infected vs non-infected | NHL | SRMA | Li 2018 | 58 | 5371 | OR | 2.50 (2.2, 2.83) | 6.33E-42 | Yes | 77.9 | NA | NA | II |
| HBV                   | HBV infected vs non-infected | BCL | SRMA | Li 2018 | 20 | >100 | OR | 2.46 (1.97, 3.07) | 1.24E-14 | Yes | 62.9 | NA | NA | II |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author | Year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Large study nominally significant (P<0.05) | I² (%) | 95% PI | Small study effect | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|-----------|--------|------|-----------------------|-------------|--------------|------------------------------------------|--------|------------------------------------------|-------|-------|-----------------|-----------------------|
| Occupation            | Teacher                   | Teacher vs non-teachers | NHL    | MA        | Boffetta | 2007 | 19                    | >100        | RR           | 1.47 (1.34, 1.61)                          | 1.60E-15 | Yes                                      | 76    | NA    | NA              | II                    |
| Occupation            | Teacher                   | Teacher vs non-teachers | HCV    | MA        | DalMaso | 2006 | 8                     | 1020        | RR           | 2.65 (1.88, 3.74)                          | 4.98E-08 | Yes                                      | 39    | (1.46, 5.81) | No              | II                    |
| HCV                   | HCV infected vs non-infected | NHL    | SRM A | Masa rone | 2019   | 27    | 3307                  | 7           | OR           | 3.36 (2.4, 4.72)                           | 7.92E-12 | Yes                                      | 88    | NA    | NA              | II                    |

BCL=B cell lymphoma; CI=confidence interval; HBV=hepatitis B virus; HCV=hepatitis C virus; MA=meta-analysis; NA=not available; NHL=non-Hodgkin lymphoma; OR=odds ratio; PI=prediction interval; SIR=standardized incidence ratio; SRMA=systematic review and meta-analysis; RR=risk ratio; TCL=T-cell lymphoma.

*P value for summary effect estimates using a random-effects DerSimonian and Laird estimator.

*P<0.1 for Egger’s test suggests the presence of small study effects.

Strength of association using the criteria listed in Table 1.
Table 3. Environmental risk factors for NHL reported in MPL with suggestive (Class III), weak (Class IV) and non-significant evidence

| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|-------------|---------------|------------------------------------------|----------|-----------------------------------|
| **Dietary factors**   |                           |                     |         |            |              |                        |             |               |                                          |          |                                   |
| Meat                  | Red meat                  | Highest vs lowest   | NHL     | MA         | Yang 2015    | 18                     | 12579       | RR            | 1.32 (1.12, 1.55) | 8.52E-04 | III                               |
| Processed meat        |                           | Highest vs lowest   | NHL     | MA         | Yang 2015    | 18                     | 14112       | RR            | 1.17 (1.07, 1.29) | 1.04E-03 | IV                                |
| Red meat              |                           | Highest vs lowest   | DLBCL   | MA         | Yang 2015    | 5                      | NA          | RR            | 1.34 (0.97, 1.86) | 7.80E-02 | NS                                |
| Processed meat        |                           | Highest vs lowest   | DLBCL   | MA         | Yang 2015    | 5                      | NA          | RR            | 1.23 (1.03, 1.48) | 2.50E-02 | IV                                |
| Processed meat        |                           | Highest vs lowest   | FL      | MA         | Yang 2015    | 5                      | NA          | RR            | 1.21 (0.98, 1.48) | 7.00E-02 | NS                                |
| Red meat              |                           | Highest vs lowest   | CLL/SL  | MA         | Yang 2015    | 5                      | NA          | RR            | 1.01 (0.84, 1.21) | 9.22E-01 | NS                                |
| Processed meat        |                           | Highest vs lowest   | CLL/SL  | MA         | Yang 2015    | 5                      | NA          | RR            | 1.06 (0.85, 1.33) | 6.22E-01 | NS                                |
| White meat/poultry    |                           | Highest vs lowest   | NHL     | MA         | Dong 2017    | 10                     | 10671       | RR            | 1.04 (0.86, 1.27) | 7.06E-01 | NS                                |
| White meat/poultry    |                           | Highest vs lowest   | DLBCL   | SRMA       | Caini 2016   | 3                      | 1134        | RR            | 0.96 (0.63, 1.48) | 8.62E-01 | NS                                |
| White meat/poultry    |                           | Highest vs lowest   | FL      | SRMA       | Caini 2016   | 3                      | 858         | RR            | 1.09 (0.51, 2.31) | 8.34E-01 | NS                                |
| White meat/poultry    |                           | Highest vs lowest   | CLL/SL  | SRMA       | Caini 2016   | 3                      | 1337        | RR            | 1.05 (0.71, 1.54) | 8.17E-01 | NS                                |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|-------------------|---------|------------|-------------|-----------------------|-------------|--------------|------------------------------------------|----------|----------------------------------|
| Fish                  | Fish                      | Highest vs lowest | NHL     | SRMA       | Caini 2016   | 11                    | 8839        | RR           | 0.93 (0.72, 1.19)                            | 5.83E-01 | NS                               |
| Fish                  | Fish                      | Highest vs lowest | DLBCL   | SRMA       | Caini 2016   | 4                     | 1228        | RR           | 0.86 (0.48, 1.56)                            | 6.29E-01 | NS                               |
| Fish                  | Fish                      | Highest vs lowest | FL      | SRMA       | Caini 2016   | 4                     | 970         | RR           | 0.86 (0.48, 1.56)                            | 6.29E-01 | NS                               |
| Fish                  | Fish                      | Highest vs lowest | CLL/SL  | SRMA       | Caini 2016   | 5                     | 1703        | RR           | 0.90 (0.72, 1.14)                            | 3.75E-01 | NS                               |
| Fruits and vegetables | Fruit and vegetable       | Highest vs lowest | NHL     | MA         | Chen 2013    | 4                     | 1747        | RR           | 0.78 (0.66, 0.92)                            | 3.00E-03 | IV                               |
| Fruit                 | Fruit                     | Highest vs lowest | NHL     | MA         | Chen 2013    | 13                   | 8476        | RR           | 0.97 (0.87, 1.08)                            | 5.93E-01 | NS                               |
| Vegetable             | Vegetable                 | Highest vs lowest | NHL     | MA         | Chen 2013    | 13                   | 8332        | RR           | 0.81 (0.71, 0.92)                            | 1.00E-03 | IV                               |
| Fruit                 | Fruit                     | Highest vs lowest | DLBCL   | MA         | Chen 2013    | 8                     | NA          | RR           | 0.94 (0.79, 1.13)                            | 5.08E-01 | NS                               |
| Vegetable             | Vegetable                 | Highest vs lowest | DLBCL   | MA         | Chen 2013    | 7                     | NA          | RR           | 0.70 (0.54, 0.91)                            | 7.00E-03 | IV                               |
| Fruit                 | Fruit                     | Highest vs lowest | FL      | MA         | Chen 2013    | 8                     | NA          | RR           | 0.96 (0.72, 1.28)                            | 7.93E-01 | NS                               |
| Vegetable             | Vegetable                 | Highest vs lowest | FL      | MA         | Chen 2013    | 7                     | NA          | RR           | 0.70 (0.53, 0.92)                            | 1.10E-02 | IV                               |
| Eggs and dairy        | Eggs                      | Highest vs lowest | NHL     | SRMA       | Caini 2016   | 10                   | 5775        | RR           | 1.17 (0.86, 1.60)                            | 3.26E-01 | NS                               |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|----------------------|-------------|---------------|-------------------------------------|----------|------------------------------------|
| Total dairy           | Highest vs lowest NHL     | MA                  | Wang 2016 | 7          | 4207 RR      | 1.20 (1.02, 1.42)    | 3.00E-02    | IV            |
| Total dairy           | Highest vs lowest DLBCL   | MA                  | Wang 2016 | 3          | 321 RR       | 1.73 (1.22, 2.45)    | 2.00E-03    | IV            |
| Total dairy           | Highest vs lowest FL      | MA                  | Wang 2016 | 3          | 355 RR       | 1.23 (0.88, 1.72)    | 2.28E-01    | NS            |
| Total dairy           | Highest vs lowest CLL/SL  | MA                  | Wang 2016 | 3          | 390 RR       | 1.35 (0.77, 2.39)    | 3.03E-01    | NS            |
| Milk                  | Highest vs lowest NHL     | MA                  | Wang 2016 | 16         | 7109 RR      | 1.41 (1.08, 1.84)    | 1.10E-02    | IV            |
| Milk                  | Highest vs lowest DLBCL   | MA                  | Wang 2016 | 3          | 352 RR       | 1.49 (1.08, 2.06)    | 1.50E-02    | IV            |
| Milk                  | Highest vs lowest FL      | MA                  | Wang 2016 | 3          | 390 RR       | 0.99 (0.47, 2.07)    | 9.81E-01    | NS            |
| Milk                  | Highest vs lowest CLL/SL  | MA                  | Wang 2016 | 3          | 477 RR       | 1.04 (0.69, 1.55)    | 8.60E-01    | NS            |
| Cheese                | Highest vs lowest NHL     | MA                  | Wang 2016 | 10         | 5519 RR      | 1.14 (0.96, 1.34)    | 1.24E-01    | NS            |
| Cheese                | Highest vs lowest DLBCL   | MA                  | Wang 2016 | 3          | 352 RR       | 0.93 (0.63, 1.37)    | 7.27E-01    | NS            |
| Cheese                | Highest vs lowest FL      | MA                  | Wang 2016 | 3          | 390 RR       | 1.04 (0.74, 1.46)    | 8.32E-01    | NS            |
| Cheese                | Highest vs lowest CLL/SL  | MA                  | Wang 2016 | 3          | 477 RR       | 1.28 (0.91, 1.81)    | 1.60E-01    | NS            |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|----------------|-----------------------------------------|---------|-------------------------------|
| Yogurt                | Highest vs lowest         | NHL                 | MA      | Wang 2016  | 4            | 2372                 | RR          | 0.78           | (0.54, 1.12)                          | 1.83E-01| NS                            |
| Yogurt                | Highest vs lowest         | DLBCL               | MA      | Wang 2016  | 3            | 352                  | RR          | 0.90           | (0.67, 1.21)                          | 4.95E-01| NS                            |
| Yogurt                | Highest vs lowest         | FL                  | MA      | Wang 2016  | 3            | 390                  | RR          | 0.89           | (0.63, 1.25)                          | 5.15E-01| NS                            |
| Yogurt                | Highest vs lowest         | CLL/SL              | MA      | Wang 2016  | 3            | 477                  | RR          | 0.97           | (0.76, 1.23)                          | 8.16E-01| NS                            |
| Yogurt                | Highest vs lowest         | NHL                 | MA      | Wang 2016  | 4            | 1534                 | RR          | 1.31           | (1.04, 1.65)                          | 2.20E-02| IV                            |
| Ice-cream             | Highest vs lowest         | NHL                 | MA      | Wang 2016  | 4            | 1598                 | RR          | 1.57           | (1.11, 2.00)                          | 1.00E-02| IV                            |
| Coffee and tea        | Coffee                    | Highest vs lowest   | NHL     | SRMA       | Mirtavoos-Mahyari 2019 | 11 | 4418 | RR | 1.21 | (0.97, 1.50) | 8.60E-02 | NS |
| Black tea             | Highest vs lowest         | NHL                 | SRMA   | Mirtavoos-Mahyari 2019 | 5 | 1600 | RR | 1.01 | (0.82, 1.24) | 9.40E-01 | NS |
| Green tea             | Highest vs lowest         | NHL                 | SRMA   | Mirtavoos-Mahyari 2019 | 3 | 637  | RR | 0.61 | (0.38, 0.99) | 4.30E-02 | IV |
| Carotenoids           | Alpha-carotene            | Highest vs lowest   | NHL     | SRMA       | Chen 2017    | 8          | 2926 | RR | 0.87 | (0.78, 0.97) | 1.20E-02 | IV |
| Carotenoids           | Alpha-carotene            | Highest vs lowest   | DLBCL   | SRMA       | Chen 2017    | 3          | NA   | RR | 0.75 | (0.59, 0.97) | 2.30E-02 | IV |
| Carotenoids           | Alpha-carotene            | Highest vs lowest   | FL      | SRMA       | Chen 2017    | 4          | NA   | RR | 0.84 | (0.60, 1.16) | 3.04E-01 | NS |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|--------------|-----------------------------------------------|-----------------------------|
| Alpha-carotene        | Highest vs lowest          | CLL/SL              | SRMA    | Chen 2017  | 2            | NA                    | RR          | 1.41         | (0.80, 2.50) 2.40E-01 | NS                          |
| Beta-carotene         | Highest vs lowest          | NHL                 | SRMA    | Chen 2017  | 10           | 3946                  | RR          | 0.80         | (0.68, 0.94) 7.00E-03 | IV                         |
| Beta-carotene         | Highest vs lowest          | DLBCL               | SRMA    | Chen 2017  | 5            | NA                    | RR          | 0.65         | (0.46, 0.91) 1.30E-02 | IV                         |
| Beta-carotene         | Highest vs lowest          | FL                  | SRMA    | Chen 2017  | 6            | NA                    | RR          | 0.80         | (0.55, 1.16) 2.44E-01 | NS                         |
| Beta-cryptoxanthin    | Highest vs lowest          | CLL/SL              | SRMA    | Chen 2017  | 4            | NA                    | RR          | 0.98         | (0.76, 1.25) 8.83E-01 | NS                         |
| Beta-cryptoxanthin    | Highest vs lowest          | NHL                 | SRMA    | Chen 2017  | 7            | 2325                  | RR          | 0.87         | (0.75, 1.01) 6.60E-02 | NS                         |
| Beta-cryptoxanthin    | Highest vs lowest          | DLBCL               | SRMA    | Chen 2017  | 4            | NA                    | RR          | 0.84         | (0.67, 1.05) 1.28E-01 | NS                         |
| Beta-cryptoxanthin    | Highest vs lowest          | FL                  | SRMA    | Chen 2017  | 4            | NA                    | RR          | 0.75         | (0.50, 1.13) 1.67E-01 | NS                         |
| Beta-cryptoxanthin    | Highest vs lowest          | CLL/SL              | SRMA    | Chen 2017  | 3            | NA                    | RR          | 0.51         | (0.15, 1.72) 2.83E-01 | NS                         |
| Lycopene              | Highest vs lowest          | NHL                 | SRMA    | Chen 2017  | 7            | 2325                  | RR          | 0.99         | (0.88, 1.12) 8.80E-01 | NS                         |
| Lycopene              | Highest vs lowest          | DLBCL               | SRMA    | Chen 2017  | 3            | NA                    | RR          | 1.04         | (0.69, 1.57) 8.62E-01 | NS                         |
| Lycopene              | Highest vs lowest          | FL                  | SRMA    | Chen 2017  | 3            | NA                    | RR          | 0.90         | (0.54, 1.49) 6.97E-01 | NS                         |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|-------------|---------------|------------------------------------------|-----------|-------------------------------|
| Lycopene              | Highest vs lowest         | CLL/SL L            | SRMA    | Chen 2017  | 2            | NA                    | RR          | 0.80          | (0.60, 1.07)                             | 1.31E-01  | NS                            |
| Andlutein/zeaxanthin  | Highest vs lowest         | NHL                 | SRMA    | Chen 2017  | 7            | 2325                  | RR          | 0.82          | (0.69, 0.97)                             | 2.20E-02  | IV                            |
| Andlutein/zeaxanthin  | Highest vs lowest         | DLBCL               | SRMA    | Chen 2017  | 3            | NA                    | RR          | 0.87          | (0.54, 1.40)                             | 5.78E-01  | NS                            |
| Andlutein/zeaxanthin  | Highest vs lowest         | FL                  | SRMA    | Chen 2017  | 3            | NA                    | RR          | 0.70          | (0.48, 1.02)                             | 6.30E-02  | NS                            |
| Andlutein/zeaxanthin  | Highest vs lowest         | CLL/SL L            | SRMA    | Chen 2017  | 2            | NA                    | RR          | 0.93          | (0.70, 1.23)                             | 6.26E-01  | NS                            |
| Micronutrient intake/supplements | Vitamin A (retinol) | Highest vs lowest | NHL | Psaltopoulou 2018 | 3 | 3314 | RR | 0.92 | (0.80, 1.07) | 2.64E-01 | NS |
| Micronutrient intake/supplements | Vitamin C | Highest vs lowest | NHL | Psaltopoulou 2018 | 5 | 3879 | RR | 1.00 | (0.90, 1.12) | 1.00E+00 | NS |
| Micronutrient intake/supplements | Vitamin D | Highest vs lowest | NHL | Lu 2014 | 6 | 4400 | OR | 1.07 | (0.82, 1.40) | 6.33E-01 | NS |
| Micronutrient intake/supplements | Vitamin D | Highest vs lowest | DLBCL | Lu 2014 | 5 | NA | OR | 1.05 | (0.73, 1.52) | 8.06E-01 | NS |
| Micronutrient intake/supplements | Vitamin D | Highest vs lowest | FL | Lu 2014 | 5 | NA | OR | 1.00 | (0.63, 1.58) | 1.00E+00 | NS |
| Micronutrient intake/supplements | Vitamin D | Highest vs lowest | CLL/SL L | Lu 2014 | 4 | NA | OR | 1.10 | (0.56, 2.14) | 7.93E-01 | NS |
| Micronutrient intake/supplements | Vitamin D | Highest vs lowest | TCL | Lu 2014 | 3 | NA | OR | 1.69 | (0.68, 4.20) | 2.62E-01 | NS |

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| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|-----------|--------------|------------------------|-------------|---------------|------------------------------------------|----------|-------------------------------|
| Vitamin E             | Highest vs lowest         | NHL                 | SRMA    | Psaltopoulou 2018 | 5   | 3879 | RR | 0.98 (0.88, 1.10) | 7.36E-01 | NS               |
| Dietary fat           | Total fat                 | Highest vs lowest   | NHL     | MA        | Han 2017     | 10 | 5042 | RR | 1.26 (1.12, 1.42) | 1.51E-04 | III              |
|                       | Total fat                 | Highest vs lowest   | DLBCL   | MA        | Han 2017     | 5  | NA  | RR | 1.41 (1.08, 1.84) | 1.10E-02 | IV               |
|                       | Total fat                 | Highest vs lowest   | FL      | MA        | Han 2017     | 5  | NA  | RR | 1.21 (0.97, 1.52) | 9.60E-02 | NS               |
|                       | Total fat                 | Highest vs lowest   | CLL/SL  | MA        | Han 2017     | 4  | NA  | RR | 0.91 (0.68, 1.23) | 5.44E-01 | NS               |
|                       | Total fat                 | Highest vs lowest   | TCL     | MA        | Han 2017     | 4  | NA  | RR | 1.12 (0.60, 2.09) | 7.35E-01 | NS               |
|                       | Animal fat                | Highest vs lowest   | NHL     | MA        | Han 2017     | 5  | 1432 | RR | 1.31 (1.08, 1.58) | 5.00E-03 | IV               |
|                       | Vegetable fat             | Highest vs lowest   | NHL     | MA        | Han 2017     | 5  | 1432 | RR | 1.00 (0.84, 1.20) | 1.00E+00 | NS               |
|                       | Dietary trans-fatty acid intake | Highest vs lowest | NHL     | SRMA    | Michels 2021 | 4   | 4701 | OR | 1.32 (0.99, 1.76) | 5.80E-02 | NS               |
|                       | Dietary nitrate and nitrite intake | Highest vs lowest | NHL     | SRMA    | Xie 2016    | 7   | 1703 | RR | 0.85 (0.68, 1.06) | 1.57E-01 | NS               |
|                       | Dietary nitrate           | Highest vs lowest   | NHL     | SRMA    | Xie 2016    | 5   | 1547 | RR | 1.54 (0.98, 2.41) | 6.00E-02 | NS               |
| Alcohol               | Ever drinking             | Ever vs never       | NHL     | SRMA    | Tramacere 2012 | 29 | 18759 | RR | 0.85 (0.79, 0.91) | 8.50E-06 | III              |
| Risk factors category | Environmental risk factors | Level of comparison | Outcomes | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|----------|------------|--------------|-----------------------|-------------|---------------|------------------------------------------|-----------|-------------------------------|
| Ever drinking         | Ever vs never             | TCL SRMA            | Tramacere 2012 | 8        | NA | RR | 0.78 (0.58, 1.05) | 1.00E-01 | NS | |
| Ever drinking         | Ever vs never             | BCL SRMA            | Tramacere 2012 | 15       | NA | RR | 0.86 (0.76, 0.97) | 1.50E-02 | IV | |
| Ever drinking         | Ever vs never             | DLBCL SRMA          | Tramacere 2012 | 14       | NA | RR | 0.79 (0.68, 0.91) | 1.60E-03 | IV | |
| Ever drinking         | Ever vs never             | FL SRMA             | Tramacere 2012 | 14       | NA | RR | 0.80 (0.69, 0.92) | 2.40E-03 | IV | |
| Ever drinking         | Ever vs never             | CLL/SL SRMA         | Tramacere 2012 | 12       | NA | RR | 1.00 (0.80, 1.26) | 1.00E+00 | NS | |
| Ever drinking         | Ever vs never             | NHL SRMA            | Tramacere 2012 | 6        | 1181 | OR | 0.84 (0.70, 1.00) | 5.50E-02 | NS | |
| Heavy drinking        | Heavy vs never            | NHL SRMA            | Martin 2005   | 7        | 477  | OR | 1.00 (0.58, 1.73) | 1.00E+00 | NS | |

**Breastfeeding**

| Ever vs never | breastfeeding | childhoud NHL SRMA | Martin 2005 | 7 | 477 | OR | 1.00 (0.58, 1.73) | 1.00E+00 | NS | |

**Drugs, vaccinations and procedures**

| Non-steroidal anti-inflammatory drugs | Aspirin | Users vs non-users | NHL SRMA | Ye 2015 | 10 | 6818 | OR | 1.02 (0.89, 1.17) | 7.89E-01 | NS | |
| Aspirin | Users vs non-users | NHL SRMA | Ye 2015 | 10 | 6818 | OR | 1.02 (0.89, 1.17) | 7.89E-01 | NS | |
| Aspirin | Users vs non-users | NHL SRMA | Ye 2015 | 10 | 6818 | OR | 1.02 (0.89, 1.17) | 7.89E-01 | NS | |
| Aspirin | Users vs non-users | NHL SRMA | Ye 2015 | 10 | 6818 | OR | 1.02 (0.89, 1.17) | 7.89E-01 | NS | |
| Aspirin | Users vs non-users | NHL SRMA | Ye 2015 | 10 | 6818 | OR | 1.02 (0.89, 1.17) | 7.89E-01 | NS | |
| Aspirin | Users vs non-users | NHL SRMA | Ye 2015 | 10 | 6818 | OR | 1.02 (0.89, 1.17) | 7.89E-01 | NS | |
| Aspirin | Users vs non-users | NHL SRMA | Ye 2015 | 10 | 6818 | OR | 1.02 (0.89, 1.17) | 7.89E-01 | NS | |
| Aspirin | Users vs non-users | NHL SRMA | Ye 2015 | 10 | 6818 | OR | 1.02 (0.89, 1.17) | 7.89E-01 | NS | |
| Aspirin | Users vs non-users | NHL SRMA | Ye 2015 | 10 | 6818 | OR | 1.02 (0.89, 1.17) | 7.89E-01 | NS | |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random $\alpha$ | Strength of reported association $b$ |
|-----------------------|---------------------------|---------------------|---------|-----------|--------------|-------------------|-------------|----------------|------------------------------------------|-----------------|-------------------------------|
| NA-NSAIDS             | Users vs non-users        | CLL/SL              | SRMA    | Ye 2015   | 3            | NA                | OR          | 1.26           | (0.86, 1.85)                           | 2.39E-01        | NS                            |
| NSAIDS                | Users vs non-users        | NHL                 | SRMA    | Ye 2015   | 13           | 9896              | OR          | 1.05           | (0.90, 1.22)                           | 5.41E-01        | NS                            |
| NSAIDS                | Users vs non-users        | DLBCL               | SRMA    | Ye 2015   | 3            | NA                | OR          | 0.99           | (0.81, 1.21)                           | 9.28E-01        | NS                            |
| NSAIDS                | Users vs non-users        | FL                  | SRMA    | Ye 2015   | 3            | NA                | OR          | 1.07           | (0.69, 1.68)                           | 7.78E-01        | NS                            |
| NSAIDS                | Users vs non-users        | CLL/SL              | SRMA    | Ye 2015   | 4            | NA                | OR          | 0.77           | (0.51, 1.15)                           | 2.09E-01        | NS                            |
| NSAIDS                | Users vs non-users        | TCL                 | SRMA    | Ye 2015   | 3            | NA                | OR          | 1.04           | (0.52, 2.07)                           | 9.19E-01        | NS                            |
| NSAIDS                | Users vs non-users        | BCL                 | SRMA    | Ye 2015   | 5            | NA                | OR          | 1.01           | (0.75, 1.36)                           | 9.52E-01        | NS                            |
| Corticosteroids       | Corticosteroids           | Users vs non-users  | NHL     | Bernatsky 2007 | 8            | 6897              | OR          | 1.13           | (0.99, 1.29)                           | 7.00E-02        | NS                            |
| Statin                | Users vs non-users        | NHL                 | SRMA    | Ye 2017   | 9            | 7825              | OR          | 0.82           | (0.69, 0.99)                           | 3.10E-02        | IV                            |
| Statin                | Users vs non-users        | DLBCL               | SRMA    | Ye 2017   | 4            | 897               | OR          | 0.78           | (0.55, 1.11)                           | 1.66E-01        | NS                            |
| Statin                | Users vs non-users        | FL                  | SRMA    | Ye 2017   | 4            | 495               | OR          | 0.89           | (0.62, 1.27)                           | 5.35E-01        | NS                            |
| Statin                | Users vs non-users        | MZL                 | SRMA    | Ye 2017   | 3            | 215               | OR          | 0.54           | (0.31, 0.94)                           | 2.90E-02        | IV                            |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|----------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|--------------|----------------------------------|----------|-------------------------------|
|                      |                            |                     |         |            |              |                       |             |              |                                  |          |                                |
|                      | Statin                     | Users vs non-users  | TCL     | SRMA       | Ye 2017      | 4                      | 227         | OR           | 0.70 (0.41, 1.19)                | 1.91E-01 | NS                             |
|                      | Paracetamol                | Paracetamol         | Users vs non-users | NHL     | SRMA       | Prego-Dominguez 2021 | 3          | 3022        | 1.20 (0.96, 1.51)                | 1.10E-01 | NS                             |
|                      | Bacillus calmette-guerin vaccination | Yes vs no | NHL     | SRMA       | Salmon 2020   | 11                     | 4350        | RR           | 1.20 (1.01, 1.43)                | 4.00E-02 | IV                             |
|                      | Insulin                    | Yes vs no           | NHL     | SRMA       | Karlstad 2013 | 4          | NA          | RR           | 1.16 (0.83, 1.62)                | 3.91E-01 | NS                             |
|                      | Inflammatory bowel disease treatment | Yes vs no | NHL     | SRMA       | Yang 2018    | 3          | 35          | RR           | 1.34 (0.62, 2.89)                | 4.70E-01 | NS                             |
|                      | Azathioprine and 6-mercaptopurine | Patients vs general population | NHL | MA         | Kandiel 2005 | 3          | 9           | SIR         | 3.92 (1.78, 7.47)                | 2.10E-04 | IV                             |
|                      | HAART among patients with HIV/AIDS | Pre vs post-HAART eras | NHL | SRMA       | Cobucci 2015   | 6          | 7701        | SIR         | 0.42 (0.26, 0.67)                | 3.00E-04 | III                           |
|                      | Red blood cell transfusions | Red blood cell transfusion | Yes vs no | NHL | MA         | Castillo 2010   | 14         | 5904        | RR           | 1.2 (1.07, 1.35)                | 2.00E-03 | IV                             |
|                      | Red blood cell transfusion  | Yes vs no           | CLL/SL  | MA         | Castillo 2010 | 5          | 3450        | RR           | 1.66 (1.08, 2.56)                | 2.10E-02 | IV                             |
|                      | Red blood cell transfusion  | Yes vs no           | FL      | MA         | Castillo 2010 | 6          | NA          | RR           | 1.02 (0.67, 1.55)                | 9.32E-01 | NS                             |
|                      | Red blood cell transfusion  | Yes vs no           | DLBCL   | MA         | Castillo 2010 | 5          | NA          | RR           | 1.06 (0.86, 1.3)                 | 5.92E-01 | NS                             |

**Non-dietary lifestyle factors**

| Risk factors category | Physical activity | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|-------------------|---------------------|---------|------------|--------------|-----------------------|-------------|--------------|----------------------------------|----------|-------------------------------|
|                      | Physical activity | Highest vs lowest   | NHL     | SRMA       | Davies 2020  | 17                     | 13425       | RR           | 0.92 (0.84, 1.00)                | 6.00E-02 | NS                             |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|-------------|--------------|----------------------------------------|-----------|-------------------------------------|
| Physical activity     | Highest vs lowest         | DLBCL               | SRMA    | Davies 2020| 10           | 1957                  | RR          |              | 0.95 (0.83, 1.09)                         | 4.70E-01  | NS                                  |
| Physical activity     | Highest vs lowest         | FL                  | SRMA    | Davies 2020| 10           | 1467                  | RR          |              | 0.95 (0.80, 1.12)                         | 5.60E-01  | NS                                  |
| Physical activity     | Highest vs lowest         | CLL/SL              | SRMA    | Davies 2020| 8            | 1452                  | RR          |              | 0.95 (0.76, 1.20)                         | 6.70E-01  | NS                                  |
| Hair dye              | Highest vs lowest         | NHL                 | MA      | Qin 2019   | 16           | 10967                 | OR          |              | 1.14 (1.01, 1.29)                         | 3.60E-02  | IV                                  |
| Hair dye              | User before 1980 vs never user | FL         | SRMA    | Odutola 2020| 4            | 439                   | OR          |              | 1.66 (1.22, 2.25)                         | 1.20E-03  | IV                                  |
| Night shift work      | Shift workers vs non shift workers | NHL          | SRMA    | Dun 2020   | 5            | >1000                 | OR          |              | 1.05 (0.99, 1.10)                         | 6.91E-02  | NS                                  |
| Indoor tanning        | Ever vs never             | NHL                 | SRMA    | O'Sullivan 2018| 10          | 14018                 | RR          |              | 0.95 (0.83, 1.08)                         | 4.54E-01  | NS                                  |
| Indoor tanning        | Ever vs never             | BCL                 | SRMA    | O'Sullivan 2018| 4            | NA                   | RR          |              | 0.82 (0.70, 0.95)                         | 1.10E-02  | NS                                  |
| Indoor tanning        | Ever vs never             | TCL                 | SRMA    | O'Sullivan 2018| 3            | NA                   | RR          |              | 1.23 (0.95, 1.59)                         | 1.15E-01  | IV                                  |
| Residential exposure to petrochemical activity | Living near vs far | NHL | SRMA | Jephcote 2020 | 9 | 1078 | RR | 1.06 (0.97, 1.17) | 2.25E-01 | NS |
| Smoking               | Ever vs never             | childhoo d NHL      | MA      | Boffetta 2000| 4            | 204                   | RR          |              | 2.08 (1.08, 3.98)                         | 2.80E-02  | IV                                  |
| Maternal smoking      | Ever vs never             | childhoo d NHL      | MA      | Antonopoul os 2011| 7            | 1072                  | OR          |              | 1.22 (1.02, 1.46)                         | 2.57E-02  | IV                                  |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|-----------|-------------|-----------------------|-------------|---------------|-----------------------------------------|-----------|-----------------------------|
| Ever smoking          | Ever vs never             | NHL                 | MA      | Sergentanis 2013 | 33          | 25891                | RR         | 1.05          | (1.00, 1.09) | 2.60E-02 | IV                          |
| Ever smoking          | Ever vs never             | DLBCL               | MA      | Sergentanis 2013 | 12          | NA                   | RR         | 1.01          | (0.95, 1.07) | 7.60E-01 | NS                          |
| Ever smoking          | Ever vs never             | FL                  | MA      | Sergentanis 2013 | 11          | NA                   | RR         | 1.05          | (0.88, 1.25) | 6.00E-01 | NS                          |
| Ever smoking          | Ever vs never             | CLL/SL              | MA      | Sergentanis 2013 | 9           | NA                   | RR         | 0.96          | (0.89, 1.04) | 3.10E-01 | NS                          |
| Ever smoking          | Ever vs never             | TCL                 | MA      | Sergentanis 2013 | 12          | NA                   | RR         | 1.23          | (1.06, 1.43) | 6.70E-03 | IV                          |
| Sun exposure          | Personal sunlight exposure| Highest vs lowest   | NHL     | Kim 2021      | 15          | 11272                | OR         | 0.81          | (0.71, 0.92) | 1.50E-03 | IV                          |
| Sun exposure          | Personal sunlight exposure| Highest vs lowest   | CLL/SL  | Kim 2021      | 4           | 1564                 | OR         | 0.80          | (0.63, 1.00) | 5.80E-02 | NS                          |
| Sun exposure          | Personal sunlight exposure| Highest vs lowest   | DLBCL   | Kim 2021      | 5           | 1843                 | OR         | 0.76          | (0.66, 0.87) | 1.10E-04 | III                         |
| Sun exposure          | Personal sunlight exposure| Highest vs lowest   | FL      | Kim 2021      | 5           | 1348                 | OR         | 0.81          | (0.67, 0.99) | 3.40E-02 | IV                          |
| Sun exposure          | Personal sunlight exposure| Highest vs lowest   | TCL     | Kim 2021      | 4           | 413                  | OR         | 1.00          | (0.68, 1.46) | 1.00E+00 | NS                          |
| Sun exposure          | Ambient sunlight exposure during lifetime| Highest vs lowest | NHL     | Kim 2021      | 7           | 19627                | OR         | 0.84          | (0.73, 0.96) | 1.30E-02 | IV                          |
| Sun exposure          | Ambient sunlight exposure during lifetime| Highest vs lowest | CLL/SL  | Kim 2021      | 4           | NA                   | OR         | 0.93          | (0.73, 1.19) | 5.70E-01 | NS                          |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|----------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|---------------|-------------------------------------------|----------|--------------------------------------|
| Ambient sunlight exposure during lifetime | Highest vs lowest | DLBCL | MA | Kim 2021 | 4 | NA | OR | 0.80 (0.69, 0.92) | 2.40E-03 | IV |
| Ambient sunlight exposure during lifetime | Highest vs lowest | FL | MA | Kim 2021 | 4 | NA | OR | 0.82 (0.72, 0.93) | 2.40E-03 | IV |
| Occupational ultraviolet exposure | Occupation vs general population | NHL | MA | Lu 2017 | 11 | 8829 | OR | 1.15 (0.99, 1.32) | 5.60E-02 | NS |
| Occupational ultraviolet exposure | Occupation vs general population | TCL | MA | Lu 2017 | 4 | NA | OR | 1.16 (0.90, 1.50) | 2.60E-01 | NS |

**Medical history and comorbid diseases**

### Autoimmune diseases

| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|----------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|---------------|-------------------------------------------|----------|--------------------------------------|
| Pernicious anemia     | Patients vs general population | NHL | SRMA | Lahner 2018 | 3 | 70 | RR | 1.16 (0.79, 1.71) | 4.60E-01 | NS |

### B-cell activating diseases

| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|----------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|---------------|-------------------------------------------|----------|--------------------------------------|
| Psoriasis             | Patients vs general population | NHL | SRMA | Vaengebjerg 2020 | 8 | 7626 | RR | 1.48 (1.30, 1.69) | 9.49E-09 | III |
| Type 1 diabetes       | Patients vs general population | NHL | MA | Wang 2020 | 3 | 1155 | RR | 1.56 (1.15, 2.08) | 4.00E-03 | IV |
| Cellulitis herpetiformis | Patients vs general population | NHL | MA | Kane 2011 | 6 | <1000 | RR | 2.75 (1.42, 5.33) | 2.60E-03 | IV |
| Systemic sclerosis    | Patients vs general population | NHL | SRMA | Zhang 2013 | 4 | 23 | SIR | 2.75 (1.42, 5.33) | 2.60E-03 | IV |

### Other
| Risk factors category | Environmental risk factors | Level of comparison | Outcome type | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|--------------------|-------------|------------|--------------|-----------------------|-------------|--------------|------------------------------------------|-----------|----------------------------------|
| Behcet's disease      | Patients vs general population | NHL | SRMA | Wang 2019 | 3 | 4 | RR | 7.79 (3.76, 16.11) | 3.16E-08 | IV |
| Ankylosing spondylitis | Patients vs general population | NHL | SRMA | Deng 2016 | 5 | >1000 | RR | 1.03 (0.83, 1.28) | 8.00E-01 | NS |
| Inflammatory bowel disease | Crohn's disease | Patients vs general population | NHL | SRMA | Lo 2021 | 6 | 30 | IRR | 1.81 (0.94, 3.49) | 7.60E-02 | NS |
| Ulcerative colitis    | Patients vs general population | NHL | SRMA | Lo 2021 | 8 | 79 | IRR | 1.34 (0.95, 1.88) | 9.30E-02 | NS |
| Allergy/Atopic diseases | Asthma | Patients vs general population | NHL | SRMA | Yang 2017 | 15 | 36903 | OR | 0.92 (0.86, 0.99) | 3.00E-02 | IV |
| Hay fever             | Patients vs general population | NHL | SRMA | Yang 2017 | 8 | 4528 | OR | 0.73 (0.62, 0.84) | 5.67E-05 | III |
| Food allergy          | Patients vs general population | NHL | SRMA | Yang 2017 | 6 | 6191 | OR | 0.71 (0.51, 0.98) | 3.90E-02 | IV |
| Eczema                | Patients vs general population | NHL | SRMA | Yang 2017 | 15 | NA | OR | 0.99 (0.81, 1.21) | 9.28E-01 | NS |
| Type 2 diabetes       | Type 2 diabetes | Patients vs general population | NHL | SRMA | Castillo 2012 | 21 | 17282 | OR | 1.22 (1.07, 1.39) | 2.94E-03 | IV |
| Parkinson's disease   | Parkinson's disease | Patients vs general population | NHL | SRMA | Zhang 2019 | 5 | 620 | OR/RR | Not specified | 0.80 (0.74, 0.87) | 1.10E-07 | IV |
| Sarcoidosis           | Sarcoidosis | Patients vs general population | NHL | SRMA | Bonifazi 2015 | 8 | 150 | RR | 1.43 (1.03, 1.99) | 3.30E-02 | IV |
| Biliary cirrhosis     | Biliary cirrhosis | Patients vs general population | NHL | SRMA | Liang 2012 | 3 | 2860 | SIR | 1.15 (0.36, 1.94) | 7.58E-01 | NS |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|-------------|--------------|------------------------------------------|-----------|-----------------------------|
| Overweight and obesity | Overweight | Overweight vs normal weight | NHL | SRMA | Larsson 2007 | 16 | 21720 | RR | 1.07 (1.01, 1.14) | 2.80E-02 | IV |
| Overweight | Overweight | Overweight vs normal weight | DLBCL | MA | Castillo 2014 | 16 | 7349 | RR | 1.14 (1.04, 1.24) | 3.50E-03 | IV |
| Overweight | Overweight | Overweight vs normal weight | CLL | MA | Castillo 2012 | 9 | 2142 | RR | 1.10 (1.03, 1.17) | 3.40E-03 | IV |
| Overweight | Overweight | Overweight vs normal weight | FL | SRMA | Odutola 2020 | 14 | 1798 | RR | 0.99 (0.92, 1.07) | 8.10E-01 | NS |
| Obesity | Obesity | Obesity vs normal weight | NHL | SRMA | Larsson 2007 | 16 | 21720 | RR | 1.20 (1.07, 1.34) | 1.50E-03 | IV |
| Obesity | Obesity | Obesity vs normal weight | DLBCL | MA | Castillo 2014 | 16 | 7349 | RR | 1.29 (1.16, 1.43) | 2.50E-06 | III |
| Obesity | Obesity | Obesity vs normal weight | CLL | MA | Castillo 2012 | 10 | 912 | RR | 1.17 (1.08, 1.27) | 1.60E-04 | IV |
| Obesity | Obesity | Obesity vs normal weight | FL | SRMA | Odutola 2020 | 13 | 903 | RR | 1.08 (0.99, 1.17) | 7.10E-02 | NS |
| Infection | Herpes zoster | Yes vs no | NHL | SRMA | Schmidt 2017 | 7 | 52134 | RR | 1.72 (1.27, 2.32) | 4.49E-04 | III |
| Herpes zoster | Yes vs no | Yes vs no | CLL | SRMA | Schmidt 2017 | 4 | >1000 | RR | 1.65 (1.20, 2.25) | 2.00E-03 | IV |
| HPgV | Yes vs no | Yes vs no | DLBCL | SRMA | Fama 2019 | 3 | 54 | OR | 3.29 (1.63, 6.62) | 1.00E-03 | IV |
| HPgV | Yes vs no | Yes vs no | FL | SRMA | Fama 2019 | 3 | 75 | OR | 3.01 (1.95, 4.63) | 8.64E-07 | IV |
| Risk factors category                  | Environmental risk factors                              | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|--------------------------------------|--------------------------------------------------------|---------------------|---------|------------|--------------|------------------------|--------------|----------------|------------------------------------------|-----------|-------------------------------|
| Epstein–Barr virus early antigen     | High (75th percentile) vs low (<25th percentile)        | NHL                 | MA      | Teras 2015 | 8            | 1421                  | RR           | 1.52           | (1.16, 1.99)                            | 2.40E-03 | IV                             |
| Epstein–Barr virus viral capsid antigen | High (75th percentile) vs low (<25th percentile)    | NHL                 | MA      | Teras 2015 | 9            | 1764                  | RR           | 1.20           | (1.00, 1.44)                            | 5.00E-02 | NS                             |
| Borrelia burgdorferi                | Yes vs no                                             | PCL                 | SRMA    | Travaglino 2020 | 10          | 410                  | OR           | 10.88          | (3.84, 30.81)                           | 8.98E-06 | IV                             |
| Borrelia burgdorferi                | Yes vs no                                             | DLBCL               | SRMA    | Travaglino 2020 | 3            | 53                   | OR           | 8.15           | (1.25, 53.06)                           | 2.80E-02 | IV                             |
| HBV                                 | Yes vs no                                             | TCL                 | SRMA    | Li 2018    | 12           | NA                   | OR           | 1.59           | (1.11, 2.26)                            | 1.07E-02 | IV                             |
| HBV                                 | Yes vs no                                             | DLBCL               | SRMA    | Li 2018    | 10           | 11943                | OR           | 2.06           | (1.48, 2.88)                            | 2.53E-05 | III                            |
| HBV                                 | Yes vs no                                             | FL                  | SRMA    | Li 2018    | 9            | 5124                 | OR           | 1.60           | (1.24, 2.07)                            | 3.50E-04 | III                            |
| HBV                                 | Yes vs no                                             | CLL/SL              | SRMA    | Li 2018    | 8            | 10738                | OR           | 1.87           | (1.34, 2.61)                            | 2.60E-04 | III                            |
| HBV                                 | Yes vs no                                             | BL                  | SRMA    | Li 2018    | 3            | 264                  | OR           | 2.12           | (0.97, 4.65)                            | 6.00E-02 | NS                             |
| HCV                                 | Patients vs general population                        | FL                  | MA      | DalMaso 2006 | 7            | 193                  | RR           | 2.73           | (2.20, 3.38)                            | 9.12E-19 | IV                             |
| HCV                                 | Patients vs general population                        | MZL                 | MA      | DalMaso 2006 | 5            | 134                  | RR           | 3.41           | (2.39, 4.87)                            | 4.48E-11 | IV                             |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|--------------|-------------------------------------------|-----------|-------------------------------|
| HCV                   | Patients vs general population | TCL | MA | DalMaso | 2006 | 4 | 122 | RR | 1.52 (1.13, 2.05) | 5.90E-03 | IV |
| HCV                   | Patients vs general population | CLL/SL | MA | DalMaso | 2006 | 5 | 88 | RR | 1.65 (1.35, 2.02) | 1.57E-06 | IV |
| Malaria infection     | Yes vs no | eBL | SRMA | Kotepui | 2021 | 5 | 6055 | OR | 0.87 (0.54, 1.39) | 5.80E-01 | NS |

### Chemicals and pesticides

| Solvent | Formaldehyde<sup>2</sup> | Ever vs never | FL | SRMA | Odutola 2021 | 3 | 292 | RR | 1.03 (0.83, 1.28) | 8.00E-01 | NS |
| Chlorinated solvents<sup>2</sup> | Ever vs never | FL | SRMA | Odutola 2021 | 3 | 143 | RR | 1.35 (1.09, 1.68) | 6.60E-03 | IV |
| Any solvent<sup>2</sup> | Ever vs never | FL | SRMA | Odutola 2021 | 3 | 669 | IRR | 1.16 (1.00, 1.34) | 4.60E-02 | IV |
| Aromatic hydrocarbons | Styrene<sup>3</sup> | Highest vs lowest | NHL | SRMA | Collins 2018 | 16 | 553 | OR/R | 1.14 (0.91, 1.43) | 2.59E-01 | NS |
| Benzene<sup>3</sup> | Ever vs never | NHL | SRMA | Kane 2010 | 24 | 1420 | OR/RR, Not specified | 1.11 (0.94, 1.30) | 2.10E-01 | NS |
| Benzene<sup>3</sup> | Ever vs never | FL | SRMA | Odutola 2021 | 3 | 333 | OR | 1.30 (0.86, 1.97) | 2.20E-01 | NS |
| Aromatic hydrocarbons<sup>3</sup> | Ever vs never | FL | SRMA | Odutola 2021 | 3 | 7262 | OR | 1.24 (0.88, 1.75) | 2.20E-01 | NS |
| Polychlorinated biphenyls | PCBs<sup>2</sup> | Highest vs lowest | NHL | SRMA | Catalani 2019 | 30 | 1439 | RR | 0.96 (0.85, 1.07) | 4.97E-01 | NS |
| PCBs<sup>2</sup> | Highest vs lowest | DLBCL | SRMA | Catalani 2019 | 6 | NA | RR | 0.68 (0.24, 1.21) | 3.31E-01 | NS |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|-------------|----------------|----------------------------------------|----------|------------------------------|
| PCBs                  | Highest vs lowest         | FL                  | SRMA    | Catalani   | 2019         | 5                      | NA          | RR             | 1.21 (0.79, 1.64)                         | 3.11E-01 | NS                           |
| PCBs                  | Highest vs lowest         | CLL                 | SRMA    | Catalani   | 2019         | 4                      | 573         | RR             | 0.63 (0.39, 0.87)                         | 2.40E-02 | IV                           |
| Dioxin                | Highest vs lowest         | NHL                 | SRMA    | Xu         | 2016         | 4                      | 4263        | RR             | 1.09 (0.92, 1.30)                         | 3.34E-01 | NS                           |
| Trichloroethylene     | Highest vs lowest         | NHL                 | SRMA    | Scott      | 2011         | 17                     | >1000       | RR             | 1.23 (1.07, 1.42)                         | 7.70E-03 | IV                           |
| Occupational exposure to methylene chloride | Highest vs lowest | NHL | MA | Liu 2013 | 6 | 3001 | OR | 1.28 (0.96, 1.70) | 9.00E-02 | NS |
| Occupational exposure to gasoline | Highest vs lowest | NHL | MA | Kane 2010 | 35 | 1042 | RR | 1.02 (0.94, 1.12) | 6.71E-01 | NS |
| Carbamate/thiocarbamate pesticides | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 3 | 1621 | RR | 1.40 (1.10, 2.00) | 2.70E-02 | IV |
| Carbamate insecticides | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 3 | 1621 | RR | 1.70 (1.30, 2.30) | 2.90E-04 | III |
| Organophosphate pesticides | Highest vs lowest | NHL | SRMA | Boffetta 2021 | 6 | 1297 | RR | 1.05 (0.90, 1.24) | 5.60E-01 | NS |
| Glyphosate             | Highest vs lowest         | NHL                 | SRMA    | Boffetta   | 2021         | 4                      | 1285        | RR             | 1.29 (1.02, 1.63)                         | 3.30E-02 | IV                           |
| Glyphosate             | Ever vs never             | FL                  | SRMA    | Odutola    | 2021         | 4                      | 897         | RR             | 0.90 (0.60, 1.34)                         | 6.20E-01 | NS                           |
| Malathion              | Yes vs no                 | NHL                 | MA       | Hu         | 2017         | 7                      | NA          | OR             | 1.17 (0.82, 1.67)                         | 3.94E-01 | NS                           |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|-----------------------|-------------|--------------|------------------------------------------|-----------|-------------------------------|
| Diazinon              | Yes vs no                 | NHL                 | MA      | Hu 2017    | 7            | NA                    | OR          | 1.39         | (1.11, 1.73)                           | 4.00E-03  | IV                            |
| Terbufos              | Yes vs no                 | NHL                 | MA      | Hu 2017    | 5            | NA                    | OR          | 1.07         | (0.85, 1.36)                           | 5.84E-01  | NS                            |
| Organophosphate pesticides | Yes vs no            | NHL                 | MA      | Hu 2017    | 10           | NA                    | OR          | 1.22         | (1.04, 1.43)                           | 1.40E-02  | IV                            |
| Organophosphate pesticides | Ever vs never        | FL                  | SRMA    | Odutola 2021 | 3            | 545                   | OR          | 1.75         | (0.46, 6.72)                           | 4.20E-01  | NS                            |
| DDT                   | Highest vs lowest         | NHL                 | MA      | Luo 2016   | 5            | 1010                  | OR          | 1.02         | (0.81, 1.28)                           | 8.73E-01  | NS                            |
| DDT                  | Highest vs lowest         | FL                  | SRMA    | Odutola 2021 | 3            | 741                   | RR          | 1.25         | (0.75, 2.07)                           | 4.00E-01  | NS                            |
| DDE                   | Highest vs lowest         | NHL                 | MA      | Luo 2016   | 11           | 1905                  | OR          | 1.38         | (1.14, 1.66)                           | 8.00E-04  | III                           |
| DDE                  | Highest vs lowest         | FL                  | SRMA    | Odutola 2021 | 4            | 255                   | RR          | 1.51         | (0.99, 2.31)                           | 5.60E-02  | NS                            |
| HCH                   | Highest vs lowest         | NHL                 | MA      | Luo 2016   | 6            | 1184                  | OR          | 1.36         | (0.95, 1.95)                           | 9.18E-02  | NS                            |
| HCB                   | Highest vs lowest         | NHL                 | MA      | Luo 2016   | 7            | 1265                  | OR          | 1.54         | (1.20, 1.99)                           | 8.00E-04  | III                           |
| Chlordane             | Highest vs lowest         | NHL                 | MA      | Luo 2016   | 8            | 1218                  | OR          | 1.89         | (1.42, 2.50)                           | 1.29E-05  | III                           |
| Organochlorine pesticides | Highest vs lowest   | NHL                 | MA      | Luo 2016   | 13           | 6582                  | OR          | 1.42         | (1.27, 1.59)                           | 2.16E-09  | III                           |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|-----------|--------------|-----------------------|-------------|---------------|------------------------------------------|-----------|-----------------------------|
| Pentachlorophenol⁴ | Highest vs lowest | NHL | SRMA | Zheng 2015 | 5 | 419 | OR | 2.65 (1.33, 5.27) | 6.00E-03 | IV |
| Phenoxy herbicides | 2,4-D | Highest vs lowest | NHL | SRMA | Smith 2017 | 11 | <1000 | OR | 1.82 (1.14, 2.92) | 1.30E-02 | IV |
| MCPA | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 5 | 3986 | RR | 1.50 (0.90, 2.50) | 1.20E-01 | NS |
| Phenoxy herbicides | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 12 | 6493 | RR | 1.40 (1.20, 1.60) | 6.00E-06 | III |
| Other pesticides | Amide herbicides | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 4 | 1155 | RR | 1.30 (0.80, 2.00) | 2.40E-01 | NS |
| Benzoic acid herbicides | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 4 | 1155 | RR | 1.30 (0.90, 1.90) | 1.70E-01 | NS |
| Triazine herbicides | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 4 | 1155 | RR | 1.50 (1.00, 2.10) | 3.20E-02 | IV |
| Trifluralin | Highest vs lowest | NHL | SRMA | Schinasi 2014 | 4 | 1346 | RR | 0.90 (0.60, 1.30) | 6.10E-01 | NS |
| Pyrethroid/pyrethrin⁵ | Ever vs never | FL | SRMA | Odutola 2021 | 4 | 697 | RR | 1.45 (0.91, 2.32) | 1.20E-01 | NS |

**Occupation**

| Flight attendant | Attendants vs general population | Attendants | NHL | MA | Buja 2006 | 3 | NA | SIR | 1.19 (0.52, 2.30) | 6.44E-01 | NS |
| Farmer | | | NA | NHL | MA | Boffetta 2007 | 50 | >1000 | RR | 1.11 (1.05, 1.17) | 1.74E-04 | III |
| Firefighter | Firefighter vs general population | NHL | SRMA | Jalilian 2019 | 14 | NA | SIR | 1.07 (0.96, 1.20) | 2.37E-01 | NS |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Strength of reported association |
|-----------------------|----------------------------|---------------------|---------|------------|--------------|------------------------|-------------|---------------|------------------------------------------|----------|------------------------------|
| Firefighter           | Ever vs never              | FL                  | SRMA    | Odutola    | 2021         | 3                      | 5           | RR            | 1.16 (0.38, 3.52)                          | 8.10E-01 | NS                           |
| Hairdresser           | Hairdresser                | NA                  | NHL     | MA         | Takkouche    | 2009                  | 13          | 22425 RR      | 1.11 (0.94, 1.32)                          | 2.30E-01 | NS                           |

Petroleum refinery worker
Worker vs general population

| Petroleum refinery worker | Worker vs general population | NHL | SRMA | Schnatter 2018 | 16 | NA | RR | 0.98 (0.89, 1.09) | 7.09E-01 | NS |

Meat worker
Worker vs general population

| Meat worker | Worker vs general population | NHL | MA | Boffetta 2007 | 9  | NA | RR | 0.99 (0.77, 1.29) | 9.40E-01 | NS |

Printer
Worker vs general population

| Printer | Worker vs general population | NHL | MA | Boffetta 2007 | 6  | >1000 | RR | 1.86 (1.38, 2.50) | 5.00E-05 | III |

Wood worker
Worker vs general population

| Wood worker | Worker vs general population | NHL | MA | Boffetta 2007 | 11 | NA | RR | 1.04 (0.79, 1.37) | 7.90E-01 | NS |

Occupational exposure to polycyclic aromatic hydrocarbons
Aluminum plant workers

| Occupational exposure to polycyclic aromatic hydrocarbons | Worker vs general population | NHL | SRMA | Alicandro 2016 | 8  | 167 | RR | 1.19 (0.98, 1.44) | 7.60E-02 | NS |

Iron and steel foundry workers

| Iron and steel foundry workers | Worker vs general population | NHL | SRMA | Alicandro 2016 | 8  | 57  | RR | 0.94 (0.73, 1.22) | 6.50E-01 | NS |

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2,4-D=2,4-Dichlorophenoxyacetic acid; ALCt=Acute lymphocytic leukemia; ALCL=Anaplastic large cell lymphoma; BL=Burkitt Lymphoma; CI=Confidence interval; CLL/SLL=Chronic lymphocytic leukemia/small lymphocytic lymphoma; DDE=dichlorodiphenyltrichloroethylene; DDT=dichlorodiphenyltrichloroethane; DLBCL=Diffuse large B-cell lymphoma; eBL=Endemic Burkitt Lymphoma; FL=Follicular lymphoma; HAART=Highly Active Antiretroviral Therapy; HBV=Hepatitis B virus; HCV=Hepatitis C virus; HIV/AIDS=Human immunodeficiency virus, acquired immunodeficiency syndrome; HPgV=Human Pegivirus; IRR=incidence rate ratio; MA=Meta-analysis; MZL=marginal zone lymphoma; MPA=2-methyl-4-chlorophenoxyacetic acid; NA=Not available; NHL=Non-Hodgkin lymphoma; OR=Odds ratio; PCBs=Polychlorinated biphenyls; PI=prediction interval; SIR=Standardized incidence ratio; SRMA=Systematic review and meta-analysis; RR=Risk ratio; TCL=T-cell lymphoma.

aP-value for summary effect estimates using a random-effects DerSimonian and Laird estimator.
bStrength of association using the criteria listed in Table 1.
cThese studies considered NHL incidence and mortality.
dSummary effect estimates were calculated using a fixed effect estimator.
eNot using inverse variance weighting. WHAT DOES THIS MEAN XS: They used Bayesian hierarchical models, I remember at some point Josh mentioned that we should make notes for this! but I'm okay with removing this footnote.
## Table 4. Suggestive risk factors and protective factors identified in meta-analyses of individual patient data from International Lymphoma Epidemiology Consortium

| NHL subtype | At least 1000 cases and $P^{\leq}10^{-3}$ | At least 1000 cases and $P^{\leq}10^{-4}$ |
|-------------|------------------------------------------|------------------------------------------|
| CLL/SLL     | Years since quitting cigarette smoking; printing pressmen | None |
| CLL/SLL/PLL/MCL | Adult infectious mononucleosis | None |
| DLBCL       | Alcohol; Any atopic disorder; Allergy; B and T-cell activating autoimmune diseases; HCV; Hay fever; Recreational sun exposure; Socioeconomic status (high vs low); BMI as young adult (25-30 kg/m$^2$); Rheumatoid arthritis; Blood transfusion; Weight | History of B-cell activating autoimmune disease; Sjogren’s syndrome; HCV; Young adult BMI (%25 kg/m$^2$); Years since quit cigarette smoking; Age first alcohol consumption (20-29 years vs. nondrinker); Current alcohol consumption status as of ~2 years prior to diagnosis/interview |
| FL          | Blood transfusions; Young adult BMI (%25 kg/m$^2$); Recreational sun exposure; History of cigarette smoking (females); Current cigarette smoking; University and higher education teachers; Male height (100% vs. 60%); Any atopic disorder | None |
| MZL         | Systemic lupus erythematosus; HCV; Peptic ulcer; Wine | History of B-cell activating autoimmune disease; Sjogren’s syndrome |
| HCL         | Current cigarette smoking | None |
| NHL         | Hormone replacement therapy; Systemic lupus erythematosus; HCV; Allergy; Food allergy; Hay fever; Blood transfusion; Height; Alcohol exposures; Recreational hair dye use; Socioeconomic status (high vs low); Secondary Sjogren’s syndrome; Childhood measles | Sjogren’s syndrome; History of B-cell activating autoimmune disease; Hay fever; Young adult BMI (%25 kg/m$^2$); Recreational sun exposure (%Q3-Q4 hours/week); Recreational hair dye use (%Q3-Q4 hours/week); Beer, wine, and liquor |

BMI=body mass index; CI=confidence interval; CLL=chronic lymphocytic leukemia; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; HCL=hairy cell leukemia; HCV=hepatitis C virus; MCL=mantle cell lymphoma; MZL=marginal zone lymphoma; NHL=non-Hodgkin lymphoma; SLL=small lymphocytic lymphoma; PLL=prolymphocytic leukemia.

* These were protective risk factors.
| Exposure [NHL subtype] | Effect estimate (95% CI) | Strength of reported association | Exposure [NHL subtype] | Effect estimate (95% CI) | Effect estimates in the same direction | Overlapping 95% confidence intervals | Same level of statistical significance \((P<0.05)\) | At least one-third of studies overlapping |
|------------------------|--------------------------|----------------------------------|------------------------|--------------------------|---------------------------------------|-----------------------------------|------------------------------------|-------------------------------|
| Red blood cell transfusion [NHL] | RR 1.20 (1.07, 1.35) | IV | History of blood transfusion [NHL] | OR 0.83 (0.77, 0.91) | No | No | Both | Yes |
| Red blood cell transfusion [CLL/SLL] | RR 1.66 (1.08, 2.56) | IV | History of blood transfusion [CLL/SLL] | OR 0.79 (0.66, 0.94) | No | No | Both | Yes |
| Red blood cell transfusion [FL] | RR 1.02 (0.67, 1.55) | NS | History of blood transfusion [FL] | OR 0.78 (0.68, 0.89) | No | Yes | MA of IPD only | Yes |
| Red blood cell transfusion [DLBCL] | RR 1.06 (0.86, 1.30) | NS | History of blood transfusion [DLBCL] | OR 0.84 (0.75, 0.95) | No | Yes | MA of IPD only | Yes |
| Ever smoking [NHL] | RR 1.05 (1.00, 1.09) | IV | Any smoking [NHL] | OR 1.02 (0.97, 1.07) | Yes | Yes | Neither | No |
| Ever smoking [DLBCL] | RR 1.01 (0.95, 1.07) | NS | Any smoking [DLBCL] | OR 1.01 (0.94, 1.08) | Yes | Yes | Neither | No |
| Ever smoking [FL] | RR 1.05 (0.88, 1.25) | NS | Any smoking [FL] | OR 1.09 (1.00, 1.18) | Yes | Yes | Neither | Yes |
| Ever smoking [CLL/SLL] | RR 0.96 (0.89, 1.04) | NS | Any smoking [CLL/SLL] | OR 0.90 (0.81, 0.99) | Yes | Yes | MA of IPD only | Yes |
| Ever smoking [TCL] | RR 1.23 (1.06, 1.43) | IV | Any smoking [TCL] | OR 1.32 (1.09, 1.59) | Yes | Yes | Both | No |
| Ever drinking [NHL] | RR 0.85 (0.79, 0.91) | III | Any alcohol [NHL] | OR 0.87 (0.81, 0.93) | Yes | Yes | Both | Yes |
| Ever drinking [TCL] | RR 0.78 (0.58, 1.05) | NS | Any alcohol [TCL] | OR 0.68 (0.53, 0.87) | Yes | Yes | MA of IPD only | Yes |
| Ever drinking [DLBCL] | RR 0.79 (0.68, 0.91) | IV | Any alcohol [DLBCL] | OR 0.81 (0.73, 0.89) | Yes | Yes | Both | Yes |
| Ever drinking [FL] | RR 0.80 (0.69, 0.92) | IV | Any alcohol [FL] | OR 0.86 (0.77, 0.96) | Yes | Yes | Both | Yes |
| Exposure [NHL subtype] | Effect estimate (95% CI) | Strength of reported association | Exposure [NHL subtype] | Effect estimate (95% CI) | Effect estimates in the same direction | Overlapping 95% confidence intervals | Same level of statistical significance (P<0.05) | At least one-third of studies overlapping |
|------------------------|--------------------------|---------------------------------|------------------------|--------------------------|----------------------------------------|----------------------------------------|---------------------------------------------|---------------------------------------------|
| Ever drinking [CLL/SLL] | RR 1.00 (0.80, 1.26)     | NS                               | Any alcohol [CLL/SLL]  | OR 1.04 (0.90, 1.19)     | Yes                                    | Yes                                    | Neither                                      | Yes                                          |
| Pernicious anemia [NHL] | RR 1.16 (0.79, 1.71)     | NS                               | Pernicious anemia [NHL]| OR 1.37 (0.62, 3.03)     | Yes                                    | Yes                                    | Neither                                      | No                                           |
| Rheumatoid arthritis [NHL] | SIR 2.26 (1.82, 2.81)   | II                               | Rheumatoid Arthritis [NHL]| OR 1.32 (0.99, 1.77)     | Yes                                    | No                                     | MA of summary level data only                | No                                           |
| Primary Sjogren's syndrome [NHL] | RR 13.76 (8.53, 18.99) | II                               | Sjogren's syndrome [NHL]| OR 7.52 (3.68, 15.36)    | Yes                                    | Yes                                    | Both                                         | No                                           |
| Systemic lupus erythematosus [NHL] | RR 5.40 (3.75, 7.77)   | II                               | Systemic Lupus Erythematosus [NHL]| OR 2.83 (1.81, 4.11) | Yes                                    | Yes                                    | Both                                         | No                                           |
| Psoriasis [NHL] | RR 1.48 (1.3, 1.69)      | III                              | Psoriasis [NHL]        | OR 1.08 (0.90, 1.29)     | Yes                                    | No                                     | MA of summary level data only                | No                                           |
| Type 1 diabetes [NHL] | RR 1.55 (1.15, 2.08)     | IV                               | Type 1 diabetes [NHL]  | OR 1.15 (0.80, 1.66)     | Yes                                    | Yes                                    | MA of summary level data only                | No                                           |
| Celiac disease [NHL] | OR 2.61 (2.04, 3.33)     | II                               | Celiac disease [NHL]   | OR 1.77 (1.05, 2.99)     | Yes                                    | Yes                                    | Both                                         | Yes                                          |
| Celiac disease [TCL] | OR 15.84 (7.85, 31.94)   | II                               | Celiac disease [TCL]   | OR 14.82 (7.27, 30.19)   | Yes                                    | Yes                                    | Both                                         | Yes                                          |
| Celiac disease [DLBCL] | OR 2.25 (1.32, 3.85)     | IV                               | Celiac disease [DLBCL] | OR 2.09 (1.04, 4.18)     | Yes                                    | Yes                                    | Both                                         | Yes                                          |
| Celiac disease [CLL]  | OR 0.80 (0.46, 1.38)     | NS                               | Celiac disease [CLL/SLL]| OR 0.60 (0.14, 2.61)     | Yes                                    | Yes                                    | Neither                                      | Yes                                          |
| Sarcoidosis [NHL] | RR 1.43 (1.03, 1.99)     | IV                               | Sarcoidosis [NHL]      | OR 0.71 (0.39, 1.29)     | No                                     | Yes                                    | Neither                                      | No                                           |
| Exposure [NHL subtype] | Effect estimate (95% CI) | Strength of reported association | Exposure [NHL subtype] | Effect estimate (95% CI) | Effect estimates in the same direction | Overlapping 95% confidence intervals | Same level of statistical significance (P<0.05) | At least one-third of studies overlapping |
|------------------------|--------------------------|----------------------------------|------------------------|--------------------------|----------------------------------------|--------------------------------------|---------------------------------------------|-------------------------------------------|
| Tuberculosis [NHL]     | RR 1.61 (1.34, 1.94)     | II                               | Adult Tuberculosis infection [NHL] | OR 1.16 (0.96, 1.39)     | Yes                                    | Yes                                  | MA of summary level data only              | No                                        |
| Herpes Zoster [NHL]    | RR 1.72 (1.27, 2.32)     | III                              | Adult shingles [NHL]         | OR 1.05 (0.93, 1.19)     | Yes                                    | No                                   | MA of summary level data only              | No                                        |
| Hepatitis C virus [NHL] | OR 3.36 (2.40, 4.72)     | II                               | Hepatitis C virus [NHL]       | OR 1.81 (1.39, 2.37)     | Yes                                    | No                                   | Both                                        | No                                        |
| Hepatitis C virus [DLBCL] | OR 2.65 (1.88, 3.74)    | II                               | hepatitis C virus [DLBCL]     | OR 2.33 (1.71, 3.19)     | Yes                                    | Yes                                  | Both                                        | Yes                                       |
| Hepatitis C virus [FL] | OR 2.73 (2.20, 3.38)     | IV                               | Hepatitis C virus [FL]        | OR 0.57 (0.30, 1.10)     | No                                     | No                                   | MA of summary level data only              | Yes                                       |
| Hepatitis C virus [MZL] | OR 3.41 (2.39, 4.87)     | IV                               | Hepatitis C virus [MZL]       | OR 3.04 (1.65, 5.60)     | Yes                                    | Yes                                  | Both                                        | Yes                                       |
| Hepatitis C virus [CLL/SLL] | OR 1.65 (1.35, 2.02)   | IV                               | Hepatitis C virus [CLL/SLL]   | OR 2.08 (1.23, 3.49)     | Yes                                    | Yes                                  | Both                                        | Yes                                       |
| Farmer [NHL]           | RR 1.11 (1.05, 1.17)     | III                              | Farmer [NHL]                 | OR 1.03 (0.95, 1.13)     | Yes                                    | Yes                                  | Neither                                      | No                                        |
| Firefighter [NHL]      | SIR 1.07 (0.96, 1.20)    | NS                               | Firefighter [NHL]            | OR 0.76 (0.53, 1.09)     | No                                     | Yes                                  | Neither                                      | No                                        |
| Hairdresser [NHL]      | RR 1.11 (0.94, 1.32)     | NS                               | Hairdresser [NHL]            | OR 1.21 (0.96, 1.52)     | Yes                                    | Yes                                  | Both                                        | No                                        |
| Petroleum refinery worker [NHL] | RR 0.98 (0.89, 1.09) | NS                               | Petroleum workers [NHL]       | OR 0.79 (0.38, 1.67)     | Yes                                    | Yes                                  | Neither                                      | No                                        |
| Teacher [NHL]          | RR 1.47 (1.34, 1.61)     | II                               | Teacher [NHL]                | OR 0.89 (0.81, 0.98)     | No                                     | No                                   | Both                                        | No                                        |
| Meat worker [NHL]      | RR 0.99 (0.77, 1.29)     | NS                               | Meat worker [NHL]            | OR 1.08 (0.81, 1.42)     | No                                     | Yes                                  | Neither                                      | No                                        |
| Printer [NHL]          | RR 1.86 (1.38, 2.50)     | III                              | Printers [NHL]               | OR 0.95 (0.78, 1.17)     | No                                     | No                                   | MA of summary level data only              | No                                        |
| Exposure [NHL subtype] | Effect estimate (95% CI) | Strength of reported association | Exposure [NHL subtype] | Effect estimate (95% CI) | Overlapping 95% confidence intervals | Same level of statistical significance (P<0.05) | At least one-third of studies overlapping |
|------------------------|--------------------------|---------------------------------|------------------------|--------------------------|---------------------------------------|-----------------------------------------------|------------------------------------------|
| Wood worker [NHL]      | RR 1.04 (0.79, 1.37)     | IV                              | Wood workers [NHL]     | OR 1.04 (0.89, 1.22)     | Yes                                   | Yes                                           | Neither                                   | No                                       |

CI=confidence interval; CLL/SLL=chronic lymphocytic leukemia/small lymphocytic lymphoma; DLBCL=diffuse large B-cell lymphoma; NA=not available; NHL=non-Hodgkin lymphoma; OR=odds ratio; SIR=standardized incidence ratio; RR=risk ratio; TCL=T-cell lymphoma.
Response letter: BMJ-2021-069314

Comments from Editors:

1) The paper assumes that IPD MAs are of high quality. This may be true but it needs some supporting evidence to match that for summary MAs. For example what % of IPD findings are non- or weakly significant?

Response: Thank you for this comment. We agree that it is important to understand the strength of associations from the individual patient-level data (IPD) meta-analyses (MAs). However, similar to previous umbrella reviews, MAs of summary-level data were our primary focus. In our evaluation, we evaluated 85 MAs of summary level data reporting 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. These evaluations took us an extensive amount of time, and it would be unrealistic to formally evaluate thousands of other associations. That being said, we do provide information about the 715 nominally significant associations from IPD MAs (please see eTable 5).

Overall, we do not assume that either IPD MAs or MAs of summary level data are higher quality. For instance, in our manuscript we outline that “… MAs of IPD contain thousands of NHL cases and are strengthened by their ability to utilize raw data that are harmonized across multiple studies, they do not include evidence from case-control and cohort studies conducted by investigators outside of the InterLymph Consortium. Therefore, MAs of summary level data and MAs of IPD evaluating the same associations between environmental risk factors and NHL may sometimes lead to discordant results and conclusions.”

To further address this concern, we have updated the Limitations section to reflect the fact that MAs of IPD and MAs of summary level data can have different strengths and limitations, and our evaluation did not focus on comparing the potential quality of these types of reviews.

Page 17, Line 11:

Ninth, MAs of IPD and MAs of summary level data have different strengths and limitations, and our evaluation did not focus on comparing the potential quality of these types of reviews.

2) Excluding non-English language reviews was a limitation.

Response: Thank you for sharing this concern. Similar to other umbrella reviews,1,2 we focused on English-language reviews. In our evaluation, we excluded 20 non-English reviews at full-text stage. We have updated the Limitations section to reflect this concern.

Page 17, Line 8

Eighth, by excluding non-English language reviews, we may have missed additional potential associations. However, we utilized the same approach as previous umbrella review focused on environmental risk factors for health outcome(s).

3) Author John Ioannides is not mentioned in the Contributors section.

Response: Thank you for pointing this out. We have further clarified Dr. Ioannidis’s contribution in this section.
Page 18, Line 5:

“XS, JPAI, and JDW designed this study ....... XS, JPAI, and JDW participated in the interpretation of the data. All authors and critically revised the manuscript for important intellectual content.”

4) Presenting the detailed AMSTAR2 scores for every MA would be helpful.

Response: Thank you for the comment. We present this information in eTable 6 and also added the information of author year in the table to make it more comprehensive. We did not evaluate the 27 MAs of IPD because the evaluation tool AMSTAR 2 was mainly designed for MAs of summary level data. Furthermore, MAs of summary level data is the major focus of our evaluation.

5) The percentages are all to one decimal place and would be simpler as whole numbers.

Response: Thanks for the comments. We have carefully revised our manuscript to make sure we reported all the percentages as whole numbers.

Comments from reviewers:

Reviewer: 1

This paper presents an umbrella review and synthesis of published meta-analyses on environmental risk factors for non-Hodgkin lymphoma. Eighty-five meta-analyses of summary-level data reporting 257 associations were identified, 11 of which were classed as providing highly suggestive evidence, for autoimmune diseases or infections- generally accepted risk factors. Further, the meta-analyses of summary-level data were compared with the InterLymph Consortium’s individual-level data analyses.

In the process of its aims, the paper collates a vast array of published meta-analyses and uses statistical criteria for evaluation. Its findings are what is already known for lymphoma. The project is undoubtedly ambitious but misses the essential narrative where the reliability of the individual studies within each meta-analysis can be assessed for generalisability, potential biases, etc. Undoubtedly more systematic reviews/meta-analyses on risk factors for NHL will continue to be published, but although there is care in the statistical criteria applied here, I am not convinced that evaluations such as this will help the overall narrative; there is a danger that purely statistical assessments could exacerbate some of the issues round assessment of the evidence by unintentionally adding weight to small risk estimates, and misses the careful attention that good reviews employ.

Response: Thank you for your careful review of our work, we appreciate the helpful feedback. To the best of our knowledge, no study has either comprehensively evaluated all the reported associations in current reviews or investigated the agreement between MAs of IPD and MAs of summary level data. Umbrella reviews can help provide information about the quality of MAs, the accumulated evidence supporting different associations, and the potential research gaps that may exist. Similar to previous high profile umbrella reviews, the primary focus of our study is to evaluate the accumulated evidence. While individual systematic reviews and meta-analyses focus on the quality of individual studies, umbrella
reviews provide information about the quality and conduct of reviews. To further address these concerns, we have updated our Limitations section.

Page 16, Line 15:

Second, we did not evaluate the quality of individual studies included in the MAs of summary level data, the impact that individual studies have on the overall heterogeneity, or the potential role that residual/unmeasured confounding could have on associations. Individual risk of bias evaluations are outside the scope of umbrella reviews, and it is the expectation that MAs have already conducted these quality assessments.

Major:

1) The criteria for selection of the meta-analyses are not clear, why are some given precedent over others? For instance, Kane et al 2011 on gluten sensitivity included over 30 studies on coeliac disease and the related dermatitis herpetiformis while the chosen Tio et al 2012 includes less of the literature at only 8 studies.

Response: Thank you for your comment. Our work focuses on the etiology of NHL risk, which specifically refers to the risk of developing NHL. In our Methods section, we mentioned that we focused on reviews “evaluating associations between environmental risk factors and incident NHL”. Although Kane et al 2011 was identified, this review included studies on coeliac disease and NHL incidence and mortality, while the eight studies included in Tio et al 2012 were all studies on NHL incidence.

2) There is no mention of the consistency of evidence within the meta-analyses using absence of heterogeneity in the study-specific risk estimates. E.g. of the 16 studies included in Qin et al 2019, the 3 which were statistically significant largely drive the overall pooled estimate of 1.14 (95%CI 1.01-1.29, heterogeneity I-squared 79.7%).

Response: Thank you for sharing this concern. Umbrella reviews focus on the totality of the evidence from meta-analyses. For these evaluations, which consider a large number of exposures and outcomes, investigating the role of individual studies is not feasible. However, our formal evaluations of the strength of evidence considers the I² value from each association.

However, to further address this comment, we have updated our Limitations section.

Page 16, Line 15:

Second, we did not evaluate the quality of individual studies included in the MAs of summary level data, the impact that individual studies have on the overall heterogeneity, or the potential role that residual/unmeasured confounding could have on associations.

3) Many of the statistically significant associations are less than 1.5 and only marginally significant (lower CI limit close to 1). This requires commentary since associations could be due to confounding, and/or scenarios such as that for Qin et al 2019.

Response: Thanks for the comment. Among the 112 statistically significant associations, we found 63 (56%) of them had effect estimates between 0.67 and 1.5. We have included this information in the revised manuscript. Please also see our response to Comment #2 above, where we note that we do not account for residual/unmeasured confounding.
Across all 112 nominally statistically significant associations, 63 (56%) had relative risk values that were between 0.67 and 1.50.

Minor:

1) There is no list of references for the meta-analyses. Those excluded because full-text could not be retrieved should also be cited. The tables should include reference numbers for the meta-analyses.

Response: Thanks for your comment. We have updated our Supplement 2 to include references to the MAs that were considered in our evaluation.

2) The items of AMSTAR2 are not mentioned.

Response: Thank you for sharing this concern. We present the items of AMSTAR 2 for each included meta-analysis in eTable 6. We also mentioned in the Results section that “The most common unfulfilled critical domains of the AMSTAR 2 tool were incomplete justification of excluded studies (74, 87%) and missing or no information about preregistered protocols (72, 85%).”

3) Tables should cite references using author name and year (missing from table 7) and repeat the header row if over more than 1 page.

Response: Thank you for this helpful suggestion. We added the author name and year information to eTable 6 and edited all our tables in the main text and supplement accordingly.

4) The authors state that InterLymph has published 1000s of associations; this statement requires qualification as like others, risk factors would have been explored based on a priori evidence, and subgroup analyses by age, sex, dose etc conducted if there is an overall association or a priori suggestion to do so. For information, InterLymph was specifically set-up in the early 2000s to explore potential risk factors for the heterogeneous subtypes of NHL; requiring international collaboration, it endeavoured to include all studies in the field at this time. The consortium has reported for most subtypes in publications by lifestyle and environmental factors as well as providing overview of each subtype in a JNCI monograph published in 2014 (please note that Morton et al 2014 in this monograph is a summary of evidence across all subtypes from the papers by Linet 2014, Cerhan 2014, Monnereau 2014, etc).

Response: Thank you for the comment. We have now updated our Discussion to improve clarity.

Furthermore, the InterLymph findings may be difficult to disentangle, with at least 700 nominally statistically significant associations among thousands of analyses conducted across different subtypes of NHL and exposure levels (e.g., different type/dosage of alcohol consumption).”
Reviewer: 2

Comments:

The authors attempted to summarize the range, strength, and validity of reported associations between environmental risk factors and NHL and evaluate the concordance between associations reported in MAs of summary level data and MAs of IPD. Please find my comments below:

1. The WCRF/AICR Continuous Update Project (CUP) is considered a gold standard reference, especially when risk factors referring to diet, nutrition, physical activity, and body fatness are concerned. The novelty of the present umbrella review will be clearer if authors indicate very specifically how their study is different or stands out from the WCRF/AICR CUP, which is supposed to be more comprehensive than any single study. The WCRF/AICR concluded that there is limited evidence for an association between excess body fatness (Lauby-Secretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, Straif K; International Agency for Research on Cancer Handbook Working Group. Body Fatness and Cancer--Viewpoint of the IARC Working Group. N Engl J Med. 2016 Aug 25;375(8):794-8.). Has the WCRF/AICR published reports on other environmental risk factors of NHL? I would like to see this mentioned in the introduction.

Response: We appreciated the comment and the helpful information. WCRF/AICR Continuous Update Project was established to answer the critical question of how diet, nutrition, and physical activity impact cancer risk. Based on our search, we were only able to identify one paper that investigated environmental risk factors for non-Hodgkin's lymphoma (NHL).\(^7\) This evaluation suggested that BMI and BMI in early adulthood (aged 18-21 years) were associated with the risk of NHL and diffuse large beta-cell lymphoma (DLBCL), which was also similar to our summary in Table 3 (obesity and overweight during adulthood were associated with the increased risk of NHL and DLBCL). Furthermore, the WCRF study only reported the relative risks for dose-response relationships (i.e., per 5 kg/m\(^2\)). As we outlined in our methods, our evaluation prioritized the effect estimates comparing ever versus never exposure (or the highest versus lowest levels of exposures). We also address this in our Limitation section, where we noted that we did not consider dose-response relationships.

We also checked the website of WCRF and it seemed that NHL is not among one of the priority areas for WCRF (https://www.wcrf.org/diet-and-cancer/cancer-types/). For the reasons outlined above, we would prefer not to mention WCRF in our Introduction, but defer to the Editors.

2. Comparing the MAs that included different study design is problematic, as different study designs have different robustness. If possible, I believe the authors should focus on the findings of MAs of prospective observational studies. Otherwise, this issue should be discussed in detail as a limitation.

Response: We are grateful for this comment. We acknowledge the fact that we did not prioritize reviews of certain study designs or address differences across different study designs. This approach has also been used for previous umbrella reviews looking at risk factors for chronic diseases.\(^8\)-\(^10\) Furthermore, certain NHL subtypes are rare, and prospective observational studies may not always be realistic. However, we have updated our
Limitation section to clarify that we did not differentiate between reviews of cohort or case-control studies.

Page 16, Line 19

...we considered MAs that included cohort and case-control studies, and our assessments did not prioritize reviews of certain study designs or address differences across different study designs. Considering that certain NHL subtypes are rare, case-control studies may often be the most realistic study design to evaluate exposure histories.

3. Since the association between environmental factors and NHL risk might be subtype-specific, the analyses should focus on NHL subtypes rather than NHL as a single exposure.

Response: Thank you for the comment. We focused on all NHL outcomes reported in MAs. In Table 2 and 3, we have one column for the outcome which specifies if it is NHL overall or a subtype of NHL. We believe that this comprehensive focus helps provide an overview of what is reported in the literature.

4. Please present the reference list of the excluded MAs. As for now, the Reviewer could not assess whether their exclusions were justified.

Response: Thanks for the comment. We have now provided a list of 904 papers that we excluded at full text stage.

5. It is not clear whether the authors only included environmental factors in adulthood. The environmental factors during childhood, adolescence, and young adulthood may be important for NHL development (Hidayat K, Li HJ, Shi BM. Anthropometric factors and non-Hodgkin's lymphoma risk: systematic review and meta-analysis of prospective studies. Crit Rev Oncol Hematol. 2018 Sep;129:113-123.; Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, Aune D, Greenwood DC, Chan DSM, Norat T. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019 Apr 1;30(4):528-541.).

Response: We appreciated the comment and also acknowledged the importance of distinguishing environmental factors during different periods. We considered any environmental exposure at any time, as defined by the authors of the individual review papers. In Table 2, we specified which risk factors were explicitly described by the authors as childhood exposures (e.g., maternal/paternal smoking).

6. The authors should also discuss that most of the meta-analyses included in their review were largely based on the data from case-control studies. Moreover, the authors did not discuss the ability of the included studies to control for important confounders. Many of the individual studies did not control for important confounders. Therefore, more long-term, well-designed prospective cohort studies are warranted to confirm or refute the current findings.

Response: We appreciated the comment. However, case-control studies are an important study design when it comes to rare outcomes. We agree that confounding is always an important issue for observational studies. The AMSTAR 2 evaluation includes a confounding-related question (item 11: “If meta-analysis was justified did the review authors use appropriate methods for statistical combination of results?”). Given our focus on accumulated evidence and the large number of associations, it would not be feasible to
examine the individual studies for their consideration of important confounders. However, we have mentioned this as a limitation in our Limitations section (see Reviewer 1 Comment #2 above).

7. “when multiple MAs of summary level data evaluated the same exposures and outcomes, we selected the association based on the largest number of included studies. Although this approach does not ensure that the highest quality MAs are selected, this methodology has been utilized by previous umbrella reviews.”

This reasoning does not provide a satisfactory rationale for utilizing the approach; please ensure that only the highest quality MAs are selected.

Response: Thank you for this comment. During the design of our study, we had several discussions about the strengths and limitations of different approaches. We reviewed previous umbrella reviews and prespecified our approach of selecting MAs with the largest number of included studies. Selecting the MAs based on the number of reviews included is one of the most extensively used approaches in current umbrella reviews.1,8 We identified 257 associations from 85 MAs in our study. For multiple risk factors (e.g., obesity/overweight, different pesticides, and some autoimmune diseases) we identified more than 5 MAs for each association. We hope that our supplementary eTable 4, which describes the overlapping MAs of summary level data, helps provide information about the associations evaluated in multiple studies.

Reference:

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3. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ.* 2017;358:j4008.
4. Neuenschwander M, Ballon A, Weber KS, et al. Role of diet in type 2 diabetes incidence: umbrella review of meta-analyses of prospective observational studies. *BMJ.* 2019;366:l2368.
5. O'Sullivan JW, Muntinga T, Grigg S, Ioannidis JPA. Prevalence and outcomes of incidental imaging findings: umbrella review. *BMJ.* 2018;361:k2387.
6. Poole R, Kennedy OJ, Roderick P, Fallowfield JA, Hayes PC, Parkes J. Coffee consumption and health: umbrella review of meta-analyses of multiple health outcomes. *BMJ.* 2017;359:j5024.
7. Abar L, Sobiecki JG, Cariolou M, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. *Ann. Oncol.* 2019;30(4):528-541.
8. Radua J, Ramella-Cravarro V, Ioannidis JPA, et al. What causes psychosis? An umbrella review of risk and protective factors. *World Psychiatry.* 2018;17(1):49-66.
9. Bellou V, Belbasis L, Tzoulaki I, Middleton LT, Ioannidis JPA, Evangelou E. Systematic evaluation of the associations between environmental risk factors and dementia: An umbrella review of systematic reviews and meta-analyses. *Alzheimers Dement.* 2017;13(4):406-418.

10. Bellou V, Belbasis L, Tzoulaki I, Evangelou E, Ioannidis JP. Environmental risk factors and Parkinson's disease: An umbrella review of meta-analyses. *Parkinsonism Relat. Disord.* 2016;23:1-9.
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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Abstract

Objectives: To summarize the range, strength, and validity of reported associations between environmental risk factors and non-Hodgkin lymphoma (NHL), and to evaluate the concordance between associations reported in meta-analyses (MAs) of summary level data and MAs of individual participant data (IPD).

Design: Umbrella review.

Data sources: MEDLINE, Embase, Scopus, Web of Science Core Collection, Cochrane Library, and Epistemonikos from inception to 23 July 2021.

Eligibility criteria: English language MAs of summary level data and MAs of IPD evaluating associations between environmental risk factors and incident NHL (overall and NHL subtypes).

Data extraction and synthesis: Summary effect estimates from MAs of summary level data comparing ever versus never exposure that were adjusted for the largest number of potential confounders were re-estimated using a random-effects model and classified as presenting non-significant, weak ($P<0.05$), suggestive ($P<10^{-3}$ and $>1000$ cases), highly suggestive ($P<10^{-6}$, $>1000$ cases, largest study reporting a significant association), or convincing ($P<10^{-6}$, $>1000$ cases, largest study reporting a significant association, $I^2<50\%$, 95% prediction interval excluding the null value, and no evidence of small study effects and excess significance bias) evidence. When the same exposures, exposure contrast levels, and outcomes were evaluated in MAs of summary level data and MAs of IPD from the International Lymphoma Epidemiology (InterLymph) Consortium, concordance in terms of direction, level of significance, and overlap of 95% confidence intervals (CI) was examined. We assessed the methodological quality of the MAs of summary level data using the A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2 tool.

Results: We identified 85 MAs of summary level data reporting 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. Nearly all (79/85, 93%) MAs of summary level data were classified as having critically low quality. Most (225, 88%) associations presented either non-significant or weak evidence. The 11 (4%) associations presenting highly suggestive evidence were primarily for autoimmune or infectious disease-related risk factors. Only 1 association, history of celiac disease and risk of NHL, presented convincing evidence. Overall, 40 associations reported in MAs of summary level data were also evaluated in InterLymph MAs of IPD. Of these, 22 (55%) pairs were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. There were 28 (70%) pairs where the summary effect sizes from the MAs of IPD were more conservative.
**Conclusion:** This umbrella review suggests that there is a mass production of low-quality MAs of summary level data, many of which report weak associations between environmental risk factors and NHL, and highlights the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.

**Systematic review registration** PROSPERO CRD42020178010.
What is already known on this topic

- Observational studies have suggested that environmental risk factors, including clinical, occupational, and lifestyle exposures, may be associated with the risk of developing non-Hodgkin lymphoma.

- As a result of the large number of observational studies evaluating the impact of environmental risk factors on non-Hodgkin lymphoma, dozens of systematic reviews and meta-analyses of summary and individual participant level data have focused on synthesizing evidence and identifying potential risk factors.

- Little is known about: (1) the range, strength, and validity of associations between environmental risk factors and non-Hodgkin lymphoma reported in meta-analyses or (2) the concordance between meta-analyses of summary level data and meta-analyses of individual participant data evaluating the same associations.

What this study adds

- This umbrella review suggests that although a large range of environmental risk factors for non-Hodgkin lymphoma have been evaluated in meta-analyses, the vast majority of meta-analyses of summary level data are low quality and present either non-significant or weak associations.

- Overall, only half of the associations that were evaluated in both meta-analyses of summary level data and meta-analyses of individual participant data were in the same direction, had the same level of statistical significance, and had overlapping 95% confidence intervals.

- Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, this umbrella review highlights the need for improving not only primary studies but also evidence synthesis in the field of non-Hodgkin lymphoma etiology.
Introduction
Non-Hodgkin lymphoma (NHL), a lymphoid cancer that originates in white blood cells called lymphocytes, is the 9th leading cause of cancer death among both men and women.\(^1\) NHL accounts for nearly 90% of all lymphomas\(^2\) and is the most common hematologic malignancy in the world.\(^3\) Although NHL can be broadly categorized into two major groups (i.e., B-cell, T-cell/natural killer-cell lymphomas), it represents a diverse group of malignant disorders with dozens of subtypes.\(^4\) Evidence suggests that NHL is more common among older adults, men, and people with a first degree relative with NHL.\(^5,6\) However, despite substantial effort to identify NHL causes and risk factors over the past few decades, the exact etiology of NHL is unknown.\(^5\)

Epidemiological studies have suggested that environmental risk factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors, may be associated with the risk of developing NHL. In particular, several prominent potential risk factors proposed in the literature include viruses (e.g., Epstein-Barr virus infection),\(^7\) autoimmune diseases (e.g., Sjogren’s syndrome, celiac disease, and rheumatoid arthritis),\(^8-10\) and immune dysregulation (i.e., patients with a history of organ transplantation, acquired immunodeficiency syndromes (HIV/AIDs), or immunosuppressive medication treatment).\(^5,6,11\) However, given that these exposures and conditions are relatively rare,\(^11\) a broad range of additional environmental risk factors, including exposure to insecticides,\(^12\) red and processed meat consumption,\(^13\) and hair dye,\(^14\) have been evaluated and proposed as potential risk factors.

As a result of the large number of observational studies evaluating the impact of environmental risk factors on NHL, dozens of systematic reviews and meta-analyses (MAs) of summary level data have focused on synthesizing evidence and identifying the most promising risk factors. Moreover, the International Lymphoma Epidemiology (InterLymph) Consortium,\(^15\) a group of investigators who pool data from their completed or ongoing NHL case-control studies, have published multiple MAs of individual participant data (IPD) evaluating associations between various environmental risk factors and NHL.\(^16-18\) Although these MAs of IPD contain thousands of NHL cases and are strengthened by their ability to utilize raw data that are harmonized across multiple studies, they do not include evidence from case-control and cohort studies conducted by investigators outside of the InterLymph Consortium. Therefore, MAs of summary level data and MAs of IPD evaluating the same associations between environmental risk factors and NHL may sometimes lead to discordant results and conclusions.
To provide an overview of the range, strength, and validity of reported associations between environmental risk factors and NHL, we conducted an umbrella review of the evidence across published systematic reviews and MAs. In addition to summarizing the results, determining hints of biases, and assessing the quality of reviews, we evaluated the consistency between all associations reported in both MAs of summary level data and InterLymph MAs of IPD.

Methods

We conducted an umbrella review on the reported associations between environmental risk factors and the risk of NHL. Umbrella reviews are used to systematically identify and evaluate evidence reported in published systematic reviews and MAs.\textsuperscript{19,20} Our study protocol was pre-registered on the International prospective register of systematic reviews (CRD42020178010) and posted on Open Science Framework (https://osf.io/6g2ev/). We did not involve patients or members of the public when designing the question and study, interpreting the results, and/or drafting the manuscript.

Database searches

Working with an experienced medical librarian (KN), we developed and performed a comprehensive search of multiple databases: MEDLINE (Ovid), Embase (Ovid), Scopus, Web of Science Core Collection (as licensed at Yale University), Cochrane Library, and Epistemonikos from inception to July 24\textsuperscript{th} 2020 (\textit{eTable 1 in Supplement 1}). In each database, we used three concepts: NHL, risk factors, and the study designs of interest (MAs, systematic reviews, and pooled analyses). The search strategy for NHL was based on the search strategy used in a published review.\textsuperscript{21} The study design search strategy used elements from a published search filter.\textsuperscript{22} Database limits were used to exclude conference papers and meeting abstracts. No language limits were used. Records were deduplicated in EndNote, the Yale Reference Deduplicator, and Covidence. No citation chaining was conducted.

On July 24\textsuperscript{th} 2020, searches were run in each database and 14,753 references were identified. After deduplication in EndNote and Covidence, 8025 unique records were uploaded for screening. On July 23\textsuperscript{th} 2021, all searches were rerun and deduplicated and 969 additional unique records were added to Covidence for manual screening. In total, our search retrieved 8994 unique records across all databases.

Eligibility criteria
We included English language systematic reviews, MAs of summary level data (i.e., MAs using effect estimates reported in individual studies), and MAs of IPD of observational studies evaluating associations between environmental risk factors and incident NHL (overall or any subtypes, eTable 2 in Supplement 1). We considered all non-genetic factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors that can affect a person’s health, as environmental risk factors. Systematic reviews and MAs were excluded if they primarily focused on genetic risk factors, evaluated risk factors for the treatment, relapse, remission, or prognosis of NHL patients, or examined NHL as a risk factor for other diseases (eText 1 in Supplement 1).

Two reviewers (XS and HZ) independently screened the titles and abstracts and then full-text versions of potentially eligible articles. Any disagreements or uncertainties were discussed with a third reviewer (JDW).

**Data extraction**

Data extraction was performed independently by two reviewers (XS and HZ), and a third reviewer (JDW) arbitrated all potential discrepancies. For each systematic review and MA, we recorded the first author, year of publication, article title, journal of publication, study design, population, examined exposures and their definitions, and examined outcomes and their definition (i.e., NHL or NHL subtypes). For all MAs of summary level data, we identified each unique exposure-outcome relationship and recorded the number of studies included, total sample size, number of cases, and study-specific adjusted relative risk estimates (e.g., relative risks, hazard ratios, or odds ratios) and corresponding 95% confidence intervals (CIs). For studies that considered multiple exposure contrast levels, control groups, and/or confounders, we prioritized the effect estimates comparing ever versus never exposure that were adjusted for the largest number of potential confounders. Whenever ever versus never exposures comparisons were not reported, we recorded the effect estimates comparing the highest versus lowest levels of exposures. When multiple MAs of summary level data were identified for the same environmental risk factor, we selected the effect estimates that were based on the largest number of component studies.

For systematic reviews with unique associations that were not investigated in MAs of summary level data, we recorded the number of studies identified, the reasons why MAs were not performed, and the main conclusions. Lastly, for all MAs of IPD, one author (JDW) identified the exposures, NHL subtypes, and number of NHL cases for: (1) all nominally
statistically significant ($P<0.05$) associations and (2) any associations that were also evaluated in MAs of summary level data.

**Quality Assessment**

Four reviewers (XS, HZ, YD, and JDW) evaluated the quality of all MAs of summary level data using A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2.33 Any discrepancies were discussed and resolved by consensus. Based on the suggested rating scheme,33 the overall confidence in the results of the MAs of summary level data were classified as high, moderate, low, or critically low. We did not examine the quality of MAs of IPD.

**Statistical analysis**

First, we used a random-effects model, which allows for unexplained between-study heterogeneity on the effect of interest, with the between-study variance estimated using the DerSimonian and Laird (DL) estimator. When summary effect estimates were reported without a corresponding $P$ value, we used the 95% CIs to calculate the $P$ value using a previously described method.24 Next, we categorized the strength of the reported associations across five levels (Table 1), following previously established methodology.25-28 All associations with $P>0.05$ were classified as non-significant. Associations with $P<0.05$ and fewer than 1000 cases were classified as weak. Associations with $P<10^{-3}$ and at least 1000 cases were classified as suggestive. For associations with $P<10^{-6}$, at least 1000 cases, and $P<0.05$ for the largest component study, we sequentially evaluated 95% prediction intervals (PIs), presence of small study effects (Egger regression asymmetry test),29 and evidence of excess significance using the Ioannidis test.30 PIs provide a potential range of the true effect and incorporate the uncertainty of whether the observed effect will arise in future studies as well.31,32 $P<0.1$ for Egger’s test suggests the presence of small study effects (i.e. small studies are more prone to report larger or more significant results while larger studies tend to report more conservative results). The Ioannidis test estimates whether the observed number of studies with nominally statistically significant ($P<0.05$) results in a MA differs from the expected number of studies with nominally statistically significant studies.30 Associations with 95% PIs including the null, statistically significant Egger’s test ($P<0.1$), and/or evidence of excess significance were classified as highly suggestive. Associations with 95% prediction intervals excluding the null, non-statistically significant Egger’s test ($P>0.1$), and no evidence of excess significance were classified as convincing.
Statistical analysis was conducted using metagen package in R version 4.1.0. (eTable 3 in Supplement 1).

Concordance between MAs of summary level data and InterLymph MAs of IPD

When the same exposures, exposure contrast levels, and NHL subtypes were examined in MAs of summary level data and InterLymph MAs of IPD, two authors (XS and JDW) determined whether the effect estimates: (1) were in the same direction, (2) had overlapping 95% CIs, and/or (3) had the same level of statistical significance ($P<0.05$ or $P\geq0.05$). Associations with all three criteria fulfilled were classified as fully concordant. Lastly, we determined how often MAs of summary level data included at least one-third of the same component studies as the InterLymph MAs of IPD.

Results

Literature search

Among 16438 records identified through the literature search, 7444 were excluded as duplicates, leaving 8994 titles and abstracts for initial screening. 7970 records were excluded based on the title and abstract and 1024 were screened at the full text stage for inclusion. After excluding 904 records at the full text stage (eTable 1 in Supplement 2), our searches identified 85 MAs of summary level data evaluating 134 unique environmental risk factors and 8 systematic reviews evaluating 8 unique risk factors (eFigure 1 and eText 2 in Supplement 1 and eTable 2 in Supplement 2). In addition, we identified 27 MAs of IPD (Supplement 2), of which 24 (89%) were conducted by the InterLymph Consortium. More than one MA of summary level data was identified for 44 (44/134, 33%) risk factors (eTable 4 in Supplement 1). Among the MAs of summary level data selected based on the largest number of component studies, approximately half were also the most recently published (25/44, 57%).

Methodological quality

The vast majority of the 85 MAs of summary level data had overall confidence ratings of low (3, 4%) or critically low (79, 93%) according to the AMSTAR 2 tool. There were 2 (2%) where the overall confidence in the results was classified as moderate. Only 1 (1%), evaluating the association between tuberculosis and risk of NHL, had an overall confidence rating of high (eTable 3 in Supplement 2). The most common unfulfilled critical domains of the
AMSTAR 2 tool were incomplete justification of excluded studies (74, 87%) and missing or no information about preregistered protocols (72, 85%).

**MAs of summary level data**

Among the 257 associations reported in the MAs of summary level data, 124 and 133 evaluated the impact of environmental risk factors on the risk of NHL overall and NHL subtypes, respectively. NHL subtypes included follicular lymphoma (FL; 43, 17%), diffuse large B-cell lymphoma (DLBCL; 35, 14%), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL; 31, 12%), T-cell lymphoma (TCL; 12, 5%), B-cell lymphoma (BCL; 4, 2%), marginal zone lymphoma (MZL; 2, 1%), endemic Burkitt Lymphoma (eBL; 1, 0.4%), Burkitt lymphoma (BL; 1, 0.4%), primary cutaneous lymphoma (PCL; 1, 0.4%). The most common exposure categories were dietary factors (90, 35%), medical histories and comorbidities (54, 21%), chemicals and pesticides (42, 16%), lifestyle factors (29, 11%), drugs, vaccinations, and medical procedures (30, 12%), and occupational (12, 5%). The median number of component studies per MA of summary level data was 5 (IQR 4-10). The median number of NHL cases, among the 64 (75%) MAs reporting this information, was 1533 (IQR, 482-5872).

**Credibility criteria**

After re-estimating the 257 associations using a random-effects DL estimator and applying the credibility criteria, 145 (56%) were classified as presenting non-significant evidence (eTable 4 in Supplement 2). There were 80 (31%) nominally statistically significant ($P<0.05$) associations that were classified as presenting weak evidence. There were 20 (8%) statistically significant associations ($P<10^{-3}$), based on analyses with at least 1000 NHL cases, that were classified as presenting suggestive evidence. Only 12 (5%) associations were classified as presenting highly suggestive or convincing evidence, with a $P<10^{-6}$, at least 1000 cases, and a $P<0.05$ for the largest component study. The 11 highly suggestive associations were for history of renal transplantation and risk of NHL, rheumatoid arthritis and risk of NHL, primary Sjogren's syndrome and risk of NHL, systemic lupus erythematosus and risk of NHL, celiac disease and risk of TCL, tuberculosis and risk of NHL, hepatitis B virus (HBV) and risk of NHL and BCL, hepatitis C virus (HCV) and risk of NHL and DLBCL, and teaching as an occupation and risk of NHL (Table 2).

There was one association, between history of celiac disease and risk of NHL (OR 2.61, 95% CI 2.04 to 3.33; 110, 245 NHL cases from 8 individual studies), that was classified as presenting convincing evidence. Although the association had $P<10^{-6}$, at least 1000 cases, a nominally significant result for the largest component study, low/moderate proportion of
total variability due to between-study variability ($I^2 < 50\%$), a $95\%$ PI excluding the null, and no evidence of small study effects, we were unable to conduct the Ioannidis test due to the incomplete information reported about the component studies. Across all the 112 nominally statistically significant associations, 63 (56\%) had relative risk values that were between 0.67 and 1.50.

**Systematic reviews**

We identified 8 systematic reviews without quantitative synthesis with 8 unique associations that were not investigated by MAs of summary level data (*eText 2 in Supplement 1*).

**MAs of IPD**

We identified 27 MAs of IPD, of which 24 were from the InterLymph Consortium. The 24 InterLymph MAs of IPD reported 715 nominally statistically significant ($P<0.05$) associations. Of these, 116 and 21 associations were based on analyses with at least 1000 NHL cases and had $P<10^{-3}$ and $P<10^{-6}$, respectively (*Table 3 and eTable 5 in Supplement 2*). Overall, the unique suggestive exposures categories were alcohol consumption on risk of DLBCL, MZL and NHL, history of Sjogren’s syndrome on risk of DLBCL, MZL and NHL, recreational sun exposure on risk of DLBCL, FL and NHL, and history of HCV on risk of DLBCL, MZL and NHL. Although the 3 non-InterLymph MAs of IPD examined 5 associations not reported in systematic reviews and/or MAs of the summary level data, including fish eaters and risk of NHL, vegetarians and vegans and risk of NHL, maternal age at the time of the child’s birth and risk of NHL, paternal age at the time of the child’s birth and risk of NHL, and leisure-time physical activity and risk of NHL, none were nominally statistically significant.

**Consistency between MAs of summary level data and InterLymph MAs of IPD**

There were 40 associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD (*eTable 6 in Supplement 2 and eFigure 1 in Supplement 1*). While 22 (55\%) evaluated the impact of environmental risk factors on the risk of NHL overall, the other half (18, 45\%) focused on various NHL subtypes (CLL/SLL, 5 (13\%); DLBCL, 5 (13\%); FL, 4 (10\%); TCL, 3 (8\%); MZL, 1 (3\%)).

Overall, 22 of 40 (55\%) of the associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD were in the same direction, had the same level of statistical significance, and had overlapping 95\% CIs. There were 10 (25\%) pairs where the effect estimates were both statistically significantly increased, 3 (8\%) where they were both statistically significantly decreased, 7 (18\%) where they were both non-statistically significantly increased, and 2 (5\%) where they were both non-statistically significantly decreased (Kappa=0.37, *eTable 6 in Supplement 2 and eFigure 1 in Supplement 1*). The 13
associations where the MAs of the summary level data and MAs of IPD effect estimates were both statistically significantly increased or decreased were for history of smoking and risk of TCL, history of drinking and risk of NHL, DLBCL, and FL, history of primary Sjogren's syndrome and risk of NHL, history of systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL, TCL and DLBCL, and history of HCV and risk of NHL, DLBCL, MZL and CLL/SLL. There were 28 (70%) pairs where the effect sizes from the MAs of IPD were more conservative than the effect sizes from the MAs of summary level data.

There were 4 suggestive associations reported in MAs of summary level data that were also evaluated in the InterLymph MAs of IPD. Of these, 3 associations from MAs of IPD had effect estimates in the same direction, had $P<10^{-3}$, and were based on analyses with at least 1000 NHL cases (i.e., history of psoriasis and risk of NHL, history of Herpes Zoster and risk of NHL, and history of farming as an occupation and risk of NHL). There were 8 highly suggestive associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD. Of these, 7 associations from the MAs of IPD had effect estimates in the same direction, had $P<10^{-6}$, and were based on analyses with at least 1000 NHL cases (i.e., history of rheumatoid arthritis and risk of NHL, history of primary Sjogren's syndrome and risk of NHL, history systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL and TCL, history of tuberculosis and risk of NHL, and history of HCV and risk of NHL).

There were 19 (48%) pairs where the MAs of summary level data included at least one-third of the same component studies as the InterLymph MAs of IPD. There was no difference in terms of concordance (direction, statistical significance of summary effect estimates and overlapping 95% CIs) between MAs of summary level data that included at least one-third versus fewer than one-third of the same component studies as the MAs of IPD (12/19 (63%) vs 10/21 (48%), $P=0.32$).

**Discussion**

In this umbrella review, we evaluated the range, strength, and validity of reported associations between environmental risk factors and NHL across 85 MAs of published observational studies. Overall, we identified 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. The vast majority of the associations, including those evaluating various dietary, clinical, lifestyle, chemical, and occupational exposures, were classified as having either non-significant or weak evidence. More than half of the nominally significant

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associations were only marginally significant. Only 5% of the associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence. When the same associations were evaluated in MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Overall, effect sizes from MAs of IPD were more conservative. This umbrella review suggests that there is a mass production of low-quality MAs of summary level data reporting weak associations between environmental risk factors and NHL. These findings highlight the need for improving not only primary studies but also evidence synthesis in this field. Moreover, given that many of the assessed risk factors are correlated, simultaneous consideration of multiple risk factors will be useful to understand which ones have the strongest, independent effects on NHL risk.

Although a wide range of environmental exposures have been evaluated and proposed as potential risk factors for NHL, our evaluation suggests that the only highly suggestive or convincing exposures proposed in MAs of summary level data and MAs of IPD are related to autoimmune and infectious diseases. In particular, the prominent autoimmune disease-related risk factors include history of celiac disease, rheumatoid arthritis, primary Sjogren's syndrome, and systemic lupus erythematosus. Although the exact mechanisms behind these associations remains unclear, many autoimmune disorders are characterized by chronic inflammation,\(^{40-42}\) which may intensify B cell or T cell activation and promote the development of lymphoma.\(^{43,44}\) Previous studies have also suggested that the dysfunction of some protein families, such as FAS and tumor necrosis factor, and the interplay between various immune cells, could be potential mechanisms.\(^{45}\) However, there is uncertainty when it comes to the temporality of these associations, with studies reporting that autoimmune diseases can occur during lymphoma.\(^{46,47}\)

Associations between viral and bacterial infections and NHL risk have been suggested for several decades.\(^{2,5,6,48,49}\) Different hypotheses for HCV-related lymphomagenesis have been proposed. For instance, chromosomal aberrations, including chromosome t(14;18) translocation, have been found to be associated with mixed cryoglobulinemia, a disorder most commonly caused by HCV infection and that can evolve into lymphoproliferative disorders.\(^{50-52}\) Furthermore, genetic variations, including Interleukin-10 polymorphisms, have also been proposed as a potential pathway between HCV infection and NHL susceptibility and development.\(^{53}\) Similar to autoimmune disease-related risk factors, it remains unclear whether these associations are driven by disease status, medication use, or disease-medication interactions.\(^{54-58}\) Considering how rare many of these autoimmune and infectious disease-
related exposures are, future efforts are necessary to determine the impact of multiple environmental as well as non-environmental risk factors simultaneously.5,6

Among 40 associations evaluated by both MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Unlike MAs of summary level data, MAs of IPD tend to focus on studies with more homogeneous designs and patient populations. Furthermore, MAs of IPD can allow for better harmonization of data across studies, more advanced one-stage meta-analytical approaches, and analyses accounting for many exposure categories and potential confounders.59,60 Although the InterLymph MAs of IPD are particularly robust due to the large number of NHL cases and subtypes considered, MAs of IPD without systematic reviews may exclude evidence from high-quality case-control or cohort studies. For instance, the InterLymph analyses only included evidence from completed and ongoing case-control studies from consortium members. Furthermore, the InterLymph findings may be difficult to disentangle, with at least 700 nominally statistically significant associations among thousands of analyses conducted across different subtypes of NHL and exposure levels (e.g., different type/dosage of alcohol consumption). In the future, it will be necessary to monitor the consistency between MAs of summary level data and MAs of IPD, especially since approximately half of the MAs of summary level data had at least one-third of the same component studies as the MAs of IPD. In addition, authors of MAs should carefully evaluate whether any external studies can and should be included in their syntheses. Of interest, we observed that more than two thirds of the effect sizes were more conservative in the InterLymph MAs of IPD than in the MAs of summary level data. This may be a reflection of greater selective reporting bias in the corpus of studies available in the literature as compared with a set of studies participating in a consortium.

Our study suggests that nearly all MAs of summary level data evaluating associations between environmental risk factors and risk of NHL could be classified as having critically low quality according to the AMSTAR 2 tool. Previous umbrella reviews focused on the associations between environmental risk factors and health outcomes have noted similar concerns. However, the proportion of low or critically low-quality NHL reviews is higher than what has been observed among umbrella reviews for inflammatory bowel diseases,61 attention-deficit/hyperactivity disorder,62 eating disorders,63 early childhood caries,64 physical activity for academic achievement,65 and physical therapy for tendinopathy.66 These findings may not be surprising considering recent concerns about the mass production of systematic reviews.67,68 In the future, authors planning systematic reviews and MAs of summary level data of the
associations between environmental exposures and NHL should adhere to reporting guidelines. Moreover, authors should also critically evaluate how their findings relate to existing MAs of IPD, focusing on the impact of different methods, populations, and other characteristics.

**Limitations**

Our umbrella review has several limitations. First, we did not identify potential environmental risk factors that were only examined in individual observational studies. Our objective was to identify and summarize the associations that were reported by the MAs of summary level data, which already covered a wide space of diverse associations. Second, we did not evaluate the quality of individual studies included in the MAs of summary level data, the impact that individual studies have on the overall heterogeneity, the magnitude of the associations, or the potential role that residual/unmeasured confounding could have on associations. Individual risk of bias evaluations are outside the scope of umbrella reviews, and it is the expectation that MAs have already conducted these quality assessments. Third, we considered MAs that included cohort and case-control studies, and our assessments did not prioritize reviews of certain study designs or address differences across different study designs. Considering that certain NHL subtypes are rare, case-control studies may often be the most realistic study design to evaluate exposure histories. Fourth, although umbrella reviews provide a comprehensive summary of the associations reported in MAs, the validity of the summary effect estimates is dependent on the quality of the individual MAs. Although we attempted to standardize associations using a random-effects DL estimator, we did not evaluate or re-conduct the literature searches for all potential exposure-outcome relationships. Fifth, we did not calculate \( I^2 \), 95% PIs, Egger’s test, and excess significance test for non-significant and nominally statistically significant associations. Given the large number of associations identified, we prioritized these calculations for associations where these values were necessary to determine the strength of associations using the previously established classification system.\(^{20}\) It is also worth noting that \( I^2 \) values should not be used to make inferences about heterogeneity, as it does not measure heterogeneity directly, but rather the proportion of total variability due to between-study variability.\(^{69}\) However, the \( I^2 \) cut-off of 50% is a standard grading criterion for evidence in umbrella reviews.\(^{25,62}\) Sixth, when summary effect estimates of multiple exposure contrast levels were reported, we focused on the risk estimates comparing ever versus never exposure (or comparing the highest versus lowest levels of exposures). Although we did not consider all potential contrast levels and dose-response relationships, our objective was to provide a universal overview of the relationships.
between examined risk factors and NHL. Specific dose-response relationships may nevertheless exist for certain associations, and they would need to be examined on a case-by-case basis. Seventh, we only identified the nominally statistically significant associations among the thousands of associations reported in InterLymph MAs of IPD. Eighth, by excluding non-English language reviews, we may have missed additional potential associations. However, we utilized the same approach as previous umbrella reviews that focused on risk factors for health outcome(s). Ninth, MAs of IPD and MAs of summary level data can have different strengths and limitations, and our evaluation did not focus on comparing the potential quality of these types of studies. We also did not focus on the impact of different methods, populations, or other characteristics when comparing the consistency of the results between the two study types. Tenth, umbrella reviews are not intended to provide information about the likelihood that associations are causal. Lastly, when multiple MAs of summary level data evaluated the same exposures and outcomes, we selected the association based on the largest number of included studies. Although this approach does not ensure that the highest quality MAs are selected, this methodology has been utilized by previous umbrella reviews.

Conclusion

In this large-scale umbrella review, we identified dozens of MAs evaluating associations between environmental risk factors and NHL. However, the vast majority of MAs of summary level data were low quality and presented either non-significant or weak evidence. When the same associations were evaluated in MAs of summary level data and MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, these findings highlight the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.
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Transparency: The senior author (manuscripts guarantor) (JDW) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant registered) have been explained.

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Tables and figures:

Table 1. Grading criteria for evidence categories

| Strength of association          | Description                                                                 |
|----------------------------------|-----------------------------------------------------------------------------|
| Convincing (class I)             | Highly statistically significant association ($P < 10^{-6}$)                  |
|                                  | At least 1000 NHL cases                                                     |
|                                  | Low/moderate proportion of total variability due to between-study variability |
|                                  | ($I^2 < 50\%$)                                                             |
|                                  | 95% prediction interval excluding the null value                            |
|                                  | Largest study reporting a nominally statistically significant ($P < 0.05$)  |
|                                  | No evidence of small-study effects                                          |
|                                  | No evidence of excess significance bias                                     |
| Highly suggestive (class II)     | Highly statistically significant association ($P < 10^{-6}$)                  |
|                                  | At least 1000 NHL cases                                                     |
|                                  | Largest study reporting a nominally statistically significant ($P < 0.05$)  |
| Suggestive (class III)           | At least 1000 NHL cases                                                     |
|                                  | Statistically significant association ($P < 10^{-3}$)                        |
| Weak (class IV)                  | Nominally statistically significant association ($P < 0.05$)                 |
| Non-significant                  | Non-statistically significant associations ($P > 0.05$)                      |

*P value for the association that calculated by random effects model.
NHL=non-Hodgkin lymphoma.
Table 2. Environmental risk factors for non-Hodgkin lymphoma reported in meta-analyses of summary level data with convincing (Class I) and highly suggestive (Class II) evidence

| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author | Year | No. of primary studies | No. of cases | Effec measure | Random effects summary effect size (95% CI) | P random | Large study nominally significant (P<0.05) | I² (%) | 95% PI | Small study effect | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|------------|--------|------|------------------------|-------------|-------------|------------------------------------------|-----------|------------------------------------------|-------|------|----------------|-------------------|
| Renal transplant      | Renal transplant          | Transplant recipients vs general population | NHL     | SRM        | Wang   | 2018 | 6                      | 770         | SIR         | 10.66 (8.54, 13.31)                           | 3.44E-86  | Yes                                      | 80.2  | NA   | NA          | II                |
| Autoimmune diseases   | Rheumatoid arthritis      | Patients vs general population | NHL     | SRM        | Simon  | 2015 | 16                     | 1531        | SIR         | 2.26 (1.82, 2.81)                           | 8.42E-13  | Yes                                      | 96    | NA   | NA          | II                |
| Primary Sjogren's syndrome | Patients vs general population | NHL     | SRM        | Liang  | 2014 | 11                    | 12325       | RR          | 13.76 (8.53, 18.99)                          | 1.62E-34  | Yes                                      | 58.8  | NA   | NA          | II                |
| Systemic lupus erythematosus | Patients vs general population | NHL     | MA         | Cao    | 2015 | 12                    | 166         | RR          | 5.4 (3.75, 7.77)                            | 1.99E-18  | Yes                                      | 74.3  | NA   | NA          | II                |
| celiac disease        | Patients vs general population | NHL     | SRM        | Tio    | 2012 | 8                     | 110245      | OR          | 2.61 (2.04, 3.33)                           | 9.32E-14  | Yes                                      | 23.4  | (1.57 , 4.33) | No | I                |
| celiac disease        | Patients vs general population | TCL     | SRM        | Tio    | 2012 | 5                     | 35358       | OR          | 15.84 (7.85, 31.94)                         | 6.90E-14  | Yes                                      | 55.5  | NA   | NA          | II                |
| Infectious diseases   | Tuberculosis             | Patients vs general population | NHL     | SRM        | Leung  | 2020 | 8                      | 2390        | RR          | 1.61 (1.34, 1.94)                           | 6.76E-07  | Yes                                      | 50.2  | NA   | NA          | II                |
| HBV                  | HBV infected vs          | NHL     | SRM        | Li     | 2018 | 58                    | 53714       | OR          | 2.50 (2.2, 2.83)                            | 6.33E-42  | Yes                                      | 77.9  | NA   | NA          | II                |
| Risk factors category | Environment risk factors | Level of comparison | Outcome | Study type | Author/year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Large study nominally significant (P<0.05) | I² (%) | 95% PI | Small study effect | Strength of reported association |
|-----------------------|--------------------------|---------------------|---------|------------|-------------|------------------------|-------------|---------------|------------------------------------------|----------|-------------------------------|--------|-------|-----------------|-------------------------------|
| HBV                  | HBV infected vs non-infected | BCL | SRMA | Li 2018 | >1000 | OR | 2.46 (1.97, 3.07) | 1.24E-14 | Yes | 62.9 | NA | NA | II |
| HCV                  | HCV infected vs non-infected | NHL | SRMA | Masa rome 2019 | 3307 | OR | 3.36 (2.4, 4.72) | 7.92E-12 | Yes | 88 | NA | NA | II |
| HCV                  | Patients vs general population | DLBCL | MA | DalMaso 2006 | 1020 | RR | 2.65 (1.88, 3.74) | 4.98E-08 | Yes | 39 | (1.46, 5.81) | No | II |
| Occupation           | Teacher vs non-teachers | NHL | MA | Boffetta 2007 | >1000 | RR | 1.47 (1.34, 1.61) | 1.60E-15 | Yes | 76 | NA | NA | II |

BCL=B cell lymphoma; CI=confidence interval; HBV=hepatitis B virus; HCV=hepatitis C virus; MA=meta-analysis; NA=not available; NHL=non-Hodgkin lymphoma; OR=odds ratio; PI=prediction interval; SIR=standardized incidence ratio; SRMA=systematic review and meta-analysis; RR=risk ratio; TCL=T-cell lymphoma.

*P value for summary effect estimates using a random-effects DerSimonian and Laird estimator.

| NHL subtype | At least 1000 cases and P<10^-3 | At least 1000 cases and P<10^-6 |
|------------|---------------------------------|---------------------------------|
| CLL/SLL    | Years since quitting cigarette smoking; printing pressmen | None |

Table 3. Suggestive risk factors and protective factors identified in meta-analyses of individual patient data from International Lymphoma Epidemiology Consortium
| CLL/SLL/PLL/MCL | Adult infectious mononucleosis | None |
|----------------|--------------------------------|------|
| DLBCL          | Alcohol; Any atopic disorder; Allergy; B and T-cell activating autoimmune diseases; HCV; Hay fever; Recreational sun exposure; Socioeconomic status (high vs low); BMI as young adult (25<30 kg/m²); Rheumatoid arthritis; Blood transfusion; Weight | History of B-cell activating autoimmune disease; Sjogren’s syndrome; HCV; Young adult BMI (%25 kg/m²+); Years since quit cigarette smoking; Age first alcohol consumption (20-29 years vs. nondrinker); Current alcohol consumption status as of ~2 years prior to diagnosis/interview |
| FL             | Blood transfusions; Young adult BMI (%25 kg/m²+); Recreational sun exposure; History of cigarette smoking (females); Current cigarette smoking; University and higher education teachers; Male height (100% vs. 60%); Any atopic disorder | None |
| MZL            | Systemic lupus erythematosus; HCV, Peptic ulcer; Wine | History of B-cell activating autoimmune disease; Sjogren’s syndrome |
| HCL            | Current cigarette smoking | None |
| NHL            | Hormone replacement therapy; Systemic lupus erythematosus; HCV; Allergy; Food allergy; Hay fever; Blood transfusion; Height; Alcohol exposures; Recreational hair dye use; Socioeconomic status (high vs low); Secondary Sjogren’s syndrome; Childhood measles | Sjogren’s syndrome; History of B-cell activating autoimmune disease; Hay fever; Young adult BMI (%25 kg/m²); Recreational sun exposure (%Q3-Q4 hours/week); Recreational hair dye use (%Q3-Q4 hours/week); Beer, wine, and liquor |

BMI=body mass index; CI=confidence interval; CLL=chronic lymphocytic leukemia; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; HCL=hairy cell leukemia; HCV=hepatitis C virus; MCL=mantle cell lymphoma; MZL=marginal zone lymphoma; NHL=non-Hodgkin lymphoma; SLL=small lymphocytic lymphoma; PLL=prolymphocytic leukemia.

*These were protective risk factors.
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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Abstract

Objectives: To summarize the range, strength, and validity of reported associations between environmental risk factors and non-Hodgkin lymphoma (NHL), and to evaluate the concordance between associations reported in meta-analyses (MAs) of summary level data and MAs of individual participant data (IPD).

Design: Umbrella review.

Data sources: MEDLINE, Embase, Scopus, Web of Science Core Collection, Cochrane Library, and Epistemonikos from inception to 23 July 2021.

Eligibility criteria: English language MAs of summary level data and MAs of IPD evaluating associations between environmental risk factors and incident NHL (overall and NHL subtypes).

Data extraction and synthesis: Summary effect estimates from MAs of summary level data comparing ever versus never exposure that were adjusted for the largest number of potential confounders were re-estimated using a random-effects model and classified as presenting non-significant, weak ($P<0.05$), suggestive ($P<10^{-3}$ and $>1000$ cases), highly suggestive ($P<10^{-6}$, $>1000$ cases, largest study reporting a significant association), or convincing ($P<10^{-6}$, $>1000$ cases, largest study reporting a significant association, $I^2<50\%$, 95% prediction interval excluding the null value, and no evidence of small study effects and excess significance bias) evidence. When the same exposures, exposure contrast levels, and outcomes were evaluated in MAs of summary level data and MAs of IPD from the International Lymphoma Epidemiology (InterLymph) Consortium, concordance in terms of direction, level of significance, and overlap of 95% confidence intervals (CI) was examined. We assessed the methodological quality of the MAs of summary level data using the A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2 tool.

Results: We identified 85 MAs of summary level data reporting 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. Nearly all (79/85, 93%) MAs of summary level data were classified as having critically low quality. Most (225, 88%) associations presented either non-significant or weak evidence. The 11 (4%) associations presenting highly suggestive evidence were primarily for autoimmune or infectious disease-related risk factors. Only 1 association, history of celiac disease and risk of NHL, presented convincing evidence. Overall, 40 associations reported in MAs of summary level data were also evaluated in InterLymph MAs of IPD. Of these, 22 (55%) pairs were in the same direction,
had the same level of statistical significance, and had overlapping 95% CIs. There were 28 (70%) pairs where the summary effect sizes from the MAs of IPD were more conservative. Nearly all (79/85, 93%) MAs of summary level data were classified as having critically low quality.

**Conclusion:** This umbrella review suggests that there is a mass production of low-quality MAs of summary level data, many of which report weak associations between environmental risk factors and NHL, and highlights the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.

**Systematic review registration** PROSPERO CRD42020178010.
What is already known on this topic

- Observational studies have suggested that environmental risk factors, including clinical, occupational, and lifestyle exposures, may be associated with the risk of developing non-Hodgkin lymphoma.
- As a result of the large number of observational studies evaluating the impact of environmental risk factors on non-Hodgkin lymphoma, dozens of systematic reviews and meta-analyses of summary and individual participant level data have focused on synthesizing evidence and identifying potential risk factors.
- Little is known about: (1) the range, strength, and validity of associations between environmental risk factors and non-Hodgkin lymphoma reported in meta-analyses or (2) the concordance between meta-analyses of summary level data and meta-analyses of individual participant data evaluating the same associations.

What this study adds

- This umbrella review suggests that although a large range of environmental risk factors for non-Hodgkin lymphoma have been evaluated in meta-analyses, the vast majority of meta-analyses of summary level data are low quality and present either non-significant or weak associations.
- Overall, only half of the associations that were evaluated in both meta-analyses of summary level data and meta-analyses of individual participant data were in the same direction, had the same level of statistical significance, and had overlapping 95% confidence intervals.
- Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, this umbrella review highlights the need for improving not only primary studies but also evidence synthesis in the field of non-Hodgkin lymphoma etiology.
Introduction

Non-Hodgkin lymphoma (NHL), a lymphoid cancer that originates in white blood cells called lymphocytes, is the 9th leading cause of cancer death among both men and women.\(^1\) NHL accounts for nearly 90% of all lymphomas\(^2\) and is the most common hematologic malignancy in the world.\(^3\) Although NHL can be broadly categorized into two major groups (i.e., B-cell, T-cell/natural killer-cell lymphomas), it represents a diverse group of malignant disorders with dozens of subtypes.\(^4\) Evidence suggests that NHL is more common among older adults, men, and people with a first degree relative with NHL.\(^5,6\) However, despite substantial effort to identify NHL causes and risk factors over the past few decades, the exact etiology of NHL is unknown.\(^5\)

Epidemiological studies have suggested that environmental risk factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors, may be associated with the risk of developing NHL. In particular, several prominent potential risk factors proposed in the literature include viruses (e.g., Epstein-Barr virus infection),\(^7\) autoimmune diseases (e.g., Sjogren’s syndrome, celiac disease, and rheumatoid arthritis),\(^8-10\) and immune dysregulation (i.e., patients with a history of organ transplantation, acquired immunodeficiency syndromes (HIV/AIDS), or immunosuppressive medication treatment).\(^5,6,11\) However, given that these exposures and conditions are relatively rare,\(^11\) a broad range of additional environmental risk factors, including exposure to insecticides,\(^12\) red and processed meat consumption,\(^13\) and hair dye,\(^14\) have been evaluated and proposed as potential risk factors.

As a result of the large number of observational studies evaluating the impact of environmental risk factors on NHL, dozens of systematic reviews and meta-analyses (MAs) of summary level data have focused on synthesizing evidence and identifying the most promising risk factors. Moreover, the International Lymphoma Epidemiology (InterLymph) Consortium,\(^15\) a group of investigators who pool data from their completed or ongoing NHL case-control studies, have published multiple MAs of individual participant data (IPD) evaluating associations between various environmental risk factors and NHL.\(^16-18\) Although
these MAs of IPD contain thousands of NHL cases and are strengthened by their ability to utilize raw data that are harmonized across multiple studies, they do not include evidence from case-control and cohort studies conducted by investigators outside of the InterLymph Consortium. Therefore, MAs of summary level data and MAs of IPD evaluating the same associations between environmental risk factors and NHL may sometimes lead to discordant results and conclusions.

To provide an overview of the range, strength, and validity of reported associations between environmental risk factors and NHL, we conducted an umbrella review of the evidence across published systematic reviews and MAs. In addition to summarizing the results, determining hints of biases, and assessing the quality of reviews, we evaluated the consistency between all associations reported in both MAs of summary level data and InterLymph MAs of IPD.

**Methods**

We conducted an umbrella review on the reported associations between environmental risk factors and the risk of NHL. Umbrella reviews are used to systematically identify and evaluate evidence reported in published systematic reviews and MAs.\(^\text{19,20}\) Our study protocol was pre-registered on the International prospective register of systematic reviews (CRD42020178010) and posted on Open Science Framework (https://osf.io/6g2ev/). We did not involve patients or members of the public when designing the question and study, interpreting the results, and/or drafting the manuscript.

**Database searches**

Working with an experienced medical librarian (KN), we developed and performed a comprehensive search of multiple databases: MEDLINE (Ovid), Embase (Ovid), Scopus, Web of Science Core Collection (as licensed at Yale University), Cochrane Library, and Epistemonikos from inception to July 24\(^\text{th}\) 2020 (eTable 1 in Supplement \textbf{41}). In each database, we used three concepts: NHL, risk factors, and the study designs of interest (MAs, systematic reviews, and pooled analyses). The search strategy for NHL was based on the search strategy used in a published review.\(^\text{21}\) The study design search strategy used elements from a published search filter.\(^\text{22}\) Database limits were used to exclude conference papers and meeting abstracts. No language limits were used. Records were deduplicated in EndNote, the Yale Reference Deduplicator, and Covidence. No citation chaining was conducted.
On July 24th 2020, searches were run in each database and 14,753 references were identified. After deduplication in EndNote and Covidence, 8025 unique records were uploaded for screening. On July 23rd 2021, all searches were rerun and deduplicated and 969 additional unique records were added to Covidence for manual screening. In total, our search retrieved 8994 unique records across all databases.

**Eligibility criteria**

We included English language systematic reviews, MAs of summary level data (i.e., MAs using effect estimates reported in individual studies), and MAs of IPD of observational studies evaluating associations between environmental risk factors and incident NHL (overall or any subtypes, eTable 2 in Supplement 1). We considered all non-genetic factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors that can affect a person’s health, as environmental risk factors.23 Systematic reviews and MAs were excluded if they primarily focused on genetic risk factors, evaluated risk factors for the treatment, relapse, remission, or prognosis of NHL patients, or examined NHL as a risk factor for other diseases (eText 1 in Supplement 1).

Two reviewers (XS and HZ) independently screened the titles and abstracts and then full-text versions of potentially eligible articles. Any disagreements or uncertainties were discussed with a third reviewer (JDW).

**Data extraction**

Data extraction was performed independently by two reviewers (XS and HZ), and a third reviewer (JDW) arbitrated all potential discrepancies. For each systematic review and MA, we recorded the first author, year of publication, article title, journal of publication, study design, population, examined exposures and their definitions, and examined outcomes and their definition (i.e., NHL or NHL subtypes). For all MAs of summary level data, we identified each unique exposure-outcome relationship and recorded the number of studies included, total sample size, number of cases, and study-specific adjusted relative risk estimates (e.g., relative risks, hazard ratios, or odds ratios) and corresponding 95% confidence intervals (CIs). For studies that considered multiple exposure contrast levels, control groups, and/or confounders, we prioritized the effect estimates comparing ever versus never exposure that were adjusted for the largest number of potential confounders. Whenever ever versus never exposures comparisons were not reported, we recorded the effect estimates comparing the highest versus lowest levels of exposures. When multiple MAs of summary level data were identified for the
same environmental risk factor, we selected the effect estimates that were based on the largest number of component studies.

For systematic reviews with unique associations that were not investigated in MAs of summary level data, we recorded the number of studies identified, the reasons why MAs were not performed, and the main conclusions. Lastly, for all MAs of IPD, one author (JDW) identified the exposures, NHL subtypes, and number of NHL cases for: (1) all nominally statistically significant ($P<0.05$) associations and (2) any associations that were also evaluated in MAs of summary level data.

**Quality Assessment**

Four reviewers (XS, HZ, YD, and JDW) evaluated the quality of all MAs of summary level data using A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2. Any discrepancies were discussed and resolved by consensus. Based on the suggested rating scheme, the overall confidence in the results of the MAs of summary level data were classified as high, moderate, low, or critically low. We did not examine the quality of MAs of IPD.

**Statistical analysis**

First, we used a random-effects model, which allows for unexplained between-study heterogeneity on the effect of interest, with the between-study variance estimated using the DerSimonian and Laird (DL) estimator. We estimated all summary effect estimates and 95% CIs using a random-effects DerSimonian and Laird (DL) estimator. When summary effect estimates were reported without a corresponding $P$ value, we used the 95% CIs to calculate the $P$ value using a previously described method. Next, we categorized the strength of the reported associations across five levels (Table 1), following previously established methodology. All associations with $P>0.05$ were classified as non-significant. Associations with $P<0.05$ and fewer than 1000 cases were classified as weak. Associations with $P<10^{-3}$ and at least 1000 cases were classified as suggestive. For associations with $P<10^{-6}$, at least 1000 cases, and $P<0.05$ for the largest component study, we sequentially evaluated 95% prediction intervals (PIs), presence of small study effects (Egger regression asymmetry test), and evidence of excess significance using the Ioannidis test. PIs provide a potential range of the true effect and incorporate the uncertainty of whether the observed effect will arise in future studies as well. $P<0.1$ for Egger’s test suggests the presence of small study effects (i.e. small studies are more prone to report larger or more significant results while larger studies tend to report more conservative results). The Ioannidis test estimates whether the observed
number of studies with nominally statistically significant \( (P<0.05) \) results in a MA differs from the expected number of studies with nominally statistically significant studies.\(^{30}\) Associations with 95\% PIs including the null, statistically significant Egger’s test \( (P<0.1) \), and/or evidence of excess significance were classified as highly suggestive. Associations with 95\% prediction intervals excluding the null, non-statistically significant Egger’s test \( (P>0.1) \), and no evidence of excess significance were classified as convincing.

Statistical analysis was conducted using \textit{metagen} \mbox{package in R version 4.1.0}. (eTable 3 in Supplement 1).

\textit{Concordance between MAs of summary level data and InterLymph MAs of IPD}

When the same exposures, exposure contrast levels, and NHL subtypes were examined in MAs of summary level data and InterLymph MAs of IPD, two authors (XS and JDW) determined whether the effect estimates: (1) were in the same direction, (2) had overlapping 95\% CIs, and/or (3) had the same level of statistical significance \( (P<0.05 \text{ or } P\geq 0.05) \). Associations with all three criteria fulfilled were classified as fully concordant. Lastly, we determined how often MAs of summary level data included at least one-third of the same component studies as the InterLymph MAs of IPD.

\textit{Quality Assessment}

Four reviewers (XS, HZ, YD, and JDW) evaluated the quality of all MAs of summary level data using \textit{A MeaSurement Tool to Assess Systematic Reviews (AMSTAR)} \(^{2,33}\) Any discrepancies were discussed and resolved by consensus. Based on the suggested rating scheme,\(^{33}\) the overall confidence in the results of the MAs of summary level data were classified as high, moderate, low, or critically low. The quality of MAs of IPD was not examined in our study.

\textit{Results}

\textit{Literature search}

Among 16438 records identified through the literature search, 7444 were excluded as duplicates, leaving 8994 titles and abstracts for initial screening. 7970 records were excluded based on the title and abstract and 1024 were screened at the full text stage for inclusion. After excluding 904 records at the full text stage (eTable 1 in Supplement 2), our searches identified 85 MAs of summary level data evaluating 134 unique environmental risk factors and 8 systematic reviews evaluating 8 unique risk factors (eFigure 1, \textit{and} eText 2 in
Supplement 1 and eTable 2 in Supplement 32). In addition, we identified 27 MAs of IPD (Supplement 32), of which 24 (89%) were conducted by the InterLymph Consortium. More than one MA of summary level data was identified for 44 (44/134, 33%) risk factors (eTable 4 in Supplement 1). Among the MAs of summary level data selected based on the largest number of component studies, approximately half were also the most recently published (25/44, 57%) (eTable 4 in Supplement 1).

**Methodological quality**

The vast majority of the 85 MAs of summary level data had overall confidence ratings of low (3, 4%) or critically low (79, 93%) according to the AMSTAR 2 tool. There were 2 (2%) where the overall confidence in the results was classified as moderate.34,35 Only 1 (1%), evaluating the association between tuberculosis and risk of NHL, had an overall confidence rating of high (eTable 643 in Supplement 42).36 The most common unfulfilled critical domains of the AMSTAR 2 tool were incomplete justification of excluded studies (74, 87%) and missing or no information about preregistered protocols (72, 85%).

**MAs of summary level data**

Among the 257 associations reported in the MAs of summary level data, 124 and 133 evaluated the impact of environmental risk factors on the risk of NHL overall and NHL subtypes, respectively. NHL subtypes included follicular lymphoma (FL; 43, 17%), diffuse large B-cell lymphoma (DLBCL; 35, 14%), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL; 31, 12%), T-cell lymphoma (TCL; 12, 5%), B-cell lymphoma (BCL; 4, 2%), marginal zone lymphoma (MZL; 2, 1%), endemic Burkitt Lymphoma (eBL; 1, 0.4%), Burkitt lymphoma (BL; 1, 0.4%), primary cutaneous lymphoma (PCL; 1, 0.4%). The most common exposure categories were dietary factors (90, 35%), medical histories and comorbidities (54, 21%), chemicals and pesticides (42, 16%), lifestyle factors (29, 11%), drugs, vaccinations, and medical procedures (30, 12%), and occupational (12, 5%). The median number of component studies per MA of summary level data was 5 (IQR 4-10). The median number of NHL cases, among the 64 (75%) MAs reporting this information, was 1533 (IQR, 482-5872).

**Credibility criteria**

After re-estimating the 257 associations using a random-effects DL estimator and applying the credibility criteria, 145 (56%) were classified as presenting non-significant evidence (eTable 324 in Supplement 2). There were 80 (31%) nominally statistically significant (P<0.05)
associations that were classified as presenting weak evidence. There were 20 (8%) statistically significant associations \( (P<10^{-3}) \), based on analyses with at least 1000 NHL cases, that were classified as presenting suggestive evidence. Only 12 (5%) associations were classified as presenting highly suggestive or convincing evidence, with a \( P<10^{-6} \), at least 1000 cases, and a \( P<0.05 \) for the largest component study. The 11 highly suggestive associations were for history of renal transplantation and risk of NHL, rheumatoid arthritis and risk of NHL, primary Sjogren's syndrome and risk of NHL, systemic lupus erythematosus and risk of NHL, celiac disease and risk of TCL, tuberculosis and risk of NHL, hepatitis B virus (HBV) and risk of NHL and BCL, hepatitis C virus (HCV) and risk of NHL and DLBCL, and teaching as an occupation and risk of NHL (Table 2).

There was one association, between history of celiac disease and risk of NHL (OR 2.61, 95% CI 2.04 to 3.33; 110, 245 NHL cases from 8 individual studies), that was classified as presenting convincing evidence. Although the association had \( P<10^{-6} \), at least 1000 cases, a nominally significant result for the largest component study, low/moderate proportion of total variability due to between-study variability (heterogeneity \( (I^2 \leqslant 50\%) \), a 95% PI excluding the null, and no evidence of small study effects, we were unable to conduct the Ioannidis test due to the incomplete information reported about the component studies. Across all the 112 nominally statistically significant associations, 63 (56%) had relative risk values that were between 0.67 and 1.50.

**Systematic reviews**

We identified 8 systematic reviews without quantitative synthesis with 8 unique associations that were not investigated by MAs of summary level data (eText 2 in Supplement 1).

**MAs of IPD**

We identified 27 MAs of IPD, of which 24 were from the InterLymph Consortium. The 24 InterLymph MAs of IPD reported 715 nominally statistically significant \( (P<0.05) \) associations. Of these, 116 and 21 associations were based on analyses with at least 1000 NHL cases and had \( P<10^{-3} \) and \( P<10^{-6} \), respectively (Table 4 and eTable 5 in Supplement 12). Overall, the unique suggestive exposures categories were alcohol consumption on risk of DLBCL, MZL and NHL, history of Sjogren’s syndrome on risk of DLBCL, MZL and NHL, recreational sun exposure on risk of DLBCL, FL and NHL, and history of HCV on risk of DLBCL, MZL and NHL. Although the 3 non-InterLymph MAs of IPD examined 5 associations not reported in systematic reviews and/or MAs of the summary level data, including fish eaters and risk of NHL, vegetarians and vegans and risk of NHL, maternal age at the time of the child’s birth.
and risk of NHL, paternal age at the time of the child’s birth and risk of NHL, and leisure-time physical activity and risk of NHL, none were nominally statistically significant.

**Consistency between MAs of summary level data and InterLymph MAs of IPD**

There were 40 associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD (eTable 5 in Supplement 2 and eFigure 1 in Supplement 1). While 22 (55%) evaluated the impact of environmental risk factors on the risk of NHL overall, the other half (18, 45%) focused on various NHL subtypes (CLL/SLL, 5 (13%); DLBCL, 5 (13%); FL, 4 (10%); TCL, 3 (8%); MZL, 1 (3%)).

Overall, 22 of 40 (55%) of the associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. There were 10 (25%) pairs where the effect estimates were both statistically significantly increased, 3 (8%) where they were both statistically significantly decreased, 7 (18%) where they were both non-statistically significantly increased, and 2 (5%) where they were both non-statistically significantly decreased (Kappa=0.37, eTable 46 in Supplement 2; eTable 7 and eFigure 1 in Supplement 1). The 13 associations where the MAs of the summary level data and MAs of IPD effect estimates were both statistically significantly increased or decreased were for history of smoking and risk of TCL, history of drinking and risk of NHL, DLBCL, and FL, history of primary Sjogren's syndrome and risk of NHL, history of systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL, TCL and DLBCL, and history of HCV and risk of NHL, DLBCL, MZL and CLL/SLL. There were 28 (70%) pairs where the effect sizes from the MAs of IPD were more conservative than the effect sizes from the MAs of summary level data.

There were 4 suggestive associations reported in MAs of summary level data that were also evaluated in the InterLymph MAs of IPD. Of these, 3 associations from MAs of IPD had effect estimates in the same direction, had \( P<10^{-3} \), and were based on analyses with at least 1000 NHL cases (i.e., history of psoriasis and risk of NHL, history of Herpes Zoster and risk of NHL, and history of farming as an occupation and risk of NHL). There were 8 highly suggestive associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD. Of these, 7 associations from the MAs of IPD had effect estimates in the same direction, had \( P<10^{-6} \), and were based on analyses with at least 1000 NHL cases (i.e., history of rheumatoid arthritis and risk of NHL, history of primary Sjogren's syndrome and risk of NHL, history systemic lupus erythematosus and risk of NHL, history of celiac...
disease and risk of NHL and TCL, history of tuberculosis and risk of NHL, and history of HCV and risk of NHL).

There were 19 (48%) pairs where the MAs of summary level data included at least one-third of the same component studies as the InterLymph MAs of IPD. There was no difference in terms of concordance (direction, statistical significance of summary effect estimates and overlapping 95% CIs) between MAs of summary level data that included at least one-third versus fewer than one-third of the same component studies as the MAs of IPD (12/19 (63%) vs 10/21 (48%), \(P = 0.32\)).

**Methodological quality**

The vast majority of the 85 MAs of summary level data had overall confidence ratings of low (3, 4%) or critically low (79, 93%) according to the AMSTAR 2 tool. There were 2 (2%) where the overall confidence in the results was classified as moderate.\(^{34,35}\) Only 1 (1%), evaluating the association between tuberculosis and risk of NHL, had an overall confidence rating of high (eTable 6 in Supplement 1).\(^{36}\) The most common unfulfilled critical domains of the AMSTAR 2 tool were incomplete justification of excluded studies (74, 87%) and missing or no information about preregistered protocols (72, 85%).

**Discussion**

In this umbrella review, we evaluated the range, strength, and validity of reported associations between environmental risk factors and NHL across 85 MAs of published observational studies. Overall, we identified 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. The vast majority of the associations, including those evaluating various dietary, clinical, lifestyle, chemical, and occupational exposures, were classified as having either non-significant or weak evidence. More than half of the nominally significant associations were only marginally significant. Only 5% of the associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence. When the same associations were evaluated in MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Overall, effect sizes from MAs of IPD were more conservative. This umbrella review suggests that there is a mass production of low-quality MAs of summary level data reporting weak associations between environmental risk factors and NHL. These findings highlight the need for improving not only primary studies but also evidence synthesis in this field. Moreover, given that many of the assessed risk factors
are correlated, simultaneous consideration of multiple risk factors will be useful to understand which ones have the strongest, independent effects on NHL risk.

Although a wide range of environmental exposures have been evaluated and proposed as potential risk factors for NHL, our evaluation suggests that the only highly suggestive or convincing exposures proposed in MAs of summary level data and MAs of IPD are related to autoimmune and infectious diseases. In particular, the prominent autoimmune disease-related risk factors include history of celiac disease, rheumatoid arthritis, primary Sjogren's syndrome, and systemic lupus erythematosus. Although the exact mechanisms behind these associations remains unclear, many autoimmune disorders are characterized by chronic inflammation, which may intensify B cell or T cell activation and promote the development of lymphoma.

Previous studies have also suggested that the dysfunction of some protein families, such as FAS and tumor necrosis factor, and the interplay between various immune cells, could be potential mechanisms. However, there is uncertainty when it comes to the temporality of these associations, with studies reporting that autoimmune diseases can occur during lymphoma.

Associations between viral and bacterial infections and NHL risk have been suggested for several decades. Different hypotheses for HCV-related lymphomagenesis have been proposed. For instance, chromosomal aberrations, including chromosome t(14;18) translocation, have been found to be associated with mixed cryoglobulinemia, a disorder most commonly caused by HCV infection and that can evolve into lymphoproliferative disorders. Furthermore, genetic variations, including Interleukin-10 polymorphisms, have also been proposed as a potential pathway between HCV infection and NHL susceptibility and development. Similar to autoimmune disease-related risk factors, it remains unclear whether these associations are driven by disease status, medication use, or disease-medication interactions. Considering how rare many of these autoimmune and infectious disease-related exposures are, future efforts are necessary to determine the impact of multiple environmental as well as non-environmental risk factors simultaneously.

Among 40 associations evaluated by both MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Unlike MAs of summary level data, MAs of IPD tend to focus on studies with more homogeneous designs and patient populations. Furthermore, MAs of IPD can allow for better harmonization of data across studies, more advanced one-stage meta-analytical approaches, and analyses accounting for many exposure categories and potential confounders. Although the InterLymph MAs of IPD are particularly robust due to the large
number of NHL cases and subtypes considered, MAs of IPD without systematic reviews may exclude evidence from high-quality case-control or cohort studies. For instance, the InterLymph analyses only included evidence from completed and ongoing case-control studies from consortium members. Furthermore, the InterLymph findings may be difficult to disentangle, with at least 700 nominally statistically significant associations among thousands of analyses conducted across different subtypes of NHL and exposure levels (e.g., different type/ dosage of alcohol consumption). In the future, it will be necessary to monitor the consistency between MAs of summary level data and MAs of IPD, especially since approximately half of the MAs of summary level data had at least one-third of the same component studies as the MAs of IPD. In addition, authors of MAs should carefully evaluate whether any external studies can and should be included in their syntheses. Of interest, we observed that more than two thirds of the effect sizes were more conservative in the InterLymph MAs of IPD than in the MAs of summary level data. This may be a reflection of greater selective reporting bias in the corpus of studies available in the literature as compared with a set of studies participating in a consortium.

Our study suggests that nearly all MAs of summary level data evaluating associations between environmental risk factors and risk of NHL could be classified as having critically low quality according to the AMSTAR 2 tool. Previous umbrella reviews focused on the associations between environmental risk factors and health outcomes have noted similar concerns. However, the proportion of low or critically low-quality NHL reviews is higher than what has been observed among umbrella reviews for inflammatory bowel diseases, attention-deficit/hyperactivity disorder, eating disorders, early childhood caries, physical activity for academic achievement, and physical therapy for tendinopathy. These findings may not be surprising considering recent concerns about the mass production of systematic reviews. In the future, authors planning systematic reviews and MAs of summary level data of the associations between environmental exposures and NHL should adhere to reporting guidelines and critically evaluate how their studies’ findings relate to existing MAs of IPD, focusing on the impact of different methods, populations, and other characteristics.

Limitations

Our umbrella review has several limitations. First, we did not identify potential environmental risk factors that were only examined in individual observational studies. Our objective was to identify and summarize the associations that were reported by the MAs of
summary level data, which already covered a wide space of diverse associations. Second, we
did not evaluate the quality of individual studies included in the MAs of summary level data,
the impact that individual studies have on the overall heterogeneity, the magnitude of the
associations, or the potential role that residual/unmeasured confounding could have on
associations. Individual risk of bias evaluations are outside the scope of umbrella reviews, and
it is the expectation that MAs have already conducted these quality assessments. Third, we
considered MAs that included cohort and case-control studies, and our assessments did not
prioritize reviews of certain study designs or address differences across different study designs.
Considering that certain NHL subtypes are rare, case-control studies may often be the most
realistic study design to evaluate exposure histories. Fourth, although umbrella reviews
provide a comprehensive summary of the associations reported in MAs, the validity of the
summary effect estimates is dependent on the quality of the individual MAs. Although we
attempted to standardize associations using a random-effects DL estimator, we did not
evaluate or re-conduct the literature searches for all potential exposure-outcome relationships.
Fifth, we did not calculate $I^2$, 95% PIs, Egger’s test, and excess significance test for non-
significant and nominally statistically significant associations. Given the large number of
associations identified, we prioritized these calculations for associations where these values
were necessary to determine the strength of associations using the previously established
classification system. It is also worth noting that $I^2$ values should not be used to make
inferences about heterogeneity, as it does not measure heterogeneity directly, but rather the
proportion of total variability due to between-study variability. However, the $I^2$ cut-off of 50%
is a standard grading criterion for evidence in umbrella reviews. Sixth, when summary
effect estimates of multiple exposure contrast levels were reported, we focused on the risk
estimates comparing ever versus never exposure (or comparing the highest versus lowest
levels of exposures). Although we did not consider all potential contrast levels and dose-
response relationships, our objective was to provide a universal overview of the relationships
between examined risk factors and NHL. Specific dose-response relationships may
nevertheless exist for certain associations, and they would need to be examined on a case-by-
case basis. Seventh, we only identified the nominally statistically significant associations
among the thousands of associations reported in InterLymph MAs of IPD. Eighth, by
excluding non-English language reviews, we may have missed additional potential
associations. However, we utilized the same approach as previous umbrella reviews that
focused on risk factors for health outcome(s). Ninth, MAs of IPD and MAs of summary
level data can have different strengths and limitations, and our evaluation did not focus on
comparing the potential quality of these types of studies. We also did not focus on the impact of different methods, populations, or other characteristics when comparing the consistency of the results between the two study types. Tenth, umbrella reviews are not intended to provide information about the likelihood that associations are causal. Lastly, when multiple MAs of summary level data evaluated the same exposures and outcomes, we selected the association based on the largest number of included studies. Although this approach does not ensure that the highest quality MAs are selected, this methodology has been utilized by previous umbrella reviews.\textsuperscript{25,70-72}

**Conclusion**

In this large-scale umbrella review, we identified dozens of MAs evaluating associations between environmental risk factors and NHL. However, the vast majority of MAs of summary level data were low quality and presented either non-significant or weak evidence. When the same associations were evaluated in MAs of summary level data and MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, these findings highlight the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.

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**Contributors:** XS and JDW originally conceived this study. XS, JPAI, and JDW designed this study. XS, HZ, YD, KN, and JDW acquired the data. XS and YD conducted the statistical analysis. XS and JDW and drafted the manuscript. XS, JPAI, and JDW participated in the interpretation of the data. All authors and critically revised the manuscript for important intellectual content. XS and JDW had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. JDW provided supervision. JDW is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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**Patient consent:** Not required

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**Data sharing:** The dataset will be made available via a publicly accessible repository on publication.

**Transparency:** The senior author (manuscripts guarantor) (JDW) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant registered) have been explained.
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## Tables and figures:

### Table 1. Grading criteria for evidence categories

| Strength of association       | Description                                                                 |
|-------------------------------|-----------------------------------------------------------------------------|
| **Convincing (class I)**      | Highly statistically significant association \( P < 10^{-6} \)               |
|                               | At least 1000 NHL cases                                                    |
|                               | Low/moderate proportion of total variability due to between-study variability |
|                               | \( I^2 \leq 50\% \)                                                        |
|                               | 95% prediction interval excluding the null value                            |
|                               | Largest study reporting a nominally statistically significant \( P < 0.05 \) |
|                               | No evidence of small-study effects                                          |
|                               | No evidence of excess significance bias                                     |
| **Highly suggestive (class II)** | Highly statistically significant association \( P < 10^{-6} \)            |
|                               | At least 1000 NHL cases                                                    |
|                               | Largest study reporting a nominally statistically significant \( P < 0.05 \) |
| **Suggestive (class III)**   | At least 1000 NHL cases                                                    |
|                               | Statistically significant association \( P < 10^{-3} \)                     |
| **Weak (class IV)**           | Nominally statistically significant association \( P < 0.05 \)              |
| **Non-significant**           | Non-statistically significant associations \( P > 0.05 \)                   |

*\( P \) value for the association that calculated by random effects model.

NHL = non-Hodgkin lymphoma.
Table 2. Environmental risk factors for non-Hodgkin lymphoma reported in meta-analyses of summary level data with convincing (Class I) and highly suggestive (Class II) evidence

| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author | Year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P randoma | Large study nominally significant (P<0.05) | I² (%) | 95% PI | Sma ll study effectb | Stren gth of reported associationc |
|-----------------------|---------------------------|---------------------|---------|------------|--------|------|------------------------|-------------|--------------|---------------------------------------------|-----------|---------------------------------|--------|------|--------------------------|-------------------------------|
| Renal transplant      | Renal transplant          | Transplant recipients vs general population | NHL | SRM A | Wang | 2018 | 6 | 770 | SIR | 10.66 (8.54, 13.31) | 3.44E-86 | Yes | 80.2 | NA | NA | II |
| Autoimmune diseases   | Rheumatoid arthritis      | Patients vs general population | NHL | SRM A | Simon | 2015 | 16 | 1531 | SIR | 2.26 (1.82, 2.81) | 8.42E-13 | Yes | 96 | NA | NA | II |
| Autoimmune diseases   | Primary Sjogren's syndrome | Patients vs general population | NHL | SRM A | Liang | 2014 | 11 | 1232 | RR | 13.76 (8.53, 18.99) | 1.62E-34 | Yes | 58.8 | NA | NA | II |
| Autoimmune diseases   | Systemic lupus erythematosus | Patients vs general population | NHL | MA | Cao | 2015 | 12 | 166 | RR | 5.4 (3.75, 7.77) | 1.99E-18 | Yes | 74.3 | NA | NA | II |
| celiac disease        | Patients vs general population | NHL | SRM A | Tio | 2012 | 8 | 1102 | OR | 2.61 (2.04, 3.33) | 9.32E-14 | Yes | 23.4 | (1.57, 4.33) | No | I |
| celiac disease        | Patients vs general population | TCL | SRM A | Tio | 2012 | 5 | 3535 | OR | 15.84 (7.85, 31.94) | 6.90E-14 | Yes | 55.5 | NA | NA | II |
| Infectious diseases   | Tuberculosis              | Patients vs general population | NHL | SRM A | Leung | 2020 | 8 | 2390 | RR | 1.61 (1.34, 1.94) | 6.76E-07 | Yes | 50.2 | NA | NA | II |
| HBV                   | HBV infected vs           | NHL | SRM A | Li | 2018 | 58 | 5371 | OR | 2.50 (2.2, 2.83) | 6.33E-42 | Yes | 77.9 | NA | NA | II |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random<sup>a</sup> | Largest study nominally significant (P<0.05) | P<sup>b</sup> (%) | 95% PI | Strength of reported association<sup>c</sup> |
|-----------------------|---------------------------|---------------------|---------|------------|--------------|------------------------|-------------|---------------|---------------------------------------------|----------------|--------------------------------------------|----------------|--------|------------------------------------------|
| HBV                  | HBV infected vs non-infected | BCL      | SRMA   | Li 2018   | 20           | >100 0               | OR          | 2.46 (1.97, 3.07) | 1.24E-14                      | Yes           | 62.9                                       | NA             | NA     | II                                       |
| HCV                  | HCV infected vs non-infected | NHL      | SRMA   | Masaione 2019 | 27         | 3307 7              | OR          | 3.36 (2.4, 4.72)  | 7.92E-12                      | Yes           | 88                                         | NA             | NA     | II                                       |
| HCV                  | Patients vs general population | DLBCL    | MA     | DalMaso 2006 | 8           | 1020               | RR          | 2.65 (1.88, 3.74) | 4.98E-08                      | Yes           | 39                                         | (1.46 , 5.81) | No     | II                                       |
| Occupation           | Teacher vs non-teachers    | NHL      | MA     | Boffetta 2007 | 19         | >100 0              | RR          | 1.47 (1.34, 1.61) | 1.60E-15                      | Yes           | 76                                         | NA             | NA     | II                                       |

BCL = B cell lymphoma; CI = confidence interval; HBV = hepatitis B virus; HCV = hepatitis C virus; MA = meta-analysis; NA = not available; NHL = non-Hodgkin lymphoma; OR = odds ratio; PI = prediction interval; SIR = standardized incidence ratio; SRMA = systematic review and meta-analysis; RR = risk ratio; TCL = T-cell lymphoma.

<sup>a</sup> P value for summary effect estimates using a random-effects DerSimonian and Laird estimator.

<sup>b</sup> P<0.1 for Egger’s test suggests the presence of small study effects.

<sup>c</sup> Strength of association using the criteria listed in Table 1.
Table 3. Suggestive risk factors and protective factors identified in meta-analyses of individual patient data from International Lymphoma Epidemiology Consortium

| NHL subtype | At least 1000 cases and P<10^-3 | At least 1000 cases and P<10^-6 |
|-------------|---------------------------------|---------------------------------|
| CLL/SLL     | Years since quitting cigarette smoking; printing pressmen | None |
| CLL/SLL/PLL/MCL | Adult infectious mononucleosis | None |
| DLBCL       | Alcohol; Any atopic disorder; Allergy; B and T-cell activating autoimmune diseases; HCV; Hay fever; Recreational sun exposure; Socioeconomic status (high vs low); BMI as young adult (25<-30 kg/m^2); Rheumatoid arthritis; Blood transfusion; Weight | History of B-cell activating autoimmune disease; Sjogren’s syndrome; HCV; Young adult BMI (%25 kg/m^2); Years since quit cigarette smoking; Age first alcohol consumption (20-29 years vs. nondrinker); Current alcohol consumption status as of ~2 years prior to diagnosis/interview* |
| FL          | Blood transfusions; Young adult BMI (%25 kg/m^2+); Recreational sun exposure; History of cigarette smoking (females); Current cigarette smoking; University and higher education teachers; Male height (100% vs. 60%); Any atopic disorder* | None |
| MZL         | Systemic lupus erythematosus; HCV, Peptic ulcer; Wine | History of B-cell activating autoimmune disease; Sjogren’s syndrome |
| HCL         | Current cigarette smoking | None |
| NHL         | Hormone replacement therapy; Systemic lupus erythematosus; HCV; Allergy; Food allergy; Hay fever; Blood transfusion; Height; Alcohol exposures; Recreational hair dye use; Socioeconomic status (high vs low); Secondary Sjogren’s syndrome; Childhood measles* | Sjogren’s syndrome; History of B-cell activating autoimmune disease; Hay fever; Young adult BMI (%25 kg/m^2); Recreational sun exposure (%Q3-Q4 hours/week); Recreational hair dye use (%Q3-Q4 hours/week); Beer, wine, and liquor* |

BMI=body mass index; CI=confidence interval; CLL=chronic lymphocytic leukemia; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; HCL=hairy cell leukemia; HCV=hepatitis C virus; MCL=mantle cell lymphoma; MZL=marginal zone lymphoma; NHL=non-Hodgkin lymphoma; SLL=small lymphocytic lymphoma; PLL=prolymphocytic leukemia.

* These were protective risk factors.
Identify correctly:
- Wrong study design: the examined study was not a systematic review, meta-analysis or pooled analysis
- Wrong topic: the examined review did not examine non-Hodgkin lymphoma or its subtypes as an outcome OR the study did not examine the impact of an environmental exposure on the risk of non-Hodgkin lymphoma development
- Wrong exposure: the examined risk factor does not meet the definition of environmental risk factor in our study
- Wrong study focus: the review did not examine the impact of an exposure on the risk of developing NHL
- Wrong component study design: the review did not synthesize observational study data
- Insufficient data for analyses: the review included fewer than 3 component studies
- Overlapping review: a larger review was identified for the same association

Figure 1: Study selection flowchart

* Web of Science Core Collection as licensed at Yale: Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years
** Wrong study design: the examined study was not a systematic review, meta-analysis or pooled analysis
Wrong topic: the examined review did not examine non-Hodgkin lymphoma or its subtypes as an outcome OR the study did not examine the impact of an environmental exposure on the risk of non-Hodgkin lymphoma development
Wrong exposure: the examined risk factor does not meet the definition of environmental risk factor in our study
Wrong study focus: the review did not examine the impact of an exposure on the risk of developing NHL
Wrong component study design: the review did not synthesize observational study data
Insufficient data for analyses: the review included fewer than 3 component studies
Overlapping review: a larger review was identified for the same association
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eTable 1: Search strategy
Database searches, 2021-07-23
Searches on the Ovid platform can be rerun at https://tools.ovid.com/ovidtools/launcher.html

| Ovid MEDLINE(R) ALL <1946 to July 22, 2021> |  |
|---|---|
| 1 [Xiaoting Shi] | 0 |
| 2 [concept two: SRs] | 0 |
| 3 (systematic adj4 review).ti. | 16047 |
| 4 systematic review.pt. | 16216 |
| 5 Cochrane Database of Systematic Reviews.jn. and review.pt. | 13658 |
| 6 [approach c: based on Lee 2012] | 0 |
| 7 medline.tw. or systematic review.ti. or meta-analysis.pt. or pubmed.tw. | 35748 |
| 8 [from our previous searches] | 0 |
| 9 (pooled analysis or pooled analyses).mp. | 11737 |
| 10 (metaanalysis or meta-analysis).af. | 22010 |
| 11 [NHL concept] | 0 |
| 12 neoplasms/ or lymphoma/ or exp lymphoma, non-hodgkin/ | 58950 |
| 13 [alternative based on https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004024.pub2/appendices#CD004024-sec1-0011] | 0 |
| 14 *Lymphoma/ | 36024 |
| 15 *hematologic neoplasms/ | 10823 |
| 16 lymphom*.mp. | 25857 |
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|   |   |
|---|---|
| 17 | non-hodgkin*.mp. | 58024 |
| 18 | nonhodgkin*.mp. | 136 |
| 19 | (non adj1 hodgkin*).mp. | 58025 |
| 20 | nhl.mp. | 13936 |
| 21 | (hemato* adj1 malign*).mp. | 26969 |
| 22 | (haemato* adj1 malign*).mp. | 5497 |
| 23 | (hemato* adj1 neoplas*).mp. | 16617 |
| 24 | (haemato* adj1 neoplas*).mp. | 415 |
| 25 | or/12,14-24 | 72171 |
| 26 | risk/ or protective factors/ or risk factors/ | 9999 |
| 27 | (risk* or protective factor*).mp. | 28997 |
| 28 | 26 or 27 | 28997 |
| 29 | or/3-10 | 42317 |
| 30 | 25 and 28 and 29 | 5543 |

Embase
<1974 to 2021 July 22>

|   |   |
|---|---|
| 1 | [NHL concept] | 0 |
| 2 | neoplasm/ or lymphoma/ or lymphatic system tumor/ or exp nonhodgkin lymphoma/ | 67263 |
| 3 | *Lymphoma/ | 1 |
| 4 | hematologic malignancy/ | 45821 |
| 5 | lymphom*.mp. | 35048 |
| 6 | non-hodgkin*.mp. | 35048 |
| 7 | nonhodgkin*.mp. | 60548 |
| 8 | (non adj1 hodgkin*).mp. | 62197 |
| 9 | (non adj1 neoplas*).mp. | 60551 |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

|   | Query                                                                                     | Results |
|---|-------------------------------------------------------------------------------------------|---------|
| 9 | nhl.mp.                                                                                    | 25440   |
| 10| (hemato* adj1 malign*).mp.                                                                 | 63015   |
| 11| (haemato* adj1 malign*).mp.                                                                | 9491    |
| 12| (hemato* adj1 neoplas*).mp.                                                               | 4590    |
| 13| (haemato* adj1 neoplas*).mp.                                                              | 689     |
| 14| or/2-13                                                                                   | 82181   |
| 15| exp risk/ or protection/                                                                  | 27149   |
| 16| (risk* or protective factor*).mp.                                                         | 43275   |
| 17| 15 or 16                                                                                  | 43681   |
| 18| [study design concept]                                                                   | 0       |
| 19| (systematic adj4 review).ti.                                                              | 19182   |
| 20| Cochrane Database of Systematic Reviews.jn. and review.pt.                               | 11247   |
| 21| medline.tw. or systematic review.ti. or pubmed.tw.                                       | 38012   |
| 22| (pooled analysis or pooled analyses).mp.                                                  | 19038   |
| 23| (metaanalysis or meta-analysis).af.                                                       | 32779   |
| 24| or/19-23                                                                                 | 56318   |
| 25| 14 and 17                                                                                | 15598   |
| 26| limit 25 to meta analysis                                                                 | 3382    |
| 27| limit 25 to systematic review                                                             | 3023    |
| 28| 25 and 24                                                                                | 6739    |
| 29| 26 or 27 or 28                                                                           | 7272    |
| 30| limit 29 to conference abstract status                                                    | 2936    |
| 31| 29 not 30                                                                                | 4336    |
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| Scopus                                           | 3173 |
|--------------------------------------------------|------|
| Web of Science Core Collection                   |      |
| TS=(lymphom* OR non-hodgkin* OR (non NEAR/1 hodgkin*) OR nhl OR ((hemato* OR haemato*) NEAR/1 (malign* OR neoplas*)) AND TS=(risk* OR protective-factor*) AND TS=((systematic W/4 review) OR medline OR pubmed OR "pooled analysis" OR "pooled analyses" OR metaanalysis OR meta-analysis)) AND (EXCLUDE (DOCTYPE, "cp") ) |      |
| Cochrane Library                                 | 2417 |
| ID                                               |      |
| #1 ((systematic NEAR/4 review)):ti OR (systematic review):pt OR (medline or pubmed or "pooled analysis" or "pooled analyses" or metaanalysis or meta-analysis):ti,ab,kw (Word variations have been searched) | 29396 |
| #2 MeSH descriptor: [Neoplasms] this term only    | 6376 |
| #3 MeSH descriptor: [Lymphoma] this term only     | 1369 |
| #4 MeSH descriptor: [Lymphoma, Non-Hodgkin] explode all trees | 2056 |
| #5 MeSH descriptor: [Hematologic Neoplasms] this term only | 466 |
| #6 (lymphom* or non-hodgkin* or nonhodgkin* or (non NEAR/1 hodgkin*) or nhl or (hemato* NEAR/1 malign*) or (haemato* NEAR/1 malign*) or (hemato* NEAR/1 neoplas*) or (haemato* NEAR/1 neoplas*)):ti,ab,kw | 14144 |
| #7 #2 or #3 or #4 or #5 or #6                    | 20192 |
| #8 (risk* or (protective NEAR/1 factor*)):ti,ab,kw | 25391 |
| #9 MeSH descriptor: [Risk] this term only         | 3322 |
| #10 MeSH descriptor: [Protective Factors] this term only | 135 |
| #11 MeSH descriptor: [Risk Factors] this term only | 24955 |
| #12 #8 or #9 or #10 or #11                       | 25391 |
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| #13 | #1 and #7 and #12 | 273 |
|-----|-------------------|-----|
|     | Limited to reviews (not trials) | 167 |

**Epistemonikos**

| SR filter | (title:(lymphoma*) OR abstract:(lymphoma*)) AND (title:(risk* OR protective) OR abstract:(risk* OR protective)) |
|-----------|----------------------------------------------------------------------------------------------------------------|
| 736       |                                                                                                                |

| broad synthesis filter | (title:(lymphoma*) OR abstract:(lymphoma*)) AND (title:(risk* OR protective) OR abstract:(risk* OR protective)) |
|------------------------|----------------------------------------------------------------------------------------------------------------|
| 24                     |                                                                                                                |

| no filter | (title:(lymphoma*) OR abstract:(lymphoma*)) AND (title:(risk* OR protective) OR abstract:(risk* OR protective)) AND (title:("pooled analysis" OR "pooled analyses") OR abstract:("pooled analysis" OR "pooled analyses")) |
|------------|------------------------------------------------------------------------------------------------------------------|
| 42         |                                                                                                                |
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eTable 2: NHL subtypes

| Category                        | Subtypes                                                                 | Eligibility as NHL |
|---------------------------------|--------------------------------------------------------------------------|--------------------|
| Mature B-cell neoplasms         | Chronic lymphocytic leukemia/small lymphocytic lymphoma                   | Yes                |
|                                 | Monoclonal B-cell lymphocytosis*                                         | No                 |
|                                 | B-cell prolymphocytic leukemia                                            | Yes                |
|                                 | Splenic marginal zone lymphoma                                            | Yes                |
|                                 | Hairy cell leukemia                                                       | Yes                |
|                                 | Splenic B-cell lymphoma/leukemia, unclassifiable                          | Yes                |
|                                 | Splenic diffuse red pulp small B-cell lymphoma                            | Yes                |
|                                 | Hairy cell leukemia-variant                                               | Yes                |
|                                 | Lymphoplasmacytic lymphoma                                                | Yes                |
|                                 | Waldenström macroglobulinemia                                              | Yes                |
|                                 | Monoclonal gammopathy of undetermined significance (MGUS), IgM*          | No                 |
|                                 | μ heavy-chain disease                                                     | No                 |
|                                 | γ heavy-chain disease                                                     | No                 |
|                                 | α heavy-chain disease                                                     | No                 |
|                                 | Monoclonal gammopathy of undetermined significance (MGUS), IgG/A*        | No                 |
|                                 | Plasma cell myeloma                                                      | No                 |
|                                 | Solitary plasmacytoma of bone                                             | No                 |
|                                 | Extraosseous plasmacytoma                                                 | No                 |
|                                 | Monoclonal immunoglobulin deposition diseases*                           | No                 |
|                                 | Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) | Yes                |
|                                 | Nodal marginal zone lymphoma                                              | Yes                |
|                                 | Pediatric nodal marginal zone lymphoma                                     | Yes                |
|                                 | Follicular lymphoma                                                       | Yes                |
|                                 | In situ follicular neoplasia*                                             | Yes                |
|                                 | Duodenal-type follicular lymphoma*                                        | Yes                |
|                                 | Pediatric-type follicular lymphoma*                                       | Yes                |
## Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Category | Subtypes | Eligibility as NHL |
|----------|----------|--------------------|
|          | Large B-cell lymphoma with IRF4 rearrangement* | Yes |
|          | Primary cutaneous follicle center lymphoma | Yes |
|          | Mantle cell lymphoma | Yes |
|          | In situ mantle cell neoplasia* | Yes |
|          | Diffuse large B-cell lymphoma (DLBCL), NOS | Yes |
|          | Germinal center B-cell type* | Yes |
|          | Activated B-cell type* | Yes |
|          | T-cell/histiocyte-rich large B-cell lymphoma | Yes |
|          | Primary DLBCL of the central nervous system (CNS) | Yes |
|          | Primary cutaneous DLBCL, leg type | Yes |
|          | EBV+ DLBCL, NOS* | Yes |
|          | EBV+ mucocutaneous ulcer* | No |
|          | DLBCL associated with chronic inflammation | Yes |
|          | Lymphomatoid granulomatosis | No |
|          | Primary mediastinal (thymic) large B-cell lymphoma | Yes |
|          | Intravascular large B-cell lymphoma | Yes |
|          | ALK+ large B-cell lymphoma | Yes |
|          | Plasmablastic lymphoma | Yes |
|          | Primary effusion lymphoma | Yes |
|          | HHV8+DLBCL, NOS* | Yes |
|          | Burkitt lymphoma | Yes |
|          | Burkitt-like lymphoma with 11q aberration* | Yes |
|          | High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements* | Yes |
|          | High-grade B-cell lymphoma, NOS* | Yes |
|          | B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma | Yes |
|          | Double hit/triple hit lymphoma | Yes |
| Mature T and NK | T-cell prolymphocytic leukemia | Yes |
|             | T-cell large granular lymphocytic leukemia | Yes |
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Category     | Subtypes                                                                 | Eligibility as NHL |
|--------------|---------------------------------------------------------------------------|--------------------|
| neoplasms    | Chronic lymphoproliferative disorder of NK cells                          | Yes                |
|              | Aggressive NK-cell leukemia                                                | Yes                |
|              | Systemic EBV+ T-cell lymphoma of childhood*                                | Yes                |
|              | Hydroa vacciniforme–like lymphoproliferative disorder*                     | Yes                |
|              | Adult T-cell leukemia/lymphoma                                             | Yes                |
|              | Extranodal NK-/T-cell lymphoma, nasal type                                 | Yes                |
|              | Enteropathy-associated T-cell lymphoma                                     | Yes                |
|              | Monomorphous epitheliotropic intestinal T-cell lymphoma*                   | Yes                |
|              | Indolent T-cell lymphoproliferative disorder of the GI tract*              | No                 |
|              | Hepatosplenic T-cell lymphoma                                              | Yes                |
|              | Subcutaneous panniculitis-like T-cell lymphoma                             | Yes                |
|              | Mycosis fungoides                                                         | Yes                |
|              | Sézary syndrome                                                           | Yes                |
|              | Primary cutaneous CD30+ T-cell lymphoproliferative disorders               | Yes                |
|              | Lymphomatoid papulosis                                                    | No                 |
|              | Primary cutaneous anaplastic large cell lymphoma                           | Yes                |
|              | Primary cutaneous γδ T-cell lymphoma                                       | Yes                |
|              | Primary cutaneous CD8+aggressive epidermotropic cytotoxic T-cell lymphoma  | Yes                |
|              | Primary cutaneous acral CD8+T-cell lymphoma*                              | Yes                |
|              | Primary cutaneous CD4+small/medium T-cell lymphoproliferative disorder*    | No                 |
|              | Peripheral T-cell lymphoma, NOS                                            | Yes                |
|              | Angioimmunoblastic T-cell lymphoma                                         | Yes                |
|              | Follicular T-cell lymphoma*                                                | Yes                |
|              | Nodal peripheral T-cell lymphoma with TFH phenotype*                       | Yes                |
|              | Anaplastic large-cell lymphoma, ALK+                                       | Yes                |
|              | Anaplastic large-cell lymphoma, ALK−*                                     | Yes                |
|              | Breast implant–associated anaplastic large-cell lymphoma*                  | Yes                |
## Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Category | Subtypes                                      | Eligibility as NHL |
|----------|-----------------------------------------------|--------------------|
|          | Acute lymphoblastic leukaemia (ALL)           | No                 |

Footnotes:
*Changes from the 2008 classification.
NOS: not otherwise specified
Information source: 2016 WHO classification of mature lymphoid neoplasms ([https://pubmed.ncbi.nlm.nih.gov/26980727/](https://pubmed.ncbi.nlm.nih.gov/26980727/))
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eTable 3: R code

```
Below is the R code example for the association between Behcet disease and NHL

# read in data_Behcet Disease
meta1 = read_excel("RR_effect_sizes_Behcet Disease_#4206.xlsx")
head(meta1)

# conduct main analysis
meta2<-metagen(meta1$LNRR,meta1$SE,
sm="R",studlab=paste(lastname,publication_year)
    ,data=meta1,method.bias="Egger",prediction = TRUE,
    level.predict =0.95)
summary(meta2)

# create forest plot, funnel plot
forest(meta2)
funnel(meta2)
meta2$pval.random

# conduct egger's test
metabias(meta2,method.bias="Egger",plotit=TRUE, correct= TRUE, k=3)
```
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**eTable 4: Overlapping meta-analyses of summary level data**

| Environmental risk factors                  | Largest review (First author, year) | Number of overlapping meta-analyses | Number of primary studies in the largest meta-analyses | Most recent (Y/N) | Highest impact factor one (Y/N) |
|---------------------------------------------|-------------------------------------|-------------------------------------|--------------------------------------------------------|------------------|-------------------------------|
| *Dietary factors*                          |                                     |                                     |                                                        |                  |                               |
| Red meat                                   | Yang 2015                           | 4                                   | 18                                                     | N                | N                             |
| Processed meat                             | Yang 2015                           | 4                                   | 18                                                     | N                | N                             |
| White meat/poultry                        | Dong 2017                           | 3                                   | 10                                                     | N                | N                             |
| Fish                                       | Caini 2016                          | 3                                   | 11                                                     | N                | N                             |
| Fruit and vegetable                       | Chen 2013                           | 2                                   | 4                                                      | N                | Y                             |
| Fruit                                      | Chen 2013                           | 2                                   | 13                                                     | N                | Y                             |
| Vegetable                                  | Chen 2013                           | 2                                   | 13                                                     | N                | Y                             |
| Eggs                                       | Caini 2016                          | 2                                   | 10                                                     | N                | N                             |
| Total dairy products                       | Wang 2016                           | 2                                   | 7                                                      | Y                | Y                             |
| Milk                                       | Wang 2016                           | 3                                   | 16                                                     | N                | Y                             |
| Cheese                                     | Wang 2016                           | 2                                   | 10                                                     | Y                | Y                             |
| Vitamin D                                  | Lu 2014                             | 2                                   | 6                                                      | N                | N                             |
| *Drugs, vaccinations and procedures*       |                                     |                                     |                                                        |                  |                               |
| Aspirin                                    | Ye 2015                             | 2                                   | 10                                                     | Y                | Y                             |
| Non-steroidal anti-inflammatory drugs      | Ye 2015                             | 2                                   | 13                                                     | Y                | N                             |
| Statin                                     | Ye 2017                             | 3                                   | 9                                                      | Y                | Y                             |
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| Environmental risk factors                        | Largest review (First author, year) | Number of overlapping meta-analyses | Number of primary studies in the largest meta-analyses | Most recent (Y/N) | Highest impact factor one (Y/N) |
|--------------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------------------------|------------------|-------------------------------|
| **Non-dietary lifestyle factors**                |                                     |                                     |                                                       |                  |                               |
| Physical activity                                | Davies 2020                         | 3                                   | 17                                                    | Y                | Y                             |
| Hair dye                                         | Qin 2019                            | 2                                   | 16                                                    | Y                | N                             |
| Petrochemical exposure                           | Jephcote 2020                       | 2                                   | 9                                                     | Y                | Y                             |
| Maternal smoking                                 | Antonopoulos 2011                   | 2                                   | 7                                                     | N                | Y                             |
| Ever smoking                                     | Sergentanis 2013                    | 2                                   | 33                                                    | Y                | N                             |
| Ever drinking                                    | Tramacere 2012                      | 3                                   | 29                                                    | N                | Y                             |
| Heavy drinking                                   | Tramacere 2012                      | 2                                   | 6                                                     | N                | Y                             |
| **Medical history and comorbid diseases**        |                                     |                                     |                                                       |                  |                               |
| Rheumatoid arthritis                             | Simon 2015                          | 2                                   | 17                                                    | Y                | N                             |
| Primary Sjogren’s syndrome                       | Liang 2014                          | 2                                   | 11                                                    | Y                | Y                             |
| Systemic lupus erythematosus                     | Cao 2015                            | 3                                   | 12                                                    | N                | N                             |
| Psoriasis                                        | Vaengebjerg 2020                    | 3                                   | 8                                                     | Y                | Y                             |
| Type 1 diabetes                                  | Wang 2020                           | 2                                   | 3                                                     | Y                | N                             |
| Celiac disease                                   | Tio 2012                            | 2                                   | 8                                                     | Y                | Y                             |
| Systemic sclerosis                               | Zhang 2013                          | 2                                   | 4                                                     | Y                | N                             |
# Environmental Risk Factors for Non-Hodgkin Lymphoma: An Umbrella Review and Comparison of Meta-Analyses of Summary and Individual Participant Level Data

| Environmental Risk Factors       | Largest Review (First Author, Year) | Number of Overlapping Meta-Analyses | Number of Primary Studies in the Largest Meta-Analyses | Most Recent (Y/N) | Highest Impact Factor One (Y/N) |
|----------------------------------|-------------------------------------|-------------------------------------|------------------------------------------------------|-------------------|-------------------------------|
| Asthma                           | Yang 2017                           | 2                                   | 15                                                   | Y                 | Y                             |
| Type 2 diabetes                  | Castillo 2012                       | 8                                   | 21                                                   | N                 | N                             |
| Overweight                       | Larsson 2007                        | 11                                  | 16                                                   | N                 | Y                             |
| Obesity                          | Larsson 2007                        | 11                                  | 16                                                   | N                 | Y                             |
| Hepatitis B virus                | Li 2018                             | 5                                   | 58                                                   | N                 | N                             |
| Hepatitis C virus                | Masarone 2019                       | 4                                   | 27                                                   | Y                 | Y                             |
| **Chemicals and Pesticides**     |                                     |                                     |                                                      |                   |                               |
| Benzene                          | Kane 2010                           | 4                                   | 24                                                   | Y                 | N                             |
| Polychlorinated biphenyls        | Catalani 2019                       | 3                                   | 30                                                   | Y                 | N                             |
| Trichloroethylene                | Scott 2011                          | 3                                   | 17                                                   | N                 | N                             |
| Glyphosate                       | Boffetta 2021                       | 4                                   | 6                                                    | Y                 | N                             |
| 2,4-Dichlorophenoxyacetic acid   | Smith 2017                          | 3                                   | 11                                                   | Y                 | Y                             |
| **Occupation**                   |                                     |                                     |                                                      |                   |                               |
| Female flight attendant          | Buja 2006                           | 4                                   | 3                                                    | Y                 | N                             |
| Farmer                           | Boffetta 2007                       | 4                                   | 50                                                   | Y                 | N                             |
| Firefighter                      | Jalilian 2019                       | 3                                   | 14                                                   | Y                 | Y                             |
| Petroleum refinery worker        | Schnatter 2018                      | 2                                   | 16                                                   | Y                 | N                             |

Y=Yes; N=No.
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**eFigure 1**

**eFigure 1:** Scatterplot of summary effect estimates in meta-analyses of summary level data and meta-analyses of IPD (pooled analyses) reporting the same associations between environmental risk factors and non-Hodgkin lymphoma. CI=confidence interval.
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eText 1: eligibility criteria

Eligibility criteria for systematic reviews and (or) meta-analyses

General inclusion criteria

Language: English only.

Study types: Systematic review and (or) meta-analysis (referred as ‘Review studies’ in the following contents).

Study designs included in review studies: Observational epidemiological studies\(^1\).

Study subjects: Human only\(^2\).

General exclusion criteria

Review studies that:

1. Focus on genetic risk factors\(^3\) for non-Hodgkin lymphoma (NHL)
2. Focus on biomarkers\(^4\) for NHL
3. Focus on risk factors for treatment, relapse, remission, or prognosis on NHL patients
4. Examine NHL as a risk factor for other diseases
5. Focus on cancer, hematological cancers, lymphoma, or any broader spectrum of diseases, but fail to provide specific data for NHL\(^5\)
6. Only include experimental studies
7. Focus on NHL as a metastasis/secondary cancer of other primary cancers
8. Focus on NHL in a particular population but fail to provide detailed information on environmental risk factors\(^6\)
9. Investigate the prevalence/incidence of NHL

\(^1\) Cohort studies or case control studies only
\(^2\) Review studies mixed with human and animal subjects will be checked in details at full text screening stage
\(^3\) Including genetic polymorphisms, family history/familial aggregation
\(^4\) Any substance, structure, or process that can be measured in the body or its products that can influence or predict the incidence of outcome or disease. Ref: http://www.inchem.org/documents/ehc/ehc/ehc222.htm (accessed 24th April, 2020)
\(^5\) This may be unclear at the title-abstract screening, therefore when in doubt, two researchers will send it on to the full text screening
\(^6\) For example, NHL in indigenous population, or men who have sex with men (MSM)
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Besides the aforementioned eligibility criteria, based on our definition of environmental risk factors, personal medical history and comorbidities (excluding metastasis of tumors) will be considered eligible in our study. In addition to the 8th General exclusion criteria, studies focus on NHL on a particular occupational population would be included since occupation can act as proxy for certain environmental exposures.

**Study types, exposures and outcome definition**

**Systematic reviews and (or) Meta-analyses of summary level data and individual participant data:**

The eligible study types in our study are systematic reviews (SRs), meta-analyses (MAs), systematic reviews and meta-analyses (SRMAs) or pooled analyses. To be eligible, SRs and SRMAs must have performed a systematic search in at least one bibliographic database. SRs, MAs and SRMAs should clearly define themselves as systematic reviews and(or) meta-analyses. For SRs in particular, we will only include exposure-outcome relationships (i.e., associations) that have not been investigated in MAs or SRMAs.

In terms of pooled analyses, the primary goal for including pooled analyses in our study is to incorporate the valuable pooled information of individual level data from scientific institutes on NHL and its subtypes, such as The International Lymphoma Epidemiology Consortium (InterLymph7) and to add to the evidence for meta-analyses on certain risk factors.

**Environmental risk factors:**

We define environmental risk factors as a broad concept of non-genetic factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors that can affect a person’s health, as environmental risk factors.4

**Outcome of interest:**

Our study outcome is non-Hodgkin lymphoma, including its subtypes (eTable 2 in Supplement 1). The classification of NHL subtypes was consulted and confirmed by an epidemiologist on NHL from InterLymph consortia. We will identify with the definition/diagnostic criteria of NHL from the original review studies.

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eText 2

Systematic reviews

We identified 8 systematic reviews without quantitative synthesis with 8 unique associations that were not investigated by meta-analyses of the published literature (Supplement). Among them, 6 (75.0%) concluded that there were weak or non-statistically significant associations between the examined risk factors (Omega-3 fatty acids, sugar intake, artificial sweetener consumption, hazardous waste, preterm birth, and prenatal/postnatal Diagnostic X-rays and childhood) and NHL risk. Two (25%) additional systematic reviews suggested possible associations between Gaucher disease and NHL risk and breast implants and anaplastic large cell lymphoma risk. Half (4, 50.0%) of the systematic reviews outlined that quantitative analyses were not conducted due to high levels of heterogeneity and/or a small number of eligible studies. The remaining 4 (50.0%) systematic reviews did not provide any reasons for not conducting quantitative analyses.

Exclusion reasons

Among the 1024 records screened at the full text level, 904 were excluded, mostly because they were for the wrong topic (442, 48.9%), they had the wrong study design (240, 26.5%), or they were not the largest meta-analysis of the published literature for a specific association (102, 11.3%).
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Physical activity in relation to risk of hematologic cancers: a systematic review and meta-analysis.

Statins use and the risk of all and subtype hematological malignancies: a meta-analysis of observational studies.

Physical activity and risk of lymphoma: a meta-analysis.

Systematic review and meta-analysis of glyphosate exposure and risk of lymphohematopoietic cancers.

Association of psoriasis with the risk of developing or dying of cancer: a systematic review and meta-analysis.

Risk of cancer in psoriasis: A systematic review and meta-analysis of epidemiological studies.

The associations of fruit and vegetable intakes with burden of diseases: A systematic review of meta-analyses.

Use of statins and risk of haematological malignancies: a meta-analysis of six randomized clinical trials and eight observational studies.

Sedentary behavior and incident cancer: a meta-analysis of prospective studies.

The risks of cancer development in systemic lupus erythematosus (SLE) patients: a systematic review and meta-analysis.

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Body mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies.

Quantitative association between body mass index and the risk of cancer: A global Meta-analysis of prospective cohort studies.

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| Year | Journal/Description                                                                 | Volume/Issue | Pages   | Authors                                                                 |
|------|-------------------------------------------------------------------------------------|--------------|---------|-----------------------------------------------------------------------|
| 2016 | Gastroenterol                                                                         | 2016         | 101475557 | 1632439                                                              |
| 2018 | Environment                                                                         | 2018         | 16        | 0147621 467-474                                                      |
| 2017 | British journal                                                                      | 2017         | 116      | 1 126-133                                                            |
| 2015 | Current Opin                                                                         | 2015         | 31       | 4 296-302                                                            |
| 2018 | Cochrane Dal                                                                         | 2018         | 1 CD005195 | 3 CD005195                                                          |
| 2004 | 8 Clinical gastro                                                                     | 2004         | 3 CD005195 | 3 CD005195                                                          |
| 2020 | The Lancet                                                                          | 2020         | 4 9609-340 | 357                                                              |
| 2012 | JBI Database                                                                          | 2012         | 10 Supplement | S259-S272                                    |
| 2014 | Asian Pacific                                                                         | 2014         | 15       | 19 8509-19                                                          |
| 2018 | Environment                                                                          | 2018         | 1 107      | 3 95-104                                                             |
| 2003 | Current Nutri                                                                        | 2003         | 1        | 1 24-29                                                              |
| 2014 | British journal                                                                      | 2014         | 111      | 5 976-80                                                             |
| 2013 | American jou                                                                          | 2013         | 109      | 3 9-Jan                                                              |
| 2000 | Gastroenterol                                                                        | 2000         | 119      | 6 1447-53                                                            |
| 2007 | 2 Asian Pacific                                                                      | 2007         | 10       | 1 11-Jun                                                             |
| 2010 | The Lancet                                                                          | 2010         | 371      | 9 609-340-357                                                      |
| 2012 | Journal of the                                                                       | 2012         | 10        | 17 3640-3649                                                      |
| 2018 | Japanese jou                                                                          | 2018         | 48       | 5 426-433                                                            |
| 2005 | American jou                                                                          | 2005         | 136      | 1 95-104                                                            |
| 2019 | BMC public h                                                                         | 2019         | 19       | 1 900                                                                |
| 2012 | 2 Obesity revi                                                                       | 2012         | 13       | 11 985-1000                                                         |
| 2018 | Environment                                                                          | 2018         | 166      | 2 0147621 628-637                                                   |
| 2012 | American Jou                                                                         | 2012         | 96       | 6 1249-1251                                                         |
| 2011 | Journal of med                                                                       | 2011         | 14       | 10 1065-78                                                          |
| 2017 | Critical review                                                                      | 2017         | 57       | 6 1153-1173                                                         |
| 2010 | Deutsches Ar                                                                         | 2010         | 107      | 37 638-43                                                           |
| 2018 | Journal of Int                                                                       | 2018         | 283      | 5 430-445                                                          |
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| 2016 | International                                                                        | 2016         | 55       | 5 487-493                                                          |
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| 2020 | Medicine                                                                             | 2020         | 99       | 15 e19698                                                           |
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| Ginseng consI (X.; Che, D)                                            | 2016 Journal of Gerontology            | 40                | 269-277     |
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| Fermented d (Zhang, K.; Da)                                           | 2019 International                      | 144               | 2099-2108   |
| Exposure to r (Zaki, A. M.; R)                                        | 2020 Middle East J                      | 11                | 11-11Jan    |
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| Collection an (Gossec, L.; Ba)                                       | 2016 Jt. Bone Spine                    | 83                | 501-509     |
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| Comparison cDe Ridder, Jo                                          | 2016 | Cancer cause                    | 27     |       | 3 291-300   |
| Associations Qiao, Yan; Ya                                         | 2018 | BMC cancer                      | 18     |       | 1 288       |
| Nut ConsumpLong, Jieyi; Ji;                                        | 2020 | Cancer epidc                    | 29     |       | 3 565-573   |
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| Muscle-strenNascimento,                                              | 2021 | The internati                   | 18     |       | 1 69        |
| ConsumptionLlaha, Fjorida                                          | 2021 | Nutrients                      | 13     |       | 2          |
| Cellular PhonChoi, Yoon-Jl                                         | 2020 | International                   | 17     |       | 21          |
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| Consumption (Makarem, Nc)                                            | 2016       | Nutrition Reviews                           | 74     | 6     |
| Thiazolidined (Colmers, I N)                                          | 2012       | Diabetes & Metabolism                       | 38     | 6     |
| Risk of lymphoma (Siegel, Corey)                                     | 2009       | Clinical Gastroenterology                   | 7      | 8     |
| The comparison (Garlethner, C)                                       | 2006       | Journal of Rheumatology                     | 33     | 12    |
| Comorbidities (Partington, R)                                         | 2018       | Arthritis Research                          | 20     | 1     |
| Dietary total (Parohan, M)                                            | 2019       | Critical Reviews                            | 138    | ago, 8916045 |
| A review and Cohen, Sarah                                            | 2014       | Occupational Reviews                        | 71     | 11    |
| Systemic sclerosis (Boni, M)                                          | 2013       | Rheumatology                                 | 52     | 1     |
| Sex Differences (Liu, Wen; Zhe)                                       | 2018       | Disease Mark                                | 2018   | dim, 8604127 |
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| Exposure to tHardell, Lenn                                             | 2002       | Leukemia & Lymphoma                         | 43     | 5     |
| Sweetened (Boyle, Peter; C)                                           | 2014       | European Journal                            | 23     | 5     |
| Risk of lymphoma (Kotylyar, David)                                   | 2015       | Clinical Gastroenterology                   | 13     | 5     |
| Hepatitis C (Khoury, Tawf)                                            | 2014       | World Journal                               | 20     | 43    |
| Association BGhasemiesfe,                                              | 2019       | JAMA Network                                | 2      | 11    |
| Cancer Risk (Wiggins, Tom)                                            | 2019       | Obesity Surgery                             | 29     | 3     |
| Effect of bariTee, May C; C                                          | 2013       | Surgical Endc                               | 27     | 12    |
| Exposure to Skim, A-Sol; Kc                                            | 2018       | International                               | 15     | 9     |
| The association (Song, Hyun Ji)                                       | 2020       | European Journal of Clinical Pharmacology   |        |       |
| Dietary fat in Bertrand, Kin                                          | 2017       | The American                                 | 106    | 2     |
| Cancer risk (Partenen, T; L)                                         | 1994       | American Journal                             | 26     | 6     |
| Exposure to tGlass, D; Sc                                             | 2017       | Journal of Occupational & Environmental     | 14     | 11    |
| Mobile phone (Myung, Seun)                                           | 2009       | Journal of Clinical Research                | 27     | 33    |
| A prospective Bertrand, Kin                                          | 2013       | Cancer Prevent                               | 6      | 8     |
| Proximity V (alefranc, A)                                             | 2020       | Environ. Risque:                            | 19     | 6     |
| Proximity to tLefranc, Agne                                          | 2020       | Environnement                                | 19     | 6     |
| [Influence of Contreras Ga]                                           | 2020       | Influencia de                               | 37     | 1     |
| Risk of cancer (Zaroushani, V)                                       | 2019       | Iran Occup. H                               | 16     | 4     |
| Meta-analysis (Wang, L.; Xie)                                         | 2010       | Journal of Preventive Medicine             | 25     | 4     |
| Pills and cancSchmidmayr, L.                                         | 2014       | Gynecologic Cancer                          | 12     | 3     |
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| Does the baris Vanderbeken                                          | 2014       | Obesite                                     | 9      | 3     |
| Domestic wa (Anzivino-Virico)                                        | 2012       | Environneme                                  | 11     | 5     |
| Parental tob (Ferris, I. Torto)                                      | 2004       | Revista Española                            | 60     | 3     |
| Research proQi, G.; Feng, J.                                         | 2018       | Chinese Journal                             | 25     | 22    |
| Correlation bSun, Y.; Wang                                         | 2019       | Chinese Journal                             | 26     | 18    |
| EnvironmentZuurbier, M.;                                             | 2007       | Environneme                                  | 6      | 1     |
| Pesticide expNicolle-Mir, L.                                         | 2012       | Environneme                                  | 11     | 3     |
| HCV-assosiat Milovanova, T.                                          | 2018       | Terapeutiche                                | 90     | 6     |
| Childhood ca Lopez Duenas                                         | 2012       | Revista Española                            | 68     | 1     |
| Non-Hodgkin Lasfargues, G.                                           | 2017       | Bulletin De L                               | 201    | 9     |
| Risk of cancer (Boaventura, I.)                                      | 2007       | Revista de Ps                               | 29     | 1     |
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2010 Psycho-Onco

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| Xue 2017 | Exclusion reason: *Overlapping studies |                          |
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| Zani 2017 | Exclusion reason: *Overlapping studies |                          |
| Starup-Linde 2013 | Exclusion reason: *Overlapping studies |                          |
| Matsuo 2004 | Exclusion reason: *Overlapping studies |                          |
| https://dx.doi.org/10.2337/dc08-1034 | Exclusion reason: *Overlapping studies |
| Mitri 2008 | Exclusion reason: *Overlapping studies |                          |
| https://dx.doi.org/10.1186/ar2404 | Exclusion reason: *Overlapping studies |
| Smitten 2008 | Exclusion reason: *Overlapping studies |                          |
| https://dx.doi.org/10.1080/10428194.2017.1339873 | Exclusion reason: *Overlapping studies |
| Sergentanis 2018 | Exclusion reason: *Overlapping studies |                          |
| https://dx.doi.org/10.1002/ijc.31330 | Exclusion reason: *Overlapping studies |
| Psaltopoulou 2018 | Exclusion reason: *Overlapping studies |                          |
| Yi 2014 | Exclusion reason: *Overlapping studies |                          |
| Baris 1998 | Exclusion reason: *Overlapping studies |                          |
| https://dx.doi.org/10.3109/10428194.2012.673225 | Exclusion reason: *Overlapping studies |
| Castillo 2012 | Exclusion reason: *Overlapping studies |                          |
| https://dx.doi.org/10.1016/j.ypmed.2019.03.035 | Exclusion reason: *Overlapping studies |
| Volesky 2019 | Exclusion reason: *Overlapping studies |                          |
| https://dx.doi.org/10.1097/MD.0000000000014755 | Exclusion reason: *Overlapping studies |
| Zhu 2019 | Exclusion reason: *Overlapping studies |                          |
| Bagnardi 2015 | Exclusion reason: *Overlapping studies |                          |
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| Buja 2005 | Exclusion reason: *Overlapping studies |                          |
| https://dx.doi.org/10.1080/10408444.2016.1214681 | Exclusion reason: *Overlapping studies |
| Acquavella 2016 | Exclusion reason: *Overlapping studies |                          |
| https://dx.doi.org/10.31557/APJCP.2019.20.11.3221 | Exclusion reason: *Overlapping studies |
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https://dx.doi.org/10.1186/s13075-018-1757-y
Partington 2018
Exclusion reason: Insufficient data for analysis;

https://dx.doi.org/10.1093/nutrit/nuw003
Makarem 2016
Exclusion reason: Insufficient data for analysis;

https://dx.doi.org/10.1016/j.diabet.2012.06.003
Colmers 2012
Exclusion reason: Insufficient data for analysis;

https://dx.doi.org/10.1016/j.cgh.2009.01.004
Siegel 2009
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Siegel 2009
Exclusion reason: Insufficient data for analysis;
Title

Postmenopausal hormone therapy and non-Hodgkin lymphoma: a pooled analysis from the InterLymph Consortium

Occupational exposure to trichloroethylene and risk of non-Hodgkin lymphoma: a pooled analysis from the InterLymph Consortium

Non-Hodgkin lymphoma and obesity: a pooled analysis from the InterLymph Consortium

Medical history, lifestyle, family history, and occupational risk factors for follicular lymphoma

Etiologic heterogeneity among non-Hodgkin lymphoma subtypes: a pooled analysis from the InterLymph Consortium

Hepatitis C and non-Hodgkin lymphoma among 4784 cases: a pooled analysis from the InterLymph Consortium

Menstrual and reproductive factors, and hormonal contraceptive use: associations with non-Hodgkin lymphoma in a pooled analysis of InterLymph case-control studies

Self-reported history of infections and the risk of non-Hodgkin lymphoma: a pooled analysis from the InterLymph Consortium

Personal sun exposure and risk of non-Hodgkin lymphoma: a pooled analysis from the InterLymph Consortium

Occupation and Risk of Non-Hodgkin Lymphoma and Its Subtypes

Medical history, lifestyle, family history, and occupational risk factors for follicular lymphoma

Medical history, lifestyle, family history, and occupational risk factors for marginal zone lymphoma

Medical history, lifestyle, family history, and occupational risk factors for follicular lymphoma

Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma

Medical history, lifestyle, family history, and occupational risk factors for mantle cell lymphoma

Medical history, lifestyle, family history, and occupational risk factors for marginal zone lymphoma

Medical history, lifestyle, family history, and occupational risk factors for mycosis fungoides and Sezary syndrome

Medical history, lifestyle, family history, and occupational risk factors for peripheral T-cell lymphomas

Medical history, lifestyle, family history, and occupational risk factors for sporadic Burkitt lymphoma/leukemia

Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: the InterLymph Non-Hodgkin Lymphoma Subtypes Project

Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: the InterLymph Non-Hodgkin Lymphoma Subtypes Project

Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: the InterLymph Non-Hodgkin Lymphoma Subtypes Project

Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: the InterLymph Non-Hodgkin Lymphoma Subtypes Project

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Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: the InterLymph Non-Hodgkin Lymphoma Subtypes Project

Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: the InterLymph Non-Hodgkin Lymphoma Subtypes Project

Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: the InterLymph Non-Hodgkin Lymphoma Subtypes Project

Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: the InterLymph Non-Hodgkin Lymphoma Subtypes Project

Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: the InterLymph Non-Hodgkin Lymphoma Subtypes Project

Medical history, lifestyle, family history, and occupational risk factors for chronic lymphocytic leukemia/small lymphocytic lymphoma: the InterLymph Non-Hodgink
Non-Hodgkin's lymphoma--meta-analyses of the effects of c
Cigarette smoking and risk of lymphoma in adults: a compre
Exposure to glyphosate and risk of non-Hodgkin lymphoma:
Fruits and vegetables consumption and risk of non-Hodgkin
Occupation and the risk of non-Hodgkin lymphoma.
Breast-feeding and childhood cancer: A systematic review w
The risk of cancer development in systemic sclerosis: a met
Occupational exposure to methylene chloride and risk of ca
Primary Sjogren's syndrome and malignancy risk: a systema
Increased risk of lymphoma among inflammatory bowel dis
Occupational exposure to pentachlorophenol causing lympl
Epstein-Barr virus and risk of non-Hodgkin lymphoma in the
Assessing the impact of HAART on the incidence of defining
Use of non-steroidal anti-inflammatory drugs and risk of no
Incidence of malignancy in adult patients with rheumatoid é
Vitamin D status and risk of non-Hodgkin lymphoma: a met
Red and Processed Meat Consumption Increases Risk for Nc
Allergic conditions are not associated with the risk of non-H
Occupational ultraviolet exposure and risk of non-Hodgkin's
Cancer risks in recipients of renal transplants: a meta-analysi
Occupational and environmental exposure to polychlorinate
Hepatitis C virus infection and non-hepatocellular malignant
Effects of Coffee, Black Tea and Green Tea Consumption on Systemic lupus erythematosus and malignancy risk: a meta-
Food of animal origin and risk of non-Hodgkin lymphoma ar
Dairy Product Consumption and Risk of Non-Hodgkin Lymph
Exposure to organochlorine pesticides and non-Hodgkin lym
Association between dietary nitrate and nitrite intake and s
Association between dioxin and cancer incidence and mort:
Associations between statin use and non-Hodgkin lymphom
Lack of association of poultry and eggs intake with risk of nc
Herpes zoster as a marker of occult cancer: A systematic rev
Carotenoid intake and risk of non-Hodgkin lymphoma: a sys
dietary Fat Consumption and Non-Hodgkin's Lymphoma Ris
Occupational exposure to polycyclic aromatic hydrocarbons
Risk of malignancy in ankylosing spondylitis: a systematic re
The association between non-Hodgkin lymphoma and organar
Incidence of cancer (other than gastric cancer) in pernicious
2,4-dichlorophenoxyacetic acid (2,4-D) and risk of non-Hodg
Systematic Review and Meta-Analysis of Selected Cancers ir
Indoor tanning and the risk of developing non-cutaneous ca
Micronutrient Intake and Risk of Hematological Malignanci
Risk of childhood cancer and adult lung cancer after childhood exposure to passive smoke: A meta-analysis.

Hepatitis B virus and risk of non-Hodgkin lymphoma: An update.

A systematic review of epidemiologic studies of styrene and cancer.

Risk of malignancy in Behcet disease: A meta-analysis with systematic review.

Alcohol drinking and non-Hodgkin lymphoma risk: a systematic review and meta-analysis.

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Risk of Lymphoma in Patients With Inflammatory Bowel Disease: A Meta-Analysis on the Relationship Between Hair Dye and Lymphoma Risk.

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Association between type 1 and type 2 diabetes and risk of lymphoma: A systematic review and meta-analysis.

Association between Bacillus Calmette-Guerin (BCG) vaccination and lymphoma risk: A systematic review and meta-analysis.

Prevalence, Incidence, and Risk of Cancer in Patients With Psoriasis and Psoriatic Arthritis: A Systematic Review and Meta-analysis.

Human Pegivirus Infection and Lymphoma Risk: A Systematic Review and Meta-analysis.

Sarcoidosis and Cancer Risk Systematic Review and Meta-analysis.

Cancer incidence attributable to tuberculosis in 2015: global, regional, and national estimates.

Non-Hodgkin lymphoma and occupational exposure to agricultural pesticide chemical groups and active ingredients: A systematic review and meta-analysis.

Cancer incidence among female flight attendants: a meta-analysis of published data.

A systematic review and meta-analysis of haematological malignancies in residents living near petrochemical facilities.

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Occupational exposure to gasoline and the risk of non-Hodgkin lymphoma: a review and meta-analysis of the literature.

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Obesity and risk of non-Hodgkin's lymphoma: a meta-analysis.

Obesity is associated with increased relative risk of diffuse large B-cell lymphoma.

Obesity but not overweight increases the incidence and mortality of leukemia in adults: A meta-analysis of prospective cohort studies.

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Hazardous waste and health impact: a systematic review of the literature.

Effects of omega-3 fatty acids on cancer risk: a systematic review.

Anaplastic Large Cell Lymphoma and Breast Implants: A Systematic Review.

Malignancies and monoclonal gammopathy in Gaucher disease: A systematic review of the relationship between artificial sweeteners and cancer risk.

Consumption of Sugars, Sugary Foods, and Sugary Beverages in Relation to Cancer Risk: A Systematic Review of Longitudinal Studies.

Are pre- or postnatal diagnostic X-rays a risk factor for childhood cancer risk in children and young adults born preterm: A systematic review?
Bernatsky 2007

Sergentanis 2013
Boffetta 2021
Chen 2013
Boffetta 2007
Martin 2005
Zhang 2013
Liu 2013
Liang 2014
Kandiel 2005
Zheng 2015
Teras 2015
Cobucci 2015
Ye 2015
Simon 2015
Lu 2014
Yang 2015
Yang 2017
Lu 2017
Wang 2017
Catalani 2019
Masarone 2019
Mirtavoos-Mahyari 2019
Cao 2015
Caini 2016
Wang 2016
Luo 2016
Xie 2016
Xu 2016
Ye 2017
Dong 2017
Schmidt 2017
Chen 2017
Han 2017
Alicandro 2016
Deng 2016
Hu 2017
Lahner 2018
Smith 2017
Schnatter 2018
O'Sullivan 2018
Psaltopoulou 2018
meta-analysis of summary level data
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### eTable 3: AMSTAR 2 evaluation

| Rating       | Title                                           | Author year | Item 1 | Item 2 | Item 3 | Item 4 |
|--------------|-------------------------------------------------|-------------|--------|--------|--------|--------|
| Critically low | Benzene exposure                               | Kane 2010   | No     | No     | NA     | No     |
| Critically low | Maternal smoking                               | Antonomopoulous 2011 | Yes | No     | NA     | Partial Yes |
| Critically low | Lifestyle factors                              | Odutola 2020 | No     | Partial Yes | NA     | No     |
| Critically low | Dietary trauma                                  | Michels 2021 | Yes    | Partial Yes | NA     | Partial Yes |
| Critically low | Sunlight exposure                               | Kim 2021    | Yes    | No     | NA     | Partial Yes |
| Critically low | Non-Hodgkin lymphoma                           | Kane 2011   | Yes    | No     | NA     | No     |
| Critically low | Trichloroethylene                               | Scott 2011  | No     | No     | NA     | Partial Yes |
| Critically low | The relationship                                | Davies 2020 | Yes    | Partial Yes | No     | Partial Yes |
| Critically low | Association                                    | Castillo 2010 | No | No     | NA     | No     |
| Critically low | A systemic factor                               | Odutola 2021 | No     | Partial Yes | NA     | No     |
| Critically low | Malaria Infection                               | Kotepui 2021 | Yes    | No     | NA     | Partial Yes |
| Critically low | Meta-analysis                                    | Tio 2012    | No     | No     | NA     | Partial Yes |
| Critically low | The Risk of                                     | Lo 2021     | Yes    | Partial Yes | NA     | Partial Yes |
| Critically low | Primary bile acids                              | Liang 2012  | Yes    | No     | NA     | No     |
| Low           | Paracetamol                                     | Prego-Dominguez 2021 | Yes | Partial Yes | No | Partial Yes |
| Critically low | Non-Hodgkin lymphoma                            | Bernatsky 2007 | No | No     | No     | No     |
| Critically low | Cigarette smoking                               | Sergentanis 2013 | No | No     | NA     | Partial Yes |
| Critically low | Exposure to                                      | Boffetta 2021 | No | No     | NA     | No     |
| Critically low | Fruits and vegetables                           | Chen 2013   | No     | No     | NA     | No     |
| Critically low | Occupation                                      | Boffetta 2007 | No | No     | No     | No     |
| Critically low | Breast-feeding                                  | Martin 2005  | Yes    | No     | NA     | No     |
| Critically low | The Risk of                                     | Zhang 2013  | No     | No     | NA     | No     |
| Critically low | Occupation                                      | Liu 2013    | No     | No     | NA     | Partial Yes |
| Critically low | Primary Sjogren's syndrome                       | Liang 2014  | Yes    | No     | NA     | No     |
| Critically low | Increased exposure                              | Kandiel 2005 | Yes | No     | No     | No     |
| Critically low | Occupation                                      | Zheng 2015  | No     | No     | NA     | No     |
| Critically low | Epstein-Ba                                      | Teras 2015  | No     | No     | NA     | No     |
| Critically low | Assessing                                       | Cobucci 2015 | Yes | No     | NA     | Partial Yes |
| Critically low | Use of non-steroidal analgesics                 | Ye 2015     | Yes    | No     | Yes    | Yes    |
| Critically low | Incidence of                                     | Simon 2015  | Yes    | No     | NA     | No     |
| Critically low | Vitamin D                                        | Lu 2014     | No     | No     | No     | Partial Yes |
| Critically low | Red and Pr                                       | Yang 2015   | No     | No     | NA     | No     |
| Critically low | Allergic conditions                             | Yang 2017   | No     | No     | NA     | Partial Yes |
| Critically low | Occupation                                      | Lu 2017     | No     | No     | NA     | Partial Yes |
| Critically low | Cancer risk                                      | Wang 2017   | Yes    | No     | NA     | Partial Yes |
| Low           | Occupation                                      | Catalani 2019 | Yes | Partial Yes | NA | Partial Yes |
| Critically low | Hepatitis C                                      | Masarone 2019 | Yes | No     | NA     | Partial Yes |
| Critically low | Effects of                                      | Mirtavoos-Mahyari 2019 | Yes | No | NA | No |
| Critically low | Systemic lupus                                   | Cao 2015    | Yes    | No     | NA     | Partial Yes |
| Critically low | Food of an                                      | Cai 2016    | No     | No     | No     | Partial Yes |
| Critically low | Dairy products                                   | Wang 2016   | No     | No     | NA     | No     |
| Critically low | Exposure to                                      | Luo 2016    | No     | No     | NA     | Partial Yes |
| Critically low | Association                                      | Xie 2016    | No     | No     | NA     | No     |
| Critically low | Association                                      | Xu 2016     | Yes    | No     | NA     | No     |
| Strength of Evidence | Association | Year | Risk | Cancer Type | Study | Meta-Analysis | Results |
|----------------------|-------------|------|------|-------------|-------|---------------|---------|
| Critically low       | Lack of ass | Dong 2017 | No   | NA          | Partial Yes |
| Critically low       | Herpes zoster | Schmidt 2017 | Yes | NA          | No |
| Critically low       | Carotenoid | Chen 2017 | No   | NA          | Partial Yes |
| Critically low       | Dietary Fat | Han 2017 | No   | NA          | No |
| Critically low       | Occupation | Alicandro 2016 | Yes | NA          | Partial Yes |
| Critically low       | Risk of mal | Deng 2016 | Yes | NA          | No |
| Critically low       | The associ | Hu 2017 | No   | NA          | No |
| Critically low       | Incidence | Lahner 2018 | No | NA          | Partial Yes |
| Critically low       | 2,4-dichlor | Smith 2017 | No | NA          | Partial Yes |
| Critically low       | Systematic | Schnatter 2018 | Yes | Yes | Partial Yes |
| Critically low       | Indoor tan | O'Sullivan 2018 | No | No | No |
| Critically low       | Micronutri | Psaltopoulou 2018 | Yes | Partial Yes | Yes |
| Critically low       | Risk of chil | Boffetta 2000 | No | No | NA |
| Critically low       | Hepatitis B | Li 2018 | Yes | No | NA |
| Critically low       | A systemat | Collins 2018 | Yes | No | NA |
| Critically low       | Risk of mal | Wang 2019 | Yes | No | NA |
| Critically low       | Alcohol dri | Tramacere 2012 | No | No | NA |
| Critically low       | Cancer inc | Jalilian 2019 | Yes | No | NA |
| Critically low       | Risk of Lyn | Yang 2018 | Yes | No | Yes |
| Critically low       | A Meta-An | Qin 2019 | No | No | NA |
| Critically low       | Association | Zhang 2019 | Yes | No | NA |
| Critically low       | Association | Wang 2020 | No | No | NA |
| Moderate             | Association | Salmon 2020 | No | Partial Yes | Yes |
| Critically low       | Prevalence | Vaengebjerg 2020 | Yes | Partial Yes | NA |
| Critically low       | Human Pe | Fama 2020 | Yes | No | NA |
| Critically low       | Sarco | Bojani 2015 | No | No | NA |
| High                 | Cancer inc | Leung 2020 | Yes | Partial Yes | NA |
| Critically low       | Non-hodgki | Schinasi 2014 | No | No | NA |
| Critically low       | Cancer inc | Buja 2006 | No | No | No |
| Low                  | A systemic | Jephcote 2020 | Yes | Partial Yes | NA |
| Critically low       | Association | Dun 2020 | Yes | No | NA |
| Critically low       | Risk of can | Takkouche 2009 | Yes | No | NA |
| Critically low       | Occupation | Kane 2010 | Yes | No | NA |
| Critically low       | Borrelia bu | Travaglino 2020 | No | No | NA |
| Moderate             | Use of insu | Karlstad 2013 | Yes | Partial Yes | No |
| Critically low       | Obesity an | Larsson 2007 | Yes | No | NA |
| Critically low       | Obesity is | Castillo 2014 | Yes | No | NA |
| Critically low       | Obesity bu | Castillo 2012 | Yes | No | NA |
| Critically low       | Increased | Castillo 2012 | Yes | No | NA |
| Critically low       | Hepatitis C | DalMaso 2006 | Yes | No | NA |
| Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 |
|--------|--------|--------|--------|--------|---------|---------|---------|--------|
| No     | No     | No     | Yes    | No     | No      | No      | No      | No     |
| No     | Yes    | No     | Partial Yes | No    | Yes     | No      | No      | No     |
| Yes    | Yes    | No     | No     | Yes    | No      | Yes     | Yes     | Yes    |
| Yes    | No     | No     | Partial Yes | Yes   | No      | Yes     | No      | No     |
| No     | Yes    | No     | Partial Yes | Yes   | No      | Yes     | Yes     | No     |
| No     | No     | No     | No     | No     | No      | No      | No      | No     |
| No     | No     | No     | Partial Yes | No    | No      | Yes     | No      | No     |
| Yes    | No     | No     | Partial Yes | Yes   | No      | Yes     | No      | No     |
| Yes    | Yes    | No     | No     | Yes    | No      | No      | No      | No     |
| No     | No     | No     | Partial Yes | Yes   | No      | Yes     | No      | No     |
| No     | No     | No     | No     | No     | No      | Yes     | No      | No     |
| No     | Yes    | No     | Yes    | No     | No      | Yes     | No      | No     |
| No     | No     | No     | No     | Yes    | No      | Yes     | No      | No     |
| No     | No     | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
| No     | No     | Yes    | No     | No     | No      | Yes     | No      | No     |
| No     | No     | No     | No     | Yes    | No      | Yes     | No      | No     |
| No     | No     | No     | No     | Yes    | No      | Yes     | No      | No     |
| No     | No     | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
| No     | No     | No     | No     | No     | No      | Yes     | No      | No     |
| No     | No     | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
| Yes    | Yes    | Partial Yes | No    | Partial Yes | No      | Yes     | No      | No     |
| No     | No     | No     | No     | No     | No      | No      | No      | No     |
| Yes    | Yes    | No     | No     | Yes    | No      | Yes     | No      | No     |
| Yes    | Yes    | No     | No     | Yes    | No      | Yes     | No      | No     |
| No     | No     | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
| No     | No     | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
| Yes    | Yes    | No     | No     | Yes    | No      | Yes     | No      | No     |
| Yes    | Yes    | No     | No     | Yes    | No      | Yes     | No      | No     |
| Yes    | Yes    | No     | No     | Yes    | No      | Yes     | No      | No     |
| No     | Yes    | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
| No     | Yes    | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
| No     | Yes    | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
| No     | Yes    | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
| No     | Yes    | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
| No     | Yes    | No     | No     | No     | Yes     | Yes     | Yes     | Yes    |
|   | Yes | Yes | No | No | No | No | Yes | No | No |
|---|-----|-----|----|----|----|----|-----|----|----|
| 1 | Yes | Yes | No | No | Yes | No | Yes | Yes | No |
| 2 | Yes | Yes | No | No | Partial Yes | Partial Yes | No | Yes | Yes | Yes |
| 3 | No | Yes | No | No | No | Yes | No | Yes | No | No |
| 4 | Yes | Yes | No | No | Yes | No | Yes | No | Yes | No |
| 5 | No | No | Yes | Yes | No | No | No | No | No | No |
| 6 | No | Yes | No | No | No | Yes | No | Yes | Yes | Yes |
| 7 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 8 | No | No | Yes | Yes | No | No | No | No | No | No |
| 9 | No | Yes | No | No | No | Yes | No | Yes | No | No |
| 10 | No | Yes | No | No | Partial Yes | Yes | No | Yes | Yes | Yes |
| 11 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 12 | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 13 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 14 | No | No | Yes | Yes | No | No | Yes | No | No | No |
| 15 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 16 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 17 | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 18 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 19 | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 20 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 21 | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 22 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 23 | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 24 | No | No | Yes | Yes | No | No | Yes | No | No | No |
| 25 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 26 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 27 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 28 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 29 | No | No | No | Partial Yes | No | No | Yes | No | No | No |
| 30 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 31 | No | Yes | No | No | Yes | No | Yes | No | No | No |
| 32 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 33 | No | No | No | No | No | Yes | No | Yes | No | No |
| 34 | Yes | Yes | No | No | Partial Yes | Yes | No | Yes | Yes | Yes |
| 35 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 36 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 37 | Yes | Yes | Yes | Yes | Yes | No | Yes | No | No | Yes |
| 38 | No | No | No | Yes | No | No | Yes | No | No | No |
| 39 | Yes | Yes | No | No | Partial Yes | Yes | No | Yes | Yes | Yes |
| 40 | No | No | No | No | No | Yes | No | Yes | No | No |
| 41 | Yes | Yes | No | No | Partial Yes | Yes | No | Yes | Yes | Yes |
| 42 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 43 | Yes | Yes | No | No | Yes | No | Yes | No | No | No |
| 44 | No | No | No | No | No | Yes | No | Yes | Yes | Yes |
| 45 | Yes | Yes | No | No | Partial Yes | Yes | No | Yes | Yes | Yes |
| 46 | Yes | No | No | No | No | Yes | No | Yes | Yes | Yes |
| 47 | Yes | No | No | Partial Yes | Yes | No | No | No | No | No |
| 48 | Yes | Yes | Partial Yes | Yes | Yes | No | Yes | No | Yes | No |
| 49 | No | No | Partial Yes | Partial Yes | No | No | Yes | No | No | No |
| 50 | No | No | No | No | Yes | No | Yes | No | No | No |
| 51 | Yes | No | No | No | Yes | No | Yes | No | No | No |
| 52 | Yes | No | No | No | Yes | No | Yes | No | No | No |
| 53 | Yes | No | No | No | Yes | No | Yes | No | No | No |
| 54 | No | Yes | No | No | Yes | No | Yes | Yes | Yes | Yes |
| 55 | No | No | No | Partial Yes | No | No | Yes | No | No | No |
| Item 14 | Item 15 | Item 16 |
|--------|--------|--------|
| Yes    | No     | Yes    |
| Yes    | Yes    | No     |
| Yes    | No     | Yes    |
| No     | No     | Yes    |
| No     | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| No     | No     | Yes    |
| No     | No     | Yes    |
| Yes    | No     | Yes    |
| Yes    | Yes    | Yes    |
| No     | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| No     | Yes    | Yes    |
| No     | No     | Yes    |
| Yes    | No     | Yes    |
| Yes    | Yes    | Yes    |
| No     | No     | Yes    |
| No     | Yes    | Yes    |
| Yes    | No     | Yes    |
| Yes    | Yes    | Yes    |
| No     | No     | Yes    |
| No     | Yes    | Yes    |
| Yes    | No     | Yes    |
| Yes    | Yes    | Yes    |
| No     | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| No     | No     | Yes    |
| No     | Yes    | Yes    |
| Yes    | No     | Yes    |
| Yes    | Yes    | Yes    |
| No     | Yes    | Yes    |
| Yes    | No     | Yes    |
| Yes    | Yes    | Yes    |
| No     | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| No     | No     | Yes    |
| Yes    | Yes    | Yes    |
| No     | Yes    | Yes    |
| Yes    | No     | Yes    |
| Yes    | Yes    | Yes    |
| No     | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| Yes    | Yes    | Yes    |
| Yes    | Yes    | Yes    |
|   | No  | Yes | Yes |
|---|-----|-----|-----|
| 1 | Yes | Yes | Yes |
| 2 | Yes | Yes | Yes |
| 3 | Yes | Yes | Yes |
| 4 | No  | Yes | Yes |
| 5 | Yes | Yes | Yes |
| 6 | Yes | Yes | Yes |
| 7 | Yes | Yes | Yes |
| 8 | Yes | Yes | Yes |
| 9 | Yes | Yes | Yes |
| 10| Yes | Yes | Yes |
| 11| Yes | Yes | Yes |
| 12| No  | No  | Yes |
| 13| Yes | Yes | Yes |
| 14| Yes | Yes | Yes |
| 15| No  | No  | Yes |
| 16| Yes | Yes | Yes |
| 17| No  | No  | Yes |
| 18| No  | Yes | No  |
| 19| Yes | Yes | Yes |
| 20| Yes | Yes | Yes |
| 21| No  | Yes | No  |
| 22| Yes | Yes | Yes |
| 23| No  | Yes | Yes |
| 24| Yes | Yes | Yes |
| 25| No  | Yes | No  |
| 26| Yes | Yes | Yes |
| 27| No  | Yes | Yes |
| 28| Yes | Yes | Yes |
| 29| No  | Yes | Yes |
| 30| Yes | Yes | Yes |
| 31| No  | Yes | Yes |
| 32| Yes | Yes | Yes |
| 33| Yes | Yes | Yes |
| 34| Yes | Yes | Yes |
| 35| No  | Yes | Yes |
| 36| Yes | Yes | Yes |
| 37| Yes | No  | Yes |
| 38| No  | Yes | No  |
| 39| Yes | Yes | Yes |
| 40| Yes | Yes | Yes |
| 41| Yes | Yes | Yes |
| 42| Yes | Yes | Yes |
| 43| Yes | Yes | Yes |
| 44| Yes | Yes | Yes |
| 45| Yes | Yes | Yes |
| 46| Yes | No  | Yes |
| 47| No  | Yes | Yes |
| 48| No  | Yes | Yes |
| 49| No  | Yes | Yes |
| 50| No  | Yes | Yes |
| 51| Yes | Yes | Yes |
| 52| Yes | Yes | Yes |
| 53| Yes | Yes | Yes |
| 54| No  | Yes | No  |
| 55| No  | Yes | No  |
| Risk factors category | Environmental risk factors |
|-----------------------|----------------------------|
| **Dietary factors**   |                            |
| Meat                  | Red meat                   |
|                       | Processed meat             |
|                       | Red meat                   |
|                       | Processed meat             |
|                       | Processed meat             |
|                       | Red meat                   |
|                       | Processed meat             |
|                       | White meat/poultry         |
|                       | White meat/poultry         |
|                       | White meat/poultry         |
|                       | White meat/poultry         |
| Fish                  | Fish                       |
|                       | Fish                       |
|                       | Fish                       |
|                       | Fish                       |
| Fruits and vegetables | Fruit and vegetable        |
|                       | Fruit                      |
|                       | Vegetable                  |
|                       | Fruit                      |
|                       | Vegetable                  |
|                       | Fruit                      |
|                       | Vegetable                  |
| Eggs and dairy        | Eggs                       |
|                       | Total dairy                |
|                       | Total dairy                |
|                       | Total dairy                |
|                       | Total dairy                |
|                       | Milk                       |
|                       | Milk                       |
|                       | Milk                       |
|                       | Milk                       |
|                       | Milk                       |
|                       | Cheese                     |
|                       | Cheese                     |
|                       | Cheese                     |
|                       | Cheese                     |
|                       | Yogurt                     |
|                       | Yogurt                     |
|                       | Yogurt                     |
|                       | Yogurt                     |
|                       | Yogurt                     |
|                       | Yogurt                     |
|                       | Yogurt                     |
|                       | Butter                     |
|                       | Ice-cream                  |
| Coffee and tea        | Coffee                     |
|                       | Black tea                  |
| Carotenoids | Micronutrient intake/supplements |
|-------------|--------------------------------|
| Green tea   | Vitamin A (retinol)            |
| Alpha-carotene | Vitamin C                  |
| Alpha-carotene | Vitamin D                   |
| Alpha-carotene | Vitamin D                   |
| Alpha-carotene | Vitamin D                   |
| Alpha-carotene | Vitamin E                   |
| Alpha-carotene | Total fat                   |
| Alpha-carotene | Total fat                   |
| Alpha-carotene | Total fat                   |
| Alpha-carotene | Total fat                   |
| Alpha-carotene | Total fat                   |
| Beta-carotene | Animal fat                  |
| Beta-carotene | Vegetable fat               |
| Beta-carotene | Dietary nitrate             |
| Beta-carotene | Dietary nitrite             |
| Beta-cryptoxanthin | Dietary trans-fatty acid intake |
| Beta-cryptoxanthin | Dietary nitrate |
| Beta-cryptoxanthin | Dietary nitrite |
| Beta-cryptoxanthin | Dietary trans-fatty acid intake |
| Lycopene   |                        |
| Lycopene   |                        |
| Lycopene   |                        |
| Lycopene   |                        |
| Lycopene   |                        |
| Lycopene   |                        |
| Lycopene   |                        |
| Andlutein/zeaxanthin |           |
| Andlutein/zeaxanthin |           |
| Andlutein/zeaxanthin |           |
| Andlutein/zeaxanthin |           |
| Andlutein/zeaxanthin |           |
| Andlutein/zeaxanthin |           |
| Vitamin D  |                        |
| Vitamin D  |                        |
| Vitamin D  |                        |
| Vitamin D  |                        |
| Vitamin E  |                        |
| Heavy drinking |                     |
| Heavy drinking |                     |
| Heavy drinking |                     |
| Heavy drinking |                     |
| Heavy drinking |                     |
| Heavy drinking |                     |
| Heavy drinking |                     |
### Breastfeeding

#### Drugs, vaccinations and procedures

| Non-steroidal anti-inflammatory drugs | Aspirin | Aspirin | Aspirin | Aspirin | NA-NSAIDS | NA-NSAIDS | NSAIDS | NSAIDS | NSAIDS | NSAIDS | NSAIDS | NSAIDS |
|---------------------------------------|---------|---------|---------|---------|-----------|-----------|--------|--------|--------|--------|--------|--------|
| Corticosteroids                       | Corticosteroids |
| Statin                                | Statin | Statin | Statin | Statin | Statin |
| Paracetamol intake                    | Paracetamol |
| Bacillus calmette-guerin vaccination  | Insulin |
| Insulin                               | Insulin |
| Anti-tumor necrosis factor alpha agents | Azathioprine and 6-mercaptopurine |

#### Inflammatory bowel disease treatment among patients with HIV/AIDS

| Red blood cell transfusion | Red blood cell transfusion | Red blood cell transfusion |

#### Non-dietary lifestyle factors

| Physical activity | Physical activity | Physical activity | Physical activity |
|-------------------|-------------------|-------------------|-------------------|
| Hair dye          | Hair dye          | Hair dye          |
| Night shift work  | Night shift work  |
| Indoor tanning    | Indoor tanning    | Indoor tanning    |
| Petrochemical exposure |
| Paternal smoking  | Paternal smoking  |
| Maternal smoking  | Maternal smoking  |
| Ever smoking      | Ever smoking      |

#### Smoking

| Smoking | Ever smoking | Ever smoking | Ever smoking |

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| Sun exposure                        | Medical history and comorbid diseases                      |
|------------------------------------|----------------------------------------------------------|
| Personal sunlight exposure         | B-cell activating diseases                                |
| Ambient sunlight exposure during lifetime | Psoriasis                                             |
| Occupational ultraviolet exposure  | Type 1 diabetes                                          |
|                                    | celiac disease                                           |
|                                    | Dermatitis herpetiformis                                 |
|                                    | Systemic sclerosis                                       |
|                                    | Crohn's disease                                          |
|                                    | Ulcerative colitis                                       |
|                                    | Sarcoidosis                                              |
|                                    | Other                                                    |
|                                    | Behcet's disease                                         |
|                                    | Ankylosing spondylitis                                   |
|                                    | Biliary cirrhosis                                        |
|                                    | Eczema                                                   |
|                                    | Allergy/Atopic diseases                                  |
| Overweight and obesity             | Type 2 diabetes                                          |
| Overweight                         | Parkinson's disease                                      |
| Overweight                         | Overweight                                               |
| Overweight                         | Overweight                                               |
| Overweight                         | Overweight                                               |
| Overweight                         | Overweight                                               |
| Obesity                            | Obesity                                                  |
| Obesity                            | Obesity                                                  |
| Obesity                            | Obesity                                                  |
| Obesity                            | Herpes zoster                                            |

Medical history and comorbid diseases

- **B-cell activating diseases**
  - Pernicious anemia

- **T-cell activating diseases**
  - Psoriasis
  - Type 1 diabetes
  - celiac disease

- **Other**
  - Behcet's disease
  - Ankylosing spondylitis
  - Biliary cirrhosis
  - Eczema

- **Allergy/Atopic diseases**
  - Asthma
  - Hay fever
  - Food allergy
  - Type 2 diabetes
  - Parkinson's disease

- **Overweight and obesity**
  - Overweight
  - Overweight
  - Overweight
  - Obese
  - Obese
  - Obese
  - Obese
| Infection                                                                 |
|---------------------------------------------------------------------------|
| Herpes zoster                                                             |
| HPV                                                                      |
| HPV                                                                      |
| Epstein–Barr virus early antigen                                         |
| Epstein–Barr virus viral capsid antigen                                  |
| Borrelia burgdorferi                                                     |
| Borrelia burgdorferi                                                     |
| HBV                                                                      |
| HBV                                                                      |
| HBV                                                                      |
| HBV                                                                      |
| HBV                                                                      |
| HBV                                                                      |
| HCV                                                                      |
| HCV                                                                      |
| HCV                                                                      |
| Malaria infection                                                        |

| Chemicals and pesticides                                                |
|------------------------------------------------------------------------|
| Solvent                                                                 |
| Formaldehyde<sup>c</sup>                                                |
| Chlorinated solvents<sup>c</sup>                                        |
| Any solvent<sup>c</sup>                                                 |
| Aromatic hydrocarbons                                                   |
| Styrene<sup>c</sup>                                                     |
| Benzene<sup>c</sup>                                                     |
| Benzene<sup>c</sup>                                                     |
| Aromatic hydrocarbons<sup>c</sup>                                       |
| Polychlorinated biphenyls                                               |
| PCB<sup>c</sup>                                                         |
| PCB<sup>c</sup>                                                         |
| PCB<sup>c</sup>                                                         |
| PCB<sup>c</sup>                                                         |
| Dioxin                                                                  |
| Dioxin                                                                  |
| Trichloroethylene                                                       |
| Trichloroethylene<sup>c</sup>                                           |
| Occupational exposure to methylene chloride                             |
| Occupational exposure to gasoline<sup>c</sup>                           |
| Carbamate/thiocarbamate pesticides                                      |
| Carbamate/thiocarbamate herbicides                                      |
| Carbamate insecticides                                                  |
| Organophosphate pesticides                                              |
| Glyphosate                                                              |
| Glyphosate<sup>c</sup>                                                  |
| Glyphosate<sup>c</sup>                                                  |
| Malathion                                                               |
| Diazinon                                                                |
| Terbufos                                                                |
| Organophosphate pesticides                                              |
| Organophosphate pesticides<sup>c</sup>                                  |
### Organochlorine pesticides

| Pesticide          |
|--------------------|
| DDT                |
| DDT<sup>c</sup>    |
| DDE                |
| DDE<sup>c</sup>    |
| HCH                |
| HCB                |
| Chlordane          |
| Pentachlorophenol<sup>c</sup> |

### Phenoxy herbicides

| Herbicide         |
|-------------------|
| 2,4-D             |
| MCPA              |
| Phenoxy herbicides |

### Other pesticides

| Pesticide                  |
|-----------------------------|
| Amide herbicides            |
| Benzoic acid herbicides     |
| Triazine herbicides         |
| Trifluralin                 |
| Pyrethroid/pyrethin<sup>c</sup> |

### Occupation

| Occupation                | Occupations                                      |
|---------------------------|---------------------------------------------------|
| Flight attendant          | Female flight attendant<sup>e</sup>              |
| Farmer                    | Farmer                                           |
| Firefighter               | Firefighter<sup>c</sup>                          |
| Hairdresser               | Hairdresser                                      |
| Petroleum refinery worker | Petroleum refinery worker                        |
| Meat worker               | Meat worker                                      |
| Printer                   | Printer                                          |
| Wood worker               | Wood worker                                      |
| Occupational exposure to  | Aluminum plant workers<sup>c</sup>              |
| polycyclic aromatic       | Iron and steel foundry workers<sup>c</sup>      |

### Footnotes

- 2,4-D=2,4-Dichlorophenoxyacetic acid; ALCL=aANaplastic largecell lymphoma; BL=Burkitt Lymphoma; CI=confidence interval; CLL=chronic lymphocytic leukaemia; CR=confidence range; CSR=case survival rate; CI=confidence interval; DR=death rate; SR=standardized mortality rate; T=total; SIR=standardized incidence ratio; SRMA=systematic review and meta-analysis; RR=risk ratio; TCL=T-cell lymphoma.
- <sup>a</sup> P value for summary effect estimates using a random-effects DerSimonian and Laird estimator.
- <sup>b</sup> Strength of association using the criteria listed in Table 1.
- <sup>c</sup> These studies considered NHL incidence and mortality.
- <sup>d</sup> Summary effect estimates were calculated using a fixed effect estimator.
- <sup>e</sup> Not using inverse variance weighting.
| Level of comparison | Outcome | Study type | Author, year | No. of primary studies | No. of cases |
|---------------------|---------|------------|--------------|------------------------|--------------|
| Highest vs lowest   | NHL     | MA         | Yang 2015    | 18                     | 12579        |
| Highest vs lowest   | NHL     | MA         | Yang 2015    | 18                     | 14112        |
| Highest vs lowest   | DLBCL   | MA         | Yang 2015    | 5                      | NA           |
| Highest vs lowest   | DLBCL   | MA         | Yang 2015    | 5                      | NA           |
| Highest vs lowest   | FL      | MA         | Yang 2015    | 5                      | NA           |
| Highest vs lowest   | CLL/SLL| MA         | Yang 2015    | 5                      | NA           |
| Highest vs lowest   | CLL/SLL| MA         | Yang 2015    | 5                      | NA           |
| Highest vs lowest   | NHL     | MA         | Dong 2017    | 10                     | 10671        |
| Highest vs lowest   | DLBCL   | SRMA       | Caini 2016   | 3                      | 1134         |
| Highest vs lowest   | FL      | SRMA       | Caini 2016   | 3                      | 858          |
| Highest vs lowest   | CLL/SLL| SRMA       | Caini 2016   | 3                      | 1337         |
| Highest vs lowest   | NHL     | SRMA       | Caini 2016   | 11                     | 8839         |
| Highest vs lowest   | DLBCL   | SRMA       | Caini 2016   | 4                      | 1228         |
| Highest vs lowest   | FL      | SRMA       | Caini 2016   | 4                      | 970          |
| Highest vs lowest   | CLL/SLL| SRMA       | Caini 2016   | 5                      | 1703         |
| Highest vs lowest   | NHL     | MA         | Chen 2013    | 4                      | 1747         |
| Highest vs lowest   | NHL     | MA         | Chen 2013    | 13                     | 8476         |
| Highest vs lowest   | NHL     | MA         | Chen 2013    | 13                     | 8332         |
| Highest vs lowest   | DLBCL   | MA         | Chen 2013    | 8                      | NA           |
| Highest vs lowest   | DLBCL   | MA         | Chen 2013    | 7                      | NA           |
| Highest vs lowest   | FL      | MA         | Chen 2013    | 8                      | NA           |
| Highest vs lowest   | FL      | MA         | Chen 2013    | 7                      | NA           |
| Highest vs lowest   | NHL     | SRMA       | Caini 2016   | 10                     | 5775         |
| Highest vs lowest   | NHL     | MA         | Wang 2016    | 7                      | 4207         |
| Highest vs lowest   | DLBCL   | MA         | Wang 2016    | 3                      | 321          |
| Highest vs lowest   | FL      | MA         | Wang 2016    | 3                      | 355          |
| Highest vs lowest   | CLL/SLL| MA         | Wang 2016    | 3                      | 390          |
| Highest vs lowest   | NHL     | MA         | Wang 2016    | 16                     | 7109         |
| Highest vs lowest   | DLBCL   | MA         | Wang 2016    | 3                      | 352          |
| Highest vs lowest   | FL      | MA         | Wang 2016    | 3                      | 390          |
| Highest vs lowest   | CLL/SLL| MA         | Wang 2016    | 3                      | 477          |
| Highest vs lowest   | NHL     | MA         | Wang 2016    | 10                     | 5519         |
| Highest vs lowest   | DLBCL   | MA         | Wang 2016    | 3                      | 352          |
| Highest vs lowest   | FL      | MA         | Wang 2016    | 3                      | 390          |
| Highest vs lowest   | CLL/SLL| MA         | Wang 2016    | 3                      | 477          |
| Highest vs lowest   | NHL     | MA         | Wang 2016    | 4                      | 1534         |
| Highest vs lowest   | NHL     | MA         | Wang 2016    | 4                      | 1598         |
| Highest vs lowest   | NHL     | SRMA       | Mirtavoos-Mahy 2019 | 11 | 4418 |
| Highest vs lowest   | NHL     | SRMA       | Mirtavoos-Mahy 2019 | 5 | 1600 |
| Study                          | Disease Type | Analysis | Reference          | Cases | Controls |
|-------------------------------|--------------|----------|--------------------|-------|----------|
| Highest vs lowest             | NHL SRMA     | Mirtavoos-Mahy 2019 | 3 | 637 |
| Highest vs lowest             | NHL SRMA     | Chen 2017 | 8 | 2926 |
| Highest vs lowest             | DLBCL SRMA   | Chen 2017 | 3 | NA |
| Highest vs lowest             | FL SRMA      | Chen 2017 | 4 | NA |
| Highest vs lowest             | CLL/SLL SRMA| Chen 2017 | 2 | NA |
| Highest vs lowest             | NHL SRMA     | Chen 2017 | 10 | 3946 |
| Highest vs lowest             | DLBCL SRMA   | Chen 2017 | 5 | NA |
| Highest vs lowest             | FL SRMA      | Chen 2017 | 6 | NA |
| Highest vs lowest             | CLL/SLL SRMA| Chen 2017 | 4 | NA |
| Highest vs lowest             | NHL SRMA     | Chen 2017 | 7 | 2325 |
| Highest vs lowest             | DLBCL SRMA   | Chen 2017 | 4 | NA |
| Highest vs lowest             | FL SRMA      | Chen 2017 | 4 | NA |
| Highest vs lowest             | CLL/SLL SRMA| Chen 2017 | 3 | NA |
| Highest vs lowest             | NHL SRMA Psaltopoulou 2018 | 3 | 3314 |
| Highest vs lowest             | NHL SRMA Psaltopoulou 2018 | 5 | 3879 |
| Highest vs lowest             | NHL MA       | Lu 2014   | 6 | 4400 |
| Highest vs lowest             | DLBCL MA     | Lu 2014   | 5 | NA |
| Highest vs lowest             | FL MA        | Lu 2014   | 5 | NA |
| Highest vs lowest             | CLL/SLL MA   | Lu 2014   | 4 | NA |
| Highest vs lowest             | TCL MA       | Lu 2014   | 3 | NA |
| Highest vs lowest             | NHL SRMA Psaltopoulou 2018 | 5 | 3879 |
| Highest vs lowest             | NHL MA       | Han 2017  | 10 | 5042 |
| Highest vs lowest             | DLBCL MA     | Han 2017  | 5 | NA |
| Highest vs lowest             | FL MA        | Han 2017  | 5 | NA |
| Highest vs lowest             | CLL/SLL MA   | Han 2017  | 4 | NA |
| Highest vs lowest             | TCL MA       | Han 2017  | 4 | NA |
| Highest vs lowest             | NHL MA       | Han 2017  | 5 | 1432 |
| Highest vs lowest             | NHL MA       | Han 2017  | 5 | 1432 |
| Highest vs lowest             | NHL SRMA Michels 2021 | 4 | 4701 |
| Highest vs lowest             | NHL SRMA Xie 2016 | 7 | 1703 |
| Highest vs lowest             | NHL SRMA Xie 2016 | 5 | 1547 |
| Ever vs never                 | NHL SRMA     | Tramacere 2012 | 29 | 18759 |
| Ever vs never                 | TCL SRMA     | Tramacere 2012 | 8 | NA |
| Ever vs never                 | BCL SRMA     | Tramacere 2012 | 15 | NA |
| Ever vs never                 | DLBCL SRMA   | Tramacere 2012 | 14 | NA |
| Ever vs never                 | FL SRMA      | Tramacere 2012 | 14 | NA |
| Ever vs never                 | CLL/SLL SRMA| Tramacere 2012 | 12 | NA |
| Heavy vs never                | NHL SRMA     | Tramacere 2012 | 6 | 1181 |
| Ever vs never | N.H. | SRMA | Year      | No.  | Count |
|---------------|------|------|-----------|------|-------|
| Users vs non-users | NHL  | SRMA | Ye 2015   | 10   | 6818  |
| Users vs non-users | DLBCL| SRMA | Ye 2015   | 3    | NA    |
| Users vs non-users | FL   | SRMA | Ye 2015   | 3    | NA    |
| Users vs non-users | CLL/SLL | SRMA | Ye 2015 | 4    | NA    |
| Users vs non-users | NHL  | SRMA | Ye 2015   | 8    | 5427  |
| Users vs non-users | CLL/SLL | SRMA | Ye 2015 | 3    | NA    |
| Users vs non-users | NHL  | SRMA | Ye 2015   | 13   | 9896  |
| Users vs non-users | DLBCL| SRMA | Ye 2015   | 3    | NA    |
| Users vs non-users | FL   | SRMA | Ye 2015   | 3    | NA    |
| Users vs non-users | CLL/SLL | SRMA | Ye 2015 | 4    | NA    |
| Users vs non-users | TCL  | SRMA | Ye 2015   | 3    | NA    |
| Users vs non-users | BCL  | SRMA | Ye 2015   | 5    | NA    |
| Users vs non-users | NHL  | MA   | Bernatsky 2007 | 8   | 6897  |
| Users vs non-users | NHL  | SRMA | Ye 2017   | 9    | 7825  |
| Users vs non-users | DLBCL| SRMA | Ye 2017   | 4    | 897   |
| Users vs non-users | FL   | SRMA | Ye 2017   | 4    | 495   |
| Users vs non-users | MZL  | SRMA | Ye 2017   | 3    | 215   |
| Users vs non-users | TCL  | SRMA | Ye 2017   | 4    | 227   |
| Users vs non-users | NHL  | SRMA | Prego-Dominguez | 3  | 3022  |
| Yes vs no | NHL  | SRMA | Salmon 2020 | 11  | 4350  |
| Yes vs no | NHL  | SRMA | Karlstad 2013 | 4   | NA    |
| Yes vs no | NHL  | SRMA | Yang 2018   | 3    | 35    |
| Patients vs general population | NHL  | MA   | Kandiel 2005 | 3   | 9     |
| Pre vs post-HAART era | NHL  | SRMA | Cobucci 2015 | 6   | 7701  |
| Yes vs no | NHL  | MA   | Castillo 2010 | 14  | 5904  |
| Yes vs no | CLL/SLL | MA  | Castillo 2010 | 5   | 3450  |
| Yes vs no | FL   | MA   | Castillo 2010 | 6   | NA    |
| Yes vs no | DLBCL| MA   | Castillo 2010 | 5   | NA    |
| Highest vs lowest | NHL  | SRMA | Davies 2020 | 17  | 13425 |
| Highest vs lowest | DLBCL| SRMA | Davies 2020 | 10  | 1957  |
| Highest vs lowest | FL   | SRMA | Davies 2020 | 10  | 1467  |
| Highest vs lowest | CLL/SLL | SRMA | Davies 2020 | 8   | 1452  |
| Highest vs lowest | NHL  | MA   | Qin 2019    | 16   | 10967 |
| User before 1980 vs never | FL   | SRMA | Odutola 2020 | 4   | 439   |
| Shift workers vs non shift | NHL  | SRMA | Dun 2020    | 5    | >1000  |
| Ever vs never | NHL  | SRMA | O’Sullivan 2018 | 10  | 14018 |
| Ever vs never | BCL  | SRMA | O’Sullivan 2018 | 4   | NA    |
| Ever vs never | TCL  | SRMA | O’Sullivan 2018 | 3   | NA    |
| Living near vs far | NHL  | SRMA | Jephcote 2020 | 9   | 1078  |
| Ever vs never | childhood | MA | Boffetta 2000 | 4   | 204   |
| Ever vs never | childhood | MA | Antonopoulos 2001 | 7   | 1072  |
| Ever vs never | NHL  | MA   | Sergentanis 201 | 33  | 25891 |
| Ever vs never | DLBCL| MA   | Sergentanis 201 | 12  | NA    |
| Comparison                        | Disease | Type | Reference       | Year | Count  |
|----------------------------------|---------|------|-----------------|------|--------|
| Ever vs never                    | FL      | MA   | Sergentanis 201 | 11   | NA     |
| Ever vs never                    | CLL/SLL | MA   | Sergentanis 201 | 9    | NA     |
| Ever vs never                    | TCL     | MA   | Sergentanis 201 | 12   | NA     |
| Highest vs lowest                | NHL     | MA   | Kim 2021        | 15   | 11272  |
| Highest vs lowest                | CLL/SLL | MA   | Kim 2021        | 4    | 1564   |
| Highest vs lowest                | DLBCL   | MA   | Kim 2021        | 5    | 1843   |
| Highest vs lowest                | FL      | MA   | Kim 2021        | 5    | 1348   |
| Highest vs lowest                | TCL     | MA   | Kim 2021        | 4    | 413    |
| Highest vs lowest                | NHL     | MA   | Kim 2021        | 7    | 196272 |
| Highest vs lowest                | CLL/SLL | MA   | Kim 2021        | 4    | NA     |
| Highest vs lowest                | DLBCL   | MA   | Kim 2021        | 4    | NA     |
| Highest vs lowest                | FL      | MA   | Kim 2021        | 4    | NA     |
| Occupation vs general population | NHL     | MA   | Lu 2017         | 11   | 8829   |
| Occupation vs general population | TCL     | MA   | Lu 2017         | 4    | NA     |
| Patients vs general population   | NHL     | SRMA | Lahner 2018     | 3    | 70     |
| Patients vs general population   | NHL     | SRMA | Vaengebjerg 202 | 8    | 7626   |
| Patients vs general population   | NHL     | MA   | Wang 2020       | 3    | 1155   |
| Patients vs general population   | DLBCL   | MA   | Tio 2012        | 3    | 13990  |
| Patients vs general population   | CLL     | MA   | Tio 2012        | 3    | 51984  |
| Patients vs general population   | NHL     | MA   | Kane 2011       | 6    | <1000  |
| Patients vs general population   | NHL     | SRMA | Zhang 2013      | 4    | 23     |
| Patients vs general population   | NHL     | SRMA | Lo 2021         | 6    | 30     |
| Patients vs general population   | NHL     | SRMA | Lo 2021         | 8    | 79     |
| Patients vs general population   | NHL     | SRMA | Bonifazi 2015   | 8    | 150    |
| Patients vs general population   | NHL     | SRMA | Wang 2019       | 3    | 4      |
| Patients vs general population   | NHL     | SRMA | Deng 2016       | 5    | >1000  |
| Patients vs general population   | NHL     | SRMA | Liang 2012      | 3    | 2860   |
| Patients vs general population   | NHL     | SRMA | Yang 2017       | 15   | NA     |
| Patients vs general population   | NHL     | SRMA | Yang 2017       | 15   | 36903  |
| Patients vs general population   | NHL     | SRMA | Yang 2017       | 8    | 4528   |
| Patients vs general population   | NHL     | SRMA | Yang 2017       | 6    | 6191   |
| Patients vs general population   | NHL     | SRMA | Castillo 2012   | 21   | 17282  |
| Patients vs general population   | NHL     | SRMA | Zhang 2019      | 5    | 620    |
| Overweight vs normal             | NHL     | SRMA | Larsson 2007    | 16   | 21720  |
| Overweight vs normal             | DLBCL   | MA   | Castillo 2014   | 16   | 7349   |
| Overweight vs normal             | CLL     | MA   | Castillo 2012   | 9    | 2142   |
| Overweight vs normal             | FL      | SRMA | Odutola 2020    | 14   | 1798   |
| Obesity vs normal weight         | NHL     | SRMA | Larsson 2007    | 16   | 21720  |
| Obesity vs normal weight         | DLBCL   | MA   | Castillo 2014   | 16   | 7349   |
| Obesity vs normal weight         | CLL     | MA   | Castillo 2012   | 10   | 912    |
| Obesity vs normal weight         | FL      | SRMA | Odutola 2020    | 13   | 903    |
| Yes vs no                        | NHL     | SRMA | Schmidt 2017    | 7    | 52134  |

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| Test            | Group 1  | Group 2 | Year       | N  | P-value |
|-----------------|----------|---------|------------|----|---------|
| Yes vs no       | CLL      | SRMA    | Schmidt 2017 | 4  | >10000  |
| Yes vs no       | DLBCL    | SRMA    | Fama 2019   | 3  | 54      |
| Yes vs no       | FL       | SRMA    | Fama 2019   | 3  | 75      |
| High (75th percentile) | NHL   | MA      | Teras 2015  | 8  | 1421    |
| High (75th percentile) | NHL   | MA      | Teras 2015  | 9  | 1764    |
| Yes vs no       | PCL      | SRMA    | Travaglino 2020 | 10 | 410     |
| Yes vs no       | DLBCL    | SRMA    | Travaglino 2020 | 3  | 53      |
| Yes vs no       | TCL      | SRMA    | Li 2018     | 12 | NA      |
| Yes vs no       | DLBCL    | SRMA    | Li 2018     | 10 | 11943   |
| Yes vs no       | FL       | SRMA    | Li 2018     | 9  | 5124    |
| Yes vs no       | CLL/SLL  | SRMA    | Li 2018     | 8  | 10738   |
| Yes vs no       | BL       | SRMA    | Li 2018     | 3  | 264     |
| Patients vs general population | FL    | MA      | DalMaso 2006 | 7  | 193     |
| Patients vs general population | MZL   | MA      | DalMaso 2006 | 5  | 134     |
| Patients vs general population | TCL   | MA      | DalMaso 2006 | 4  | 122     |
| Patients vs general population | CLL/SLL | MA    | DalMaso 2006 | 5  | 88      |
| Yes vs no       | eBL      | SRMA    | Kotepeui 2021 | 5  | 6055    |
| Ever vs never   | FL       | SRMA    | Odutola 2021 | 3  | 292     |
| Ever vs never   | FL       | SRMA    | Odutola 2021 | 3  | 143     |
| Ever vs never   | FL       | SRMA    | Odutola 2021 | 3  | 669     |
| Highest vs lowest | NHL  | SRMA    | Collins 2018 | 16 | 553     |
| Ever vs never   | NHL      | SRMA    | Kane 2010   | 24 | 1420    |
| Ever vs never   | FL       | SRMA    | Odutola 2021 | 3  | 333     |
| Ever vs never   | FL       | SRMA    | Odutola 2021 | 3  | 7262    |
| Highest vs lowest | NHL  | SRMA    | Catalani 2019 | 30 | 1439    |
| Highest vs lowest | DLBCL | SRMA    | Catalani 2019 | 6  | NA      |
| Highest vs lowest | FL     | SRMA    | Catalani 2019 | 5  | NA      |
| Highest vs lowest | CLL    | SRMA    | Catalani 2019 | 4  | 573     |
| Highest vs lowest | NHL    | SRMA    | Xu 2016     | 4  | 4263    |
| Highest vs lowest | NHL    | SRMA    | Scott 2011  | 17 | >1000   |
| Highest vs lowest | NHL    | MA      | Liu 2013    | 6  | 3001    |
| Highest vs lowest | NHL    | MA      | Kane 2010   | 35 | 1042    |
| Highest vs lowest | NHL    | SRMA    | Schinasi 2014 | 3  | 1621    |
| Highest vs lowest | NHL    | SRMA    | Schinasi 2014 | 3  | 1621    |
| Highest vs lowest | NHL    | SRMA    | Boffetta 2021 | 6  | 1297    |
| Highest vs lowest | DLBCL  | SRMA    | Boffetta 2021 | 4  | 1285    |
| Ever vs never   | FL       | SRMA    | Odutola 2021 | 4  | 897     |
| Yes vs no       | NHL      | MA      | Hu 2017     | 7  | NA      |
| Yes vs no       | NHL      | MA      | Hu 2017     | 7  | NA      |
| Yes vs no       | NHL      | MA      | Hu 2017     | 5  | NA      |
| Yes vs no       | NHL      | MA      | Hu 2017     | 10 | NA      |
| Ever vs never   | FL       | SRMA    | Odutola 2021 | 3  | 545     |
| Study                      | Disease  | Group 1 | Group 2 | Year | p-value |
|---------------------------|----------|---------|---------|------|---------|
| Highest vs lowest         | NHL MA   | Luo 2016| 5 1010  |      |         |
| Highest vs lowest         | FL SRMA  | Odutola21| 3 741   |      |         |
| Highest vs lowest         | NHL MA   | Luo 2016| 6 1184  |      |         |
| Highest vs lowest         | FL SRMA  | Odutola21| 4 255   |      |         |
| Highest vs lowest         | NHL MA   | Luo 2016| 7 1265  |      |         |
| Highest vs lowest         | NHL MA   | Luo 2016| 8 1218  |      |         |
| Highest vs lowest         | NHL MA   | Luo 2016| 13 6582 |      |         |
| Highest vs lowest         | NHL SRMA | Zheng 2015| 5 419   |      |         |
| Highest vs lowest         | NHL SRMA | Smith 2017| 11 <1000|      |         |
| Highest vs lowest         | NHL SRMA | Schinasi 2014| 5 3986  |      |         |
| Highest vs lowest         | NHL SRMA | Schinasi 2014| 12 6493 |      |         |
| Highest vs lowest         | NHL SRMA | Schinasi 2014| 4 1155  |      |         |
| Highest vs lowest         | NHL SRMA | Schinasi 2014| 4 1155  |      |         |
| Highest vs lowest         | NHL SRMA | Schinasi 2014| 4 1346  |      |         |
| Ever vs never             | FL SRMA  | Odutola21| 4 697   |      |         |

| Study                      | Disease  | Group 1 | Group 2 | Year | p-value |
|---------------------------|----------|---------|---------|------|---------|
| Attendants vs general     | NHL MA   | Buja 2006| 3 NA    |      |         |
| NA                        | NHL MA   | Boffetta 2007| 50 >1000|      |         |
| Firefighter vs general    | NHL SRMA | Jalilian 2019| 14 NA   |      |         |
| Ever vs never             | FL SRMA  | Odutola21| 3 5     |      |         |
| NA                        | NHL MA   | Takkouche 2009| 13 22425|      |         |
| Worker vs general population | NHL SRMA | Schnatter 2018| 16 NA   |      |         |
| Worker vs general population | NHL MA | Boffetta 2007| 9 NA    |      |         |
| Worker vs general population | NHL MA | Boffetta 2007| 6 >1000 |      |         |
| Worker vs general population | NHL MA | Boffetta 2007| 11 NA   |      |         |
| Worker vs general population | NHL SRMA | Alicandro 2016| 8 167   |      |         |
| Worker vs general population | NHL SRMA | Alicandro 2016| 8 57   |      |         |

ir kitt Lymphoma; CI=confidence interval; CLL/SLL=chronic lymphocytic leukemia/small lymphocytic rd estimator.
| Effect measure | Random effects summary | P random | Strength of reported association |
|---------------|------------------------|----------|---------------------------------|
| RR 1.32 (1.12, 1.55) | 8.52E-04 | III |  |
| RR 1.17 (1.07, 1.29) | 1.04E-03 | IV |  |
| RR 1.34 (0.97, 1.86) | 7.80E-02 | NS |  |
| RR 1.23 (1.03, 1.48) | 2.50E-02 | IV |  |
| RR 1.21 (0.98, 1.48) | 7.00E-02 | NS |  |
| RR 1.01 (0.84, 1.21) | 9.22E-01 | NS |  |
| RR 1.06 (0.85, 1.33) | 6.22E-01 | NS |  |
| RR 1.04 (0.86, 1.27) | 7.06E-01 | NS |  |
| RR 0.96 (0.63, 1.48) | 8.62E-01 | NS |  |
| RR 1.09 (0.51, 2.31) | 8.34E-01 | NS |  |
| RR 1.05 (0.71, 1.54) | 8.17E-01 | NS |  |
| RR 0.93 (0.72, 1.19) | 5.83E-01 | NS |  |
| RR 0.86 (0.48, 1.56) | 6.29E-01 | NS |  |
| RR 0.86 (0.48, 1.56) | 6.29E-01 | NS |  |
| RR 0.90 (0.72, 1.14) | 3.75E-01 | NS |  |
| RR 0.78 (0.66, 0.92) | 3.00E-03 | IV |  |
| RR 0.97 (0.87, 1.08) | 5.93E-01 | NS |  |
| RR 0.81 (0.71, 0.92) | 1.00E-03 | IV |  |
| RR 0.94 (0.79, 1.13) | 5.08E-01 | NS |  |
| RR 0.70 (0.54, 0.91) | 7.00E-03 | IV |  |
| RR 0.96 (0.72, 1.28) | 7.93E-01 | NS |  |
| RR 0.70 (0.53, 0.92) | 1.10E-02 | IV |  |
| RR 1.17 (0.86, 1.60) | 3.26E-01 | NS |  |
| RR 1.20 (1.02, 1.42) | 3.00E-02 | IV |  |
| RR 1.73 (1.22, 2.45) | 2.00E-03 | IV |  |
| RR 1.23 (0.88, 1.72) | 2.28E-01 | NS |  |
| RR 1.35 (0.77, 2.39) | 3.03E-01 | NS |  |
| RR 1.41 (1.08, 1.84) | 1.10E-02 | IV |  |
| RR 1.49 (1.08, 2.06) | 1.50E-02 | IV |  |
| RR 0.99 (0.47, 2.07) | 9.81E-01 | NS |  |
| RR 1.04 (0.69, 1.55) | 8.60E-01 | NS |  |
| RR 1.14 (0.96, 1.34) | 1.24E-01 | NS |  |
| RR 0.93 (0.63, 1.37) | 7.27E-01 | NS |  |
| RR 1.04 (0.74, 1.46) | 8.32E-01 | NS |  |
| RR 1.28 (0.91, 1.81) | 1.60E-01 | NS |  |
| RR 0.78 (0.54, 1.12) | 1.83E-01 | NS |  |
| RR 0.90 (0.67, 1.21) | 4.95E-01 | NS |  |
| RR 0.89 (0.63, 1.25) | 5.15E-01 | NS |  |
| RR 0.97 (0.76, 1.23) | 8.16E-01 | NS |  |
| RR 1.31 (1.04, 1.65) | 2.20E-02 | IV |  |
| RR 1.57 (1.11, 2.20) | 1.00E-02 | IV |  |
| RR 1.21 (0.97, 1.50) | 8.60E-02 | NS |  |
| RR 1.01 (0.82, 1.24) | 9.40E-01 | NS |  |
|   | RR     | CI             | P-value | Category |
|---|--------|----------------|---------|----------|
| 1 | 0.61   | (0.38, 0.99)   | 4.30E-02| IV       |
| 2 | 0.87   | (0.78, 0.97)   | 1.20E-02| IV       |
| 3 | 0.75   | (0.59, 0.97)   | 2.30E-02| IV       |
| 4 | 0.84   | (0.60, 1.16)   | 3.04E-01| NS       |
| 5 | 1.41   | (0.80, 2.50)   | 2.40E-01| NS       |
| 6 | 0.80   | (0.68, 0.94)   | 7.00E-03| IV       |
| 7 | 0.65   | (0.46, 0.91)   | 1.30E-02| IV       |
| 8 | 0.80   | (0.55, 1.16)   | 2.30E-02| NS       |
| 9 | 0.84   | (0.67, 1.05)   | 1.28E-01| NS       |
| 10| 0.75   | (0.50, 1.13)   | 1.67E-01| NS       |
| 11| 0.51   | (0.15, 1.72)   | 2.83E-01| NS       |
| 12| 0.99   | (0.88, 1.12)   | 8.80E-01| NS       |
| 13| 1.04   | (0.69, 1.57)   | 8.62E-01| NS       |
| 14| 0.90   | (0.54, 1.49)   | 6.97E-01| NS       |
| 15| 0.80   | (0.60, 1.07)   | 1.31E-01| NS       |
| 16| 0.82   | (0.69, 0.97)   | 2.20E-02| IV       |
| 17| 0.87   | (0.54, 1.40)   | 5.78E-01| NS       |
| 18| 0.70   | (0.48, 1.02)   | 6.30E-02| NS       |
| 19| 0.93   | (0.70, 1.23)   | 6.26E-01| NS       |
| 20| 0.92   | (0.80, 1.07)   | 2.64E-01| NS       |
| 21| 1.00   | (0.90, 1.12)   | 1.00E+00| NS       |
| 22| 1.07   | (0.82, 1.40)   | 6.33E-01| NS       |
| 23| 1.05   | (0.73, 1.52)   | 8.06E-01| NS       |
| 24| 1.00   | (0.63, 1.58)   | 1.00E+00| NS       |
| 25| 1.10   | (0.56, 2.14)   | 7.93E-01| NS       |
| 26| 1.69   | (0.68, 4.20)   | 2.62E-01| NS       |
| 27| 0.98   | (0.88, 1.10)   | 7.36E-01| NS       |
| 28| 1.26   | (1.12, 1.42)   | 1.51E-04| III      |
| 29| 1.41   | (1.08, 1.84)   | 1.10E-02| IV       |
| 30| 1.21   | (0.97, 1.52)   | 9.60E-02| NS       |
| 31| 0.91   | (0.68, 1.23)   | 5.44E-01| NS       |
| 32| 1.12   | (0.60, 2.09)   | 7.35E-01| NS       |
| 33| 1.31   | (1.08, 1.58)   | 5.00E-03| IV       |
| 34| 1.00   | (0.84, 1.20)   | 1.00E+00| NS       |
| 35| 1.32   | (0.99, 1.76)   | 5.80E-02| NS       |
| 36| 0.85   | (0.68, 1.06)   | 1.57E-01| NS       |
| 37| 1.54   | (0.98, 2.41)   | 6.00E-02| NS       |
| 38| 0.85   | (0.79, 0.91)   | 8.50E-06| III      |
| 39| 0.78   | (0.58, 1.05)   | 1.00E-01| NS       |
| 40| 0.86   | (0.76, 0.97)   | 1.50E-02| IV       |
| 41| 0.79   | (0.68, 0.91)   | 1.60E-03| IV       |
| 42| 0.80   | (0.69, 0.92)   | 2.40E-03| IV       |
| 43| 1.00   | (0.80, 1.26)   | 1.00E+00| NS       |
| 44| 0.84   | (0.70, 1.00)   | 5.50E-02| NS       |
| OR  | 1.00 (0.58, 1.73) | 1.00E+00 | NS |
|-----|------------------|----------|----|
| OR  | 1.02 (0.89, 1.17) | 7.89E-01 | NS |
| OR  | 1.06 (0.85, 1.33) | 6.22E-01 | NS |
| OR  | 1.15 (0.83, 1.59) | 4.07E-01 | NS |
| OR  | 0.70 (0.54, 0.91) | 7.00E-03 | IV |
| OR  | 1.33 (1.11, 1.60) | 2.00E-03 | IV |
| OR  | 1.26 (0.86, 1.85) | 2.39E-01 | NS |
| OR  | 0.95 (0.90, 1.22) | 5.41E-01 | NS |
| OR  | 0.99 (0.81, 1.21) | 9.28E-01 | NS |
| OR  | 1.07 (0.69, 1.68) | 7.78E-01 | NS |
| OR  | 0.77 (0.51, 1.15) | 2.09E-01 | NS |
| OR  | 1.04 (0.52, 2.07) | 9.19E-01 | NS |
| OR  | 1.01 (0.75, 1.36) | 9.52E-01 | NS |
| OR  | 1.13 (0.99, 1.29) | 7.00E-02 | NS |
| OR  | 0.82 (0.69, 0.99) | 3.10E-02 | IV |
| OR  | 0.78 (0.55, 1.11) | 1.66E-01 | NS |
| OR  | 0.89 (0.62, 1.27) | 5.35E-01 | NS |
| OR  | 0.54 (0.31, 0.94) | 2.90E-02 | IV |
| OR  | 0.70 (0.41, 1.19) | 1.91E-01 | NS |
| RR  | 1.20 (0.96, 1.51) | 1.10E-01 | NS |
| RR  | 1.20 (1.01, 1.43) | 4.00E-02 | IV |
| RR  | 1.16 (0.83, 1.62) | 3.91E-01 | NS |
| RR  | 1.34 (0.62, 2.89) | 4.70E-01 | NS |
| SIR | 3.92 (1.78, 7.47) | 2.10E-04 | IV |
| SIR | 0.42 (0.26, 0.67) | 3.00E-04 | III |
| RR  | 1.2 (1.07, 1.35)  | 2.00E-03 | IV |
| RR  | 1.66 (1.08, 2.56) | 2.10E-02 | IV |
| RR  | 1.02 (0.67, 1.55) | 9.32E-01 | NS |
| RR  | 1.06 (0.86, 1.3)  | 5.92E-01 | NS |
| RR  | 0.92 (0.84, 1.00) | 6.00E-02 | NS |
| RR  | 0.95 (0.83, 1.09) | 4.70E-01 | NS |
| RR  | 0.95 (0.80, 1.12) | 5.60E-01 | NS |
| RR  | 0.95 (0.76, 1.20) | 6.70E-01 | NS |
| OR  | 1.14 (1.01, 1.29) | 3.60E-02 | IV |
| OR  | 1.66 (1.22, 2.25) | 1.20E-03 | IV |
| OR  | 1.05 (0.99, 1.10) | 6.91E-02 | NS |
| RR  | 0.95 (0.83, 1.08) | 4.54E-01 | NS |
| RR  | 0.82 (0.70, 0.95) | 1.10E-02 | IV |
| RR  | 1.23 (0.95, 1.59) | 1.15E-01 | NS |
| RR  | 1.06 (0.97, 1.17) | 2.25E-01 | NS |
| RR  | 2.08 (1.08, 3.98) | 2.80E-02 | IV |
| OR  | 1.22 (1.02, 1.46) | 2.57E-02 | IV |
| RR  | 1.05 (1.00, 1.09) | 2.60E-02 | IV |
| RR  | 1.01 (0.95, 1.07) | 7.60E-01 | NS |
|   | RR     | CI            | p-value | Category |
|---|--------|---------------|---------|----------|
| 1 | 1.05   | (0.88, 1.25)  | 6.00E-01 | NS       |
| 2 | 0.96   | (0.89, 1.04)  | 3.10E-01 | NS       |
| 3 | 1.23   | (1.06, 1.43)  | 6.70E-03 | IV       |
| 4 | 0.81   | (0.71, 0.92)  | 1.50E-03 | IV       |
| 5 | 0.80   | (0.63, 1.00)  | 5.80E-02 | NS       |
| 6 | 0.76   | (0.66, 0.87)  | 1.10E-04 | III      |
| 7 | 0.81   | (0.67, 0.99)  | 3.40E-02 | IV       |
| 8 | 1.00   | (0.68, 1.46)  | 1.00E+00 | NS       |
| 9 | 0.84   | (0.73, 0.96)  | 1.30E-02 | IV       |
|10 | 0.93   | (0.73, 1.19)  | 5.70E-01 | NS       |
|11 | 0.80   | (0.69, 0.92)  | 2.40E-03 | IV       |
|12 | 0.82   | (0.72, 0.93)  | 2.40E-03 | IV       |
|13 | 1.15   | (0.99, 1.32)  | 5.60E-02 | NS       |
|14 | 1.16   | (0.90, 1.50)  | 2.60E-01 | NS       |
|---|--------|---------------|---------|----------|
| 15| 1.16   | (0.79, 1.71)  | 4.60E-01 | NS       |
|16 | 1.48   | (1.30, 1.69)  | 9.49E-09 | III      |
|17 | 1.55   | (1.15, 2.08)  | 4.00E-03 | IV       |
|18 | 2.25   | (1.32, 3.85)  | 3.03E-03 | IV       |
|19 | 0.80   | (0.46, 1.38)  | 4.34E-01 | NS       |
|20 | 6.48   | (2.32, 18.1)  | 3.91E-04 | IV       |
|21 | 2.75   | (1.42, 5.33)  | 2.60E-03 | IV       |
|22 | 1.81   | (0.94, 3.49)  | 7.60E-02 | NS       |
|23 | 1.34   | (0.95, 1.88)  | 9.30E-02 | NS       |
|24 | 1.43   | (1.03, 1.99)  | 3.30E-02 | IV       |
|25 | 7.79   | (3.76, 16.11)| 3.16E-08 | IV       |
|26 | 1.03   | (0.83, 1.28)  | 8.00E-01 | NS       |
|27 | 1.15   | (0.36, 1.94)  | 7.58E-01 | NS       |
|28 | 0.99   | (0.81, 1.21)  | 9.28E-01 | NS       |
|29 | 0.92   | (0.86, 0.99)  | 3.00E-02 | IV       |
|30 | 0.73   | (0.62, 0.84)  | 5.67E-05 | III      |
|31 | 0.71   | (0.51, 0.98)  | 3.90E-02 | IV       |
|32 | 1.22   | (1.07, 1.39)  | 2.94E-03 | IV       |
|33 | 0.80   | (0.74, 0.87)  | 1.10E-07 | IV       |
|34 | 1.07   | (1.01, 1.14)  | 2.80E-02 | IV       |
|35 | 1.14   | (1.04, 1.24)  | 3.50E-03 | IV       |
|36 | 1.10   | (1.03, 1.17)  | 3.40E-03 | IV       |
|37 | 0.99   | (0.92, 1.07)  | 8.10E-01 | NS       |
|38 | 1.20   | (1.07, 1.34)  | 1.50E-03 | IV       |
|39 | 1.29   | (1.16, 1.43)  | 2.50E-06 | III      |
|40 | 1.17   | (1.08, 1.27)  | 1.60E-04 | IV       |
|41 | 1.08   | (0.99, 1.17)  | 7.10E-02 | NS       |
|42 | 1.72   | (1.27, 2.32)  | 4.49E-04 | III      |
|    | RR       | 95% CI       | P Value | Stage |
|----|----------|--------------|---------|-------|
| 1  | 1.65     | (1.20, 2.25) | 2.00E-03 | IV    |
| 2  | 3.29     | (1.63, 6.62) | 1.00E-03 | IV    |
| 3  | 3.01     | (1.95, 4.63) | 8.64E-07 | IV    |
| 4  | 1.52     | (1.16, 1.99) | 2.40E-03 | IV    |
| 5  | 1.20     | (1.00, 1.44) | 5.00E-02 | NS    |
| 6  | 10.88    | (3.84, 30.81)| 8.98E-06 | IV    |
| 7  | 8.15     | (1.25, 53.06)| 2.80E-02 | IV    |
| 8  | 1.59     | (1.11, 2.26) | 1.07E-02 | IV    |
| 9  | 2.06     | (1.48, 2.88) | 2.53E-05 | III   |
| 10 | 1.60     | (1.24, 2.07) | 3.50E-04 | III   |
| 11 | 1.87     | (1.34, 2.61) | 2.60E-04 | III   |
| 12 | 2.12     | (0.97, 4.65) | 6.00E-02 | NS    |
| 13 | 2.73     | (2.20, 3.38) | 9.12E-19 | IV    |
| 14 | 3.41     | (2.39, 4.87) | 4.48E-11 | IV    |
| 15 | 1.52     | (1.13, 2.05) | 5.90E-03 | IV    |
| 16 | 1.65     | (1.35, 2.02) | 1.57E-06 | IV    |
| 17 | 0.87     | (0.54, 1.39) | 5.80E-01 | NS    |
|    | RR       | 1.03 (0.83, 1.28)| 8.00E-01 | NS    |
| 18 | 1.35     | (1.09, 1.68) | 6.60E-03 | IV    |
| 19 | IRR      | 1.16 (1.00, 1.34)| 4.60E-02 | IV    |
| 20 | RR, Not specified | 1.14 (0.91, 1.43) | 2.59E-01 | NS    |
| 21 | OR       | 1.11 (0.94, 1.30)| 2.10E-01 | NS    |
| 22 | OR       | 1.30 (0.86, 1.97)| 2.20E-01 | NS    |
| 23 | OR       | 1.24 (0.88, 1.75)| 2.20E-01 | NS    |
| 24 | RR       | 0.96 (0.85, 1.07)| 4.97E-01 | NS    |
| 25 | RR       | 0.68 (0.24, 1.12)| 3.31E-01 | NS    |
| 26 | RR       | 1.21 (0.79, 1.64)| 3.11E-01 | NS    |
| 27 | RR       | 0.63 (0.39, 0.87)| 2.40E-02 | IV    |
| 28 | RR       | 1.09 (0.92, 1.30)| 3.34E-01 | NS    |
| 29 | RR       | 1.23 (1.07, 1.42)| 7.70E-03 | IV    |
| 30 | OR       | 1.28 (0.96, 1.70)| 9.00E-02 | NS    |
| 31 | RR       | 1.02 (0.94, 1.12)| 6.71E-01 | NS    |
| 32 | RR       | 1.40 (1.10, 2.00)| 2.70E-02 | IV    |
| 33 | RR       | 1.70 (1.30, 2.30)| 2.90E-04 | III   |
| 34 | RR       | 1.05 (0.90, 1.24)| 5.60E-01 | NS    |
| 35 | RR       | 1.29 (1.02, 1.63)| 3.30E-02 | IV    |
| 36 | RR       | 0.90 (0.60, 1.34)| 6.20E-01 | NS    |
| 37 | OR       | 1.17 (0.82, 1.67)| 3.94E-01 | NS    |
| 38 | OR       | 1.39 (1.11, 1.73)| 4.00E-03 | IV    |
| 39 | OR       | 1.07 (0.85, 1.36)| 5.84E-01 | NS    |
| 40 | OR       | 1.22 (1.04, 1.43)| 1.40E-02 | IV    |
| 41 | OR       | 1.75 (0.46, 6.72)| 4.20E-01 | NS    |
|   | OR     | CI      |   |
|---|--------|---------|---|
|   | 1.02 (0.81, 1.28) | 8.73E-01 | NS |
| RR| 1.25 (0.75, 2.07)  | 4.00E-01 | NS |
| OR| 1.38 (1.14, 1.66)  | 8.00E-04 | III |
| RR| 1.51 (0.99, 2.31)  | 5.60E-02 | NS |
| OR| 1.36 (0.95, 1.95)  | 9.18E-02 | NS |
| RR| 1.54 (1.20, 1.99)  | 8.00E-04 | III |
| OR| 1.89 (1.42, 2.50)  | 1.29E-05 | III |
| RR| 1.42 (1.27, 1.59)  | 2.16E-09 | III |
| OR| 2.65 (1.33, 5.27)  | 6.00E-03 | IV |
| OR| 1.82 (1.14, 2.92)  | 1.30E-02 | IV |
| RR| 1.50 (0.90, 2.50)  | 1.20E-01 | NS |
| RR| 1.40 (1.20, 1.60)  | 6.00E-06 | III |
| RR| 1.30 (0.80, 1.90)  | 2.40E-01 | NS |
| RR| 1.30 (0.90, 1.90)  | 1.70E-01 | NS |
| RR| 1.50 (1.00, 2.10)  | 3.20E-02 | IV |
| RR| 0.90 (0.60, 1.30)  | 6.10E-01 | NS |
| RR| 1.45 (0.91, 2.32)  | 1.20E-01 | NS |
| SIR| 1.19 (0.52, 2.15)  | 6.44E-01 | NS |
| RR| 1.11 (1.05, 1.17)  | 1.74E-04 | III |
| SIR| 1.07 (0.96, 1.20)  | 2.37E-01 | NS |
| RR| 1.16 (0.38, 3.52)  | 8.10E-01 | NS |
| RR| 1.11 (0.94, 1.32)  | 2.30E-01 | NS |
| RR| 0.98 (0.89, 1.09)  | 7.09E-01 | NS |
| RR| 0.99 (0.77, 1.29)  | 9.40E-01 | NS |
| RR| 1.86 (1.38, 2.50)  | 5.00E-05 | III |
| RR| 1.04 (0.79, 1.37)  | 7.90E-01 | NS |
| RR| 1.19 (0.98, 1.44)  | 7.60E-02 | NS |
| RR| 0.94 (0.73, 1.22)  | 6.50E-01 | NS |

lymphoma; DDE=dichlorodiphenyldichloroethylene; DDT=dichlorodiphenyltrichloroethane; DLB
CL=diffuse large B-cell lymphoma; eBL=endemic Burkitt Lymphoma; FL=follicular lymphoma; HAART=
=Highly Active Antiretroviral Therapy; HBV=hepatitis B virus; HCB=hexachlorobenzene; HCH=hexachlorobenzene
orocyclohexane; HCV=hepatitis C virus; HIV/AIDS=human immunodeficiency virus, acquired immunodeficiency syndrome.
deficiency syndrome; HPgV=Human Pegivirus; IRR= incidence rate ratio; MA= meta-analysis; MZL=mili
arginal zone lymphoma; MCPA=2-methyl-4-chlorophenoxyacetic acid; NA-NSAIDS=non-aspirin non-st
teroidal anti-inflammatory drugs; NSAIDS=non-steroidal anti-inflammatory drugs; NA=not available;
NHL= non-Hodgkin lymphoma; OR=odds ratio; PCBs=Polychlorinated biphenyls; PI=prediction interval.
T-cell lymphoma.
| Study      | Outcome |
|-----------|---------|
| Kane 2013 | NHL     |
| Kane 2013 | NHL     |
| Kane 2013 | NHL     |
| Kane 2013 | NHL     |
| Kane 2013 | NHL     |
| Kane 2013 | NHL     |
| Kane 2013 | NHL     |
| Kane 2013 | NHL     |
| Kane 2013 | DLBCL   |
| Kane 2013 | DLBCL   |
| Kane 2013 | DLBCL   |
| Kane 2013 | DLBCL   |
| Kane 2013 | FL      |
| Cocco 2013| DLBCL   |
| Cocco 2013| DLBCL   |
| Cocco 2013| FL      |
| Cocco 2013| FL      |
| Willet 2008| NHL    |
| Willet 2008| FL     |
| Willet 2008| CLL/SLL|
| Willet 2008| Other BCL|
| Willet 2008| Other BCL|
| Willet 2008| DLBCL   |
| Willet 2008| BL      |
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Slager 2014| CLL/SLL|
| Reference | Diagnosis  |
|-----------|------------|
| Slager 2014 | CLL/SLL    |
| Slager 2014 | CLL/SLL    |
| Slager 2014 | CLL/SLL    |
| Slager 2014 | CLL/SLL    |
| Slager 2014 | CLL/SLL    |
| Slager 2014 | CLL/SLL    |
| Slager 2014 | CLL/SLL    |
| Slager 2014 | CLL/SLL    |
| Morton 2014 | NHL        |
| Morton 2014 | MZL        |
| Morton 2014 | LPL/WM     |
| Morton 2014 | DLBCL      |
| Morton 2014 | NHL        |
| Morton 2014 | DLBCL      |
| Morton 2014 | MZL        |
| Morton 2014 | DLBCL      |
| Morton 2014 | NHL        |
| Morton 2014 | MZL        |
| Morton 2014 | LPL/WM     |
| Morton 2014 | DLBCL      |
| Morton 2014 | FL         |
| Morton 2014 | NHL        |
| Morton 2014 | MF/SS      |
| Morton 2014 | PTCL       |
| Morton 2014 | MZL        |
| Morton 2014 | LPL/WM     |
| Morton 2014 | DLBCL      |
| Morton 2014 | MF/SS      |
| Morton 2014 | PTCL       |
| Morton 2014 | NHL        |
| Morton 2014 | PTCL       |
| Morton 2014 | DLBCL      |
| Morton 2014 | PTCL       |
| Morton 2014 | MF/SS      |
| Morton 2014 | HCL        |
| Morton 2014 | NHL        |
| Morton 2014 | MZL        |
| Morton 2014 | LPL/WM     |
| Morton 2014 | DLBCL      |
| Morton 2014 | CLL/SLL    |
| Morton 2014 | MZL        |
| Morton 2014 | NHL        |
| Morton 2014 | DLBCL      |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL |
| Morton 2014 | MCL |
| Morton 2014 | MCL |
| Morton 2014 | NHL |
| Morton 2014 | DLBCL |
| Morton 2014 | DlBCL |
| Morton 2014 | FL |
| Morton 2014 | NHL |
| Morton 2014 | BL |
| Morton 2014 | BL |
| Morton 2014 | LPL/WM |
| Morton 2014 | DLBCL |
| Morton 2014 | FL |
| Morton 2014 | FL |
| Morton 2014 | NHL |
| Morton 2014 | DLBCL |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL |
| Morton 2014 | HCL |
| Morton 2014 | NHL |
| Morton 2014 | DLBCL |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL |
| Morton 2014 | HCL |
| Morton 2014 | NHL |
| Morton 2014 | DLBCL |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL |
| Morton 2014 | NHL |
| Morton 2014 | DLBCL |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL |
| Morton 2014 | HCL |
| Morton 2014 | DLBCL |
| Morton 2014 | MF/SS |
| Morton 2014 | LPL/WM |
| Morton 2014 | DLBCL |
| Morton 2014 | DLBCL |
| Morton 2014 | FL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | CLL/SLL |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL |
| Morton 2014 | HCL |
| Morton 2014 | MF/SS |
| Morton 2014 | MF/SS |
| Morton 2014 | MZL |
| Morton 2014 | LPL/WM |
| Morton 2014 | DLBCL |
| Morton 2014 | MCL |
| Morton 2014 | NHL |
| Morton 2014 | NHL |
| Morton 2014 | NHL |
| Morton 2014 | NHL |
| Morton 2014 | PTCL |
| Morton 2014 | MZL |
| Morton 2014 | DLBCL |
| Morton 2014 | FL |
| Morton 2014 | NHL |
| Morton 2014 | MZL |
| Morton 2014 | BL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | NHL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | FL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | NHL |
| Morton 2014 | MZL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | FL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | NHL |
| Morton 2014 | PTCL |
| Morton 2014 | DLBCL |
| Morton 2014 | NHL |
| Morton 2014 | PTCL |
| Morton 2014 | DLBCL |
| Morton 2014 | DLBCL |
| Morton 2014 | FL |
| Morton 2014 | NHL |
|------------|-----|
| Morton 2014 | NHL |
| Morton 2014 | MF/SS |
| Morton 2014 | MF/SS |
| Morton 2014 | MZL |
| Morton 2014 | DLBCL |
| Morton 2014 | FL |
| Morton 2014 | NHL |
| Morton 2014 | MZL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | FL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | FL |
| Morton 2014 | NHL |
| Morton 2014 | PTCL |
| Morton 2014 | MZL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | BL |
| Morton 2014 | DLBCL |
| Morton 2014 | PTCL |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL |
| Morton 2014 | HCL |
| Morton 2014 | PTCL |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL |
| Morton 2014 | HCL |
| Morton 2014 | HCL |
| Morton 2014 | HCL |
| Morton 2014 | HCL |
| Morton 2014 | PTCL |
| Morton 2014 | LPL/WM |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL       |
| Morton 2014 | PTCL    |
| Morton 2014 | LPL/WM   |
| Morton 2014 | FL       |
| Morton 2014 | PTCL    |
| Morton 2014 | CLL/SLL |
| Morton 2014 | PTCL    |
| Morton 2014 | MZL     |
| Morton 2014 | LPL/WM   |
| Morton 2014 | LPL/WM   |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL       |
| Morton 2014 | PTCL    |
| Morton 2014 | CLL/SLL |
| Morton 2014 | FL       |
| Morton 2014 | NHL     |
| Morton 2014 | MZL     |
| Morton 2014 | NHL     |
| Morton 2014 | NHL     |
| Morton 2014 | NHL     |
| Morton 2014 | FL       |
| Morton 2014 | NHL     |
| Morton 2014 | NHL     |
| Morton 2014 | FL       |
| Morton 2014 | NHL     |
| Morton 2014 | DLBCL   |
| Morton 2014 | NHL     |
| Morton 2014 | DLBCL   |
| Morton 2014 | FL       |
| Morton 2014 | FH       |
| Morton 2014 | FL       |
| Morton 2014 | FL       |
| Morton 2014 | NHL     |
| Morton 2014 | DLBCL   |
| Morton 2014 | HCL     |
| Morton 2014 | PTCL    |
| Morton 2014 | CLL/SLL |
| Morton 2014 | HCL     |
| Morton 2014 | MCL     |
| Morton 2014 | PTCL    |
| Morton 2014 | PTCL    |
| Morton 2014 | MCL     |
| Morton 2014 | CLL/SLL |
| Morton 2014 | NHL     |
| Morton 2014 | NHL     |
| Morton 2014 | MF/SS   |
| Morton 2014 | MF/SS   |
| Morton 2014 | DLBCL |
| Morton 2014 | CLL/SLL |
| Morton 2014 | HCL |
| Morton 2014 | NHL |
| Morton 2014 | MF/SS |
| Morton 2014 | CLL/SLL |
| Morton 2014 | NHL |
| Morton 2014 | DLBCL |
| Morton 2014 | CLL/SLL |
| Morton 2014 | ALL |
| Morton 2014 | MF/SS |
| Morton 2014 | PTCL |
| Morton 2014 | DLBCL |
| Morton 2014 | DLBCL |
| Morton 2005 | NHL |
| Morton 2005 | NHL |
| Morton 2005 | NHL |
| Morton 2005 | NHL |
| Morton 2005 | NHL |
| Morton 2005 | NHL |
| Morton 2005 | Other T-cell |
| Morton 2005 | BL |
| Morton 2005 | BL |
| Morton 2005 | DLBCL |
| Morton 2005 | DLBCL |
| Morton 2005 | FL |
| Morton 2005 | CL/L/SLL |
| Morton 2005 | DLBCL |
| Morton 2005 | DLBCL |
| Morton 2005 | DLBCL |
| Morton 2005 | DLBCL |
| Morton 2005 | FL |
| Morton 2005 | FL    | Morton 2005 | BL    | Morton 2005 | BL    | Morton 2005 | DLBCL | Morton 2005 | DLBCL | Morton 2005 | DLBCL | Morton 2005 | DLBCL |
|------------|-------|------------|-------|------------|-------|------------|-------|------------|-------|------------|-------|------------|-------|
| Ekstrom 2008 | NHL  | Ekstrom 2008 | NHL  | Ekstrom 2008 | NHL  | Ekstrom 2008 | NHL  | Ekstrom 2008 | DLBCL | Ekstrom 2008 | DLBCL | Ekstrom 2008 | DLBCL |
| Ekstrom 2008 | FL    | Ekstrom 2008 | FL    | Ekstrom 2008 | CLL/SLL/PLL | Ekstrom 2008 | MZL  | Ekstrom 2008 | MZL  | Ekstrom 2008 | MZL  | Ekstrom 2008 | MZL  |
| Cerhan 2019 | NHL  | Cerhan 2019 | NHL  | Cerhan 2019 | NHL  | Cerhan 2019 | NHL  | Cerhan 2019 | NHL  | Cerhan 2019 | NHL  | Cerhan 2019 | NHL  |
| Cerhan 2019 | NHL  | Cerhan 2019 | NFL  | Cerhan 2019 | NHL  | Cerhan 2019 | NHL  | Cerhan 2019 | NHL  | Cerhan 2019 | FL    | Cerhan 2019 | DLBCL |
| Cerhan 2019 | CLL/SLL | Cerhan 2019 | FL    | Morton 2005 (Cigarette smoking) | NHL  | Morton 2005 (Cigarette smoking) | NHL  | Morton 2005 (Cigarette smoking) | NHL  | Morton 2005 (Cigarette smoking) | NHL  |
| Reference        | NHL                      | Other B-cell lymphoma |
|------------------|--------------------------|-----------------------|
| Morton 2005      | NHL                      |                       |
| Morton 2005      | FL                       |                       |
| Morton 2005      | DLBCL                    |                       |
| Morton 2005      | PTCL                     |                       |
| Morton 2005      | MCL                      |                       |
| Morton 2005      | Other T-cell             |                       |
| De Sanjose 2008  | NHL                      |                       |
| De Sanjose 2008  | DLBCL                    |                       |
| De Sanjose 2008  | LPL                      |                       |
| De Sanjose 2008  | MZL                      |                       |
| De Sanjose 2008  | Other B-cell             |                       |
| Becker 2012      | NHL                      |                       |
| Becker 2012      | CLL/SLL/PLL              |                       |
| Becker 2012      | T-cell                   |                       |
| Becker 2012      | PTCL                     |                       |
| Mbulaiteye 2014  | BL                       |                       |
| Mbulaiteye 2014  | BL                       |                       |
| Mbulaiteye 2014  | BL                       |                       |
| Mbulaiteye 2014  | BL                       |                       |
| Mbulaiteye 2014  | BL                       |                       |
| Mbulaiteye 2014  | BL                       |                       |
| Mbulaiteye 2014  | BL                       |                       |
| Mbulaiteye 2014  | BL                       |                       |
| Wang 2014        | PTCL                     |                       |
| Wang 2014        | PTCL                     |                       |
| Wang 2014        | PTCL                     |                       |
| Authors      | Diagnosis               |
|--------------|-------------------------|
| Wang 2014    | PTCL                    |
| Wang 2014    | PTCL                    |
| Wang 2014    | PTCL                    |
| Wang 2014    | PTCL                    |
| Wang 2014    | PTCL                    |
| Wang 2014    | PTCL                    |
| Wang 2014    | PTCL-NOS                |
| Wang 2014    | PTCL-NOS                |
| Wang 2014    | PTCL-NOS                |
| Wang 2014    | PTCL-NOS                |
| Wang 2014    | PTCL-NOS                |
| Wang 2014    | PTCL-NOS                |
| Wang 2014    | ALCL                    |
| Wang 2014    | ALCL                    |
| Wang 2014    | ALCL                    |
| Wang 2014    | ALCL                    |
| Wang 2014    | ALCL                    |
| Wang 2014    | ALCL                    |
| Wang 2014    | ALCL                    |
| Wang 2014    | Mycosis fungoides       |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides |
| Aschebrook-Kilfoy 2014 | Mycosis fungoides |
| Bracci 2014  | MZL                     |
| Bracci 2014  | MZL                     |
| Bracci 2014  | MZL                     |
| Bracci 2014  | MZL                     |
| Bracci 2014  | MZL                     |
| Bracci 2014  | MZL                     |
| Bracci 2014 | MZL |
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| Bracci 2014 | MZL |
| Bracci 2014 | MZL |
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| Bracci 2014 | MZL |
| Bracci 2014 | MZL |
| Bracci 2014 | MZL |
| Bracci 2014 | MZL |
| Bracci 2014 | MZL |
| Bracci 2014 | MZL |
| Bracci 2014 | EMZL |
| Bracci 2014 | EMZL |
| Bracci 2014 | EMZL |
| Bracci 2014 | EMZL |
| Bracci 2014 | EMZL |
| Bracci 2014 | EMZL |
| Bracci 2014 | EMZL |
| Bracci 2014 | EMZL |
| Bracci 2014 | NMZL |
| Bracci 2014 | NMZL |
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| Bracci 2014 | NMZL |
| Bracci 2014 | NMZL |
| Bracci 2014 | NMZL |
| Bracci 2014 | NMZL |
| Bracci 2014 | NMZL |
| Bracci 2014 | NMZL |
| Bracci 2014 | NMZL |
| Bracci 2014 | NMZL |
| Bracci 2014 | SMZL |
| Bracci 2014 | SMZL |
| Bracci 2014 | SMZL |
| Bracci 2014 | SMZL |
| Bracci 2014 | SMZL |
| Bracci 2014 | SMZL |
| Bracci 2014 | SMZL |
| Date     | Code       |
|----------|------------|
| Bracci 2014 | SMZL       |
| Smedby 2014 | MCL       |
| Smedby 2014 | MCL       |
| Smedby 2014 | MCL       |
| Smedby 2014 | MCL       |
| Smedby 2014 | MCL       |
| Smedby 2014 | MCL       |
| Smedby 2014 | MCL       |
| Vajdic 2014 | LPL/WM     |
| Vajdic 2014 | LPL/WM     |
| Vajdic 2014 | LPL/WM     |
| Vajdic 2014 | LPL/WM     |
| Vajdic 2014 | LPL/WM     |
| Vajdic 2014 | LPL/WM     |
| Vajdic 2014 | LPL/WM     |
| Vajdic 2014 | LPL/WM     |
| Vajdic 2014 | LPL/WM     |
| Linet 2014  | FL         |
| Linet 2014  | FL         |
| Linet 2014  | FL         |
| Linet 2014  | FL         |
| Linet 2014  | FL         |
| Linet 2014  | FL         |
| Linet 2014  | FL         |
| Linet 2014  | FL         |
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| Linet 2014  | FL         |
| Linet 2014  | FL         |
| Linet 2014  | FL         |
| Linet 2014  | FL         |
| Linet 2014  | FL         |
| Year | Type     |
|------|----------|
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | FL       |
| 2014 | DLBCL    |
| 2014 | DLBCL    |
| 2014 | DLBCL    |
| 2014 | DLBCL    |
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| Kane 2012      | FL  |
| Kane 2012      | FL  |
| tMannetje 2016 | NHL |
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| tMannetje 2016 | DLBCL |
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| Reference     | Type     |
|---------------|----------|
| tMannetje 2016 | DLBCL    |
| tMannetje 2016 | DLBCL    |
| tMannetje 2016 | DLBCL    |
| tMannetje 2016 | DLBCL    |
| tMannetje 2016 | DLBCL    |
| tMannetje 2016 | FL       |
| tMannetje 2016 | FL       |
| tMannetje 2016 | FL       |
| tMannetje 2016 | CLL/SLL  |
| tMannetje 2016 | CLL/SLL  |
| tMannetje 2016 | CLL/SLL  |
| tMannetje 2016 | CLL/SLL  |
| tMannetje 2016 | CLL/SLL  |
| tMannetje 2016 | CLL/SLL  |
| tMannetje 2016 | CLL/SLL  |
| tMannetje 2016 | PTCL     |
| tMannetje 2016 | PTCL     |
| tMannetje 2016 | PTCL     |
| tMannetje 2016 | PTCL     |
| tMannetje 2016 | PTCL     |
| Kricker 2008   | NHL      |
| Kricker 2008   | FL       |
| Kricker 2008   | FL       |
| Kricker 2008   | DLBCL    |
| Kricker 2008   | DLBCL    |
**Exposure**

| Exposure                                                                 |   |
|-------------------------------------------------------------------------|---|
| Hormone therapy (ever vs. never)                                        |   |
| Hormone therapy age first used (50-54 years vs. never used)            |   |
| Hormone therapy age first used (55+ years vs. never used)              |   |
| Hormone therapy years used (<2 years vs. never used)                   |   |
| Hormone therapy years used (5 to <10 years vs. never used)             |   |
| Hormone therapy years since last used (current vs. never used)         |   |
| Hormone therapy (ever vs. never)                                        |   |
| Hormone therapy age first used (50-54 years vs. never used)            |   |
| Hormone therapy years used (5 to <10 years vs. never used)             |   |
| Hormone therapy years since last used (current vs. never used)         |   |
| Hormone therapy years since last used (current vs. never used)         |   |
| Duration trichloroethylene exposure (30-39 years vs. unexposed)        |   |
| Frequency trichloroethylene exposure (<5% work time vs. unexposed)     |   |
| Frequency trichloroethylene exposure (31%+ work time vs. unexposed)    |   |
| Intensity of trichloroethylene exposure (>150 ppm vs. unexposed)       |   |
| Male height (100% vs. 60%)                                             |   |
| Male height (100% vs. 60%)                                             |   |
| Female height (20% vs. 60%)                                            |   |
| Male height (100% vs. 60%)                                             |   |
| Female height (80% vs. 60%)                                            |   |
| Weight (Grade 3 obese vs. normal weight)                               |   |
| Weight (Underweight vs. normal weight)                                 |   |
| Any atopic disease (yes vs. no)                                        |   |
| Allergy (yes vs. no)                                                   |   |
| Blood transfusion (yes vs. no)                                         |   |
| Total number of transfusions (1 vs none)                               |   |
| Number of years from first transfusion to date of diagnosis (<20 years vs. no treatment) |   |
| Transfusion before 1990 (Transfusion 1990+ vs. No transfusion)         |   |
| Adult height (Q4 vs Q1)                                                |   |
| Adult height (continuous, 10 cm)                                       |   |
| HCV                                                                     |   |
| Ever lived or worked on a farm (yes vs. no)                            |   |
| Farmer (yes vs. no)                                                    |   |
| Animal farmer (yes vs. no)                                             |   |
| Mixed animal and crop farmer (yes vs. no)                              |   |
| Hairdresser (yes vs. no)                                               |   |
| Total sun exposure (quartile 4 (high) vs. 1 (low))                     |   |
| Recreational sun exposure (Quartile 4 (high) vs 1 (low))               |   |
| Recreational sun exposure (Quartile 2 vs. 1)                           |   |
| History of cigarette smoking (yes vs. no)                              |   |
| Smoking status as of ~1 year before diagnosis/interview (current vs. nonsmoker) |   |
| Question                                                                 |
|-------------------------------------------------------------------------|
| Age started smoking cigarettes (14-<18 years)                          |
| Age started smoking cigarettes (18-<20 years)                          |
| Frequency of cigarette smoking (30+ cigarettes/day vs. nonsmoker)      |
| Duration of cigarette smoking (30-39 years vs. nonsmoker)              |
| Years since quitting cigarette smoking (former smoker unknown when quit vs.) |
| Lifetime cigarette exposure (>20-35 plac-years vs. nonsmoker)           |
| Lifetime cigarette exposure (>35 plac-years vs. nonsmoker)             |
| Frequency of hair dye use (12+ times/year vs. never hair dye)          |
| History of B-cell activating autoimmune disease (any vs. none)          |
| History of B-cell activating autoimmune disease (any vs. none)          |
| History of B-cell activating autoimmune disease (any vs. none)          |
| History of B-cell activating autoimmune disease (any vs. none)          |
| Hemolytic anemia (any vs. non)                                         |
| Hemolytic anemia (any vs. non)                                         |
| Pernicious anemia                                                      |
| Rheumatoid arthritis (any vs. none)                                    |
| Sjogren's syndrome (any vs. none)                                      |
| Sjogren's syndrome (any vs. none)                                      |
| Sjogren's syndrome (any vs. none)                                      |
| Sjogren's syndrome (any vs. none)                                      |
| Sjogren's syndrome (any vs. none)                                      |
| Sjogren's syndrome (any vs. none)                                      |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| Systemic lupus erythematosus (any vs. none)                            |
| History of T-cell activating autoimmune disease                        |
| History of T-cell activating autoimmune disease                        |
| Celiac disease (any vs. none)                                          |
| Celiac disease (any vs. none)                                          |
| Celiac disease (any vs. none)                                          |
| Psoriasis (any vs. none)                                               |
| Systemic sclerosis/scleroderma                                          |
| Systemic sclerosis/scleroderma                                          |
| Hepatitis C virus seropositivity                                       |
| Hepatitis C virus seropositivity                                       |
| HCV                                                                     |
| HCV                                                                     |
| HCV                                                                     |
| Peptic ulcer                                                           |
| Allergy                                                                |
| Allergy                                                                |
| Condition                  |
|---------------------------|
| Allergy                   |
| Allergy                   |
| Hay fever                 |
| Allergy                   |
| Food allergy              |
| Asthma                    |
| Food allergy              |
| Food allergy              |
| Hay fever                 |
| Systemic sclerosis/scleroderma |
| Hay fever                 |
| History of blood transfusion (any vs. none) |
| History of blood transfusion (any vs. none) |
| History of blood transfusion (any vs. none) |
| History of blood transfusion (any vs. none) |
| History of blood transfusion (any vs. none) |
| Age at least transfusion (%>40 years) |
| Age at least transfusion (%>40 years) |
| Age at least transfusion (%>40 years) |
| Age at least transfusion (%>40 years) |
| Age at least transfusion (%>40 years) |
| No. transfusions (% 2+)    |
| No. transfusions (% 2+)    |
| No. transfusions (% 2+)    |
| Blood transfusion <1990    |
| Blood transfusion <1991    |
| Blood transfusion <1992    |
| Blood transfusion <1993    |
| Blood transfusion <1994    |
| Year first Ocs use (%<1970) |
| Ever used HRT             |
| Usual adult BMI (% 25 kg/m^2+) |
| Usual adult BMI (% 25 kg/m^2+) |
| Usual adult BMI (% 25 kg/m^2+) |
| Young adult BMI (% 25 kg/m^2+) |
| Young adult BMI (% 25 kg/m^2+) |
| Height (% Q3-Q4)          |
| Height (% Q3-Q4)          |
| Parameter                                      |
|-----------------------------------------------|
| Physical activity (%≥moderate)                |
| Height (% Q3-Q4)                              |
| Height (% Q3-Q4)                              |
| Height (% Q3-Q4)                              |
| Physical activity (%≥moderate)                |
| Weight (% Q3-Q4)                              |
| Weight (% Q3-Q4)                              |
| Weight (% Q3-Q4)                              |
| Physical activity (%≥moderate)                |
| Ever used HRT                                 |
| Young adult BMI (% 25 kg/m^2+)                 |
| Height (% Q3-Q4)                              |
| Any alcohol                                   |
| Any alcohol                                   |
| Any alcohol                                   |
| Any alcohol                                   |
| Any alcohol                                   |
| Status (% current)                            |
| Status (% current)                            |
| Any alcohol                                   |
| Status (% current) alcohol                    |
| Status (% current) alcohol                    |
| Age at initiation (% <20 years)               |
| Age at initiation (% <20 years) alcohol       |
| Age at initiation (% <20 years) alcohol       |
| Frequency (%>14 servings/week) alcohol        |
| Frequency (%>14 servings/week)                |
| Frequency (%>14 servings/week) alcohol        |
| Frequency (%>14 servings/week) alcohol        |
| Frequency (%>14 servings/week) alcohol        |
| Duration (%>30 years) alochol                 |
| Duration (%>30 years) alochol                 |
| Lifetime (%>200 kg) alcohol                   |
| Lifetime (%>200 kg) alcohol                   |
| Any beer                                      |
| Any beer                                      |
| Any beer                                      |
| Frequency (%>14 servings/week) beer           |
| Frequency (%>14 servings/week) beer           |
| Lifetime (%>200 kg) beer                      |
| Frequency (%>14 servings/week) beer           |
| Description                                                                 | Count |
|----------------------------------------------------------------------------|-------|
| Lifetime (%>200 kg) beer                                                   |       |
| Any liquor                                                                 |       |
| Eczema                                                                     |       |
| Any liquor                                                                 |       |
| Any liquor                                                                 |       |
| Any liquor                                                                 |       |
| Any liquor                                                                 |       |
| Frequency (%>=14 servings/week) any liquor                                  |       |
| Frequency (%>=14 servings/week) any liquor                                  |       |
| Frequency (%>=14 servings/week) any liquor                                  |       |
| Frequency (%>=14 servings/week) any liquor                                  |       |
| Frequency (%>=23 servings/week) any liquor                                  |       |
| Lifetime (%>200 kg) any liquor                                             |       |
| Lifetime (%>200 kg) any liquor                                             |       |
| Any wine                                                                   |       |
| Any wine                                                                   |       |
| Any wine                                                                   |       |
| Any wine                                                                   |       |
| Any wine                                                                   |       |
| Frequency (%>=14 servings/week) wine                                        |       |
| Frequency (%>=14 servings/week) wine                                        |       |
| Frequency (%>=14 servings/week) wine                                        |       |
| Frequency (%>=14 servings/week) wine                                        |       |
| Frequency (%>=14 servings/week) wine                                        |       |
| Frequency (%>=14 servings/week) wine                                        |       |
| Lifetime (%>200 kg) any wine                                               |       |
| Lifetime (%>200 kg) any wine                                               |       |
| History of ciagrette smoking (any vs. none)                                |       |
| History of ciagrette smoking (any vs. none)                                |       |
| History of ciagrette smoking (any vs. none)                                |       |
| History of ciagrette smoking (any vs. none)                                |       |
| Status (% current) cigarette smoking                                       |       |
| Status (% current) cigarette smoking                                       |       |
| Status (% current) cigarette smoking                                       |       |
| Years since quitting (%>15 years) cigarette smoking                        |       |
| Age at initiation (%<20 years) cigarette smoking                           |       |
| Frequency (%>20 years) cigarette smoking                                    |       |
| Duration (%>=20 years) cigarette smoking                                   |       |
| Packyears (%>20) cigarette smoking                                         |       |
| Status (% current) cigarette smoking                                       |       |
| Years since quitting (%>15 years)                                          |       |
| Years since quitting (%>15 years) cigarette smoking                        |       |
| Years since quitting (%>15 years)                                          |       |
| Description                                                                 | Percentage |
|----------------------------------------------------------------------------|------------|
| Years since quitting (%>15 years)                                         |            |
| Age since initiation (% <20 years) cigarette smoking                      |            |
| Age since initiation (% <20 years) cigarette smoking                      |            |
| Age since initiation (% <20 years) cigarette smoking                      |            |
| Frequency (%>20) cigarette smoking                                         |            |
| Frequency (%>20) cigarette smoking                                         |            |
| Duration (%>=20 years) cigarette smoking                                   |            |
| Duration (%>=20 years) cigarette smoking                                   |            |
| Duration (%>=20 years) cigarette smoking                                   |            |
| Forestry worker                                                           |            |
| Duration (%>=20 years) cigarette smoking                                   |            |
| Duration (%>=20 years) cigarette smoking                                   |            |
| Duration (%>=20 years) cigarette smoking                                   |            |
| Packyears (%>20) cigarette smoking                                         |            |
| Packyears (%>20) cigarette smoking                                         |            |
| Packyears (%>20) cigarette smoking                                         |            |
| Frequency (%>-12 times/year) personal hairdye use                          |            |
| Frequency (%>-12 times/year) personal hairdye use                          |            |
| Frequency (%>-12 times/year) personal hairdye use                          |            |
| Duration of hairdye use (%>=20 years)                                      |            |
| Any hairdye use <1980                                                      |            |
| Any hairdye use <1980                                                      |            |
| Recreational hairdye use (%Q3-Q4 hours/week)                              |            |
| Sun exposure (%Q3-Q4 hours/week)                                           |            |
| Sun exposure (%Q3-Q4 hours/week)                                           |            |
| Recreational sun exposure (%Q3-Q4 hours/week)                             |            |
| Recreational sun exposure (%Q3-Q4 hours/week)                             |            |
| General unspecified laborer                                                |            |
| Baker/miller                                                              |            |
| Recreational sun exposure (%Q3-Q4 hours/week)                             |            |
| Socioeconomic status (% low)                                               |            |
| Socioeconomic status (% low)                                               |            |
| Socioeconomic status (% low)                                               |            |
| History of living or working on a farm                                     |            |
| History of living or working on a farm                                     |            |
| History of living or working on a farm                                     |            |
| Ever lived on a farm                                                       |            |
| Mixed/unspecified farmer                                                   |            |
| Ever worked on a farm                                                      |            |
| Electonical/electronics worker                                             |            |
| Farmer any type                                                            |            |
| Animal farmer                                                              |            |
| Field crop/vegetable farmer                                                |            |
| Lifetime liquor (%>200 kg)                                                 |            |
| Field crop/vegetable farmer                                                |            |
| Field crop/vegetable farmer | Mixed/unspecified farmer | Mixed/unspecified farmer | General farmer worked | General farmer worked | General farm worker |
|---------------------------|-------------------------|-------------------------|-----------------------|-----------------------|-------------------|
| Hairdresser               |                         |                         |                       |                       |                   |
| Hairdresser               |                         |                         |                       |                       |                   |
| Hairdresser               |                         |                         |                       |                       |                   |
| Women's hairdresser       |                         |                         |                       |                       |                   |
| Women's hairdresser       |                         |                         |                       |                       |                   |
| Women's hairdresser       |                         |                         |                       |                       |                   |
| Leather worker            |                         |                         |                       |                       |                   |
| Painter                   |                         |                         |                       |                       |                   |
| Textile worker            |                         |                         |                       |                       |                   |
| Textile worker            |                         |                         |                       |                       |                   |
| Welder/flamecutter        |                         |                         |                       |                       |                   |
| Wine and beer             |                         |                         |                       |                       |                   |
| Ever drinker vs. never drinker |                   |                         |                       |                       |                   |
| Wine and liquor           |                         |                         |                       |                       |                   |
| Beer, wine, and liquor    |                         |                         |                       |                       |                   |
| Frequency (1-6 servings per week vs. none) alcohol |                   |                         |                       |                       |                   |
| Frequency (7-13 servings per week vs. none) alcohol |                   |                         |                       |                       |                   |
| Frequency (14-27 servings per week vs. none) alcohol |                   |                         |                       |                       |                   |
| Frequency (>=28 servings per week vs. none) alcohol |                   |                         |                       |                       |                   |
| Beer                      |                         |                         |                       |                       |                   |
| Ever vs. non-drinker      |                         |                         |                       |                       |                   |
| Current vs. non-drinker   |                         |                         |                       |                       |                   |
| Ever vs. non-drinker      |                         |                         |                       |                       |                   |
| Current vs. non-drinker   |                         |                         |                       |                       |                   |
| Ever vs. non-drinker      |                         |                         |                       |                       |                   |
| Ever vs. non-drinker      |                         |                         |                       |                       |                   |
| Frequency (1-6 servings per week vs. none) drinking |                   |                         |                       |                       |                   |
| Frequency (7-13 servings per week vs. none) drinking |                   |                         |                       |                       |                   |
| Frequency (14-27 servings per week vs. none) drinking |                   |                         |                       |                       |                   |
| Frequency (>=28 servings per week vs. none) drinking |                   |                         |                       |                       |                   |

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| Variable                                                                 | Description                                                                 |
|-------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Frequency                                                               | (7-13 servings per week vs. none) drinking                                  |
| Duration                                                                | (21-30 years) drinking                                                      |
| Duration                                                                | (31-40 years) drinking                                                      |
| Duration                                                                | (1-20 years) drinking                                                       |
| Duration                                                                | (21-30 years) drinking                                                      |
| Duration                                                                | (31-40 years) drinking                                                      |
| Duration                                                                | (>=41 years) drinking                                                       |
| Hemolytic anemia                                                        | (any vs. non)                                                               |
| Systemic lupus erythematosus                                           | (any vs. none)                                                              |
| Hemolytic anemia                                                        | (any vs. non)                                                               |
| Sjogren's syndrome                                                      | (any vs. none)                                                              |
| Primary sjogren's syndrome                                             |                                                                            |
| Secondary sjogren's syndrome                                           |                                                                            |
| Hemolytic anemia                                                        | (any vs. non)                                                               |
| Systemic lupus erythematosus                                           | (any vs. none)                                                              |
| Sjogren's syndrome                                                      | (any vs. none)                                                              |
| Primary sjogren's syndrome                                             |                                                                            |
| Secondary sjogren's syndrome                                           |                                                                            |
| Sjogren's syndrome                                                      | (any vs. none)                                                              |
| Secondary sjogren's syndrome                                           |                                                                            |
| Type 1 diabetes                                                         |                                                                            |
| Sjogren's syndrome                                                      | (any vs. none)                                                              |
| Systemic lupus erythematosus                                           | (any vs. none)                                                              |
| Primary sjogren's syndrome                                             |                                                                            |
| Secondary sjogren's syndrome                                           |                                                                            |
| Sjogren's syndrome                                                      | (any vs. none)                                                              |
| Secondary sjogren's syndrome                                           |                                                                            |
| History of blood transfusion                                           | (any vs. none) white men                                                   |
| Number of blood transfusions                                           | (One vs none) white men                                                    |
| Age of 1st transfusion                                                 | (21-30 years vs. none) white men                                           |
| Age of 1st transfusion                                                 | (31-40 years vs. none) white men                                           |
| Age of 1st transfusion                                                 | (41-50 years vs. none) white men                                           |
| Era first transfusion                                                  | (<1970) white men                                                          |
| Era first transfusion                                                  | (1970s) white men                                                          |
| Era first transfusion                                                  | (1990+) white men                                                          |
| Number of blood transfusions                                           | (two vs none) white women                                                   |
| Age of 1st transfusion                                                 | (31-40 years vs. none) white women                                         |
| Age of 1st transfusion                                                 | (51-60 years vs. none) white women                                         |
| History of blood transfusion                                           | (any vs. none) white men                                                   |
| Status (%) current cigarette smoking                                   |                                                                            |
| Intensity                                                               | (11-20 cigarettes/d)                                                       |
| Intensity                                                               | (21-30 cigarettes/d)                                                       |
| Duration (21-35 years) cigarette smoking |
|----------------------------------------|
| Duration (>=36 years) cigarette smoking |
| Pack-years (21-35) cigarette smoking   |
| Pack-years (>=36) cigarette smoking   |
| Ever vs. never smoker                  |
| Status (% current) cigarette smoking   |
| Age at initiation (% >-20 years)       |
| Intensity (21-30 cigarettes/d)         |
| Pack-years (>=36) cigarette smoking   |
| Age at initiation (18-19 years vs. nonsmoker) |
| Pack-years (>=36) cigarette smoking   |
| Intensity (11-20 cigarettes/d)         |
| Years since quit cigarette smoking (>=31 vs. nonsmoker) |
| Intensity (11-20 cigarettes/d)         |
| Intensity (21-30 cigarettes/d)         |
| Duration (21-35 years) cigarette smoking |
| Duration (>=36 years) cigarette smoking |
| Pack-years (>=36) cigarette smoking   |
| HCV                                    |
| Childhood measles                      |
| Childhood whooping cough/pertussis     |
| Adult infectious mononucleosis         |
| Adult infectious mononucleosis         |
| Adult infectious mononucleosis         |
| Asthma (<50 years age)                 |
| Number of blood transfusions (>=3 vs. no transfusion), <50 years age |
| Lifetime alcohol consumed (>400 kg vs. nondrinker), >=50 years age |
| Lifetime alcohol consumed (drinker, consumption unknown), >=50 years age |
| Duration of employment as cleaner (1-10 years vs. never) |
| Eczema with no other atopic conditions (<50 years age) |
| Usual adult height (Q4 vs. Q1, <50 years age) |
| Charworker cleaner or related work (<50 years age) |
| HCV (>50 years)                        |
| Usual adult body mass index (25-<30 Kg/m^2) (>=50 years age) |
| Drinker (at least 1 drink per month vs. non-drinker) |
| Celiac disease (any vs. none)          |
| Allergy                                |
| Eczema                                 |
| Feature                                    |
|--------------------------------------------|
| Psoriasis (any vs. none)                   |
| Duration of cigarette smoking (40+ years)  |
| Smoker, duration unknown                   |
| Drinker (at least 1 drink per month vs. non-drinker) |
| Electrical fitters                         |
| Textile worker                             |
| Ever lived or worked on a farm             |
| Celiac disease (any vs. none)              |
| Allergy                                    |
| Psoriasis (any vs. none)                   |
| Duration of cigarette smoking (40+ years)  |
| Smoker, duration unknown                   |
| Drinker (at least 1 drink per month vs. non-drinker) |
| Celiac disease (any vs. none)              |
| Duration of cigarette smoking (40+ years)  |
| Smoker, duration unknown                   |
| Recreation sun exposure (Q4 (high) vs. Q1) |
| Electrical fitters                         |
| Textile worker                             |
| Electrical fitters                         |
| Hay fever                                  |
| Celiac disease (any vs. none)              |
| Duration of cigarette smoking (1-19 years) |
| Duration of cigarette smoking (40+ years)  |
| Smoker, duration unknown                   |
| Asthma with allergy, hay fever, and/or eczema |
| Fire fighter                               |
| Duration (>=40 years) cigarette smoking    |
| Usual adult body mass index (30-50 kg/m^2) |
| B and T-cell activation                    |
| History of eczema                          |
| Multiple myeloma                           |
| Crop and vegetable farm workers            |
| Painter                                    |
| Woodworkers                                |
| General carpenter                          |
| Physical activity (%>=vigorous)            |
| Physical activity (%>=moderate)            |
| Sjogren's syndrome (any vs. none)          |
| Systemic lupus erythematosus (any vs. none) |
| B-cell activation                          |
| HCV                                        |
| Ulcer                                      |
| Subject                                                                 |
|------------------------------------------------------------------------|
| Asthma with out other atopy                                           |
| Recreational sun exposure (Q2 vs Q1 hours/week)                       |
| Recreational sun exposure (Q3 vs Q1 hours/week)                       |
| Recreational sun exposure (Q4 vs Q1 hours/week)                       |
| Years since quit cigarette smoking (Former <5 years vs. nonsmoker)    |
| Years since quit cigarette smoking (Former unknown years)             |
| Any type of alcohol (Q1 vs nondrinker g/wk)                           |
| Any type of alcohol (Q3 vs nondrinker g/wk)                           |
| Any type of alcohol (Q4 vs nondrinker g/wk)                           |
| Wine (Q2 vs. nondrinker g/wk)                                         |
| Wine (Q3 vs. nondrinker g/wk)                                         |
| Wine (Q4 vs. nondrinker g/wk)                                         |
| Teacher                                                               |
| General carpenter                                                     |
| Sjogren's syndrome (any vs. none)                                     |
| Systemic lupus erythematosus (any vs. none)                           |
| B-cell activation                                                     |
| HCV                                                                   |
| Ulcer                                                                 |
| Years since quit cigarette smoking (Former <5 years vs. nonsmoker)    |
| Years since quit cigarette smoking (Former unknown years)             |
| Any type of alcohol (Q3 vs nondrinker g/wk)                           |
| Any type of alcohol (Q4 vs nondrinker g/wk)                           |
| Wine (Q2 vs. nondrinker g/wk)                                         |
| Wine (Q3 vs. nondrinker g/wk)                                         |
| Wine (Q4 vs. nondrinker g/wk)                                         |
| Any type of alcohol (Q1 vs nondrinker g/wk)                           |
| Any type of alcohol (Q2 vs nondrinker g/wk)                           |
| Wine (Q1 vs. nondrinker g/wk)                                         |
| Wine (Q2 vs. nondrinker g/wk)                                         |
| Wine (Q3 vs. nondrinker g/wk)                                         |
| Sjogren's syndrome (any vs. none)                                     |
| Systemic lupus erythematosus (any vs. none)                           |
| B and T-cell activation                                               |
| Metal worker                                                          |
| B-cell activation                                                     |
| Asthma no other atopy                                                 |
| General unspecified laborer                                           |
| Teacher                                                               |
| Use hair dyes before 1980                                             |
| Color of hairdye used (women only; light vs. never)                   |
| Color of hairdye used (women only; dark vs. never)                    |
| Type of hairdye used (women only; permanent vs. never)                |
| Physical activity (%>=vigorous)                                       |
| Ever used hairdye                        |
| Any atopic disorder                      |
| Allergy                                  |
| Allergy and asthma, hay fever, or eczema |
| Hay fever                                |
| Hay fever but no other atopic conditions  |
| Hay fever and asthma, allergy, or eczema  |
| Ever lived on a farm                      |
| Divers: material handling equipment operators |
| Electrical and electronics workers        |
| Sjogren’s syndrome (any vs. none)         |
| Systemic lupus erythematosus (any vs. none) |
| HCV                                      |
| B-cell activation                         |
| Hay fever                                |
| Usual adult weight (Q2 vs Q1)             |
| Usual adult weight (Q3 vs Q1)             |
| Usual adult weight (Q4 vs Q1)             |
| Duration (>=40 years) cigarette smoking   |
| Age started smoking cigarettes (>=20 years vs. nonsmoker) |
| Medical doctor                           |
| Sjogren's syndrome (any vs. none)         |
| Any atopic disorder                       |
| Allergy                                  |
| Food allergy                             |
| Astma                                    |
| Hay fever                                |
| Blood transfusion, Male                   |
| Blood transfusion, Female                 |
| BMI as young adult (kg/m^2) continuous, Female |
| Physical activity (Mild), Female          |
| Recreational sun exposure (Q2 vs Q1 hours/week), Male |
| Recreational sun exposure (Q3 vs Q1 hours/week), Male |
| Recreational sun exposure (Q4 vs Q1 hours/week), Male |
| Spray-painter (except construction), Male  |
| University and higher education teachers, Male |
| History of cigarette smoking (any vs. none), Female |
| Drinker (at least 1 drink per month vs. non-drinker), Female |
| Recreational sun exposure (Q2 vs Q1 hours/week), Female |
| Recreational sun exposure (Q3 vs Q1 hours/week), Female |
| Recreational sun exposure (Q4 vs Q1 hours/week), Female |
| Blood transfusion                         |
| Blood transfusion 1 vs none               |
| Blood transfusion 2 vs none                        |
|--------------------------------------------------|
| Number of years from 1st blood transfusion to date of diagnosis/interview (<20 years) |
| Number of years from 1st blood transfusion to date of diagnosis/interview (20-39 years) |
| Blood transfusion <1990                          |
| Blood transfusion after 1990                     |
| BMI as young adult (25-<30 kg/m^2)               |
| BMI as young adult (kg/m^2) continuous (5 kg/m^2 increase) |
| Usual adult height (Q4 vs. Q1)                   |
| Physical activity (mild vs. no)                  |
| Status (% current) cigarette smoking             |
| Age started smoking cigarettes regularly (14-17 years) |
| Frequency of cigarette smoking (11-20 per day)    |
| Duration (>=40 years) cigarette smoking          |
| Pack-years (21-35) cigarette smoking             |
| Drinker (at least 1 drink per month vs. non-drinker) |
| Alcohol consumption status (Drinker status unknown vs. nondrinker) |
| Duration of alcohol consumption (Drinker duration unknown vs. nondrinker) |
| Servings of alcohol per week as an adult (1-6 drinks/week vs. nondrinker) |
| Servings of alcohol per week as an adult (7-13 drinks/week vs. nondrinker) |
| Servings of alcohol per week as an adult (>=28 drinks/week vs. nondrinker) |
| Servings of alcohol per week as an adult (Drinker drinks/week unknown vs. nondrinker) |
| Grams of ethanol per week as adult (Q1 vs nondrinker) |
| Grams of ethanol per week as adult (Q2 vs nondrinker) |
| Grams of ethanol per week as adult (Q4 vs nondrinker) |
| Lifetime alcohol consumption (1-100 kg vs nondrinker) |
| Lifetime alcohol consumption (101-200 kg vs nondrinker) |
| Total sun exposure (Q2 vs Q1 hours/week)         |
| Total sun exposure (Q4 vs Q1 hours/week)         |
| Recreational sun exposure (Q2 vs Q1 hours/week)  |
| Recreational sun exposure (Q3 vs Q1 hours/week)  |
| Recreational sun exposure (Q4 vs Q1 hours/week)  |
| Bakers and millers                               |
| Spray-painter (except construction)              |
| University and higher education teachers         |
| Sjogren's syndrome (any vs. none)                |
| Systemic lupus erythematosus (any vs. none)      |
| Hemolytic anemia (any vs. non)                   |
| Celiac disease (any vs. none)                    |
| Rheumatoid arthritis (any vs. none)              |
| Allergy                                          |
| Asthma                                           |
| Hay fever                                        |
| Age at first blood transfusion                   |
| Description                                                                 | Comparison 1          | Comparison 2          |
|---------------------------------------------------------------------------|-----------------------|-----------------------|
| Total number of blood transfusions (2+ vs none)                           |                       |                       |
| Number of transfusions unknown                                            |                       |                       |
| Number of years from 1st blood transfusion to date of diagnosis/interview | <20 years             |                       |
| Transfusions before 1990                                                  |                       |                       |
| Usual adult height (Q4 vs Q1)                                             |                       |                       |
| Usual adult weight (Q4 vs Q1)                                             |                       |                       |
| Usual adult body mass index (15-<18.5 vs. 18.5-<22.5)                     |                       |                       |
| Usual adult body mass index (35-50 vs. 18.5-<22.5)                        |                       |                       |
| Smoking status as of ~1 year before diagnosis/interview (status unknown vs|                       |                       |
| Frequency of cigarette smoking (21-30 cigarettes/day vs. nonsmoker)       |                       |                       |
| Smoker, duration unknown                                                  |                       |                       |
| Years since quit cigarette smoking (Former unknown years)                |                       |                       |
| History of alcohol consumption (>=1 drink/month v. non-drinker)           |                       |                       |
| Alcohol consumption status as of ~2 years prior to diagnosis/interview (current drinker vs. nondrinker) |                       |                       |
| Age first alcohol consumption (20-29 years vs. nondrinker)                |                       |                       |
| Duration of alcohol consumption (1-20 years vs. nondrinker)              |                       |                       |
| Duration of alcohol consumption (21-30 years vs. nondrinker)              |                       |                       |
| Duration of alcohol consumption (30-39 years vs. nondrinker)              |                       |                       |
| Duration of alcohol consumption (40+ years vs. nondrinker)                |                       |                       |
| Duration of alcohol consumption (Drinker duration unknown vs. nondrinker) |                       |                       |
| Servings of alcohol per week as an adult (1-6 drinks/week vs. nondrinker) |                       |                       |
| Servings of alcohol per week as an adult (7-13 drinks/week vs. nondrinker) |                       |                       |
| Servings of alcohol per week as an adult (14-27 drinks/week vs. nondrinker) |                       |                       |
| Servings of alcohol per week as an adult (>=28 drinks/week vs. nondrinker) |                       |                       |
| Servings of beer per week as an adult (<1 drinks/week vs. nondrinker)     |                       |                       |
| Servings of beer per week as an adult (1-6 drinks/week vs. nondrinker)    |                       |                       |
| Servings of liquor per week as an adult (<1 drinks/week vs. nondrinker)   |                       |                       |
| Servings of liquor per week as an adult (1-6 drinks/week vs. nondrinker)  |                       |                       |
| Servings of wine per week as an adult (1-6 drinks/week vs. nondrinker)    |                       |                       |
| Servings of wine per week as an adult (7-13 drinks/week vs. nondrinker)   |                       |                       |
| Servings of wine per week as an adult (14-27 drinks/week vs. nondrinker)  |                       |                       |
| Servings of wine per week as an adult (>=28 drinks/week vs. nondrinker)   |                       |                       |
| Grams of ethanol per week as adult (Q1 vs nondrinker)                     |                       |                       |
| Grams of ethanol per week as adult (Q2 vs nondrinker)                     |                       |                       |
| Grams of ethanol per week as adult (Q3 vs nondrinker)                     |                       |                       |
| Grams of ethanol per week as adult (Q4 vs nondrinker)                     |                       |                       |
| Grams of ethanol per week as adult, Beer (Q1 vs nondrinker)              |                       |                       |
| Grams of ethanol per week as adult, beer (Q2 vs nondrinker)               |                       |                       |
| Grams of ethanol per week as adult, beer (Q4 vs nondrinker)               |                       |                       |
| Drinker, wine & liquor (no beer)                                          |                       |                       |
| Grams of ethanol per week as adult, wine (Q1 vs nondrinker)               |                       |                       |
| Grams of ethanol per week as adult, wine (Q2 vs nondrinker)               |                       |                       |
| Grams of ethanol per week as adult, wine (Q3 vs nondrinker) |
| Grams of ethanol per week as adult, wine (Q4 vs nondrinker) |
| Grams of ethanol per week as adult, liquor (Q1 vs nondrinker) |
| Grams of ethanol per week as adult, liquor (Q2 vs nondrinker) |
| Grams of ethanol per week as adult, liquor (Q3 vs nondrinker) |
| Grams of ethanol per week as adult, liquor (Q4 vs nondrinker) |
| Drinker, wine & beer (no liquor) |
| Lifetime beer consumption (1-100 kg vs. nondrinker) |
| Lifetime wine consumption (201-400 kg vs. nondrinker) |
| Lifetime wine consumption (unknown vs. nondrinker) |
| Drinker, wine, & liquor (no beer) |
| Lifetime liquor consumption (1-100 kg vs. nondrinker) |
| Lifetime liquor consumption (201-400 kg vs. nondrinker) |
| Lifetime liquor consumption (unknown vs. nondrinker) |
| Lifetime wine consumption (1-100 kg vs. nondrinker) |
| Lifetime wine consumption (101-200 kg vs. nondrinker) |
| Lifetime wine consumption (201-400 kg vs. nondrinker) |
| Lifetime wine consumption (400+ kg vs. nondrinker) |
| Lifetime wine consumption (unknown vs. nondrinker) |
| Color of hair dye used (unknown vs. never) |
| Drivers: material handling equiment |
| Cleaners and related workers |
| Hairdresser |
| Textile worker |
| Fiber preparers |
| Socioeconomic status (medium vs. low) |
| Socioeconomic status (high vs. low) |
| B-cell activation |
| B and T-cell activation |
| Any atopic disorder |
| HCV |
| Blood transfusion |
| BMI as young adult (25-<30 kg/m^2) |
| BMI as young adult (30-50 kg/m^2) |
| Lifetime alcohol consumption (1-100 kg vs nondrinker) |
| Lifetime alcohol consumption (101-200 kg vs nondrinker) |
| Lifetime alcohol consumption (201-400 kg vs nondrinker) |
| Lifetime alcohol consumption (unknown) |
| Recreational sun exposure (Q3 vs Q1 hours/week) |
| Recreational sun exposure (Q4 vs Q1 hours/week) |
| Field crop/vegetable farmer |
| Sewer and embroiderer |
| Women's hairdresser |
| Variable                                                                 |
|-------------------------------------------------------------------------|
| Lifetime cigarette exposure (11-20 pack-years vs. nonsmoker)            |
| Lifetime cigarette exposure (21-35 pack-years vs. nonsmoker)            |
| Lifetime cigarette exposure (>35 pack-years)                           |
| Ever lived on a farm                                                   |
| Height (Q3 vs. Q1)                                                     |
| Height (Q4 vs. Q1)                                                     |
| History of cigarette smoking (any vs. none)                            |
| Status (% current) cigarette smoking                                   |
| Age started smoking cigarettes regularly (14-17 years)                 |
| Age started smoking cigarettes regularly (18-19 years)                 |
| Frequency of cigarette smoking (11-20 per day)                         |
| Frequency of cigarette smoking (21-30 per day)                         |
| Frequency of cigarette smoking (>30 per day)                           |
| Duration of cigarette smoking (21-30 years)                            |
| Duration of cigarette smoking (30-39 years)                            |
| Duration of cigarette smoking (40+ years)                              |
| Lifetime cigarette exposure (continuous)                               |
| Ever worked as a mixed animal and crop farmer                          |
| Duration as mixed animal and crop farmer (10 years+ vs. never)          |
| Years since last child (<10 years)                                     |
| Contraception among women born in 1925 or later                        |
| Charworkers, cleaners and related                                      |
| Railway-engine drivers and firemen                                     |
| Vehicle electrician                                                    |
| Other motor-vehicle drivers                                           |
| Field crop/vegetable farmer                                            |
| Field crop farm worker general                                         |
| General farmer worked                                                 |
| Women's hairdresser                                                   |
| Medical assistants                                                    |
| Spray-painter (except construction)                                    |
| Teachers                                                               |
| University and higher education teachers                               |
| Secondary education teachers                                           |
| Head teacher                                                           |
| Other teachers                                                        |
| Milliners and hatmakers                                               |
| Carpenter, general                                                    |
| Charworkers, cleaners and related                                     |
| Field crop/vegetable farmer                                           |
| Field crop farm worker general                                         |
| Hairdresser                                                           |
| Women's hairdresser                                                  |
| Occupation                                      |
|------------------------------------------------|
| Medical workers                                |
| Metal melters and reheaters                    |
| Special education teachers                     |
| Textile worker                                 |
| Milliners and hatmakers                        |
| Sewer and embroiderer                          |
| Bakers and millers                             |
| Spray-painter (except construction)            |
| University and higher education teachers       |
| Farmer-animal                                  |
| Farmers-mix and unspecified                    |
| General farm worker                            |
| Hairdresser                                    |
| Women's hairdresser                            |
| Printing pressmen                              |
| Preprimary education teachers                  |
| Carpenter, general                             |
| Electric fitters                               |
| Metal workers                                  |
| Painters                                       |
| Textile worker                                 |
| Spinners, weavers, knitters, dyers, and related workers |
| Wood workers                                   |
| Cabinetmakers                                  |
| Recreational sun exposure (Q4 vs Q1 hours/week) |
| Recreational sun exposure (Q2 vs Q1 hours/week) |
| Recreational sun exposure (Q4 vs Q1 hours/week) |
| Recreational sun exposure (Q3 vs Q1 hours/week) |
| Recreational sun exposure (Q4 vs Q1 hours/week) |
| Number of cases |
|-----------------|
| 2094            |
| 1987            |
| 1987            |
| 2094            |
| 2094            |
| 2035            |
| 675             |
| 637             |
| 675             |
| 637             |
| 637             |
| 552             |
| 418             |
| 1251            |
| 1251            |
| 639             |
| 639             |
| 5731            |
| 1047            |
| 625             |
| 228             |
| 174             |
| 6285            |
| 90              |
| 2345            |
| 2182            |
| 1168            |
| 1168            |
| 1168            |
| 1168            |
| 1168            |
| 1794            |
| 1794            |
| 994             |
| 1595            |
| 1042            |
| 1042            |
| 1013            |
| 1042            |
| 685             |
| 1301            |
| 1301            |
| 2191            |
| 2191            |
| 1 | 3034 |
|---|------|
| 2 | 3034 |
| 3 | 3034 |
| 4 | 3034 |
| 5 | 3034 |
| 6 | 3034 |
| 7 | 3034 |
| 8 | 3034 |
| 9 | 3034 |
| 10 | 3034 |
| 11 | 3034 |
| 12 | 3034 |
| 13 | 3034 |
| 14 | 3034 |
| 15 | 3034 |
| 16 | 3034 |
| 17 | 3034 |
| 18 | 3034 |
| 19 | 3034 |
| 20 | 3034 |
| 21 | 3034 |
| 22 | 3034 |
| 23 | 3034 |
| 24 | 3034 |
| 25 | 3034 |
| 26 | 3034 |
| 27 | 3034 |
| 28 | 1155 |
| 29 | 3064 |
| 30 | 3064 |
| 31 | 3066 |
| 32 | 3066 |
| 33 | 1645 |
| 34 | 4667 |
| 35 | 4667 |
| 36 | 4546 |
| 37 | 4546 |
| 38 | 4577 |
| 39 | 2382 |
| 40 | 3264 |
| 41 | 3645 |
| 42 | 3645 |
| 43 | 4124 |
| 44 | 4124 |
| 45 | 4124 |
| 46 | 4124 |
| 47 | 2863 |
| 48 | 2863 |
| 49 | 2765 |
| 50 | 3086 |
| 51 | 2983 |
| Effect estimate (95% CI) |
|--------------------------|
| 0.79 (0.69-0.90)         |
| 0.74 (0.61-0.91)         |
| 0.78 (0.62-0.98)         |
| 0.78 (0.62-0.98)         |
| 0.72 (0.57-0.91)         |
| 0.70 (0.54-0.90)         |
| 0.66 (0.54-0.80)         |
| 0.58 (0.42-0.80)         |
| 0.59 (0.40-0.86)         |
| 0.57 (0.44-0.74)         |
| 0.76 (0.58-0.99)         |
| 0.4 (0.2-1.0)            |
| 0.6 (0.4-1.0)            |
| 1.8 (1.1-2.9)            |
| 2.2 (1.1-4.2)            |
| 1.19 (1.06-1.34)         |
| 1.47 (1.18-1.84)         |
| 0.72 (0.56-0.93)         |
| 1.71 (1.14-2.58)         |
| 1.87 (1.14-3.05)         |
| 1.80 (1.23-2.62)         |
| 3.13 (1.19-8.25)         |
| 0.86 (0.78-0.95)         |
| 0.87 (0.77-0.98)         |
| 0.79 (0.66-0.94)         |
| 0.81 (0.66-0.99)         |
| 0.71 (0.55-0.92)         |
| 0.68 (0.49-0.94)         |
| 1.23 (1.05-1.44)         |
| 1.10 (1.02-1.19)         |
| 1.99 (1.16-3.41)         |
| 1.21 (1.07-1.36)         |
| 1.20 (1.06-1.35)         |
| 0.64 (0.43-0.96)         |
| 1.32 (1.08-1.61)         |
| 1.77 (1.05-3.01)         |
| 0.75 (0.59-0.96)         |
| 0.80 (0.69-0.94)         |
| 0.81 (0.68-0.96)         |
| 0.90 (0.81-0.99)         |
| 0.82 (0.71-0.94)         |
| Value          | Lower CI  | Upper CI  |
|---------------|-----------|-----------|
| 0.87          | 0.76      | 0.99      |
| 0.83          | 0.71      | 0.98      |
| 0.72          | 0.57      | 0.90      |
| 0.82          | 0.71      | 0.96      |
| 2.54          | 1.53      | 4.21      |
| 0.84          | 0.72      | 0.98      |
| 0.82          | 0.70      | 0.95      |
| 1.51          | 1.09      | 2.10      |
| 1.96          | 1.60      | 2.40      |
| 5.46          | 3.81      | 7.83      |
| 2.61          | 1.34      | 5.08      |
| 2.45          | 1.91      | 3.16      |
| 2.24          | 1.03      | 4.87      |
| 2.72          | 1.13      | 6.57      |
| 3.45          | 1.07      | 11.15     |
| 1.94          | 1.35      | 2.79      |
| 7.52          | 3.68      | 15.36     |
| 38.07         | 16.94     | 85.55     |
| 12.14         | 3.16      | 46.58     |
| 8.77          | 3.94      | 19.54     |
| 3.23          | 1.19      | 8.80      |
| 2.83          | 1.82      | 4.41      |
| 5.03          | 1.16      | 21.57     |
| 3.90          | 1.24      | 12.30     |
| 6.54          | 3.10      | 13.82     |
| 8.41          | 2.81      | 25.20     |
| 2.49          | 1.42      | 4.37      |
| 1.66          | 1.00      | 2.75      |
| 1.95          | 1.37      | 2.77      |
| 1.77          | 1.05      | 2.99      |
| 14.82         | 7.27      | 30.19     |
| 2.09          | 1.04      | 4.18      |
| 2.05          | 1.23      | 3.42      |
| 8.87          | 1.11      | 71.25     |
| 12.74         | 1.49      | 108.84    |
| 1.81          | 1.39      | 2.37      |
| 3.04          | 1.65      | 5.60      |
| 2.70          | 1.11      | 6.56      |
| 2.33          | 1.71      | 3.19      |
| 2.08          | 1.23      | 3.49      |
| 1.56          | 1.21      | 2.03      |
| 0.86          | 0.81      | 0.92      |
| 0.82          | 0.74      | 0.90      |
|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
| 0.80 (0.65-0.99) | 1.29 (1.06-1.57) | 1.20 (1.02-1.40) | 3.46 (1.62-7.39) | 0.53 (0.30-0.93) | 1.68 (1.06-2.67) | 0.74 (0.58-0.95) | 0.55 (0.36-0.82) | 1.26 (1.10-1.44) | 2.09 (1.24-3.51) | 0.84 (0.73-0.96) | 1.95 (1.51-2.53) | 1.20 (1.08-1.32) | 0.87 (0.81-0.93) | 0.68 (0.53-0.87) | 0.75 (0.62-0.91) | 0.81 (0.73-0.89) | 0.86 (0.77-0.96) | 0.86 (0.78-0.94) | 0.73 (0.55-0.98) | 0.64 (0.48-0.87) | 0.53 (0.31-0.91) | 0.70 (0.62-0.80) | 0.85 (0.75-0.97) | 0.44 (0.21-0.92) | 0.73 (0.62-0.86) | 0.82 (0.75-0.91) | 0.61 (0.45-0.84) | 0.49 (0.31-0.76) | 0.73 (0.64-0.83) | 0.82 (0.69-0.96) | 0.44 (0.21-0.93) | 0.73 (0.62-0.86) | 0.28 (0.12-0.70) | 0.64 (0.52-0.79) | 0.90 (0.84-0.97) | 0.61 (0.46-0.80) | 0.84 (0.76-0.93) | 0.83 (0.71-0.96) | 0.49 (0.27-0.88) | 0.64 (0.46-0.87) | 0.67 (0.55-0.83) | 0.78 (0.61-0.99) |
|   |   |
|---|---|
| 0.74 (0.58-0.94) |   |
| 0.84 (0.78-0.91) |   |
| 2.31 (1.68-3.17) |   |
| 0.66 (0.47-0.92) |   |
| 0.71 (0.58-0.88) |   |
| 0.81 (0.73-0.90) |   |
| 0.86 (0.76-0.97) |   |
| 0.77 (0.64-0.93) |   |
| 0.37 (0.19-0.70) |   |
| 0.33 (0.15-0.74) |   |
| 0.65 (0.50-0.84) |   |
| 1.70 (1.15-2.52) |   |
| 0.15 (0.03-0.84) |   |
| 0.57 (0.41-0.79) |   |
| 0.85 (0.79-0.91) |   |
| 0.67 (0.52-0.86) |   |
| 0.64 (0.53-0.78) |   |
| 0.69 (0.51-0.95) |   |
| 0.81 (0.73-0.89) |   |
| 0.85 (0.76-0.95) |   |
| 0.81 (0.72-0.92) |   |
| 0.61 (0.39-0.95) |   |
| 0.45 (0.30-0.69) |   |
| 0.41 (0.23-0.73) |   |
| 0.67 (0.57-0.80) |   |
| 0.17 (0.05-0.65) |   |
| 0.52 (0.39-0.70) |   |
| 1.32 (1.09-1.59) |   |
| 0.90 (0.81-0.99) |   |
| 1.09 (1.00-1.18) |   |
| 0.51 (0.37-0.71) |   |
| 1.46 (1.16-1.84) |   |
| 0.83 (0.73-0.94) |   |
| 1.18 (1.06-1.31) |   |
| 0.40 (0.26-0.61) |   |
| 0.49 (0.30-0.81) |   |
| 0.23 (0.12-0.44) |   |
| 0.37 (0.22-0.62) |   |
| 0.30 (0.18-0.51) |   |
| 0.37 (0.23-0.57) |   |
| 1.54 (1.23-1.94) |   |
| 1.37 (1.01-1.85) |   |
| 0.82 (0.72-0.94) |   |
|   |   |
|---|---|
|   | 1.17 (1.06-1.29) |
|   | 1.29 (1.00-1.66) |
|   | 1.38 (1.02-1.86) |
|   | 1.13 (1.02-1.26) |
|   | 1.60 (1.16-2.19) |
|   | 0.78 (0.66-0.93) |
|   | 1.75 (1.33-2.30) |
|   | 1.27 (1.03-1.57) |
|   | 3.17 (1.08-9.31) |
|   | 1.50 (1.10-2.04) |
|   | 0.84 (0.74-0.96) |
|   | 1.19 (1.06-1.33) |
|   | 1.67 (1.28-2.18) |
|   | 0.80 (0.70-0.91) |
|   | 1.13 (1.01-1.27) |
|   | 1.16 (1.00-1.35) |
|   | 1.55 (1.05-2.29) |
|   | 1.18 (1.02-1.35) |
|   | 1.23 (1.06-1.42) |
|   | 1.32 (1.05-1.65) |
|   | 0.74 (0.66-0.83) |
|   | 0.79 (0.68-0.91) |
|   | 0.79 (0.64-0.98) |
|   | 0.74 (0.66-0.83) |
|   | 0.75 (0.64-0.88) |
|   | 1.28 (1.06-1.55) |
|   | 0.51 (0.28-0.93) |
|   | 0.70 (0.58-0.84) |
|   | 0.88 (0.83-0.93) |
|   | 0.82 (0.76-0.90) |
|   | 1.72 (1.13-2.63) |
|   | 0.73 (0.55-0.95) |
|   | 1.21 (1.07-1.36) |
|   | 1.68 (1.04-2.71) |
|   | 1.40 (1.03-1.90) |
|   | 0.56 (0.31-0.98) |
|   | 0.68 (0.47-0.99) |
|   | 1.63 (1.09-2.44) |
|   | 1.23 (1.04-1.45) |
|   | 0.77 (0.63-0.94) |
|   | 1.32 (1.06-1.61) |
|   | 3.18 (1.44-7.05) |
|   | 2.80 (1.38-5.68) |
| Value | 95% CI  |
|-------|--------|
| 1.48  | (1.14-1.93) |
| 1.31  | (1.07-1.60) |
| 2.34  | (1.36-4.01) |
| 1.28  | (1.10-1.50) |
| 2.07  | (1.06-4.07) |
| 1.46  | (1.15-1.85) |
| 1.34  | (1.05-1.72) |
| 1.49  | (1.10-2.03) |
| 1.77  | (1.05-2.98) |
| 1.42  | (1.07-1.89) |
| 1.63  | (1.15-2.31) |
| 2.46  | (1.31-4.62) |
| 3.89  | (1.34-11.33) |
| 3.42  | (1.81-6.47) |
| 1.55  | (1.03-2.33) |
| 1.20  | (1.02-1.41) |
| 1.33  | (1.00-1.77) |
| 0.85  | (0.75-0.96) |
| 0.83  | (0.76-0.89) |
| 0.79  | (0.70-0.90) |
| 0.76  | (0.68-0.84) |
| 0.81  | (0.74-0.88) |
| 0.83  | (0.74-0.92) |
| 0.85  | (0.76-0.95) |
| 0.87  | (0.76-0.99) |
| 0.85  | (0.76-0.95) |
| 0.85  | (0.74-0.99) |
| 0.51  | (0.33-0.77) |
| 0.29  | (0.13-0.64) |
| 0.75  | (0.66-0.84) |
| 0.64  | (0.53-0.77) |
| 0.84  | (0.73-0.97) |
| 0.66  | (0.45-0.98) |
| 0.60  | (0.37-0.96) |
| 0.42  | (0.21-0.85) |
| 0.41  | (0.19-0.92) |
| 0.36  | (0.14-0.89) |
| 0.80  | (0.65-0.99) |
| 0.76  | (0.67-0.87) |
| 0.73  | (0.62-0.85) |
| 0.73  | (0.61-0.86) |
| 0.73  | (0.60-0.90) |
| 0.82  | (0.70-0.96) |
|   |   |
|---|---|
| 0.80 (0.65-0.98) |   |
| 0.24 (0.08-0.76) |   |
| 0.27 (0.07-0.99) |   |
| 0.72 (0.56-0.92) |   |
| 0.74 (0.57-0.94) |   |
| 0.72 (0.57-0.93) |   |
| 0.67 (0.53-0.85) |   |
| 2.57 (1.27-5.21) |   |
| 2.69 (1.68-4.30) |   |
| 2.57 (1.27-5.21) |   |
| 6.56 (3.10-13.9) |   |
| 4.75 (1.79-12.6) |   |
| 9.57 (2.90-31.6) |   |
| 3.22 (1.31-7.89) |   |
| 2.74 (1.47-5.11) |   |
| 8.92 (3.82-20.7) |   |
| 6.57 (2.12-20.3) |   |
| 6.57 (2.12-20.3) |   |
| 3.91 (1.39-11.0) |   |
| 7.55 (1.75-32.7) |   |
| 1.97 (1.00-3.88) |   |
| 30.6 (12.3-76.1) |   |
| 7.52 (3.39-16.7) |   |
| 23.1 (7.16-74.5) |   |
| 44.6 (10.6-187) |   |
| 0.74 (0.65-0.83) |   |
| 0.70 (0.60-0.81) |   |
| 0.61 (0.45-0.82) |   |
| 0.71 (0.51-0.97) |   |
| 0.68 (0.50-0.92) |   |
| 0.77 (0.61-0.98) |   |
| 0.58 (0.42-0.79) |   |
| 0.66 (0.52-0.84) |   |
| 0.76 (0.63-0.92) |   |
| 0.78 (0.63-0.97) |   |
| 0.70 (0.50-0.97) |   |
| 0.70 (0.56-0.88) |   |
| 0.72 (0.59-0.87) |   |
| 0.67 (0.52-0.87) |   |
| 0.77 (0.64-0.92) |   |
| 1.10 (1.00-1.20) |   |
| 1.12 (1.02-1.22) |   |
| 1.19 (1.04-1.36) |   |
| Value  | 95% CI     |
|--------|------------|
| 1.12   | 1.02-1.23  |
| 1.16   | 1.05-1.28  |
| 1.14   | 1.02-1.27  |
| 1.21   | 1.09-1.34  |
| 1.15   | 1.12-1.52  |
| 1.31   | 1.12-1.52  |
| 1.24   | 1.05-1.46  |
| 1.27   | 1.05-1.53  |
| 1.24   | 1.06-1.44  |
| 0.34   | 0.12-0.96  |
| 0.38   | 0.15-0.97  |
| 0.63   | 0.40-0.98  |
| 2.04   | 1.14-3.65  |
| 1.25   | 1.08-1.46  |
| 1.33   | 1.06-1.67  |
| 1.21   | 1.03-1.42  |
| 1.28   | 1.08-1.53  |
| 1.30   | 1.08-1.56  |
| 1.78   | 1.40-2.25  |
| 2.24   | 1.68-2.99  |
| 2.57   | 1.14-5.79  |
| 2.47   | 1.44-4.23  |
| 2.36   | 1.11-5.01  |
| 0.84   | 0.76-0.93  |
| 0.85   | 0.78-0.93  |
| 1.26   | 1.01-1.57  |
| 1.71   | 1.30-2.25  |
| 1.41   | 1.01-1.97  |
| 1.72   | 1.14-2.59  |
| 0.35   | 0.13-0.95  |
| 6.46   | 1.75-23.81 |
| 0.22   | 0.06-0.86  |
| 0.63   | 0.40-0.98  |
| 3.27   | 1.24-8.60  |
| 2.54   | 1.20-5.40  |
| 2.17   | 1.08-4.36  |
| 3.49   | 1.13-10.7  |
| 4.19   | 1.05-16.61 |
| 0.27   | 0.08-0.98  |
| 0.63   | 0.40-0.98  |
| 17.80  | 8.61-36.79 |
| 0.69   | 0.54-0.87  |
| 1.41   | 1.07-1.85  |
|   |   |   |
|---|---|---|
| 1 | 1.97 (1.17-3.32) |   |
| 2 | 1.92 (1.41-2.62) |   |
| 3 | 4.44 (2.14-9.25) |   |
| 4 | 0.64 (0.49-0.82) |   |
| 5 | 2.89 (1.41-5.95) |   |
| 6 | 1.58 (1.05-2.38) |   |
| 7 | 0.72 (0.55-0.95) |   |
| 8 | 8.66 (1.97-38.1) |   |
| 9 | 0.67 (0.46-0.98) |   |
| 10 | 2.41 (1.15-5.04) |   |
| 11 | 1.76 (1.14-2.72) |   |
| 12 | 3.61 (1.26-10.4) |   |
| 13 | 0.65 (0.45-0.93) |   |
| 14 | 16.59 (3.27-84.3) |   |
| 15 | 2.46 (1.30-4.65) |   |
| 16 | 5.26 (1.31-21.1) |   |
| 17 | 0.48 (0.26-0.88) |   |
| 18 | 4.08 (1.36-12.2) |   |
| 19 | 2.60 (1.21-5.58) |   |
| 20 | 5.45 (1.20-24.7) |   |
| 21 | 6.38 (1.77-23.0) |   |
| 22 | 39.91 (3.15-506.4) |   |
| 23 | 3.62 (1.13-11.55) |   |
| 24 | 5.82 (1.63-20.80) |   |
| 25 | 16.37 (1.49-183.4) |   |
| 26 | 10.2 (2.90-35.5) |   |
| 27 | 15.2 (2.69-85.7) |   |
| 28 | 1.55 (1.04-2.31) |   |
| 29 | 1.57 (1.03-2.40) |   |
| 30 | 9.45 (1.80-49.60) |   |
| 31 | 2.38 (1.73-3.29) |   |
| 32 | 6.17 (2.39-15.91) |   |
| 33 | 2.37 (1.14-4.92) |   |
| 34 | 3.71 (1.94-7.07) |   |
| 35 | 2.20 (1.18-4.08) |   |
| 36 | 4.07 (1.54-10.75) |   |
| 37 | 0.50 (0.28-0.90) |   |
| 38 | 0.46 (0.22-0.97) |   |
| 39 | 38.38 (17.04-86.48) |   |
| 40 | 6.57 (3.11-13.86) |   |
| 41 | 5.74 (3.97-8.33) |   |
| 42 | 3.04 (1.65-5.60) |   |
| 43 | 1.56 (1.21-2.03) |   |
| Value   | 95% CI       |
|---------|--------------|
| 1.42    | (1.03-1.97)  |
| 0.66    | (0.52-0.84)  |
| 0.78    | (0.62-0.97)  |
| 0.68    | (0.54-0.85)  |
| 1.62    | (1.17-2.24)  |
| 3.24    | (1.49-7.05)  |
| 0.76    | (0.59-0.98)  |
| 0.60    | (0.44-0.82)  |
| 0.61    | (0.42-0.88)  |
| 0.62    | (0.46-0.84)  |
| 0.60    | (0.44-0.80)  |
| 0.59    | (0.37-0.95)  |
| 0.50    | (0.35-0.70)  |
| 2.34    | (1.23-4.45)  |
| 40.25   | (17.5-92.6)  |
| 8.44    | (3.58-19.91) |
| 6.40    | (4.24-9.68)  |
| 5.29    | (2.48-11.28) |
| 1.83    | (1.35-2.49)  |
| 1.55    | (1.03-2.33)  |
| 3.58    | (1.65-7.78)  |
| 0.55    | (0.36-0.84)  |
| 0.48    | (0.28-0.82)  |
| 0.61    | (0.41-0.92)  |
| 0.65    | (0.43-0.98)  |
| 0.50    | (0.29-0.88)  |
| 0.41    | (0.21-0.83)  |
| 0.38    | (0.20-0.72)  |
| 0.37    | (0.17-0.78)  |
| 0.45    | (0.22-0.90)  |
| 141     | (25.01-800)  |
| 9.24    | (1.95-43.74) |
| 11.67   | (1.33-103)   |
| 3.56    | (1.67-7.58)  |
| 4.25    | (1.49-12.14) |
| 2.28    | (1.23-4.23)  |
| 2.10    | (1.15-3.84)  |
| 0.33    | (0.12-0.91)  |
| 14.85   | (1.94-114)   |
| 9.69    | (2.12-44.34) |
| 5.30    | (1.19-23.66) |
| 6.59    | (1.54-28.17) |
| 0.44    | (0.22-0.90)  |
|   | 6.54 (1.53-27.85) |
|---|------------------|
| 2 | 0.74 (0.61-0.89) |
| 3 | 0.79 (0.63-0.98) |
| 4 | 0.68 (0.52-0.88) |
| 5 | 0.63 (0.48-0.82) |
| 6 | 0.55 (0.33-0.93) |
| 7 | 0.66 (0.49-0.89) |
| 8 | 1.40 (1.03-1.90) |
| 9 | 3.05 (1.47-6.31) |
| 10 | 1.63 (1.09-2.44) |
| 11 | 14.0 (3.60-54.5) |
| 12 | 8.23 (2.69-25.2) |
| 13 | 2.51 (1.03-6.17) |
| 14 | 2.78 (1.43-5.43) |
| 15 | 0.73 (0.44-0.99) |
| 16 | 0.71 (0.51-0.99) |
| 17 | 0.72 (0.53-0.98) |
| 18 | 0.61 (0.44-0.85) |
| 19 | 1.46 (1.04-2.05) |
| 20 | 1.45 (1.05-2.00) |
| 21 | 5.54 (2.19-14.0) |
| 22 | 3.37 (1.23-9.19) |
| 23 | 0.87 (0.80-0.94) |
| 24 | 0.88 (0.79-0.98) |
| 25 | 0.79 (0.67-0.94) |
| 26 | 0.85 (0.74-0.97) |
| 27 | 0.82 (0.73-0.91) |
| 28 | 0.74 (0.59-0.92) |
| 29 | 0.80 (0.68-0.95) |
| 30 | 1.25 (1.09-1.44) |
| 31 | 1.53 (1.02-2.30) |
| 32 | 0.77 (0.61-0.96) |
| 33 | 0.74 (0.58-0.93) |
| 34 | 0.77 (0.62-0.95) |
| 35 | 3.83 (1.87-7.84) |
| 36 | 0.53 (0.31-0.90) |
| 37 | 1.22 (1.09-1.37) |
| 38 | 0.79 (0.68-0.91) |
| 39 | 0.77 (0.64-0.93) |
| 40 | 0.78 (0.64-0.95) |
| 41 | 0.70 (0.58-0.85) |
| 42 | 0.78 (0.68-0.89) |
| 43 | 0.83 (0.71-0.97) |
|   |   |   |   |
|---|---|---|---|
| 0.63 | 0.46 | 0.86 |   |
| 0.77 | 0.63 | 0.94 |   |
| 0.76 | 0.62 | 0.93 |   |
| 0.83 | 0.71 | 0.96 |   |
| 0.62 | 0.45 | 0.86 |   |
| 1.49 | 1.21 | 1.83 |   |
| 1.21 | 1.09 | 1.35 |   |
| 1.15 | 1.02 | 1.30 |   |
| 1.41 | 1.04 | 1.91 |   |
| 1.19 | 1.07 | 1.32 |   |
| 1.12 | 1.01 | 1.25 |   |
| 1.13 | 1.02 | 1.25 |   |
| 1.18 | 1.04 | 1.35 |   |
| 1.18 | 1.04 | 1.34 |   |
| 0.86 | 0.77 | 0.96 |   |
| 0.81 | 0.69 | 0.95 |   |
| 0.80 | 0.69 | 0.93 |   |
| 0.85 | 0.75 | 0.97 |   |
| 0.84 | 0.72 | 0.99 |   |
| 0.78 | 0.64 | 0.96 |   |
| 3.00 | 1.25 | 7.23 |   |
| 0.79 | 0.68 | 0.92 |   |
| 0.83 | 0.71 | 0.97 |   |
| 0.79 | 0.66 | 0.94 |   |
| 0.75 | 0.60 | 0.93 |   |
| 0.68 | 0.51 | 0.91 |   |
| 0.83 | 0.69 | 0.99 |   |
| 0.82 | 0.69 | 0.99 |   |
| 0.77 | 0.67 | 0.90 |   |
| 0.77 | 0.66 | 0.89 |   |
| 0.74 | 0.65 | 0.86 |   |
| 0.51 | 0.28 | 0.93 |   |
| 2.66 | 1.36 | 5.34 |   |
| 0.58 | 0.41 | 0.83 |   |
| 9.35 | 4.20 | 20.86 |   |
| 2.53 | 1.44 | 4.43 |   |
| 2.72 | 1.13 | 6.57 |   |
| 2.14 | 1.07 | 4.28 |   |
| 1.94 | 1.35 | 2.79 |   |
| 0.82 | 0.74 | 0.90 |   |
| 0.87 | 0.77 | 0.98 |   |
| 0.78 | 0.70 | 0.86 |   |
| 0.69 | 0.54 | 0.88 |   |
|   |   |
|---|---|
| 1 | 0.70 (0.53-0.92) |
| 2 | 0.44 (0.20-0.96) |
| 3 | 0.83 (0.70-0.98) |
| 4 | 0.87 (0.76-0.99) |
| 5 | 1.12 (1.01-1.25) |
| 6 | 1.20 (1.07-1.33) |
| 7 | 0.60 (0.41-0.88) |
| 8 | 1.26 (1.04-1.53) |
| 9 | 1.26 (1.01-1.57) |
| 10 | 1.17 (1.01-1.35) |
| 11 | 1.42 (1.04-1.95) |
| 12 | 2.20 (1.65-2.95) |
| 13 | 0.81 (0.73-0.89) |
| 14 | 0.71 (0.63-0.80) |
| 15 | 0.71 (0.62-0.82) |
| 16 | 0.79 (0.65-0.95) |
| 17 | 0.60 (0.60-0.91) |
| 18 | 0.82 (0.68-0.99) |
| 19 | 0.71 (0.60-0.85) |
| 20 | 0.86 (0.75-0.98) |
| 21 | 0.81 (0.73-0.91) |
| 22 | 0.76 (0.67-0.87) |
| 23 | 0.77 (0.67-0.89) |
| 24 | 0.77 (0.66-0.90) |
| 25 | 0.80 (0.69-0.92) |
| 26 | 0.82 (0.72-0.94) |
| 27 | 0.75 (0.62-0.92) |
| 28 | 0.71 (0.62-0.82) |
| 29 | 0.78 (0.67-0.90) |
| 30 | 0.75 (.66-0.85) |
| 31 | 0.70 (0.58-0.83) |
| 32 | 0.78 (0.65-0.93) |
| 33 | 0.75 (0.61-0.92) |
| 34 | 0.84 (0.75-0.96) |
| 35 | 0.79 (0.70-0.90) |
| 36 | 0.77 (0.68-0.88) |
| 37 | 0.78 (0.67-0.90) |
| 38 | 0.80 (0.69-0.92) |
| 39 | 0.78 (0.66-0.91) |
| 40 | 0.75 (0.63-0.88) |
| 41 | 0.81 (0.72-0.91) |
| 42 | 0.78 (0.68-0.90) |
| 43 | 0.78 (0.68-0.90) |
|   |   |
|---|---|
| 0.75 (0.65-0.86) |   |
| 0.78 (0.66-0.91) |   |
| 0.70 (0.59-0.83) |   |
| 0.79 (0.67-0.93) |   |
| 0.74 (0.62-0.89) |   |
| 0.81 (0.68-0.98) |   |
| 0.84 (0.76-0.94) |   |
| 0.78 (0.66-0.92) |   |
| 0.63 (0.44-0.91) |   |
| 0.82 (0.72-0.93) |   |
| 0.81 (0.72-0.93) |   |
| 0.74 (0.62-0.89) |   |
| 0.67 (0.47-0.94) |   |
| 0.79 (0.69-0.89) |   |
| 0.74 (0.53-0.86) |   |
| 0.70 (0.53-0.92) |   |
| 0.71 (0.52-0.98) |   |
| 0.56 (0.40-0.79) |   |
| 0.83 (0.74-0.94) |   |
| 1.41 (1.07-1.87) |   |
| 1.56 (1.03-2.37) |   |
| 1.27 (1.03-1.57) |   |
| 1.49 (1.10-2.03) |   |
| 1.20 (1.02-1.41) |   |
| 2.21 (1.21-4.03) |   |
| 0.88 (0.81-0.95) |   |
| 0.86 (0.79-0.94) |   |
| 2.36 (1.80-3.09) |   |
| 4.86 (2.31-10.25) |   |
| 0.82 (0.76-0.89) |   |
| 2.02 (1.47-2.76) |   |
| 0.81 (0.72-0.91) |   |
| 1.47 (1.22-1.77) |   |
| 1.58 (1.12-2.23) |   |
| 0.80 (0.68-0.95) |   |
| 0.79 (0.63-0.98) |   |
| 0.66 (0.53-0.83) |   |
| 0.87 (0.77-0.97) |   |
| 0.79 (0.69-0.90) |   |
| 0.78 (0.69-0.89) |   |
| 1.49 (1.14-1.95) |   |
| 1.43 (1.10-1.87) |   |
| 1.61 (1.13-2.31) |   |
|   |   |   |
|---|---|---|
| 1 | 0.56 (0.34-0.95) |   |
| 2 | 0.48 (0.28-0.83) |   |
| 3 | 0.29 (0.14-0.58) |   |
| 4 | 1.70 (1.02-2.82) |   |
| 5 | 2.40 (1.23-4.70) |   |
| 6 | 2.59 (1.32-5.07) |   |
| 7 | 0.51 (0.37-0.71) |   |
| 8 | 0.34 (0.21-0.55) |   |
| 9 | 0.46 (0.30-0.72) |   |
| 10 | 0.48 (0.25-0.91) |   |
| 11 | 0.49 (0.32-0.75) |   |
| 12 | 0.34 (0.13-0.85) |   |
| 13 | 0.22 (0.07-0.71) |   |
| 14 | 0.39 (0.22-0.69) |   |
| 15 | 0.44 (0.25-0.78) |   |
| 16 | 0.49 (0.27-0.91) |   |
| 17 | 0.98 (0.96-0.99) |   |
| 18 | 2.34 (1.36-4.01) |   |
| 19 | 2.98 (1.50-5.93) |   |
| 20 | 1.87 (1.02-3.40) |   |
| 21 | 1.30 (1.04-1.63) |   |
| 22 | 1.17 (1.01-1.36) |   |
| 23 | 0.45 (0.22-0.94) |   |
| 24 | 2.58 (1.20-5.55) |   |
| 25 | 0.65 (0.46-0.92) |   |
| 26 | 1.26 (1.05-1.51) |   |
| 27 | 1.38 (1.07-1.77) |   |
| 28 | 1.19 (1.03-1.37) |   |
| 29 | 1.34 (1.02-1.74) |   |
| 30 | 0.69 (0.50-0.95) |   |
| 31 | 2.07 (1.30-3.29) |   |
| 32 | 0.89 (0.81-0.98) |   |
| 33 | 0.75 (0.61-0.90) |   |
| 34 | 0.82 (0.69-0.98) |   |
| 35 | 2.16 (1.15-4.06) |   |
| 36 | 0.63 (0.40-0.98) |   |
| 37 | 2.46 (1.28-4.74) |   |
| 38 | 1.42 (1.04-1.93) |   |
| 39 | 1.27 (1.03-1.58) |   |
| 40 | 1.50 (1.15-1.97) |   |
| 41 | 1.48 (1.01-2.17) |   |
| 42 | 1.47 (1.08-2.00) |   |
| 43 | 1.60 (1.13-2.27) |   |
| Value | 95% CI       |
|-------|-------------|
| 0.85  | (0.72-0.99) |
| 2.31  | (1.01-5.26) |
| 1.94  | (1.01-3.71) |
| 1.19  | (1.01-1.41) |
| 2.90  | (1.30-6.45) |
| 1.51  | (1.16-1.96) |
| 0.54  | (0.30-0.99) |
| 2.67  | (1.36-5.25) |
| 0.62  | (0.44-0.89) |
| 0.63  | (0.42-0.96) |
| 1.30  | (1.06-1.60) |
| 1.44  | (1.13-1.84) |
| 1.79  | (1.06-3.03) |
| 2.69  | (1.43-5.06) |
| 6.52  | (2.79-15.21)|
| 2.00  | (1.04-3.87) |
| 2.10  | (1.08-4.09) |
| 2.02  | (1.03-3.97) |
| 0.66  | (0.45-0.99) |
| 1.80  | (1.14-2.84) |
| 1.60  | (1.18-2.17) |
| 1.85  | (1.21-2.83) |
| 1.54  | (1.04-2.27) |
| 2.41  | (1.22-4.74) |
| 0.76  | (0.63-0.91) |
| 0.83  | (0.71-0.96) |
| 0.73  | (0.62-0.86) |
| 0.75  | (0.61-0.93) |
| 0.69  | (0.55-0.87) |
| Classification of evidence | |
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|21 | Suggestive |
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|52 | Suggestive |
|53 | Weak   |
|54 | Highly suggestive |
|55 | Weak   |
|56 | Suggestive |
|57 | Suggestive |
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|   | Weak   | Weak | Weak | Weak | Suggestive | Weak | Weak | Weak | Suggestive | Weak | Weak | Weak | Suggestive | Weak | Weak | Weak | Suggestive | Weak | Weak | Weak | Suggestive | Weak | Weak | Weak | Suggestive | Weak | Weak | Weak | Highly suggestive | Suggestive | Weak | Weak |
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| 25 | Weak |
| 26 | Weak |
| 27 | Suggestive |
| 28 | Suggestive |
| 29 | Highly suggestive |
| 30 | Suggestive |
| 31 | Suggestive |
| 32 | Suggestive |
| 33 | Weak |
| 34 | Weak |
| 35 | Weak |
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| 37 | Weak |
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| 41 | Weak |
| 42 | Suggestive |
| 43 | Suggestive |
| 44 | Suggestive |
| 45 | Weak |
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| 49 | Weak |
| 50 | Weak |
| 51 | Weak |
| 52 | Weak |
| 53 | Weak |
| 54 | Weak |
| 55 | Weak |
| 56 | Weak |
| 57 | Weak |
| 58 | Weak |
| 59 | Weak |
| 60 | Weak |
### Table 6. Concordance between meta-analyses of summary level data and MAs of individual participant data from International Lymphoma Epidemiology Consortium

| Exposure [NHL subtype] | Effect estimate (95% CI) | Strength of reported association |
|------------------------|---------------------------|----------------------------------|
| Red blood cell transfusion [NHL] | RR 1.20 (1.07, 1.35) | IV |
| Red blood cell transfusion [CLL/SLL] | RR 1.66 (1.08, 2.56) | IV |
| Red blood cell transfusion [FL] | RR 1.02 (0.67, 1.55) | NS |
| Red blood cell transfusion [DLBCL] | RR 1.06 (0.86, 1.30) | NS |
| Ever smoking [NHL] | RR 1.05 (1.00, 1.09) | IV |
| Ever smoking [DLBCL] | RR 1.01 (0.95, 1.07) | NS |
| Ever smoking [FL] | RR 1.05 (0.88, 1.25) | NS |
| Ever smoking [CLL/SLL] | RR 0.96 (0.89, 1.04) | NS |
| Ever smoking [TCL] | RR 1.23 (1.06, 1.43) | IV |
| Ever drinking [NHL] | RR 0.85 (0.79, 0.91) | III |
| Ever drinking [TCL] | RR 0.78 (0.58, 1.05) | NS |
| Ever drinking [DLBCL] | RR 0.79 (0.68, 0.91) | IV |
| Ever drinking [FL] | RR 0.80 (0.69, 0.92) | IV |
| Ever drinking [CLL/SLL] | RR 1.00 (0.80, 1.26) | NS |
| Pernicious anemia [NHL] | RR 1.16 (0.79, 1.71) | NS |
| Rheumatoid arthritis [NHL] | SIR 2.26 (1.82, 2.81) | II |
| Primary Sjogren's syndrome [NHL] | RR 13.76 (8.53, 18.99) | II |
| Systemic lupus erythematosus [NHL] | RR 5.40 (3.75, 7.77) | II |
| Psoriasis [NHL] | RR 1.48 (1.3, 1.69) | III |
| Type 1 diabetes [NHL] | RR 1.55 (1.15, 2.08) | IV |
| Celiac disease [NHL] | OR 2.61 (2.04, 3.33) | II |
| Celiac disease [TCL] | OR 15.84 (7.85, 31.94) | II |
| Celiac disease [DLBCL] | OR 2.25 (1.32, 3.85) | IV |
| Celiac disease [CLL] | OR 0.80 (0.46, 1.38) | NS |
| Sarcoidosis [NHL] | RR 1.43 (1.03, 1.99) | IV |
| Tuberculosis [NHL] | RR 1.61 (1.34, 1.94) | II |
| Herpes Zoster [NHL] | RR 1.72 (1.27, 2.32) | III |
| Hepatitis C virus [NHL] | OR 3.36 (2.40, 4.72) | II |
| Hepatitis C virus [DLBCL] | OR 2.65 (1.88, 3.74) | II |
| Hepatitis C virus [FL] | OR 2.73 (2.20, 3.38) | IV |
| Hepatitis C virus [MZL] | OR 3.41 (2.39, 4.87) | IV |
| Hepatitis C virus [CLL/SLL] | OR 1.65 (1.35, 2.02) | IV |
| Farmer [NHL] | RR 1.11 (1.05, 1.17) | III |
| Firefighter [NHL] | SIR 1.07 (0.96, 1.20) | NS |
| Hairdresser [NHL] | RR 1.11 (0.94, 1.32) | NS |
| Petroleum refinery worker [NHL] | RR 0.98 (0.89, 1.09) | NS |
| Teacher [NHL] | RR 1.47 (1.34, 1.61) | II |
| Meat worker [NHL] | RR 0.99 (0.77, 1.29) | NS |
| Printer [NHL] | RR 1.86 (1.38, 2.50) | III |
| Wood worker [NHL] | RR 1.04 (0.79, 1.37) | IV |

**Footnotes**

CI=confidence interval; CLL/SLL=chronic lymphocytic leukemia/small lymphocytic lymphoma.
| Exposure [NHL subtype] | Effect estimate (95% CI) | Effect estimates in the same direction | Overlapping 95% confidence intervals | Same level of statistical significance (P<0.05) |
|------------------------|--------------------------|---------------------------------------|--------------------------------------|-----------------------------------|
| History of blood transfusion | MA of IPD | OR 0.83 (0.77, 0.91) | No | No | Both |
| History of blood transfusion | MA of IPD | OR 0.79 (0.66, 0.94) | No | No | Both |
| History of blood transfusion | MA of IPD | OR 0.78 (0.68, 0.89) | No | Yes | MA of IPD |
| History of blood transfusion | MA of IPD | OR 0.84 (0.75, 0.95) | No | Yes | MA of IPD |
| Any smoking [NHL] | Both | OR 1.02 (0.97, 1.07) | Yes | Yes | Neither |
| Any smoking [DLBCL] | Both | OR 1.01 (0.94, 1.08) | Yes | Yes | Neither |
| Any smoking [FL] | MA of IPD | OR 0.90 (0.81, 0.99) | Yes | Yes | MA of IPD |
| Any smoking [TCL] | MA of IPD | OR 1.32 (1.09, 1.59) | Yes | Yes | Both |
| Any alcohol [NHL] | MA of IPD | OR 0.87 (0.81, 0.93) | Yes | Yes | Both |
| Any alcohol [TCL] | MA of IPD | OR 0.68 (0.53, 0.87) | Yes | Yes | MA of IPD |
| Any alcohol [DLBCL] | MA of IPD | OR 0.81 (0.73, 0.89) | Yes | Yes | Both |
| Any alcohol [FL] | MA of IPD | OR 0.86 (0.77, 0.96) | Yes | Yes | Both |
| Any alcohol [CLL/SLL] | MA of IPD | OR 1.04 (0.90, 1.19) | Yes | Yes | Neither |
| Pernicious anemia [NHL] | MA of IPD | OR 1.37 (0.62, 3.03) | Yes | Yes | Neither |
| Rheumatoid Arthritis [NHL] | MA of IPD | OR 1.32 (0.99, 1.77) | Yes | No | MA of sum |
| Sjogren’s syndrome [NHL] | MA of IPD | OR 7.52 (3.68, 15.36) | Yes | Yes | Both |
| Systemic Lupus Erythematosus [NHL] | MA of IPD | OR 2.83 (1.81, 4.11) | Yes | Yes | Both |
| Psoriasis [NHL] | MA of IPD | OR 1.08 (0.90, 1.29) | Yes | No | MA of sum |
| Type 1 diabetes [NHL] | MA of IPD | OR 1.15 (0.80, 1.66) | Yes | Yes | MA of sum |
| celiac disease [NHL] | MA of IPD | OR 1.77 (1.05, 2.99) | Yes | Yes | Both |
| celiac disease [TCL] | MA of IPD | OR 14.82 (7.27, 30.19) | Yes | Yes | Both |
| celiac disease [DLBCL] | MA of IPD | OR 2.09 (1.04, 4.18) | Yes | Yes | Both |
| celiac disease [CLL/SLL] | MA of IPD | OR 0.60 (0.14, 2.61) | Yes | Yes | Neither |
| Sarcoidosis [NHL] | MA of IPD | OR 0.71 (0.39, 1.29) | No | Yes | Neither |
| Adult Tuberculosis infection | MA of IPD | OR 1.16 (0.96, 1.39) | Yes | Yes | MA of sum |
| Adult shingles [NHL] | MA of IPD | OR 1.05 (0.93, 1.19) | Yes | No | MA of sum |
| Hepatitis C virus [NHL] | MA of IPD | OR 1.81 (1.39, 2.37) | Yes | No | Both |
| hepatitis C virus [DLBCL] | MA of IPD | OR 2.33 (1.71, 3.19) | Yes | Yes | Both |
| Hepatitis C virus [FL] | MA of IPD | OR 0.57 (0.30, 1.10) | No | No | MA of sum |
| Hepatitis C virus [MZL] | MA of IPD | OR 3.04 (1.65, 5.60) | Yes | Yes | Both |
| Hepatitis C virus [CLL/SLL] | MA of IPD | OR 2.08 (1.23, 3.49) | Yes | Yes | Both |
| Farmer [NHL] | MA of IPD | OR 1.03 (0.95, 1.13) | Yes | Yes | Neither |
| Firefighter [NHL] | MA of IPD | OR 0.76 (0.53, 1.09) | No | Yes | Neither |
| Hairdresser [NHL] | MA of IPD | OR 1.21 (0.96, 1.52) | Yes | Yes | Both |
| Petroleum workers [NHL] | MA of IPD | OR 0.79 (0.38, 1.67) | Yes | Yes | Neither |
| Teacher [NHL] | MA of IPD | OR 0.89 (0.81, 0.98) | No | No | Both |
| Meat worker [NHL] | MA of IPD | OR 1.08 (0.81, 1.42) | No | Yes | Neither |
| Printers [NHL] | MA of IPD | OR 0.95 (0.78, 1.17) | No | No | MA of sum |
| Wood workers [NHL] | MA of IPD | OR 1.04 (0.89, 1.22) | Yes | Yes | Neither |

NHL = non-Hodgkin lymphoma; DLBCL = diffuse large B-cell lymphoma; NA = not available; MAs of IPD = meta-analyses of individual participant data from International Lymphoma Epidemiology Consortium.
| Overlapping evidence |
|-----------------------|
| At least one-third of studies overlapping |
| Yes |
| Yes |
| Yes |
| Yes |
| No |
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CI=confidence interval; CLL/SLL=chronic lymphocytic leukemia/small lymphocytic lymphoma; DLBCL=diffuse large B-cell lymphoma; NHL=non-Hodgkin lymphoma; OR=odds ratio; SIR=standardized incidence ratio; RR=risk ratio; TCL=T-cell lymphoma.
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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Abstract

**Objectives:** To summarize the range, strength, and validity of reported associations between environmental risk factors and non-Hodgkin lymphoma (NHL), and to evaluate the concordance between associations reported in meta-analyses (MAs) of summary level data and MAs of individual participant data (IPD).

**Design:** Umbrella review.

**Data sources:** MEDLINE, Embase, Scopus, Web of Science Core Collection, Cochrane Library, and Epistemonikos from inception to 23 July 2021.

**Eligibility criteria:** English language MAs of summary level data and MAs of IPD evaluating associations between environmental risk factors and incident NHL (overall and NHL subtypes).

**Data extraction and synthesis:** Summary effect estimates from MAs of summary level data comparing ever versus never exposure that were adjusted for the largest number of potential confounders were re-estimated using a random-effects model and classified as presenting non-significant, weak ($P<0.05$), suggestive ($P<10^{-3}$ and $>1000$ cases), highly suggestive ($P<10^{-6}$, $>1000$ cases, largest study reporting a significant association), or convincing ($P<10^{-6}$, $>1000$ cases, largest study reporting a significant association, $I^2 < 50\%$, 95% prediction interval excluding the null value, and no evidence of small study effects and excess significance bias) evidence. When the same exposures, exposure contrast levels, and outcomes were evaluated in MAs of summary level data and MAs of IPD from the International Lymphoma Epidemiology (InterLymph) Consortium, concordance in terms of direction, level of significance, and overlap of 95% confidence intervals (CIs) was examined. We assessed the methodological quality of the MAs of summary level data using the A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2 tool.

**Results:** We identified 85 MAs of summary level data reporting 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. Nearly all (79/85, 93%) MAs of summary level data were classified as having critically low quality. Most (225, 88%) associations presented either non-significant or weak evidence. The 11 (4%) associations presenting highly suggestive evidence were primarily for autoimmune or infectious disease-related risk factors. Only 1 association, history of celiac disease and risk of NHL, presented convincing evidence. Overall, 40 associations reported in MAs of summary level data were also evaluated in InterLymph MAs of IPD. Of these, 22 (55%) pairs were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. There were 28 (70%) pairs where the summary effect sizes from the MAs of IPD were more conservative.
**Conclusion:** This umbrella review suggests that there is a mass production of MAs of summary level data, many of which report weak associations between environmental risk factors and NHL, and highlights the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.

**Systematic review registration** PROSPERO CRD42020178010.
What is already known on this topic

- Observational studies have suggested that environmental risk factors, including clinical, occupational, and lifestyle exposures, may be associated with the risk of developing non-Hodgkin lymphoma.

- As a result of the large number of observational studies evaluating the impact of environmental risk factors on non-Hodgkin lymphoma, dozens of systematic reviews and meta-analyses of summary and individual participant level data have focused on synthesizing evidence and identifying potential risk factors.

- Little is known about: (1) the range, strength, and validity of associations between environmental risk factors and non-Hodgkin lymphoma reported in meta-analyses or (2) the concordance between meta-analyses of summary level data and meta-analyses of individual participant data evaluating the same associations.

What this study adds

- This umbrella review suggests that although a large range of environmental risk factors for non-Hodgkin lymphoma have been evaluated in meta-analyses, the vast majority of meta-analyses of summary level data are low quality and present either non-significant or weak associations.

- Overall, only half of the associations that were evaluated in both meta-analyses of summary level data and meta-analyses of individual participant data were in the same direction, had the same level of statistical significance, and had overlapping 95% confidence intervals.

- Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, this umbrella review highlights the need for improving not only primary studies but also evidence synthesis in the field of non-Hodgkin lymphoma etiology.
Introduction

Non-Hodgkin lymphoma (NHL), a lymphoid cancer that originates in white blood cells called lymphocytes, is the 9th leading cause of cancer death among both men and women.1 NHL accounts for nearly 90% of all lymphomas2 and is the most common hematologic malignancy in the world.3 Although NHL can be broadly categorized into two major groups (i.e., B-cell, T-cell/natural killer-cell lymphomas), it represents a diverse group of malignant disorders with dozens of subtypes.4 Evidence suggests that NHL is more common among older adults, men, and people with a first degree relative with NHL.5,6 However, despite substantial effort to identify NHL causes and risk factors over the past few decades, the exact etiology of NHL is unknown.5

Epidemiological studies have suggested that environmental risk factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors, may be associated with the risk of developing NHL. In particular, several prominent potential risk factors proposed in the literature include viruses (e.g., Epstein-Barr virus infection),7 autoimmune diseases (e.g., Sjogren’s syndrome, celiac disease, and rheumatoid arthritis),8-10 and immune dysregulation (i.e., patients with a history of organ transplantation, acquired immunodeficiency syndromes (HIV/AIDS), or immunosuppressive medication treatment).5,6,11 However, given that these exposures and conditions are relatively rare,11 a broad range of additional environmental risk factors, including exposure to insecticides,12 red and processed meat consumption,13 and hair dye,14 have been evaluated and proposed as potential risk factors.

As a result of the large number of observational studies evaluating the impact of environmental risk factors on NHL, dozens of systematic reviews and meta-analyses (MAs) of summary level data have focused on synthesizing evidence and identifying the most promising risk factors. Moreover, the International Lymphoma Epidemiology (InterLymph) Consortium,15 a group of investigators who pool data from their completed or ongoing NHL case-control studies, have published multiple MAs of individual participant data (IPD) evaluating associations between various environmental risk factors and NHL.16-18 Although these MAs of IPD contain thousands of NHL cases and are strengthened by their ability to utilize raw data that are harmonized across multiple studies, they do not include evidence from case-control and cohort studies conducted by investigators outside of the InterLymph Consortium. Therefore, MAs of summary level data and MAs of IPD evaluating the same associations between environmental risk factors and NHL may sometimes lead to discordant results and conclusions.
To provide an overview of the range, strength, and validity of reported associations between environmental risk factors and NHL, we conducted an umbrella review of the evidence across published systematic reviews and MAs. In addition to summarizing the results, determining hints of biases, and assessing the quality of reviews, we evaluated the consistency between all associations reported in both MAs of summary level data and InterLymph MAs of IPD.

Methods
We conducted an umbrella review on the reported associations between environmental risk factors and the risk of NHL. Umbrella reviews are used to systematically identify and evaluate evidence reported in published systematic reviews and MAs.\textsuperscript{19,20} Our study protocol was pre-registered on the International prospective register of systematic reviews (CRD42020178010) and posted on Open Science Framework (https://osf.io/6g2ev/). We did not involve patients or members of the public when designing the question and study, interpreting the results, and/or drafting the manuscript.

Database searches
Working with an experienced medical librarian (KN), we developed and performed a comprehensive search of multiple databases: MEDLINE (Ovid), Embase (Ovid), Scopus, Web of Science Core Collection (as licensed at Yale University), Cochrane Library, and Epistemonikos from inception to July 24\textsuperscript{th} 2020 (eTable 1 in Supplement 1). In each database, we used three concepts: NHL, risk factors, and the study designs of interest (MAs, systematic reviews, and pooled analyses). The search strategy for NHL was based on the search strategy used in a published review.\textsuperscript{21} The study design search strategy used elements from a published search filter.\textsuperscript{22} Database limits were used to exclude conference papers and meeting abstracts. No language limits were used. Records were deduplicated in EndNote, the Yale Reference Deduplicator, and Covidence. No citation chaining was conducted.

On July 24\textsuperscript{th} 2020, searches were run in each database and 14,753 references were identified. After deduplication in EndNote and Covidence, 8025 unique records were uploaded for screening. On July 23\textsuperscript{th} 2021, all searches were rerun and deduplicated and 969 additional unique records were added to Covidence for manual screening. In total, our search retrieved 8994 unique records across all databases.

Eligibility criteria
We included English language systematic reviews, MAs of summary level data (i.e., MAs using effect estimates reported in individual studies), and MAs of IPD of observational studies evaluating associations between environmental risk factors and incident NHL (overall or any subtypes, eTable 2 in Supplement 1). We considered all non-genetic factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors that can affect a person’s health, as environmental risk factors. Systematic reviews and MAs were excluded if they primarily focused on genetic risk factors, evaluated risk factors for the treatment, relapse, remission, or prognosis of NHL patients, or examined NHL as a risk factor for other diseases (eText 1 in Supplement 1).

Two reviewers (XS and HZ) independently screened the titles and abstracts and then full-text versions of potentially eligible articles. Any disagreements or uncertainties were discussed with a third reviewer (JDW).

Data extraction

Data extraction was performed independently by two reviewers (XS and HZ), and a third reviewer (JDW) arbitrated all potential discrepancies. For each systematic review and MA, we recorded the first author, year of publication, article title, journal of publication, study design, population, examined exposures and their definitions, and examined outcomes and their definition (i.e., NHL or NHL subtypes). For all MAs of summary level data, we identified each unique exposure-outcome relationship and recorded the number of studies included, total sample size, number of cases, and study-specific adjusted relative risk estimates (e.g., relative risks, hazard ratios, or odds ratios) and corresponding 95% confidence intervals (CIs). For studies that considered multiple exposure contrast levels, control groups, and/or confounders, we prioritized the effect estimates comparing ever versus never exposure that were adjusted for the largest number of potential confounders. Whenever ever versus never exposures comparisons were not reported, we recorded the effect estimates comparing the highest versus lowest levels of exposures. When multiple MAs of summary level data were identified for the same environmental risk factor, we selected the effect estimates that were based on the largest number of component studies.

For systematic reviews with unique associations that were not investigated in MAs of summary level data, we recorded the number of studies identified, the reasons why MAs were not performed, and the main conclusions. Lastly, for all MAs of IPD, one author (JDW) identified the exposures, NHL subtypes, and number of NHL cases for: (1) all nominally
statistically significant ($P<0.05$) associations and (2) any associations that were also evaluated in MAs of summary level data.

**Quality Assessment**

Four reviewers (XS, HZ, YD, and JDW) evaluated the quality of all MAs of summary level data using A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2. Any discrepancies were discussed and resolved by consensus. Based on the suggested rating scheme, the overall confidence in the results of the MAs of summary level data were classified as high, moderate, low, or critically low. We did not examine the quality of MAs of IPD.

**Statistical analysis**

First, we used a random-effects model, which allows for unexplained between-study heterogeneity on the effect of interest, with the between-study variance estimated using the DerSimonian and Laird (DL) estimator. When summary effect estimates were reported without a corresponding $P$ value, we used the 95% CIs to calculate the $P$ value using a previously described method. Next, we categorized the strength of the reported associations across five levels (Table 1), following previously established methodology. All associations with $P>0.05$ were classified as non-significant. Associations with $P<0.05$ and fewer than 1000 cases were classified as weak. Associations with $P<10^{-3}$ and at least 1000 cases were classified as suggestive. For associations with $P<10^{-6}$, at least 1000 cases, and $P<0.05$ for the largest component study, we sequentially evaluated 95% prediction intervals (PIs), presence of small study effects (Egger regression asymmetry test), and evidence of excess significance using the Ioannidis test. PIs provide a potential range of the true effect and incorporate the uncertainty of whether the observed effect will arise in future studies as well. $P<0.1$ for Egger’s test suggests the presence of small study effects (i.e. small studies are more prone to report larger or more significant results while larger studies tend to report more conservative results). The Ioannidis test estimates whether the observed number of studies with nominally statistically significant ($P<0.05$) results in a MA differs from the expected number of studies with nominally statistically significant studies. Associations with 95% PIs including the null, statistically significant Egger’s test ($P<0.1$), and/or evidence of excess significance were classified as highly suggestive. Associations with 95% prediction intervals excluding the null, non-statistically significant Egger’s test ($P>0.1$), and no evidence of excess significance were classified as convincing. Statistical analysis was conducted using metagen package in R version 4.1.0. (eTable 3 in Supplement 1).
Table 1. Grading criteria for evidence categories

| Strength of association | Description |
|-------------------------|-------------|
| Convincing (class I)    | Highly statistically significant association ($P < 10^{-6}$) |
|                         | At least 1000 NHL cases |
|                         | Low/moderate proportion of total variability due to between-study variability ($I^2 < 50\%$) |
|                         | 95% prediction interval excluding the null value |
|                         | Largest study reporting a nominally statistically significant ($P < 0.05$) |
|                         | No evidence of small-study effects |
|                         | No evidence of excess significance bias |
| Highly suggestive (class II) | Highly statistically significant association ($P < 10^{-6}$) |
|                         | At least 1000 NHL cases |
|                         | Largest study reporting a nominally statistically significant ($P < 0.05$) |
| Suggestive (class III)  | At least 1000 NHL cases |
|                         | Statistically significant association ($P < 10^{-3}$) |
| Weak (class IV)         | Nominally statistically significant association ($P < 0.05$) |
| Non-significant         | Non-statistically significant associations ($P > 0.05$) |

* $P$ value for the association that calculated by random effects model.
NHL=non-Hodgkin lymphoma.

Concordance between MAs of summary level data and InterLymph MAs of IPD

When the same exposures, exposure contrast levels, and NHL subtypes were examined in MAs of summary level data and InterLymph MAs of IPD, two authors (XS and JDW) determined whether the effect estimates: (1) were in the same direction, (2) had overlapping 95% CIs, and/or (3) had the same level of statistical significance ($P<0.05$ or $P\geq 0.05$). Associations with all three criteria fulfilled were classified as fully concordant. Lastly, we determined how often MAs of summary level data included at least one-third of the same component studies as the InterLymph MAs of IPD.

Results

Literature search

Among 16438 records identified through the literature search, 7444 were excluded as duplicates, leaving 8994 titles and abstracts for initial screening (Figure 1). 7970 records were excluded based on the title and abstract and 1024 were screened at the full text stage for inclusion. After excluding 904 records at the full text stage (eTable 1 in Supplement 2), our
searches identified 85 MAs of summary level data evaluating 134 unique environmental risk factors and 8 systematic reviews evaluating 8 unique risk factors (eFigure 1 and eText 2 in Supplement 1 and eTable 2 in Supplement 2). In addition, we identified 27 MAs of IPD (Supplement 2), of which 24 (89%) were conducted by the InterLymph Consortium. More than one MA of summary level data was identified for 44 (44/134, 33%) risk factors (eTable 4 in Supplement 1). Among the MAs of summary level data selected based on the largest number of component studies, approximately half were also the most recently published (25/44, 57%).

**Methodological quality**

The vast majority of the 85 MAs of summary level data had overall confidence ratings of low (3, 4%) or critically low (79, 93%) according to the AMSTAR 2 tool. There were 2 (2%) where the overall confidence in the results was classified as moderate.\(^{34,35}\) Only 1 (1%), evaluating the association between tuberculosis and risk of NHL, had an overall confidence rating of high (eTable 3 in Supplement 2).\(^{36}\) The most common unfulfilled critical domains of the AMSTAR 2 tool were incomplete justification of excluded studies (74, 87%) and missing or no information about preregistered protocols (72, 85%).

**MAs of summary level data**

Among the 257 associations reported in the MAs of summary level data, 124 and 133 evaluated the impact of environmental risk factors on the risk of NHL overall and NHL subtypes, respectively. NHL subtypes included follicular lymphoma (FL; 43, 17%), diffuse large B-cell lymphoma (DLBCL; 35, 14%), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL; 31, 12%), T-cell lymphoma (TCL; 12, 5%), B-cell lymphoma (BCL; 4, 2%), marginal zone lymphoma (MZL; 2, 1%), endemic Burkitt Lymphoma (eBL; 1, 0.4%), Burkitt lymphoma (BL; 1, 0.4%), primary cutaneous lymphoma (PCL; 1, 0.4%). The most common exposure categories were dietary factors (90, 35%), medical histories and comorbidities (54, 21%), chemicals and pesticides (42, 16%), lifestyle factors (29, 11%), drugs, vaccinations, and medical procedures (30, 12%), and occupational (12, 5%). The median number of component studies per MA of summary level data was 5 (IQR 4-10). The median number of NHL cases, among the 64 (75%) MAs reporting this information, was 1533 (IQR, 482-5872).

**Credibility criteria**

After re-estimating the 257 associations using a random-effects DL estimator and applying the credibility criteria, 145 (56%) were classified as presenting non-significant evidence (eTable 4 in Supplement 2). There were 80 (31%) nominally statistically significant (\(P<0.05\))
associations that were classified as presenting weak evidence. There were 20 (8%) statistically
significant associations ($P<10^{-3}$), based on analyses with at least 1000 NHL cases, that were
classified as presenting suggestive evidence. Only 12 (5%) associations were classified as
presenting highly suggestive or convincing evidence, with a $P<10^{-6}$, at least 1000 cases, and a
$P<0.05$ for the largest component study. The 11 highly suggestive associations were for history
of renal transplantation and risk of NHL, rheumatoid arthritis and risk of NHL, primary
Sjogren's syndrome and risk of NHL, systemic lupus erythematosus and risk of NHL, celiac
disease and risk of TCL, tuberculosis and risk of NHL, hepatitis B virus (HBV) and risk of
NHL and BCL, hepatitis C virus (HCV) and risk of NHL and DLBCL, and teaching as an
occupation and risk of NHL (Table 2).

| Risk factors category | Environmental risk factors | Level of comparison | Outcomes type | Author | Year | N. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | $P$ random | Largest study nominally significant ($P<0.05$) | $I^2$ (%) | 95% PI | Strength of association |
|-----------------------|-----------------------------|---------------------|---------------|--------|------|----------------------|-------------|---------------|------------------------------------------|-----------|---------------------------------|---------|------|------------------------|
| Renal transplant      | Renal transplant recipients vs general population | NHL | SR MA | Wang 2018 | 6 | 770 | SI R | 10.66 (8.54, 13.31) | 3.44E-86 | Yes | 80.2 | NA | NA | II |
| Autoimmune diseases   | Rheumatoid arthritis patients vs general population | NHL | SR MA | Simon 2015 | 16 | 153 | SI R | 2.26 (1.82, 2.81) | 8.42E-13 | Yes | 96 | N A | NA | NA | II |
| Primary Sjogren's syndrome patients vs general population | NHL | SR MA | Lian 2014 | 11 | 123 | R R | 13.76 (8.53, 18.99) | 1.62E-34 | Yes | 58.8 | N A | NA | NA | II |
| Systemic lupus patients vs general | NHL | MA | Cao 2015 | 12 | 166 | R R | 5.4 (3.75, 7.77) | 1.99E-18 | Yes | 74.3 | N A | NA | NA | II |

Table 2. Environmental risk factors for non-Hodgkin lymphoma reported in meta-analyses of summary level data with convincing (Class I) and highly suggestive (Class II) evidence.
| Disease             | Patients vs general population | NHL | SR/MA | Tio 2012 | 8 | 110/245 | OR   | 2.61 (2.04, 3.33) | 9.32 E-14 | Yes | 23/4 | (1.57, 5.33) | No | I       |
|---------------------|--------------------------------|-----|-------|----------|---|---------|------|-----------------|----------|-----|------|-------------|----|---------|
| Celiac disease      | Patients vs general population | TCL | SR/MA | Tio 2012 | 5 | 353/58  | OR   | 15.84 (7.85, 31.94) | 6.70 E-14 | Yes | 55/5 | NA        | NA | II      |
| Tuberculosis        | Patients vs general population | NHL | SR/MA | Leung 2020 | 8 | 239/14  | RR   | 1.61 (1.34, 1.94) | 6.76 E-07 | Yes | 50/2 | NA        | NA | II      |
| HBV                 | HBV infected vs non-infected   | NHL | SR/MA | Li 2018  | 58| 537/14  | OR   | 2.50 (2.2, 2.83)  | 6.33 E-42 | Yes | 77/9 | NA        | NA | II      |
| HBV                 | HBV infected vs non-infected   | NHL | SR/MA | Li 2018  | 20| >10/00  | OR   | 2.46 (1.97, 3.07) | 1.24 E-14 | Yes | 62/9 | NA        | NA | II      |
| HCV                 | HCV infected vs non-infected   | NHL | SR/MA | Masaroni 2019 | 27| 330/77  | OR   | 3.36 (2.4, 4.72)  | 7.92 E-12 | Yes | 65/12 | NA        | NA | II      |
| HCV                 | Patients vs general population | DLBCL | MA | Dal Maso 2006 | 8 | 102/0   | RR   | 2.65 (1.88, 3.74) | 4.98 E-08 | Yes | 39/17 | NA        | NA | II      |

| Occupation          | Teachers vs non-teachers       | NHL | MA  | Boffetta 2007 | 19| >10/00  | RR   | 1.47 (1.34, 1.61) | 1.60 E-15 | Yes | 76/15 | NA        | NA | II      |

BCL=B cell lymphoma; CI=confidence interval; HBV=hepatitis B virus; HCV=hepatitis C virus; MA=meta-analysis; NA=not available; NHL=non-Hodgkin lymphoma; OR=odds ratio; PI=prediction interval; SIR=standardized incidence ratio; SRMA=systematic review and meta-analysis; RR=risk ratio; TCL=T-cell lymphoma.

*P* value for summary effect estimates using a random-effects DerSimonian and Laird estimator.

*P*<0.1 for Egger’s test suggests the presence of small study effects.

Strength of association using the criteria listed in Table 1.

There was one association, between history of celiac disease and risk of NHL (OR 2.61, 95% CI 2.04 to 3.33; 110, 245 NHL cases from 8 individual studies), that was classified as presenting convincing evidence. Although the association had *P*<10^-6, at least 1000 cases, a nominally significant result for the largest component study, low/moderate proportion of total variability due to between-study variability (*I^2*<50%), a 95% PI excluding the null, and no evidence of small study effects, we were unable to conduct the Ioannidis test due to the incomplete information reported about the component studies. Across all the 112 nominally...
statistically significant associations, 63 (56%) had relative risk values that were between 0.67 and 1.50.

**Systematic reviews**

We identified 8 systematic reviews without quantitative synthesis with 8 unique associations that were not investigated by MAs of summary level data (*eText 2 in Supplement 1*).

**MAs of IPD**

We identified 27 MAs of IPD, of which 24 were from the InterLymph Consortium. The 24 InterLymph MAs of IPD reported 715 nominally statistically significant (*P*<0.05) associations. Of these, 116 and 21 associations were based on analyses with at least 1000 NHL cases and had *P*<10^-3 and *P*<10^-6, respectively (*Table 3 and eTable 5 in Supplement 2*). Overall, the unique suggestive exposures categories were alcohol consumption on risk of DLBCL, MZL and NHL, history of Sjogren’s syndrome on risk of DLBCL, MZL and NHL, recreational sun exposure on risk of DLBCL, FL and NHL, and history of HCV on risk of DLBCL, MZL and NHL. Although the 3 non-InterLymph MAs of IPD examined 5 associations not reported in systematic reviews and/or MAs of the summary level data, including fish eaters and risk of NHL, vegetarians and vegans and risk of NHL, maternal age at the time of the child’s birth and risk of NHL, paternal age at the time of the child’s birth and risk of NHL, and leisure-time physical activity and risk of NHL, none were nominally statistically significant.

| Table 3. Suggestive risk factors and protective factors identified in meta-analyses of individual patient data from International Lymphoma Epidemiology Consortium |
|-----------------|---------------------------------|---------------------------------|
| **NHL subtype** | **At least 1000 cases and *P*<10^-3** | **At least 1000 cases and *P*<10^-6** |
| CLL/SLL         | Years since quitting cigarette smoking; printing pressmen | None |
| CLL/SLL/PLL/MCL | Adult infectious mononucleosis | None |
| DLBCL           | Alcohol; Any atopic disorder; Allergy; B and T-cell activating autoimmune diseases; HCV; Hay fever; Recreational sun exposure; Socioeconomic status (high vs low); BMI as young adult (25-<30 kg/m²); Rheumatoid arthritis; Blood transfusion; Weight | History of B-cell activating autoimmune disease; Sjogren’s syndrome; HCV; Young adult BMI (%25 kg/m²²); Years since quit cigarette smoking; Age first alcohol consumption (20-29 years vs. nondrinker); Current alcohol consumption status as of ~2 years prior to diagnosis/interview |
| FL              | Blood transfusions; Young adult BMI (%25 kg/m²²); Recreational sun exposure; History of cigarette smoking (females); Current cigarette smoking; University and higher education teachers; Male height | None |
Consistency between MAs of summary level data and InterLymph MAs of IPD

There were 40 associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD (eTable 6 in Supplement 2 and eFigure 1 in Supplement 1). While 22 (55%) evaluated the impact of environmental risk factors on the risk of NHL overall, the other half (18, 45%) focused on various NHL subtypes (CLL/SLL, 5 (13%); DLBCL, 5 (13%); FL, 4 (10%); TCL, 3 (8%); MZL, 1 (3%)).

Overall, 22 of 40 (55%) of the associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. There were 10 (25%) pairs where the effect estimates were both statistically significantly increased, 3 (8%) where they were both statistically significantly decreased, 7 (18%) where they were both non-statistically significantly increased, and 2 (5%) where they were both non-statistically significantly decreased (Kappa=0.37, eTable 6 in Supplement 2 and eFigure 1 in Supplement 1). The 13 associations where the MAs of the summary level data and MAs of IPD effect estimates were both statistically significantly increased or decreased were for history of smoking and risk of TCL, history of drinking and risk of NHL, DLBCL, and FL, history of primary Sjogren’s syndrome and risk of NHL, history of systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL, TCL and DLBCL, and history of HCV and risk of NHL, DLBCL, MZL and CLL/SLL. There were 28 (70%) pairs where the effect sizes from the MAs of IPD were more conservative than the effect sizes from the MAs of summary level data.

There were 4 suggestive associations reported in MAs of summary level data that were also evaluated in the InterLymph MAs of IPD. Of these, 3 associations from MAs of IPD had effect estimates in the same direction, had P<10^-3, and were based on analyses with at least 1000 NHL cases (i.e., history of psoriasis and risk of NHL, history of Herpes Zoster and risk...
of NHL, and history of farming as an occupation and risk of NHL). There were 8 highly suggestive associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD. Of these, 7 associations from the MAs of IPD had effect estimates in the same direction, had $P<10^{-6}$, and were based on analyses with at least 1000 NHL cases (i.e., history of rheumatoid arthritis and risk of NHL, history of primary Sjogren's syndrome and risk of NHL, history systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL and TCL, history of tuberculosis and risk of NHL, and history of HCV and risk of NHL).

There were 19 (48%) pairs where the MAs of summary level data included at least one-third of the same component studies as the InterLymph MAs of IPD. There was no difference in terms of concordance (direction, statistical significance of summary effect estimates and overlapping 95% CIs) between MAs of summary level data that included at least one-third versus fewer than one-third of the same component studies as the MAs of IPD (12/19 (63%) vs 10/21 (48%), $P=0.32$).

**Discussion**

In this umbrella review, we evaluated the range, strength, and validity of reported associations between environmental risk factors and NHL across 85 MAs of published observational studies. Overall, we identified 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. The vast majority of the associations, including those evaluating various dietary, clinical, lifestyle, chemical, and occupational exposures, were classified as having either non-significant or weak evidence. More than half of the nominally significant associations were only marginally significant. Only 5% of the associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence. When the same associations were evaluated in MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Overall, effect sizes from MAs of IPD were more conservative. This umbrella review suggests that there is a mass production of low-quality MAs of summary level data reporting weak associations between environmental risk factors and NHL. These findings highlight the need for improving not only primary studies but also evidence synthesis in this field. Moreover, given that many of the assessed risk factors are correlated, simultaneous consideration of multiple risk factors will be useful to understand which ones have the strongest, independent effects on NHL risk.
Although a wide range of environmental exposures have been evaluated and proposed as potential risk factors for NHL, our evaluation suggests that the only highly suggestive or convincing exposures proposed in MAs of summary level data and MAs of IPD are related to autoimmune and infectious diseases. In particular, the prominent autoimmune disease-related risk factors include history of celiac disease, rheumatoid arthritis, primary Sjogren's syndrome, and systemic lupus erythematosus. Although the exact mechanisms behind these associations remains unclear, many autoimmune disorders are characterized by chronic inflammation, which may intensify B cell or T cell activation and promote the development of lymphoma. Previous studies have also suggested that the dysfunction of some protein families, such as FAS and tumor necrosis factor, and the interplay between various immune cells, could be potential mechanisms. However, there is uncertainty when it comes to the temporality of these associations, with studies reporting that autoimmune diseases can occur during lymphoma.

Associations between viral and bacterial infections and NHL risk have been suggested for several decades. Different hypotheses for HCV-related lymphomagenesis have been proposed. For instance, chromosomal aberrations, including chromosome t(14;18) translocation, have been found to be associated with mixed cryoglobulinemia, a disorder most commonly caused by HCV infection and that can evolve into lymphoproliferative disorders. Furthermore, genetic variations, including Interleukin-10 polymorphisms, have also been proposed as a potential pathway between HCV infection and NHL susceptibility and development. Similar to autoimmune disease-related risk factors, it remains unclear whether these associations are driven by disease status, medication use, or disease-medication interactions. Considering how rare many of these autoimmune and infectious disease-related exposures are, future efforts are necessary to determine the impact of multiple environmental as well as non-environmental risk factors simultaneously.

Among 40 associations evaluated by both MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Unlike MAs of summary level data, MAs of IPD tend to focus on studies with more homogeneous designs and patient populations. Furthermore, MAs of IPD can allow for better harmonization of data across studies, more advanced one-stage meta-analytical approaches, and analyses accounting for many exposure categories and potential confounders. Although the InterLymph MAs of IPD are particularly robust due to the large number of NHL cases and subtypes considered, MAs of IPD without systematic reviews may exclude evidence from high-quality case-control or cohort studies. For instance, the
InterLymph analyses only included evidence from completed and ongoing case-control studies from consortium members. Furthermore, the InterLymph findings may be difficult to disentangle, with at least 700 nominally statistically significant associations among thousands of analyses conducted across different subtypes of NHL and exposure levels (e.g., different type/dosage of alcohol consumption). In the future, it will be necessary to monitor the consistency between MAs of summary level data and MAs of IPD, especially since approximately half of the MAs of summary level data had at least one-third of the same component studies as the MAs of IPD. In addition, authors of MAs should carefully evaluate whether any external studies can and should be included in their syntheses. Of interest, we observed that more than two thirds of the effect sizes were more conservative in the InterLymph MAs of IPD than in the MAs of summary level data. This may be a reflection of greater selective reporting bias in the corpus of studies available in the literature as compared with a set of studies participating in a consortium.

Our study suggests that nearly all MAs of summary level data evaluating associations between environmental risk factors and risk of NHL could be classified as having critically low quality according to the AMSTAR 2 tool. Previous umbrella reviews focused on the associations between environmental risk factors and health outcomes have noted similar concerns. However, the proportion of low or critically low-quality NHL reviews is higher than what has been observed among umbrella reviews for inflammatory bowel diseases,\textsuperscript{61} attention-deficit/hyperactivity disorder,\textsuperscript{62} eating disorders,\textsuperscript{63} early childhood caries,\textsuperscript{64} physical activity for academic achievement,\textsuperscript{65} and physical therapy for tendinopathy.\textsuperscript{66} These findings may not be surprising considering recent concerns about the mass production of systematic reviews.\textsuperscript{67,68} In the future, authors planning systematic reviews and MAs of summary level data of the associations between environmental exposures and NHL should adhere to reporting guidelines. Moreover, authors should also critically evaluate how their findings relate to existing MAs of IPD, focusing on the impact of different methods, populations, and other characteristics.

Limitations
Our umbrella review has several limitations. First, we did not identify potential environmental risk factors that were only examined in individual observational studies. Our objective was to identify and summarize the associations that were reported by the MAs of summary level data, which already covered a wide space of diverse associations. Second, we did not evaluate the quality of individual studies included in the MAs of summary level data, the impact that individual studies have on the overall heterogeneity, the magnitude of the
associations, or the potential role that residual/unmeasured confounding could have on associations. Individual risk of bias evaluations are outside the scope of umbrella reviews, and it is the expectation that MAs have already conducted these quality assessments. Third, we considered MAs that included cohort and case-control studies, and our assessments did not prioritize reviews of certain study designs or address differences across different study designs. Considering that certain NHL subtypes are rare, case-control studies may often be the most realistic study design to evaluate exposure histories.

Fourth, although umbrella reviews provide a comprehensive summary of the associations reported in MAs, the validity of the summary effect estimates depends on the quality of the individual MAs. Although we attempted to standardize associations using a random-effects DL estimator, we did not evaluate or re-conduct the literature searches for all potential exposure-outcome relationships. Different approaches can impact the width of the CIs (i.e., Wald vs. Hartung-Knapp-Sidik-Jonkman). In our evaluation, it is unlikely that these differences would impact the associations that were classified as highly suggestive or convincing. Given that the Hartung-Knapp-Sidik-Jonkman method has been found to outperform the standard DL method in certain scenarios, future MAs should consider this approach in their analyses.69-71

Fifth, we did not calculate $I^2$, 95% PIs, Egger’s test, and excess significance test for non-significant and nominally statistically significant associations. Given the large number of associations identified, we prioritized these calculations for associations where these values were necessary to determine the strength of associations using the previously established classification system.20 It is also worth noting that other tests may be more appropriate (e.g., Peter’s test vs. Egger’s test to examine small study effects72), and that $I^2$ values should not be used to make inferences about heterogeneity, as it does not measure heterogeneity directly, but rather the proportion of total variability due to between-study variability.73 However, we used the same approaches as previous umbrella reviews.26,62

Sixth, when summary effect estimates of multiple exposure contrast levels were reported, we focused on the risk estimates comparing ever versus never exposure (or comparing the highest versus lowest levels of exposures). Although we did not consider all potential contrast levels and dose-response relationships, our objective was to provide a universal overview of the relationships between examined risk factors and NHL. Specific dose-response relationships may nevertheless exist for certain associations, and they would need to be examined on a case-by-case basis. Seventh, we only identified the nominally statistically significant associations among the thousands of associations reported in
InterLymph MAs of IPD. Eighth, by excluding non-English language reviews, we may have missed additional potential associations. However, we utilized the same approach as previous umbrella reviews that focused on risk factors for health outcome(s).\textsuperscript{51,74}

Ninth, MAs of IPD and MAs of summary level data can have different strengths and limitations, and our evaluation did not focus on comparing the potential quality of these types of studies. We also did not focus on the impact of different methods, populations, or other characteristics when comparing the consistency of the results between the two study types. Tenth, umbrella reviews are not intended to provide information about the likelihood that associations are causal. Lastly, when multiple MAs of summary level data evaluated the same exposures and outcomes, we selected the association based on the largest number of included studies. Although this approach does not ensure that the highest quality MAs are selected, this methodology has been utilized by previous umbrella reviews.\textsuperscript{26,74-76}

**Conclusion**

In this large-scale umbrella review, we identified dozens of MAs evaluating associations between environmental risk factors and NHL. However, the vast majority of MAs of summary level data were low quality and presented either non-significant or weak evidence. When the same associations were evaluated in MAs of summary level data and MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95\% CIs. Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, these findings highlight the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.

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participated in the interpretation of the data. All authors and critically revised the manuscript for important intellectual content. XS and JDW had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. JDW provided supervision. JDW is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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**Patient consent:** Not required

**Ethical approval:** Not required

**Data sharing:** All data are included in the supplementary materials.

**Transparency:** The senior author (manuscripts guarantor) (JDW) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant registered) have been explained.

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**Figure 1: Study selection flowchart**

* Web of Science Core Collection as licensed at Yale: Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years

** Wrong study design: the examined study was not a systematic review, meta-analysis or pooled analysis

Wrong topic: the examined review did not examine non-Hodgkin lymphoma or its subtypes as an outcome OR the study did not examine the impact of an environmental exposure on the risk of non-Hodgkin lymphoma development

Wrong exposure: the examined risk factor does not meet the definition of environmental risk factor in our study

Wrong study focus: the review did not examine the impact of an exposure on the risk of developing NHL

Wrong component study design: the review did not synthesize observational study data

Insufficient data for analyses: the review included fewer than 3 component studies

Overlapping review: a larger review was identified for the same association
Response letter: bmjmed-2022-000184

Response: We would like to thank the BMJ Medicine Editors for considering our revised manuscript. Although we truly appreciate the additional feedback, we are unable to make the changes requested with the data that we currently have. We hope that the Editors and Dr. Riley will consider our explanations and proposed additions to the Limitations section. Please find more details responses below. Once again, thank you for considering a revised version of our manuscript.

Reviewer 1:

I thank the authors for their clear response and improved revision. I flag again the considerable work the authors have done.

Response: We would like to thank Dr. Riley for considering our revised manuscript. We appreciate the opportunity to respond to the remaining comments below.

We are close, but an issue remains, in that there continues to be inappropriate methods in places, and the authors decide to stick with them because that is what previous umbrella reviews did. E.g. they say in their response: “We completely agree that other approaches may be more appropriate than Egger’s test. However, to ensure that our umbrella review is aligned with current practices, we did not use Peter’s or Debray’s tests in this study.” The same is true with their sticking to the use of a Wald-based confidence interval rather than the Hartung-Knapp confidence interval, simply because the former is what umbrella reviews have used before.

I urge the authors to reconsider this for their next revision. At the least, the better methods can be applied and shown in a supplementary material, for completeness. There is a chance to demonstrate better practice than previous umbrella reviews, as otherwise sub-standard methods will continue to be used simply because that is what previously has always been done. I appreciate that the conclusions are unlikely to change (as they are actually flagging the poor quality of the field primarily), but at least reconsider the confidence interval derivation in key analyses to demonstrate robustness.

Response: We appreciate Dr. Riley’s attention to detail and helpful feedback. However, at this stage, we are unable to conduct the analyses requested above. In order to perform Peter’s tests and update our analyses using HKSJ confidence intervals, we would need to identify all the individual studies included in 257 associations from 85 separate meta-analyses. This is very challenging given the incomplete reporting across individual meta-analyses. Moreover, given that we have worked on this project since July 2020, it is not feasible for us to re-abstract the data from the individual studies to re-run each meta-analysis.

Although we are not able to fully respond to Dr. Riley’s requests, we are assured that our findings are unlikely to change. In fact, for the 12 associations classified as presenting highly suggestive or convincing evidence, applying the HKSJ method did not change any
conclusions. This may not be surprising given that none of these associations are close to the null OR value of 1.0 (i.e., they are highly significant).

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Different approaches can impact the width of the CIs (i.e., Wald vs. Hartung-Knapp-Sidik-Jonkman). In our evaluation, it is unlikely that these differences would impact the associations that were classified as highly suggestive or convincing. Given that the Hartung-Knapp-Sidik-Jonkman method has been found to outperform the standard DL method in certain scenarios, future MAs should consider this approach in their analyses.

It is also worth noting that other tests may be more appropriate (e.g., Peter’s test vs. Egger’s test to examine small study effects). However, we used the same approaches as previous umbrella reviews.

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Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

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**Appendix:** 2
Abstract

Objectives: To summarize the range, strength, and validity of reported associations between environmental risk factors and non-Hodgkin lymphoma (NHL), and to evaluate the concordance between associations reported in meta-analyses (MAs) of summary level data and MAs of individual participant data (IPD).

Design: Umbrella review.

Data sources: MEDLINE, Embase, Scopus, Web of Science Core Collection, Cochrane Library, and Epistemonikos from inception to 23 July 2021.

Eligibility criteria: English language MAs of summary level data and MAs of IPD evaluating associations between environmental risk factors and incident NHL (overall and NHL subtypes).

Data extraction and synthesis: Summary effect estimates from MAs of summary level data comparing ever versus never exposure that were adjusted for the largest number of potential confounders were re-estimated using a random-effects model and classified as presenting non-significant, weak ($P<0.05$), suggestive ($P<10^{-3}$ and $>1000$ cases), highly suggestive ($P<10^{-6}$, $>1000$ cases, largest study reporting a significant association), or convincing ($P<10^{-6}$, $>1000$ cases, largest study reporting a significant association, $I^2<50\%$, 95% prediction interval excluding the null value, and no evidence of small study effects and excess significance bias) evidence. When the same exposures, exposure contrast levels, and outcomes were evaluated in MAs of summary level data and MAs of IPD from the International Lymphoma Epidemiology (InterLymph) Consortium, concordance in terms of direction, level of significance, and overlap of 95% confidence intervals (CIs) was examined. We assessed the methodological quality of the MAs of summary level data using the A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2 tool.

Results: We identified 85 MAs of summary level data reporting 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. Nearly all (79/85, 93%) MAs of summary level data were classified as having critically low quality. Most (225, 88%) associations presented either non-significant or weak evidence. The 11 (4%) associations presenting highly suggestive evidence were primarily for autoimmune or infectious disease-related risk factors. Only 1 association, history of celiac disease and risk of NHL, presented convincing evidence. Overall, 40 associations reported in MAs of summary level data were also evaluated in InterLymph MAs of IPD. Of these, 22 (55%) pairs were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. There were 28 (70%) pairs where the summary effect sizes from the MAs of IPD were more conservative.
**Conclusion:** This umbrella review suggests that there is a mass production of low-quality MAs of summary level data, many of which report weak associations between environmental risk factors and NHL, and highlights the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.

**Systematic review registration** PROSPERO CRD42020178010.
What is already known on this topic

- Observational studies have suggested that environmental risk factors, including clinical, occupational, and lifestyle exposures, may be associated with the risk of developing non-Hodgkin lymphoma.
- As a result of the large number of observational studies evaluating the impact of environmental risk factors on non-Hodgkin lymphoma, dozens of systematic reviews and meta-analyses of summary and individual participant level data have focused on synthesizing evidence and identifying potential risk factors.
- Little is known about: (1) the range, strength, and validity of associations between environmental risk factors and non-Hodgkin lymphoma reported in meta-analyses or (2) the concordance between meta-analyses of summary level data and meta-analyses of individual participant data evaluating the same associations.

What this study adds

- This umbrella review suggests that although a large range of environmental risk factors for non-Hodgkin lymphoma have been evaluated in meta-analyses, the vast majority of meta-analyses of summary level data are low quality and present either non-significant or weak associations.
- Overall, only half of the associations that were evaluated in both meta-analyses of summary level data and meta-analyses of individual participant data were in the same direction, had the same level of statistical significance, and had overlapping 95% confidence intervals.
- Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, this umbrella review highlights the need for improving not only primary studies but also evidence synthesis in the field of non-Hodgkin lymphoma etiology.
Introduction

Non-Hodgkin lymphoma (NHL), a lymphoid cancer that originates in white blood cells called lymphocytes, is the 9th leading cause of cancer death among both men and women.\(^1\) NHL accounts for nearly 90% of all lymphomas\(^2\) and is the most common hematologic malignancy in the world.\(^3\) Although NHL can be broadly categorized into two major groups (i.e., B-cell, T-cell/natural killer-cell lymphomas), it represents a diverse group of malignant disorders with dozens of subtypes.\(^4\) Evidence suggests that NHL is more common among older adults, men, and people with a first degree relative with NHL.\(^5,6\) However, despite substantial effort to identify NHL causes and risk factors over the past few decades, the exact etiology of NHL is unknown.\(^5\)

Epidemiological studies have suggested that environmental risk factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors, may be associated with the risk of developing NHL. In particular, several prominent potential risk factors proposed in the literature include viruses (e.g., Epstein-Barr virus infection),\(^7\) autoimmune diseases (e.g., Sjogren’s syndrome, celiac disease, and rheumatoid arthritis),\(^8-10\) and immune dysregulation (i.e., patients with a history of organ transplantation, acquired immunodeficiency syndromes (HIV/AIDS), or immunosuppressive medication treatment).\(^5,6,11\) However, given that these exposures and conditions are relatively rare,\(^11\) a broad range of additional environmental risk factors, including exposure to insecticides,\(^12\) red and processed meat consumption,\(^13\) and hair dye,\(^14\) have been evaluated and proposed as potential risk factors.

As a result of the large number of observational studies evaluating the impact of environmental risk factors on NHL, dozens of systematic reviews and meta-analyses (MAs) of summary level data have focused on synthesizing evidence and identifying the most promising risk factors. Moreover, the International Lymphoma Epidemiology (InterLymph) Consortium,\(^15\) a group of investigators who pool data from their completed or ongoing NHL case-control studies, have published multiple MAs of individual participant data (IPD) evaluating associations between various environmental risk factors and NHL.\(^16-18\) Although these MAs of IPD contain thousands of NHL cases and are strengthened by their ability to utilize raw data that are harmonized across multiple studies, they do not include evidence from case-control and cohort studies conducted by investigators outside of the InterLymph Consortium. Therefore, MAs of summary level data and MAs of IPD evaluating the same associations between environmental risk factors and NHL may sometimes lead to discordant results and conclusions.
To provide an overview of the range, strength, and validity of reported associations between environmental risk factors and NHL, we conducted an umbrella review of the evidence across published systematic reviews and MAs. In addition to summarizing the results, determining hints of biases, and assessing the quality of reviews, we evaluated the consistency between all associations reported in both MAs of summary level data and InterLymph MAs of IPD.

**Methods**

We conducted an umbrella review on the reported associations between environmental risk factors and the risk of NHL. Umbrella reviews are used to systematically identify and evaluate evidence reported in published systematic reviews and MAs. Our study protocol was pre-registered on the International prospective register of systematic reviews (CRD42020178010) and posted on Open Science Framework (https://osf.io/6g2ev/). We did not involve patients or members of the public when designing the question and study, interpreting the results, and/or drafting the manuscript.

**Database searches**

Working with an experienced medical librarian (KN), we developed and performed a comprehensive search of multiple databases: MEDLINE (Ovid), Embase (Ovid), Scopus, Web of Science Core Collection (as licensed at Yale University), Cochrane Library, and Epistemonikos from inception to July 24th 2020 (**Table 1 in Supplement 1**). In each database, we used three concepts: NHL, risk factors, and the study designs of interest (MAs, systematic reviews, and pooled analyses). The search strategy for NHL was based on the search strategy used in a published review. The study design search strategy used elements from a published search filter. Database limits were used to exclude conference papers and meeting abstracts. No language limits were used. Records were deduplicated in EndNote, the Yale Reference Deduplicator, and Covidence. No citation chaining was conducted.

On July 24th 2020, searches were run in each database and 14,753 references were identified. After deduplication in EndNote and Covidence, 8025 unique records were uploaded for screening. On July 23th 2021, all searches were rerun and deduplicated and 969 additional unique records were added to Covidence for manual screening. In total, our search retrieved 8994 unique records across all databases.

**Eligibility criteria**
We included English language systematic reviews, MAs of summary level data (i.e., MAs using effect estimates reported in individual studies), and MAs of IPD of observational studies evaluating associations between environmental risk factors and incident NHL (overall or any subtypes, eTable 2 in Supplement 1). We considered all non-genetic factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors that can affect a person’s health, as environmental risk factors. Systematic reviews and MAs were excluded if they primarily focused on genetic risk factors, evaluated risk factors for the treatment, relapse, remission, or prognosis of NHL patients, or examined NHL as a risk factor for other diseases (eText 1 in Supplement 1).

Two reviewers (XS and HZ) independently screened the titles and abstracts and then full-text versions of potentially eligible articles. Any disagreements or uncertainties were discussed with a third reviewer (JDW).

Data extraction
Data extraction was performed independently by two reviewers (XS and HZ), and a third reviewer (JDW) arbitrated all potential discrepancies. For each systematic review and MA, we recorded the first author, year of publication, article title, journal of publication, study design, population, examined exposures and their definitions, and examined outcomes and their definition (i.e., NHL or NHL subtypes). For all MAs of summary level data, we identified each unique exposure-outcome relationship and recorded the number of studies included, total sample size, number of cases, and study-specific adjusted relative risk estimates (e.g., relative risks, hazard ratios, or odds ratios) and corresponding 95% confidence intervals (CIs). For studies that considered multiple exposure contrast levels, control groups, and/or confounders, we prioritized the effect estimates comparing ever versus never exposure that were adjusted for the largest number of potential confounders. Whenever ever versus never exposures comparisons were not reported, we recorded the effect estimates comparing the highest versus lowest levels of exposures. When multiple MAs of summary level data were identified for the same environmental risk factor, we selected the effect estimates that were based on the largest number of component studies.

For systematic reviews with unique associations that were not investigated in MAs of summary level data, we recorded the number of studies identified, the reasons why MAs were not performed, and the main conclusions. Lastly, for all MAs of IPD, one author (JDW) identified the exposures, NHL subtypes, and number of NHL cases for: (1) all nominally
statistically significant ($P<0.05$) associations and (2) any associations that were also evaluated in MAs of summary level data.

**Quality Assessment**

Four reviewers (XS, HZ, YD, and JDW) evaluated the quality of all MAs of summary level data using A MeaSurement Tool to Assess Systematic Reviews (AMSTAR) 2. Any discrepancies were discussed and resolved by consensus. Based on the suggested rating scheme, the overall confidence in the results of the MAs of summary level data were classified as high, moderate, low, or critically low. We did not examine the quality of MAs of IPD.

**Statistical analysis**

First, we used a random-effects model, which allows for unexplained between-study heterogeneity on the effect of interest, with the between-study variance estimated using the DerSimonian and Laird (DL) estimator. When summary effect estimates were reported without a corresponding $P$ value, we used the 95% CIs to calculate the $P$ value using a previously described method. Next, we categorized the strength of the reported associations across five levels (Table 1), following previously established methodology. All associations with $P>0.05$ were classified as non-significant. Associations with $P<0.05$ and fewer than 1000 cases were classified as weak. Associations with $P<10^{-3}$ and at least 1000 cases were classified as suggestive. For associations with $P<10^{-6}$, at least 1000 cases, and $P<0.05$ for the largest component study, we sequentially evaluated 95% prediction intervals (PIs), presence of small study effects (Egger regression asymmetry test), and evidence of excess significance using the Ioannidis test. PIs provide a potential range of the true effect and incorporate the uncertainty of whether the observed effect will arise in future studies as well. $P<0.1$ for Egger’s test suggests the presence of small study effects (i.e. small studies are more prone to report larger or more significant results while larger studies tend to report more conservative results). The Ioannidis test estimates whether the observed number of studies with nominally statistically significant ($P<0.05$) results in a MA differs from the expected number of studies with nominally statistically significant studies. Associations with 95% PIs including the null, statistically significant Egger’s test ($P<0.1$), and/or evidence of excess significance were classified as highly suggestive. Associations with 95% prediction intervals excluding the null, non-statistically significant Egger’s test ($P>0.1$), and no evidence of excess significance were classified as convincing. Statistical analysis was conducted using metagen package in R version 4.1.0. (eTable 3 in Supplement 1).
### Table 1. Grading criteria for evidence categories

| Strength of association       | Description                                                                 |
|------------------------------|-----------------------------------------------------------------------------|
| Convincing (class I)         | Highly statistically significant association \( (P < 10^{-6}) \)              |
|                              | At least 1000 NHL cases                                                     |
|                              | Low/moderate proportion of total variability due to between-study variability \( (I^2 < 50\%) \) |
|                              | 95% prediction interval excluding the null value                            |
|                              | Largest study reporting a nominally statistically significant \( (P < 0.05) \) |
|                              | No evidence of small-study effects                                          |
|                              | No evidence of excess significance bias                                     |
| Highly suggestive (class II) | Highly statistically significant association \( (P < 10^{-6}) \)              |
|                              | At least 1000 NHL cases                                                     |
|                              | Largest study reporting a nominally statistically significant \( (P < 0.05) \) |
| Suggestive (class III)       | At least 1000 NHL cases                                                     |
| Weak (class IV)              | Statistically significant association \( (P < 10^{-3}) \)                    |
| Non-significant              | Nominally statistically significant association \( (P < 0.05) \)             |
|                              | Non-statistically significant associations \( (P > 0.05) \)                  |

\(^aP\) value for the association that calculated by random effects model.

NHL = non-Hodgkin lymphoma.

Statistical analysis was conducted using metagen package in R version 4.1.0. (eTable 3 in Supplement 1).

**Concordance between MAs of summary level data and InterLymph MAs of IPD**

When the same exposures, exposure contrast levels, and NHL subtypes were examined in MAs of summary level data and InterLymph MAs of IPD, two authors (XS and JDW) determined whether the effect estimates: (1) were in the same direction, (2) had overlapping 95% CIs, and/or (3) had the same level of statistical significance \( (P < 0.05 \) or \( P \geq 0.05) \). Associations with all three criteria fulfilled were classified as fully concordant. Lastly, we determined how often MAs of summary level data included at least one-third of the same component studies as the InterLymph MAs of IPD.

**Results**

https://mc.manuscriptcentral.com/bmjmedicine
Literature search

Among 16438 records identified through the literature search, 7444 were excluded as duplicates, leaving 8994 titles and abstracts for initial screening (Figure 1). 7970 records were excluded based on the title and abstract and 1024 were screened at the full text stage for inclusion. After excluding 904 records at the full text stage (eTable 1 in Supplement 2), our searches identified 85 MAs of summary level data evaluating 134 unique environmental risk factors and 8 systematic reviews evaluating 8 unique risk factors (eFigure 1 and eText 2 in Supplement 1 and eTable 2 in Supplement 2). In addition, we identified 27 MAs of IPD (Supplement 2), of which 24 (89%) were conducted by the InterLymph Consortium. More than one MA of summary level data was identified for 44 (44/134, 33%) risk factors (eTable 4 in Supplement 1). Among the MAs of summary level data selected based on the largest number of component studies, approximately half were also the most recently published (25/44, 57%).

Methodological quality

The vast majority of the 85 MAs of summary level data had overall confidence ratings of low (3, 4%) or critically low (79, 93%) according to the AMSTAR 2 tool. There were 2 (2%) where the overall confidence in the results was classified as moderate. Only 1 (1%), evaluating the association between tuberculosis and risk of NHL, had an overall confidence rating of high (eTable 3 in Supplement 2). The most common unfulfilled critical domains of the AMSTAR 2 tool were incomplete justification of excluded studies (74, 87%) and missing or no information about preregistered protocols (72, 85%).

MAs of summary level data

Among the 257 associations reported in the MAs of summary level data, 124 and 133 evaluated the impact of environmental risk factors on the risk of NHL overall and NHL subtypes, respectively. NHL subtypes included follicular lymphoma (FL; 43, 17%), diffuse large B-cell lymphoma (DLBCL; 35, 14%), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL; 31, 12%), T-cell lymphoma (TCL; 12, 5%), B-cell lymphoma (BCL; 4, 2%), marginal zone lymphoma (MZL; 2, 1%), endemic Burkitt Lymphoma (eBL; 1, 0.4%), Burkitt lymphoma (BL; 1, 0.4%), primary cutaneous lymphoma (PCL; 1, 0.4%). The most common exposure categories were dietary factors (90, 35%), medical histories and comorbidities (54, 21%), chemicals and pesticides (42, 16%), lifestyle factors (29, 11%), drugs, vaccinations, and medical procedures (30, 12%), and occupational (12, 5%). The median number of component studies per MA of summary level data was 5 (IQR 4-10). The median
number of NHL cases, among the 64 (75%) MAs reporting this information, was 1533 (IQR, 482-5872).

**Credibility criteria**

After re-estimating the 257 associations using a random-effects DL estimator and applying the credibility criteria, 145 (56%) were classified as presenting non-significant evidence (eTable 4 in Supplement 2). There were 80 (31%) nominally statistically significant ($P<0.05$) associations that were classified as presenting weak evidence. There were 20 (8%) statistically significant associations ($P<10^{-3}$), based on analyses with at least 1000 NHL cases, that were classified as presenting suggestive evidence. Only 12 (5%) associations were classified as presenting highly suggestive or convincing evidence, with a $P<10^{-6}$, at least 1000 cases, and a $P<0.05$ for the largest component study. The 11 highly suggestive associations were for history of renal transplantation and risk of NHL, rheumatoid arthritis and risk of NHL, primary Sjogren's syndrome and risk of NHL, systemic lupus erythematosus and risk of NHL, celiac disease and risk of TCL, tuberculosis and risk of NHL, hepatitis B virus (HBV) and risk of NHL and BCL, hepatitis C virus (HCV) and risk of NHL and DLBCL, and teaching as an occupation and risk of NHL (Table 2).

### Table 2. Environmental risk factors for non-Hodgkin lymphoma reported in meta-analyses of summary level data with convincing (Class I) and highly suggestive (Class II) evidence

| Risk factors category | Environmental risk factors | Level of comparison | Outcomes | Study type | Author year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random* | Largest study nominally significant ($P<0.05$) | 95% PI | Small study effect² | Strength of reported association³ |
|-----------------------|---------------------------|---------------------|-----------|------------|--------------|------------------------|--------------|--------------|------------------------------------------|-----------|---------------------------------------------|-------|---------------------|-------------------------|
| Renal transplant      | Renal transplant recipients vs general population | NHL | SR MA | Wang 2018 | 6 | 770 | SI R | 10.66 (8.54, 13.31) | 3.44 E-86 | Ye s | 80 | NA | NA | II |
| Autoimmune Rheumatology | Patients | NHL | SR | Sim | 16 | 153 | SI | 2.26 | 8.42 | Ye s | 96 | N | NA | II |
| Risk factors category | Environmental risk factors | Level of comparison | Outcome | Study type | Author year | No. of cases | Effect summary (95% CI) | Effect size | No. of studies | Effect | Strength of reported association |
|-----------------------|---------------------------|---------------------|---------|-----------|-------------|--------------|------------------------|------------|----------------|--------|--------------------------|
| HCV                   | HCV                       | NHL                 | SR      | Mas       | 2015        | 123 25       | 1.82 (1.81, 1.83)      | 1.62       | Ye a         | A      | 58.3 1.62 (E-34) |
| Sjogren's syndrome    | Patients vs general population | NHL | SR | MA | Liang 2014 | 11 | 162 13 | 3.75 (18.99) 5.4 (3.75, 7.72) 1.99 | Ye a | 74.3 | NA | NA II |
| celiac disease       | Patients vs general population | NHL | SR | MA | Cao 2015 | 12 | 166 | 5.4 (3.75, 7.77) 1.99 | Ye a | 74.3 | NA | NA II |
| Tuberculosis         | Patients vs general population | NHL | SR | MA | Leung 2020 | 8 | 239 0 | 1.61 (1.34, 1.94) 6.76 | Ye a | 50.3 | NA | NA II |
| HBV                  | HBV infected vs non-infected | NHL | SR | MA | Li 2018 | 58 | 537 14 | 2.50 (2.23, 2.83) 6.33 | Ye a | 77.3 | N A | NA II |
| HBV                  | HBV infected vs non-infected | BCL | SR | MA | Li 2018 | 20 | >10 00 | 2.46 (1.97, 3.07) 1.24 | Ye a | 62.9 | N A | NA II |
There was one association, between history of celiac disease and risk of NHL (OR 2.61, 95% CI 2.04 to 3.33; 110, 245 NHL cases from 8 individual studies), that was classified as presenting convincing evidence. Although the association had \( P < 10^{-6} \), at least 1000 cases, a nominally significant result for the largest component study, low/moderate proportion of total variability due to between-study variability (\( I^2 < 50\% \)), a 95% PI excluding the null, and no evidence of small study effects, we were unable to conduct the Ioannidis test due to the incomplete information reported about the component studies. Across all the 112 nominally statistically significant associations, 63 (56%) had relative risk values that were between 0.67 and 1.50.

**Systematic reviews**

We identified 8 systematic reviews without quantitative synthesis with 8 unique associations that were not investigated by MAs of summary level data (eText 2 in Supplement 1).

**MAs of IPD**

We identified 27 MAs of IPD, of which 24 were from the InterLymph Consortium. The 24 InterLymph MAs of IPD reported 715 nominally statistically significant (\( P < 0.05 \)) associations. Of these, 116 and 21 associations were based on analyses with at least 1000 NHL cases and had \( P < 10^{-3} \) and \( P < 10^{-6} \), respectively (Table 3 and eTable 5 in Supplement 2). Overall, the unique suggestive exposures categories were alcohol consumption on risk of DLBCL, MZL and NHL, history of Sjogren’s syndrome on risk of DLBCL, MZL and NHL, recreational sun exposure on risk of DLBCL, FL and NHL, and history of HCV on risk of DLBCL, MZL and NHL. Although the 3 non-InterLymph MAs of IPD examined 5 associations not reported in...
systematic reviews and/or MAs of the summary level data, including fish eaters and risk of NHL, vegetarians and vegans and risk of NHL, maternal age at the time of the child’s birth and risk of NHL, paternal age at the time of the child’s birth and risk of NHL, and leisure-time physical activity and risk of NHL, none were nominally statistically significant.

| NHL subtype       | At least 1000 cases and \( P<10^{-3} \) | At least 1000 cases and \( P<10^{-6} \) |
|-------------------|-----------------------------------------|-----------------------------------------|
| CLL/SLL           | Years since quitting cigarette smoking; printing pressmen | None |
| CLL/SLL/PLL/MCL   | Adult infectious mononucleosis            | None |
| DLBCL             | Alcohol; Any atopic disorder; Allergy; B and T-cell activating autoimmune diseases; HCV; Hay fever; Recreational sun exposure; Socioeconomic status (high vs low); BMI as young adult (25<30 kg/m\(^2\)); Rheumatoid arthritis; Blood transfusion; Weight | History of B-cell activating autoimmune disease; Sjogren’s syndrome; HCV; Young adult BMI (%25 kg/m\(^2\)); Years since quit cigarette smoking; Age first alcohol consumption (20-29 years vs. nondrinker); Current alcohol consumption status as of ~2 years prior to diagnosis/interview; |
| FL                | Blood transfusions; Young adult BMI (%25 kg/m\(^2\)); Recreational sun exposure (%); History of cigarette smoking (females); Current cigarette smoking; University and higher education teachers; Male height (100% vs. 60%); Any atopic disorder; | None |
| MZL               | Systemic lupus erythematosus; HCV; Peptic ulcer; Wine | History of B-cell activating autoimmune disease; Sjogren’s syndrome |
| HCL               | Current cigarette smoking | None |
| NHL               | Hormone replacement therapy; Systemic lupus erythematosus; HCV; Allergy; Food allergy; Hay fever; Blood transfusion; Height; Alcohol exposures; Recreational hair dye use; Socioeconomic status (high vs low); Secondary Sjogren’s syndrome; Childhood measles; | Sjogren’s syndrome; History of B-cell activating autoimmune disease; Hay fever; Young adult BMI (%25 kg/m\(^2\)); Recreational sun exposure (%Q3-Q4 hours/week); Recreational hair dye use (%Q3-Q4 hours/week); Beer, wine, and liquor; |

BMI=body mass index; CI=confidence interval; CLL=chronic lymphocytic leukemia; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; HCL=hairy cell leukemia; HCV=hepatitis C virus; MCL=mantle cell lymphoma; MZL=marginal zone lymphoma; NHL=non-Hodgkin lymphoma; SLL=small lymphocytic lymphoma; PLL=prolymphocytic leukemia.

* These were protective risk factors.
Consistency between MAs of summary level data and InterLymph MAs of IPD

There were 40 associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD (eTable 6 in Supplement 2 and eFigure 1 in Supplement 1). While 22 (55%) evaluated the impact of environmental risk factors on the risk of NHL overall, the other half (18, 45%) focused on various NHL subtypes (CLL/SLL, 5 (13%); DLBCL, 5 (13%); FL, 4 (10%); TCL, 3 (8%); MZL, 1 (3%)).

Overall, 22 of 40 (55%) of the associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. There were 10 (25%) pairs where the effect estimates were both statistically significantly increased, 3 (8%) where they were both statistically significantly decreased, 7 (18%) where they were both non-statistically significantly increased, and 2 (5%) where they were both non-statistically significantly decreased (Kappa=0.37, eTable 6 in Supplement 2 and eFigure 1 in Supplement 1). The 13 associations where the MAs of the summary level data and MAs of IPD effect estimates were both statistically significantly increased or decreased were for history of smoking and risk of TCL, history of drinking and risk of NHL, DLBCL, and FL, history of primary Sjogren's syndrome and risk of NHL, history of systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL, TCL and DLBCL, and history of HCV and risk of NHL, DLBCL, MZL and CLL/SLL. There were 28 (70%) pairs where the effect sizes from the MAs of IPD were more conservative than the effect sizes from the MAs of summary level data.
There were 4 suggestive associations reported in MAs of summary level data that were also evaluated in the InterLymph MAs of IPD. Of these, 3 associations from MAs of IPD had effect estimates in the same direction, had $P<10^{-3}$, and were based on analyses with at least 1000 NHL cases (i.e., history of psoriasis and risk of NHL, history of Herpes Zoster and risk of NHL, and history of farming as an occupation and risk of NHL). There were 8 highly suggestive associations reported in MAs of summary level data that were also evaluated in InterLymph MAs of IPD. Of these, 7 associations from the MAs of IPD had effect estimates in the same direction, had $P<10^{-6}$, and were based on analyses with at least 1000 NHL cases (i.e., history of rheumatoid arthritis and risk of NHL, history of primary Sjogren's syndrome and risk of NHL, history systemic lupus erythematosus and risk of NHL, history of celiac disease and risk of NHL and TCL, history of tuberculosis and risk of NHL, and history of HCV and risk of NHL).

There were 19 (48%) pairs where the MAs of summary level data included at least one-third of the same component studies as the InterLymph MAs of IPD. There was no difference in terms of concordance (direction, statistical significance of summary effect estimates and overlapping 95% CIs) between MAs of summary level data that included at least one-third versus fewer than one-third of the same component studies as the MAs of IPD (12/19 (63%) vs 10/21 (48%), $P=0.32$).

Discussion
In this umbrella review, we evaluated the range, strength, and validity of reported associations between environmental risk factors and NHL across 85 MAs of published observational studies. Overall, we identified 257 associations for 134 unique environmental risk factors and 10 NHL subtypes. The vast majority of the associations, including those evaluating various dietary, clinical, lifestyle, chemical, and occupational exposures, were classified as having either non-significant or weak evidence. More than half of the nominally significant associations were only marginally significant. Only 5% of the associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence. When the same associations were evaluated in MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Overall, effect sizes from MAs of IPD were more conservative. This umbrella review suggests that there is a mass production of low-quality MAs of summary level data reporting weak associations between environmental risk
factors and NHL. These findings highlight the need for improving not only primary studies but also evidence synthesis in this field. Moreover, given that many of the assessed risk factors are correlated, simultaneous consideration of multiple risk factors will be useful to understand which ones have the strongest, independent effects on NHL risk.

Although a wide range of environmental exposures have been evaluated and proposed as potential risk factors for NHL, our evaluation suggests that the only highly suggestive or convincing exposures proposed in MAs of summary level data and MAs of IPD are related to autoimmune and infectious diseases. In particular, the prominent autoimmune disease-related risk factors include history of celiac disease, rheumatoid arthritis, primary Sjogren's syndrome, and systemic lupus erythematosus. Although the exact mechanisms behind these associations remains unclear, many autoimmune disorders are characterized by chronic inflammation, which may intensify B cell or T cell activation and promote the development of lymphoma. Previous studies have also suggested that the dysfunction of some protein families, such as FAS and tumor necrosis factor, and the interplay between various immune cells, could be potential mechanisms. However, there is uncertainty when it comes to the temporality of these associations, with studies reporting that autoimmune diseases can occur during lymphoma.

Associations between viral and bacterial infections and NHL risk have been suggested for several decades. Different hypotheses for HCV-related lymphomagenesis have been proposed. For instance, chromosomal aberrations, including chromosome t(14;18) translocation, have been found to be associated with mixed cryoglobulinemia, a disorder most commonly caused by HCV infection and that can evolve into lymphoproliferative disorders. Furthermore, genetic variations, including Interleukin-10 polymorphisms, have also been proposed as a potential pathway between HCV infection and NHL susceptibility and development. Similar to autoimmune disease-related risk factors, it remains unclear whether these associations are driven by disease status, medication use, or disease-medication interactions. Considering how rare many of these autoimmune and infectious disease-related exposures are, future efforts are necessary to determine the impact of multiple environmental as well as non-environmental risk factors simultaneously.

Among 40 associations evaluated by both MAs of summary level data and InterLymph MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Unlike MAs of summary level data, MAs of IPD tend to focus on studies with more homogeneous designs and patient populations. Furthermore, MAs of IPD can allow for better harmonization of data across studies, more advanced one-stage meta-
analytical approaches, and analyses accounting for many exposure categories and potential confounders. Although the InterLymph MAs of IPD are particularly robust due to the large number of NHL cases and subtypes considered, MAs of IPD without systematic reviews may exclude evidence from high-quality case-control or cohort studies. For instance, the InterLymph analyses only included evidence from completed and ongoing case-control studies from consortium members. Furthermore, the InterLymph findings may be difficult to disentangle, with at least 700 nominally statistically significant associations among thousands of analyses conducted across different subtypes of NHL and exposure levels (e.g., different type/dosage of alcohol consumption). In the future, it will be necessary to monitor the consistency between MAs of summary level data and MAs of IPD, especially since approximately half of the MAs of summary level data had at least one-third of the same component studies as the MAs of IPD. In addition, authors of MAs should carefully evaluate whether any external studies can and should be included in their syntheses. Of interest, we observed that more than two thirds of the effect sizes were more conservative in the InterLymph MAs of IPD than in the MAs of summary level data. This may be a reflection of greater selective reporting bias in the corpus of studies available in the literature as compared with a set of studies participating in a consortium.

Our study suggests that nearly all MAs of summary level data evaluating associations between environmental risk factors and risk of NHL could be classified as having critically low quality according to the AMSTAR 2 tool. Previous umbrella reviews focused on the associations between environmental risk factors and health outcomes have noted similar concerns. However, the proportion of low or critically low-quality NHL reviews is higher than what has been observed among umbrella reviews for inflammatory bowel diseases, attention-deficit/hyperactivity disorder, eating disorders, early childhood caries, physical activity for academic achievement, and physical therapy for tendinopathy. These findings may not be surprising considering recent concerns about the mass production of systematic reviews. In the future, authors planning systematic reviews and MAs of summary level data of the associations between environmental exposures and NHL should adhere to reporting guidelines. Moreover, authors should also critically evaluate how their findings relate to existing MAs of IPD, focusing on the impact of different methods, populations, and other characteristics.

**Limitations**

Our umbrella review has several limitations. First, we did not identify potential environmental risk factors that were only examined in individual observational studies. Our
objective was to identify and summarize the associations that were reported by the MAs of summary level data, which already covered a wide space of diverse associations. Second, we did not evaluate the quality of individual studies included in the MAs of summary level data, the impact that individual studies have on the overall heterogeneity, the magnitude of the associations, or the potential role that residual/unmeasured confounding could have on associations. Individual risk of bias evaluations are outside the scope of umbrella reviews, and it is the expectation that MAs have already conducted these quality assessments. Third, we considered MAs that included cohort and case-control studies, and our assessments did not prioritize reviews of certain study designs or address differences across different study designs. Considering that certain NHL subtypes are rare, case-control studies may often be the most realistic study design to evaluate exposure histories.

Fourth, although umbrella reviews provide a comprehensive summary of the associations reported in MAs, the validity of the summary effect estimates is dependent on the quality of the individual MAs. Although we attempted to standardize associations using a random-effects DL estimator, we did not evaluate or re-conduct the literature searches for all potential exposure-outcome relationships. It has been shown that different approaches can impact the width of the CIs (i.e., Wald-type vs. Hartung-Knapp-Sidik-Jonkman). In our evaluation, however, it is unlikely that these differences would impact the associations that were classified as highly suggestive or convincing. Given that the Hartung-Knapp-Sidik-Jonkman method has been found to outperform the standard DL method in certain scenarios, future UR evaluations should consider this approach in their analyses.

Fifth, we did not calculate I^2, 95% PIs, Egger’s test, and excess significance test for non-significant and nominally statistically significant associations. Given the large number of associations identified, we prioritized these calculations for associations where these values were necessary to determine the strength of associations using the previously established classification system. It is also worth noting that other tests may be more appropriate (e.g., Peter’s test vs. Egger’s test to examine small study effects), and that I^2 values should not be used to make inferences about heterogeneity, as it does not measure heterogeneity directly, but rather the proportion of total variability due to between-study variability. However, the I^2 cut-off of 50% is a standard grading criterion for we used the same approaches as previous evidence in umbrella reviews.

Sixth, when summary effect estimates of multiple exposure contrast levels were reported, we focused on the risk estimates comparing ever versus never exposure (or...
comparing the highest versus lowest levels of exposures). Although we did not consider all potential contrast levels and dose-response relationships, our objective was to provide a universal overview of the relationships between examined risk factors and NHL. Specific dose-response relationships may nevertheless exist for certain associations, and they would need to be examined on a case-by-case basis. Seventh, we only identified the nominally statistically significant associations among the thousands of associations reported in InterLymph MAs of IPD. Eighth, by excluding non-English language reviews, we may have missed additional potential associations. However, we utilized the same approach as previous umbrella reviews that focused on risk factors for health outcome(s).

Ninth, MAs of IPD and MAs of summary level data can have different strengths and limitations, and our evaluation did not focus on comparing the potential quality of these types of studies. We also did not focus on the impact of different methods, populations, or other characteristics when comparing the consistency of the results between the two study types. Tenth, umbrella reviews are not intended to provide information about the likelihood that associations are causal. Lastly, when multiple MAs of summary level data evaluated the same exposures and outcomes, we selected the association based on the largest number of included studies. Although this approach does not ensure that the highest quality MAs are selected, this methodology has been utilized by previous umbrella reviews.

Conclusion

In this large-scale umbrella review, we identified dozens of MAs evaluating associations between environmental risk factors and NHL. However, the vast majority of MAs of summary level data were low quality and presented either non-significant or weak evidence. When the same associations were evaluated in MAs of summary level data and MAs of IPD, only half were in the same direction, had the same level of statistical significance, and had overlapping 95% CIs. Although several associations, primarily those for autoimmune and infectious disease-related risk factors, presented either highly suggestive or convincing evidence, these findings highlight the need for improving not only primary studies but also evidence synthesis in the field of NHL etiology.
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Transparency: The senior author (manuscripts guarantor) (JDW) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant registered) have been explained.

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### Table 1: Grading criteria for evidence categories

| Strength of association                  | Description                                                                 |
|------------------------------------------|------------------------------------------------------------------------------|
| **Convincing (class I)**                 | Highly statistically significant association ($P < 10^{-6}$)                  |
|                                          | At least 1000 NHL cases                                                      |
|                                          | Low/moderate proportion of total variability due to between-study variability ($I^2 < 50\%$) |
|                                          | 95% prediction interval excluding the null value                            |
|                                          | Largest study reporting a nominally statistically significant ($P < 0.05$)     |
|                                          | No evidence of small-study effects                                           |
|                                          | No evidence of excess significance bias                                     |
| **Highly suggestive (class II)**         | Highly statistically significant association ($P < 10^{-6}$)                  |
|                                          | Largest study reporting a nominally statistically significant ($P < 0.05$)     |
| **Suggestive (class III)**               | At least 1000 NHL cases                                                      |
|                                          | Statistically significant association ($P < 10^{-3}$)                         |
| **Weak (class IV)**                      | Nominally statistically significant association ($P < 0.05$)                  |
| **Non-significant**                      | Non-statistically significant associations ($P > 0.05$)                      |

* $P$-value for the association calculated by random-effects model.

NHL = non-Hodgkin lymphoma.
Environmental risk factors for non-Hodgkin lymphoma reported in meta-analyses of summary-level data with convincing (Class I) and highly suggestive (Class II) evidence

| Level of comparison | Outcome | Study type | Author/year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Large study nominally significant (P<0.05) | $I^2$ (%) | 95% CI of effect estimate |
|---------------------|---------|------------|-------------|------------------------|-------------|---------------|-----------------------------------|----------|------------------------------------------|-----------|--------------------------|
| Renal transplant    | Transplant recipients vs. general population | NHL | Wang 2018 | 6 | 770 | SIR | 10.66 (8.54, 13.31) | 0.005 | Yes | 80.2 | NA | NA |
| Rheumatoid arthritis | Patients vs general population | NHL | Simo 2015 | 16 | 1534 | SIR | 2.26 (1.82, 2.81) | 0.003 | Yes | 96 | NA | NA |
| Primary Sjögren's syndrome | Patients vs. general population | NHL | Liang 2014 | 11 | 1233 | RR | 1.76 (1.53, 1.99) | 0.003 | Yes | 58.8 | NA | NA |
| Systemic lupus erythematosus | Patients vs. general population | NHL | Cao 2015 | 12 | 166 | RR | 1.44 (1.25, 1.65) | 0.003 | Yes | 24.3 | NA | NA |
| Colitis disease | Patients vs. general population | NHL | Tio 2012 | 5 | 1102 | OR | 2.61 (2.04, 3.33) | 0.003 | Yes | 33.4 (1.57, 7.22) | No |
| Colitis disease | Patients vs. general population | TCI | Tio 2012 | 5 | 1353 | OR | 1.84 (1.25, 2.64) | 0.003 | Yes | 55.5 | NA | NA |
| Tuberculosis | Patients vs. general population | NHL | Leung 2020 | 5 | 2300 | RR | 1.61 (1.34, 1.94) | 0.003 | Yes | 50.2 | NA | NA |
| HBV infected vs. non-infected | HBV infected vs. non-infected | NHL | Li 2016 | 58 | 5334 | OR | 2.60 (2.23, 3.02) | 0.003 | Yes | 37.9 | NA | NA |
| HDV infected vs. non-infected | HDV infected vs. non-infected | BCL | Li 2015 | 20 | 1000 | OR | 2.46 (1.97, 3.07) | 0.003 | Yes | 62.0 | NA | NA |
| Environmental risk factors | Level of comparison | Outcome | Study type | Author/year | No. of primary studies | No. of cases | Effect measure | Random effects summary effect size (95% CI) | P random | Large study nominally significant (P<0.05) | $I^2$ (%) | 95% CI of effect estimate |
| HCV infected vs. non-infected | HCV infected vs. non-infected | NHL | Mane 2010 | 22 | 2307 | OR | 3.36 (2.49, 4.52) | 0.003 | Yes | 68 | NA | NA |
| HCV infected vs. non-infected | Patients vs. general population | DHB | MA 2006 | 8 | 1020 | RR | 2.65 (1.88, 3.74) | 0.003 | Yes | 29.8 | 0.006 | NA |
Table 3. Suggestive risk factors and protective factors identified in meta-analyses of individual patient data from International Lymphoma Epidemiology Consortium

| NHL subtype | At least 1000 cases and P<10^-4 | At least 1000 cases and P<10^-6 |
|-------------|----------------------------------|----------------------------------|
| CLL/SLL     | Years since quitting cigarette smoking, printing pressman | None |
| CLL/SLL/PLL/MCL | Alcohol, Any atopic disorder, Allergy, B and T cell activating autoimmune disease, HCV, Hay fever, Recreational sun exposure, Socioeconomic status (high vs low), BMI as young adult (25<30 kg/m^2), Rheumatoid arthritis, Blood transfusion, Weight, Occupation | History of B cell activating autoimmune disease, Siogren’s syndrome, HCV, Young BMI (%25 kg/m^2), Years since quitting smoking, Age first alcohol consumption (20-29 years vs. nondrinker), Current alcohol consumption status as of ~2 years prior to diagnosis/interview |
| DLBCL       | Blood transfusion, Young adult BMI (%25 kg/m^2), Recreational sun exposure, History of cigarette smoking (female), Current cigarette smoking, University and higher education teachers, Male height (100% vs. 60%), Any atopic disorder | None |
| FL          | Blood transfusion, Young adult BMI (%25 kg/m^2), Recreational sun exposure, History of cigarette smoking (female), Current cigarette smoking, University and higher education teachers, Male height (100% vs. 60%), Any atopic disorder | None |
| MZL         | Systemic lupus erythematosus, HCV, Peptic ulcer, Wine | History of B cell activating autoimmune disease, Siogren’s syndrome |
| HCL         | Current cigarette smoking | None |
| NHL         | Hormone replacement therapy, Systemic lupus erythematosus, HCV, Allergy, Food allergy, Hay fever, Blood transfusion, Height, Alcohol exposure, Recreational hair dye use, Socioeconomic status (high vs low), Secondary Sjoogren’s syndrome, Childhood measles | Siogren’s syndrome, History of B cell activating autoimmune disease, Hay fever, Young BMI (%25 kg/m^2), Recreational sun exposure (%Q3 Q4 hours/week), Recreational hair use (%Q3 Q4 hours/week), Beer, wine, and liquor |

BMI, body mass index; CI, confidence interval; CLL, chronic lymphocytic leukemia; DLBCL, diffuse large B cell lymphoma; FL, follicular lymphoma; HCL, hairy cell leukemia; HCV, hepatitis C virus; HLA, human leukocyte antigen; MA, meta-analysis; NA, not available; NHL, non-Hodgkin lymphoma; OR, odds ratio; PI, prediction interval; SIR, standardized incidence ratio; SRMA, systematic review and meta-analysis; RR, risk ratio; TCL, T-cell lymphoma.

a These were protective risk factors.
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

Supplementary materials summary

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eTable 1: Search strategy
Database searches, 2021-07-23
Searches on the Ovid platform can be rerun at https://tools.ovid.com/ovidtools/launcher.html

| Ovid MEDLINE(R) ALL <1946 to July 22, 2021> |  |
|-------------------------------------------|--|
| 1 [Xiaoting Shi]                          | 0 |
| 2 [concept two: SRs]                      | 0 |
| 3 (systematic adj4 review).ti.            | 16047 |
| 4 systematic review.pt.                   | 3 |
| 5 Cochrane Database of Systematic Reviews.jn. and review.pt. | 16216 |
| 6 [approach c: based on Lee 2012]         | 2 |
| 7 medline.tw. or systematic review.ti. or meta-analysis.pt. or pubmed.tw. | 13658 |
| 8 [from our previous searches]            | 0 |
| 9 (pooled analysis or pooled analyses).mp. | 35748 |
| 10 (metaanalysis or meta-analysis).af.    | 3 |
| 11 [NHL concept]                          | 0 |
| 12 neoplasms/ or lymphoma/ or exp lymphoma, non-hodgkin/ | 58950 |
| 13 [alternative based on https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004024.pub2/appendices#CD004024-sec1-0011] | 0 |
| 14 *Lymphoma/                             | 36024 |
| 15 *hematologic neoplasms/                | 10823 |
| 16 lymphom*.mp.                           | 25857 |
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|   |   |
|---|---|
| 17 | non-hodgkin*.mp. | 58024 |
| 18 | nonhodgkin*.mp. | 136 |
| 19 | (non adj1 hodgkin*).mp. | 58025 |
| 20 | nhl.mp. | 13936 |
| 21 | (hemato* adj1 malign*).mp. | 26969 |
| 22 | (haemato* adj1 malign*).mp. | 5497 |
| 23 | (hemato* adj1 neoplas*).mp. | 16617 |
| 24 | (haemato* adj1 neoplas*).mp. | 415 |
| 25 | or/12,14-24 | 72171 |
| 26 | risk/ or protective factors/ or risk factors/ | 99999 |
| 27 | (risk* or protective factor*).mp. | 28997 |
| 28 | 26 or 27 | 28997 |
| 29 | or/3-10 | 42317 |
| 30 | 25 and 28 and 29 | 5543 |

Embase <1974 to 2021 July 22>

|   |   |
|---|---|
| 1 | [NHL concept] | 0 |
| 2 | neoplasm/ or lymphoma/ or lymphatic system tumor/ or exp nonhodgkin lymphoma/ | 67263 |
| 3 | *Lymphoma/ | 45821 |
| 4 | hematologic malignancy/ | 35985 |
| 5 | lymphom*.mp. | 35048 |
| 6 | non-hodgkin*.mp. | 60548 |
| 7 | nonhodgkin*.mp. | 62197 |
| 8 | (non adj1 hodgkin*).mp. | 60551 |
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| 9  | nhl.mp.                                                   | 25440 |
| 10 | (hemato* adj1 malign*).mp.                               | 63015 |
| 11 | (haemato* adj1 malign*).mp.                              | 9491  |
| 12 | (hemato* adj1 neoplas*).mp.                              | 4590  |
| 13 | (haemato* adj1 neoplas*).mp.                             | 689   |
| 14 | or/2-13                                                   | 82181 |
| 15 | exp risk/ or protection/                                 | 27149 |
| 16 | (risk* or protective factor*).mp.                        | 43275 |
| 17 | 15 or 16                                                  | 43681 |
| 18 | [study design concept]                                   | 0     |
| 19 | (systematic adj4 review).ti.                             | 19182 |
| 20 | Cochrane Database of Systematic Reviews.jn. and review.pt.| 11247 |
| 21 | medline.tw. or systematic review.ti. or pubmed.tw.       | 38012 |
| 22 | (pooled analysis or pooled analyses).mp.                 | 19038 |
| 23 | (metaanalysis or meta-analysis).af.                      | 32779 |
| 24 | or/19-23                                                  | 56318 |
| 25 | 14 and 17                                                 | 15598 |
| 26 | limit 25 to meta analysis                                | 3382  |
| 27 | limit 25 to systematic review                            | 3023  |
| 28 | 25 and 24                                                 | 6739  |
| 29 | 26 or 27 or 28                                           | 7272  |
| 30 | limit 29 to conference abstract status                   | 2936  |
| 31 | 29 not 30                                                 | 4336  |
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| Scopus | ((TITLE-ABS-KEY (lymphom* OR non-hodgkin* OR (non W/1 hodgkin*) OR nhl OR ((hemato* OR haemato*) W/1 (malign* OR neoplas*))) AND (TITLE-ABS-KEY (risk* OR protective-factor*)))) AND (TITLE-ABS-KEY ((systematic W/4 review) OR medline OR pubmed OR "pooled analysis" OR "pooled analyses" OR metaanalysis OR meta-analysis)) AND (EXCLUDE (DOCTYPE, "cp")) | 3173 |
| Web of Science Core Collection | TS=(lymphom* OR non-hodgkin* OR (non NEAR/1 hodgkin*) OR nhl OR ((hemato* OR haemato*) NEAR/1 (malign* OR neoplas*)) AND TS=(risk* OR protective-factor*) AND TS=((systematic NEAR/4 review) OR medline OR pubmed OR "pooled analysis" OR "pooled analyses" OR metaanalysis OR meta-analysis) | 2417 |
| Cochrane Library | Refined by excluding the Web of Science document types proceedings papers and meeting abstracts | |
| ID | Search | Hits |
| #1 | ((systematic NEAR/4 review)):ti OR (systematic review):pt OR (medline or pubmed or "pooled analysis" or "pooled analyses" or metaanalysis or meta-analysis):ti,ab,kw (Word variations have been searched) | 29396 |
| #2 | MeSH descriptor: [Neoplasms] this term only | 6376 |
| #3 | MeSH descriptor: [Lymphoma] this term only | 1369 |
| #4 | MeSH descriptor: [Lymphoma, Non-Hodgkin] explode all trees | 2056 |
| #5 | MeSH descriptor: [Hematologic Neoplasms] this term only | 466 |
| #6 | (lymphom* or non-hodgkin* or nonhodgkin* or (non NEAR/1 hodgkin*) or nhl or (hemato* NEAR/1 malign*) or (haemato* NEAR/1 malign*) or (hemato* NEAR/1 neoplas*) or (haemato* NEAR/1 neoplas*)):ti,ab,kw | 14144 |
| #7 | #2 or #3 or #4 or #5 or #6 | 20192 |
| #8 | (risk* or (protective NEAR/1 factor*)):ti,ab,kw | 25391 |
| #9 | MeSH descriptor: [Risk] this term only | 3322 |
| #10 | MeSH descriptor: [Protective Factors] this term only | 135 |
| #11 | MeSH descriptor: [Risk Factors] this term only | 24955 |
| #12 | #8 or #9 or #10 or #11 | 25391 |
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| #13 | #1 and #7 and #12 | 273 |
|-----|-------------------|-----|
| Epistemikon | Limited to reviews (not trials) | 167 |

| SR filter | (title:(lymphoma*) OR abstract:(lymphoma*)) AND (title:(risk* OR protective) OR abstract:(risk* OR protective)) | 736 |
| broad synthesis filter | (title:(lymphoma*) OR abstract:(lymphoma*)) AND (title:(risk* OR protective) OR abstract:(risk* OR protective)) | 24 |
| no filter | (title:(lymphoma*) OR abstract:(lymphoma*)) AND (title:(risk* OR protective) OR abstract:(risk* OR protective)) | 42 |
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**eTable 2: NHL subtypes**

| Category                        | Subtypes                                                                 | Eligibility as NHL |
|---------------------------------|--------------------------------------------------------------------------|--------------------|
| **Mature B-cell neoplasms**     | Chronic lymphocytic leukemia/small lymphocytic lymphoma                   | Yes                |
|                                 | Monoclonal B-cell lymphocytosis*                                         | No                 |
|                                 | B-cell prolymphocytic leukemia                                            | Yes                |
|                                 | Splenic marginal zone lymphoma                                            | Yes                |
|                                 | Hairy cell leukemia                                                       | Yes                |
|                                 | Splenic B-cell lymphoma/leukemia, unclassifiable                         | Yes                |
|                                 | Splenic diffuse red pulp small B-cell lymphoma                           | Yes                |
|                                 | Hairy cell leukemia-variant                                              | Yes                |
|                                 | Lymphoplasmacytic lymphoma                                               | Yes                |
|                                 | Waldenström macroglobulinemia                                             | Yes                |
|                                 | Monoclonal gammopathy of undetermined significance (MGUS), IgM*          | No                 |
|                                 | μ heavy-chain disease                                                     | No                 |
|                                 | γ heavy-chain disease                                                     | No                 |
|                                 | α heavy-chain disease                                                     | No                 |
|                                 | Monoclonal gammopathy of undetermined significance (MGUS), IgG/A*        | No                 |
|                                 | Plasma cell myeloma                                                      | No                 |
|                                 | Solitary plasmacytoma of bone                                             | No                 |
|                                 | Extraosseous plasmacytoma                                                | No                 |
|                                 | Monoclonal immunoglobulin deposition diseases*                           | No                 |
|                                 | Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue    | Yes                |
|                                 | (MALT lymphoma)                                                          |                    |
|                                 | Nodal marginal zone lymphoma                                              | Yes                |
|                                 | Pediatric nodal marginal zone lymphoma                                    | Yes                |
|                                 | Follicular lymphoma                                                      | Yes                |
|                                 | In situ follicular neoplasia*                                             | Yes                |
|                                 | Duodenal-type follicular lymphoma*                                        | Yes                |
|                                 | Pediatric-type follicular lymphoma*                                       | Yes                |
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| Category | Subtypes                                                                 | Eligibility as NHL |
|----------|---------------------------------------------------------------------------|--------------------|
|          | Large B-cell lymphoma with IRF4 rearrangement*                           | Yes                |
|          | Primary cutaneous follicle center lymphoma                                | Yes                |
|          | Mantle cell lymphoma                                                     | Yes                |
|          | In situ mantle cell neoplasia*                                           | Yes                |
|          | Diffuse large B-cell lymphoma (DLBCL), NOS                               | Yes                |
|          | Germinal center B-cell type*                                              | Yes                |
|          | Activated B-cell type*                                                   | Yes                |
|          | T-cell/histiocyte-rich large B-cell lymphoma                             | Yes                |
|          | Primary DLBCL of the central nervous system (CNS)                        | Yes                |
|          | Primary cutaneous DLBCL, leg type                                         | Yes                |
|          | EBV+ DLBCL, NOS*                                                         | Yes                |
|          | EBV+ mucocutaneous ulcer*                                                | No                 |
|          | DLBCL associated with chronic inflammation                               | Yes                |
|          | Lymphomatoid granulomatosis                                              | No                 |
|          | Primary mediastinal (thymic) large B-cell lymphoma                        | Yes                |
|          | Intravascular large B-cell lymphoma                                       | Yes                |
|          | ALK+ large B-cell lymphoma                                               | Yes                |
|          | Plasmablastic lymphoma                                                   | Yes                |
|          | Primary effusion lymphoma                                                | Yes                |
|          | HHV8+DLBCL, NOS*                                                         | Yes                |
|          | Burkitt lymphoma                                                         | Yes                |
|          | Burkitt-like lymphoma with 11q aberration*                              | Yes                |
|          | High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements*| Yes                |
|          | High-grade B-cell lymphoma, NOS*                                         | Yes                |
|          | B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma | Yes |
|          | Double hit/triple hit lymphoma                                           | Yes                |
|          | T-cell prolymphocytic leukemia                                           | Yes                |
|          | T-cell large granular lymphocytic leukemia                               | Yes                |
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| Category                        | Subtypes                                                                 | Eligibility as NHL |
|---------------------------------|---------------------------------------------------------------------------|--------------------|
| Chronic lymphoproliferative disorder of NK cells | Yes                                                                 |                    |
| Aggressive NK-cell leukemia      | Yes                                                                 |                    |
| Systemic EBV+ T-cell lymphoma of childhood* | Yes                                                                |                    |
| Hydroa vacciniforme–like lymphoproliferative disorder* | Yes                                                                |                    |
| Adult T-cell leukemia/lymphoma  | Yes                                                                 |                    |
| Extranodal NK-/T-cell lymphoma, nasal type | Yes                                                                |                    |
| Enteropathy-associated T-cell lymphoma | Yes                                                                |                    |
| Monomorphic epitheliotropic intestinal T-cell lymphoma* | Yes                                                                |                    |
| Indolent T-cell lymphoproliferative disorder of the GI tract* | No                                                                 |                    |
| Hepatosplenic T-cell lymphoma    | Yes                                                                 |                    |
| Subcutaneous panniculitis-like T-cell lymphoma | Yes                                                                |                    |
| Mycosis fungoides               | Yes                                                                 |                    |
| Sézary syndrome                 | Yes                                                                 |                    |
| Primary cutaneous CD30+ T-cell lymphoproliferative disorders | Yes                                                                |                    |
| Lymphomatoid papulosis          | No                                                                   |                    |
| Primary cutaneous anaplastic large cell lymphoma | Yes                                                                |                    |
| Primary cutaneous γδ T-cell lymphoma | Yes                                                                |                    |
| Primary cutaneous CD8+aggressive epidermotropic cytotoxic T-cell lymphoma | Yes                                                                |                    |
| Primary cutaneous acral CD8+T-cell lymphoma* | Yes                                                                |                    |
| Primary cutaneous CD4+small/medium T-cell lymphoproliferative disorder* | No                                                                 |                    |
| Peripheral T-cell lymphoma, NOS  | Yes                                                                 |                    |
| Angioimmunoblastic T-cell lymphoma | Yes                                                                |                    |
| Follicular T-cell lymphoma*      | Yes                                                                 |                    |
| Nodal peripheral T-cell lymphoma with TFH phenotype* | Yes                                                                |                    |
| Anaplastic large-cell lymphoma, ALK+ | Yes                                                                |                    |
| Anaplastic large-cell lymphoma, ALK−* | Yes                                                                |                    |
| Breast implant–associated anaplastic large-cell lymphoma* | Yes                                                                |                    |
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| Category          | Subtypes                      | Eligibility as NHL |
|-------------------|-------------------------------|--------------------|
|                   | Acute lymphoblastic leukaemia (ALL) | No                 |

Footnotes:
*Changes from the 2008 classification.
NOS: not otherwise specified
Information source: 2016 WHO classification of mature lymphoid neoplasms (https://pubmed.ncbi.nlm.nih.gov/26980727/)
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eTable 3: R code

```
# read in data_Behcet Disease
meta1 = read_excel("RR_effect_sizes_Behcet Disease_#4206.xlsx")
head(meta1)

# conduct main analysis
meta2<-metagen(meta1$LNRR,meta1$SE,
sm="R",studlab=paste(lastname,publication_year)
 ,data=meta1,method.bias="Egger",prediction = TRUE,
 level.predict =0.95)
summary(meta2)

# create forest plot, funnel plot
forest(meta2)
funnel(meta2)
meta2$pval.random

# conduct egger's test
metabias(meta2,method.bias="Egger",plotit=TRUE, correct= TRUE, k=3)
```
Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

**eTable 4: Overlapping meta-analyses of summary level data**

| Environmental risk factors                      | Largest review (First author, year) | Number of overlapping meta-analyses | Number of primary studies in the largest meta-analyses | Most recent (Y/N) | Highest impact factor one (Y/N) |
|------------------------------------------------|-------------------------------------|-------------------------------------|--------------------------------------------------------|-------------------|--------------------------------|
| **Dietary factors**                             |                                     |                                     |                                                        |                   |                                 |
| Red meat                                        | Yang 2015                           | 4                                   | 18                                                     | N                 | N                              |
| Processed meat                                  | Yang 2015                           | 4                                   | 18                                                     | N                 | N                              |
| White meat/poultry                             | Dong 2017                           | 3                                   | 10                                                     | N                 | N                              |
| Fish                                            | Caini 2016                          | 3                                   | 11                                                     | N                 | N                              |
| Fruit and vegetable                            | Chen 2013                           | 2                                   | 4                                                      | N                 | Y                              |
| Fruit                                           | Chen 2013                           | 2                                   | 13                                                     | N                 | Y                              |
| Vegetable                                       | Chen 2013                           | 2                                   | 13                                                     | N                 | Y                              |
| Eggs                                            | Caini 2016                          | 2                                   | 10                                                     | N                 | N                              |
| Total dairy products                            | Wang 2016                           | 2                                   | 7                                                      | Y                 | Y                              |
| Milk                                            | Wang 2016                           | 3                                   | 16                                                     | N                 | Y                              |
| Cheese                                          | Wang 2016                           | 2                                   | 10                                                     | Y                 | Y                              |
| Vitamin D                                       | Lu 2014                             | 2                                   | 6                                                      | N                 | N                              |
| **Drugs, vaccinations and procedures**          |                                     |                                     |                                                        |                   |                                 |
| Aspirin                                         | Ye 2015                             | 2                                   | 10                                                     | Y                 | Y                              |
| Non-steroidal anti-inflammatory drugs           | Ye 2015                             | 2                                   | 13                                                     | Y                 | N                              |
| Statin                                          | Ye 2017                             | 3                                   | 9                                                      | Y                 | Y                              |
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| Environmental risk factors                      | Largest review (First author, year) | Number of overlapping meta-analyses | Number of primary studies in the largest meta-analyses | Most recent (Y/N) | Highest impact factor one (Y/N) |
|------------------------------------------------|-------------------------------------|-------------------------------------|------------------------------------------------------|------------------|--------------------------------|
| **Non-dietary lifestyle factors**               |                                     |                                     |                                                      |                  |                                |
| Physical activity                               | Davies 2020                         | 3                                   | 17                                                   | Y                | Y                              |
| Hair dye                                        | Qin 2019                            | 2                                   | 16                                                   | Y                | N                              |
| Petrochemical exposure                          | Jephcote 2020                       | 2                                   | 9                                                    | Y                | Y                              |
| Maternal smoking                                | Antonopoulos 2011                   | 2                                   | 7                                                    | N                | Y                              |
| Ever smoking                                    | Sergentanis 2013                    | 2                                   | 33                                                   | Y                | N                              |
| Ever drinking                                   | Tramacere 2012                      | 3                                   | 29                                                   | N                | Y                              |
| Heavy drinking                                  | Tramacere 2012                      | 2                                   | 6                                                    | N                | Y                              |
| **Medical history and comorbid diseases**       |                                     |                                     |                                                      |                  |                                |
| Rheumatoid arthritis                            | Simon 2015                          | 2                                   | 17                                                   | Y                | N                              |
| Primary Sjogren’s syndrome                      | Liang 2014                          | 2                                   | 11                                                   | Y                | Y                              |
| Systemic lupus erythematosus                    | Cao 2015                            | 3                                   | 12                                                   | N                | N                              |
| Psoriasis                                       | Vaengebjerg 2020                    | 3                                   | 8                                                    | Y                | Y                              |
| Type 1 diabetes                                 | Wang 2020                           | 2                                   | 3                                                    | Y                | N                              |
| Celiac disease                                  | Tio 2012                            | 2                                   | 8                                                    | Y                | Y                              |
| Systemic sclerosis                              | Zhang 2013                          | 2                                   | 4                                                    | Y                | N                              |
### Environmental risk factors for non-Hodgkin lymphoma: an umbrella review and comparison of meta-analyses of summary and individual participant level data

| Environmental risk factors | Largest review (First author, year) | Number of overlapping meta-analyses | Number of primary studies in the largest meta-analyses | Most recent (Y/N) | Highest impact factor one (Y/N) |
|----------------------------|-------------------------------------|-------------------------------------|-------------------------------------------------------|------------------|-------------------------------|
| Asthma                     | Yang 2017                           | 2                                   | 15                                                    | Y                | Y                             |
| Type 2 diabetes            | Castillo 2012                       | 8                                   | 21                                                    | N                | N                             |
| Overweight                 | Larsson 2007                        | 11                                  | 16                                                    | N                | Y                             |
| Obesity                    | Larsson 2007                        | 11                                  | 16                                                    | N                | Y                             |
| Hepatitis B virus          | Li 2018                             | 5                                   | 58                                                    | N                | N                             |
| Hepatitis C virus          | Masarone 2019                       | 4                                   | 27                                                    | Y                | Y                             |
| **Chemicals and pesticides** |                                      |                                      |                                                       |                  |                               |
| Benzene                    | Kane 2010                           | 4                                   | 24                                                    | Y                | N                             |
| Polychlorinated biphenyls  | Catalani 2019                       | 3                                   | 30                                                    | Y                | N                             |
| Trichloroethylene          | Scott 2011                          | 3                                   | 17                                                    | N                | N                             |
| Glyphosate                 | Boffetta 2021                       | 4                                   | 6                                                     | Y                | N                             |
| 2,4-Dichlorophenoxyacetic acid | Smith 2017                        | 3                                   | 11                                                    | Y                | Y                             |
| **Occupation**             |                                      |                                      |                                                       |                  |                               |
| Female flight attendant    | Buja 2006                           | 4                                   | 3                                                     | Y                | N                             |
| Farmer                     | Boffetta 2007                       | 4                                   | 50                                                    | Y                | N                             |
| Firefighter                | Jalilian 2019                       | 3                                   | 14                                                    | Y                | Y                             |
| Petroleum refinery worker  | Schnatter 2018                      | 2                                   | 16                                                    | Y                | N                             |

Y=Yes; N=No.
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eFigure 1: Scatterplot of summary effect estimates in meta-analyses of summary level data and meta-analyses of individual participant data

CI=confidence interval.
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eText 1: Eligibility criteria

Eligibility criteria for systematic reviews and (or) meta-analyses

General inclusion criteria

Language: English only.

Study types: Systematic review and (or) meta-analysis (referred as ‘Review studies’ in the following contents).

Study designs included in review studies: Observational epidemiological studies.

Study subjects: Human only.

General exclusion criteria

Review studies that:

1. Focus on genetic risk factors3 for non-Hodgkin lymphoma (NHL)
2. Focus on biomarkers4 for NHL
3. Focus on risk factors for treatment, relapse, remission, or prognosis on NHL patients
4. Examine NHL as a risk factor for other diseases
5. Focus on cancer, hematological cancers, lymphoma, or any broader spectrum of diseases, but fail to provide specific data for NHL5
6. Only include experimental studies
7. Focus on NHL as a metastasis/secondary cancer of other primary cancers
8. Focus on NHL in a particular population but fail to provide detailed information on environmental risk factors6
9. Investigate the prevalence/incidence of NHL

---

1 Cohort studies or case control studies only
2 Review studies mixed with human and animal subjects will be checked in details at full text screening stage
3 Including genetic polymorphisms, family history/familial aggregation
4 Any substance, structure, or process that can be measured in the body or its products that can influence or predict the incidence of outcome or disease. Ref: http://www.inchem.org/documents/ehc/ehc/ehc222.htm (accessed 24th April, 2020)
5 This may be unclear at the title-abstract screening, therefore when in doubt, two researchers will send it on to the full text screening
6 For example, NHL in indigenous population, or men who have sex with men (MSM)
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Besides the aforementioned eligibility criteria, based on our definition of environmental risk factors, personal medical history and comorbidities (excluding metastasis of tumors) will be considered eligible in our study. In addition to the 8th General exclusion criteria, studies focus on NHL on a particular occupational population would be included since occupation can act as proxy for certain environmental exposures.

**Study types, exposures and outcome definition**

**Systematic reviews and (or) Meta-analyses of summary level data and individual participant data:**

The eligible study types in our study are systematic reviews (SRs), meta-analyses (MAs), systematic reviews and meta-analyses (SRMAs) or pooled analyses. To be eligible, SRs and SRMAs must have performed a systematic search in at least one bibliographic database. SRs, MAs and SRMAs should clearly define themselves as systematic reviews and(or) meta-analyses. For SRs in particular, we will only include exposure-outcome relationships (i.e., associations) that have not been investigated in MAs or SRMAs.

In terms of pooled analyses, the primary goal for including pooled analyses in our study is to incorporate the valuable pooled information of individual level data from scientific institutes on NHL and its subtypes, such as The International Lymphoma Epidemiology Consortium (InterLymph) and to add to the evidence for meta-analyses on certain risk factors.

**Environmental risk factors:**

We define environmental risk factors as a broad concept of non-genetic factors, including physical, natural, chemical, biological, psychosocial, occupational, and lifestyle factors that can affect a person’s health, as environmental risk factors.

**Outcome of interest:**

Our study outcome is non-Hodgkin lymphoma, including its subtypes (eTable 2 in Supplement 1). The classification of NHL subtypes was consulted and confirmed by an epidemiologist on NHL from InterLymph consortia. We will identify with the definition/diagnostic criteria of NHL from the original review studies.

**References**

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---

7 An open scientific forum for epidemiologic research in non-Hodgkin's lymphoma and a group of international investigators who have completed or have ongoing case-control studies and who discuss and undertake research projects that pool data across studies or otherwise undertake collaborative research. Ref: https://epi.grants.cancer.gov/interlymph/ (accessed 24th April, 2020)
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4. Prüss-Ustün A, van Deventer E, Mudu P, et al. Environmental risks and non-communicable diseases. BMJ. 2019;364:l265.
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eText 2: Systematic reviews without quantitative synthesis

Systematic reviews

We identified 8 systematic reviews without quantitative synthesis with 8 unique associations that were not investigated by meta-analyses of the published literature (Supplement). Among them, 6 (75.0%) concluded that there were weak or non-statistically significant associations between the examined risk factors (Omega-3 fatty acids,1 sugar intake,2 artificial sweetener consumption,3 hazardous waste,4 preterm birth,5 and prenatal/postnatal Diagnostic X-rays and childhood6) and NHL risk. Two (25%) additional systematic reviews suggested possible associations between Gaucher disease7 and NHL risk and breast implants and anaplastic large cell lymphoma risk.8 Half (4, 50.0%) of the systematic reviews outlined that quantitative analyses were not conducted due to high levels of heterogeneity and/or a small number of eligible studies.1,3,6,7 The remaining 4 (50.0%) systematic reviews did not provide any reasons for not conducting quantitative analyses.2,4,5,8

Exclusion reasons

Among the 1024 records screened at the full text level, 904 were excluded, mostly because they were for the wrong topic (442, 48.9%), they had the wrong study design (240, 26.5%), or they were not the largest meta-analysis of the published literature for a specific association (102, 11.3%).
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1. MacLean CH, Newberry SJ, Mojica WA, Khanna P, Issa AM, Suttrop MJ, Lim YW, Traina SB, Hilton L, Garland R, Morton SC. Effects of omega-3 fatty acids on cancer risk: a systematic review. Jama. 2006 Jan 25;295(4):403-15.

2. Makarem N, Bandera EV, Nicholson JM, Parekh N. Consumption of sugars, sugary foods, and sugary beverages in relation to cancer risk: a systematic review of longitudinal studies. Annual review of nutrition. 2018 Aug 21;38:17-39.

3. Mishra A, Ahmed K, Froghi S, Dasgupta P. Systematic review of the relationship between artificial sweetener consumption and cancer in humans: analysis of 599,741 participants. International journal of clinical practice. 2015 Dec;69(12):1418-26.

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8. Kim B, Roth C, Chung KC, Young VL, van Busum K, Schnyer C, Mattke S. Anaplastic large cell lymphoma and breast implants: a systematic review. Plastic and reconstructive surgery. 2011 Jun 1;127(6):2141-50.
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Supplementary materials summary

Supplement 2

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| Title | Authors | PubMed | Journal | Volume | Issue | Pages | DOI | Study | Notes |
|-------|---------|--------|---------|--------|-------|-------|-----|-------|-------|
| Body mass index and the risk of cancer in women compared with men: a meta-analysis of prospective cohort studies. | Xue, Kai; Li, Feng; Chen, Yi-Wei; Zhou, Yu-Hao; He, Jia | 2017 | European journal of cancer prevention | 16 | 64 | 104-105 | | Xue 2017 | Exclusion reason: "Overlapping studies;" |
| Do polychlorinated biphenyls cause cancer? A systematic review and meta-analysis of epidemiological studies on risk of cutaneous melanoma and non-Hodgkin lymphoma. | Zani, Claudia; Ceretti, Elisabetta; Covolo, Loredana; Donato, Francesco | 2017 | Chemosphere | 183 | 4 | 97-106 | https://dx.doi.org/10.1016/j.chemosphere.2017.08.044 | Zani 2017 | Exclusion reason: "Overlapping studies;" |
| CARING (Cancer Risk and Nutritional Guesstimates): the association of diabetes mellitus and cancer risk with focus on possible determinants - a systematic review and a meta-analysis. | Starup-Linde, Jakob; Karlstad, Øystein; Eriksen, Stine Aistrup; Vestergaard, Peter; Bronsveld, Heleen K.; de Vries, Frank; Andersen, Morten; Auvinen, Ari; Haukkka, Jari; Hjelvik, Vidar; Bazelier, Marco; Boer, Anthonius de; Furu, Kari; De Bruin, Marie L. | 2013 | Current drug safety | 8 | 5 | 296-332 | | Starup-Linde 2013 | Exclusion reason: "Overlapping studies;" |
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| A meta-analysis of the incidence of malignancy in adult patients with rheumatoid arthritis. | Simmen, Allison L.; Simon, Teresa A.; Hochberg, Marc C.; Sussia, Sany | 2008 | Arthritis research & therapy | 10 | 2 | 645 | https://dx.doi.org/10.1186/ar1654 | Simmen 2008 | Exclusion reason: "Overlapping studies;" |
| Consumption of fruits, vegetables, and risk of hematological malignancies: a systematic review and meta-analysis of prospective studies. | Sergentanis, Theodoros N.; Psaltopoulos, Theodoros; Tzaninisis, Ioannis-Georgios; Dimopoulos, Meletios-Athanasiou. | 2018 | Leukemia & lymphoma | 59 | 2 | 434-447 | https://dx.doi.org/10.1080/10428194.2017.1380978 | Sergentanis 2018 | Exclusion reason: "Overlapping studies;" |
| Alcohol consumption and risk of hematological malignancies: A meta-analysis of prospective studies. | Psaltopoulos, Theodoros; Sergentanis, Theodoros N.; Tzaninisis, Ioannis-Georgios; Tzanninis, Ioannis-Georgios; Kusano, Aaron; De Bruin, Marie L. | 2018 | International journal of cancer | 143 | 3 | 486-495 | https://dx.doi.org/10.1002/ijc.31468 | Psaltopoulos 2018 | Exclusion reason: "Overlapping studies;" |
| Association between infection of hepatitis B virus and onset risk of B-cell non-Hodgkin’s lymphoma: a systematic review and a meta-analysis. | Yi, Hai-zen; Chen, Jin; Ding, Cen; Hong; Yan; Wei; Tan, Xiao-hong | 2014 | Medical oncology (Northwood, London, England) | 31 | 8 | 84 | https://dx.doi.org/10.1007/s10830-014-0176-7 | Yi 2014 | Exclusion reason: "Overlapping studies;" |
| Agricultural use of DDT and risk of non-Hodgkin’s lymphoma: pooled analysis of three case-control studies in the United States. | Baris, D.; Zahn, S. H.; Cantor, K. P.; Blair, A. | 1998 | Occupational and environmental medicine | 55 | 8 | 522-7 | | Baris 1998 | Exclusion reason: "Overlapping studies;" |
| Cigarette smoking is associated with a small increase in the incidence of non-Hodgkin lymphoma: a meta-analysis of 24 studies. | Castillo, J. J.; Dalia, S. | 2012 | Leukemia & lymphoma | 53 | 10 | 1911-1917 | https://dx.doi.org/10.1016/j.leukres.2012.06.006 | Castillo 2012 | Exclusion reason: "Overlapping studies;" |
| Title                                                                 | Authors | Year | Journal/Conference | Volume/Issue | Pages | DOI                                                                 |
|----------------------------------------------------------------------|---------|------|--------------------|--------------|-------|---------------------------------------------------------------------|
| Is prevention of cancer by sun exposure more than just the effect of vitamin D? A systematic review of epidemiological studies. | van der Rhee, Han; Coebergh, Jan Willem; de Vries, Esther | 2013 | European journal of cancer (Oxford, England : 1990) | 49 | 6 1422-36 | https://dx.doi.org/10.1016/j.ej cancer.2013 | Exclusion reason: *Overlapping studies ; |
| Hepatitis B infection increases the risk of non-Hodgkin lymphoma: a meta-analysis of observational studies. | Dalia, Samir; Chavez, Julio; Castillo, Jorge J; Sokol, Lubomir | 2013 | Leukemia research | 37 | 9 1107-15 | https://dx.doi.org/10.1016/j.leuk.2013 | Exclusion reason: *Overlapping studies ; |
| 2,4-Dichlorophenoxyacetic acid and non-Hodgkin’s lymphoma: results from the Agricultural Health Study and an updated meta-analysis | Goodman, J. E.; Loftus, C. T.; Zu, K. | 2017 | Annals of Epidemiology | 27 | 4 290 | http://dx.doi.org/10.1016/j.anedem.2017 | Exclusion reason: *Overlapping studies ; |
| Animal farming and the risk of lympho-haematopoietic cancers: a meta-analysis of three cohort studies within the AGRICROC consortium. | El-Zaemey, Sonia; Schirnasi, Leah H; Ferro, Gilles; Tu, Severeine; Lebailly, Pierre; Baldi, Isabelle; Nordby, Karl-Christian; Kjaerheim, Kristina; Schur, Joachim; Monnereau, Alain; Brouwer, Maartje; Koutros, Stella; Hofmann, Jonathan; Kristensen, Petter; Kronbou, Hans; Leon, | 2019 | Occupational and environmental medicine | 76 | 11 827-837 | https://dx.doi.org/10.1136/oem.2019.010542 | Exclusion reason: *Overlapping studies ; |
| Coffee and the Risk of Lymphoma: A Meta-analysis Article. | Han, Tianjie; L; Junshan; Wang, Ling; Xu, Hongyi | 2016 | Iranian journal of public health | 45 | 9 1126-1130 | https://dx.doi.org/10.1136/ijph.2016.082412 | Exclusion reason: *Overlapping studies ; |
| A Systematic Review of Carcinogenic Outcomes and Potential Mechanisms from Exposure to 2,4-D and MCPA in the Environment. | von Stackelberg, Katherine | 2013 | Journal of Toxicology | 2013 10159097 | 371610 | https://dx.doi.org/10.1155/2013/10159097 | Exclusion reason: *Overlapping studies ; |
| Benzene exposure and non-Hodgkin lymphoma: a meta-analysis of epidemiologic studies. | Alexander, Dominik D; Wagner, Meghan E | 2010 | Journal of occupational and environmental medicine | 52 | 2 169-89 | https://dx.doi.org/10.1097/JOC.0b013e3181d754d | Exclusion reason: *Overlapping studies ; |
| Association of risk of non-Hodgkin’s lymphoma with hepatitis B virus infection: a meta-analysis. | Qi, Zhen; Wang, Hao; Gao, Guangxun | 2015 | International journal of clinical and experimental medicine | 8 | 12 22167-74 | https://dx.doi.org/10.1186/0007-0994-2015-22167 | Exclusion reason: *Overlapping studies ; |
| Association of diabetes mellitus with non-Hodgkin lymphoma risk: a meta-analysis of cohort studies. | Xu, Jian; Wang, Tingting | 2019 | Hematology (Amsterdam, Netherlands) | 24 | 1 527-532 | https://dx.doi.org/10.1080/00070002.2019.1664972 | Exclusion reason: *Overlapping studies ; |
| Exposure to glyphosate-based herbicides and risk for non-Hodgkin lymphoma: A meta-analysis and supporting evidence. | Zhang, Luoping; Rana, Iman; Shaffer, Rachel M; Taill, Emanuela; Sheppard, Lianne | 2018 | Mutation research | 781 | 040078 166-206 | https://dx.doi.org/10.1016/j.mma.2018 | Exclusion reason: *Overlapping studies ; |
| Hematopoietic and lymphatic cancers in patients with periodontitis: a systematic review and meta-analysis. | Wu, Y; Shi, X; Li, Y; Gu, Y; Qian, Q; Hong, Y | 2020 | Medicina oral, patologia oral y cirugia bucal | 25 | 1 e21-e28 | https://dx.doi.org/10.4317/medicina.2020 | Exclusion reason: *Overlapping studies ; |
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| An integrated safety profile analysis of belatacept in kidney transplant recipients | Oriinyo, J.; Charpentier, B.; Pestana, J. M.; Varenterghem, Y.; Vincenti, F.; Reyes-Acevedo, R.; Apanovich, A. M.; Gujrathi, S.; Aganwal, M.; Thomas, D.; Larsen, C. P. | 2010 | Transplantation                   | 90     | 12 1521-152 | http://dx.doi.org/10.1097/TP.0b013e3181ed3a0c                    | Exclusion reason: Incorrect component study design                      |                                                                                     |
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| Consumption of sugar-sweetened beverages and fruit juice and human cancer: A systematic review and dose-response meta-analysis of observational studies | Li, Yuting; Guo, Liliazzi; He, Kailin; Tang, Shaozhi; Huang, Changbing | 2021 | 12     | 10 3077-3088 | http://dx.doi.org/10.7150/jca.21205 | Li 2021 |       |
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| Subclinical hypothyroidism and the risk of cancer incidence and     | Gomez-Izquierdo, Juan; Filion, Kristen B.; Boivin, Jean-Francois; Azoulay, Laurent; Poliak, Michael; Yu, Oriana Hoi Yun                  | 2020 | BMC endocrine disorders                                                          | 20     | 1    | 83    | https://dx.doi.org/10.1186/s11686-020-20146-9 | Exclusion reason: Incorrect indication |
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| The risk of malignancies in patients receiving hematopoietic stem   | Loff-Forusiani, P.; Heydari, K.; Shamsbrian, A.; Hadayatvakkah-Hashem, A.; Ahmad, M.; Janabi, G.; Zabol, E.; Alisadeh-Navaei, R.; Aref, A.; Keyhani, S.; Ghasemzadeh, S. M. | 2020 | Clinical and Translational Oncology                                             | 22     | 10   | 1825-1830 | http://dx.doi.org/10.1007/s10786-020-06240-4 | Exclusion reason: Incorrect indication |
| cell transplantation: a systematic review and meta-analysis         |                                                                                                                                          |      |                                                                                 |        |      |       |                             |                                         |
| Risk of Malignancy in Spontaneous Infections: A Systematic Review   | Karmecharya, Paras; Shahuulkal, Ravi; Ogdie, Alexs                                                                                         | 2020 | Rheumatic Disease Clinics of North America                                      | 46     | 3    | 463-511| https://dx.doi.org/10.1016/j.reda.2020.09.002 | Exclusion reason: Incorrect indication |
| Donor-transmitted cancer in kidney transplant recipients:           | Echer, Albino; Ciolfi, Babina; Marletta, Stefano; Motter, Jennifer Daniel; Segev, Dorny; Lidor, Gambaro; Giovanni, Zaza; Gianluigi, Momo; Rosand Emmanuell Angel; Nacchia, Francesco; Donato, Paola; Boschiere, Luigi; Boggi, Ugo; Lombardini, Letizia | 2020 | Journal of Nephrology                                                           | 33     | 6    | 1321-1331| https://dx.doi.org/10.1007/s40464-020-06240-4 | Exclusion reason: Incorrect indication |
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| Whole Grains, Refined Grains, and Cancer Risk: A Systematic Review of Meta-Analyses of Observational Studies | Gaesser, Glenn A.                                                         | 2020 | Nutrients                                                               | 12     |      | 12                             | https://dx.doi.org/10.3390/nu.12050731                                | Exclusion reason: Incorrect indication |
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| Bisphosphonates and risk of cancers: a systematic review and meta-analysis | Li, Yuan-Yuan; Gao, Li-Jie; Zhang, Yu-Xue; Lu, Shu-Juan; Cheng, Shuo; Liu, Yu-Peng; Jia, Cun-Xian | 2020 | British journal of cancer                                              | 123    |      | 1570-1580                       | https://dx.doi.org/10.1038/s41406-020-00050                          | Exclusion reason: Incorrect indication |
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| Association Between Alzheimer Disease and Cancer With Evaluation of Study Biases: A Systematic Review and Meta-analysis | Osprina-Romero, Monica; Glymour, M. Maria; Hayes-Larson, Eleanor; Mayeda, Elizabeth Rose; Graff, Rebecca E.; Brenowitz, Willa D.; Ackley, Sarah F.; Witte, John S.; Kobayashi, Lindsay C. | 2020       | JAMA network open         | 3      | 11 e202551 | https://dx.doi.org/10.1001/jamanetworkopen.2020.2551             | Exclusion reason: Incorrect indication   |
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| Immunosuppression in patients with Crohn's disease and neoplasia: An ongoing clinical dilemma | Dasari, B. V. M.; McCreany, A.; Gardiner, K.                              | 2012 | Diseases of the Colon and Rectum            | 10.1097/OCP.2012.1008-10              |
| Exam 1: Risks of Serious Infection or Lymphoma With Anti-Tumor Necrosis Factor Therapy for Pediatric Inflammatory Bowel Disease: A Systematic Review | Anonymous                                                               | 2014 | Clinical Gastroenterology and Hepatology     | 10.1016/j.cgjo.2014.09.001 (Epub 2014 Sept 25) |
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Olive oil intake is inversely related to cancer prevalence: a systematic review and a meta-analysis of 13,800 patients and 23,340 controls in 19 observational studies.

Psaltopoulou, Theodora; Kosti, Rena I; Haidopoulous, Dimitrios; Dimopoulous, Meletios; Panagiotakos, Demetrios B

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https://dx.doi.org/10.1186/1424-3106-10-14

Psaltopoulou 2011

Exclusion reason: Incorrect indication

Dietary phytochemicals and cancer chemoprevention: A meta-analysis of prospective studies.

Kamangar, Farin; Shakeri, Ramin; Malekzadeh, Reza; Ismail, Farshad

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Kamangar 2014

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Obesity and cancer: the role of vitamin D.

Shanmugalingam, Thukral; Crawley, Danielle; Bosco, Cecilia; Melvin, Jennifer; Rohrmann, Sabine; Chowdhury, Simon; Holmeirick, Mieke

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Shanmugalingam 2014

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409-25

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Nut consumption and risk of cancer and type 2 diabetes: a systematic review and meta-analysis.

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Nutrition reviews

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125-134

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Exclusion reason: Incorrect indication

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Lee, P. N.

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125-134

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Exclusion reason: Incorrect indication

Green tea (Camellia sinensis) for the prevention of cancer.

Filippini, T; Malavoltil, M; Borelli, P; Iizzo, A; Fairweather-Tait, S J; Hornet, M; vincelli, M

2020

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10.1002/14651858.CD008590

Filippini 2020

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Ginseng consumption and risk of cancer: A meta-analysis.

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| Health effects associated with smokeless tobacco: a systematic review.  | Critchley, J A; Unal, B                                                  | 2003 | Thorax                                                                  | 58     | 5     | 435-43                                                                                     | Exclusion reason: Incorrect indication                                           |
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| Household physical activity and cancer risk: a systematic review and dose-response meta-analysis of epidemiological studies. | Shi, Yun; Li, Tingling; Wang, Ying; Zhou, Lingling; Qin, Qin; Yin, Jieyun; Wei, Sheng; Liu, Li; Nie, Shaofa | 2015 | Scientific Reports                                                      | 5      | 101563288 | 14961                                                                                       | Exclusion reason: Incorrect indication                                           |
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| Intensified low-density lipoprotein-cholesterol target of statin therapy and cancer risk: a meta-analysis. | Sun, Haixia; Yuan, Yang; Wang, Pin; Cai, Rongrong; Xia, Wenqing; Huang, Rong; Wang, Shaohua | 2015 | Lipids in Health and Disease                                           | 14     | 101147896 | 140                                                                                          | Exclusion reason: Incorrect indication                                           |
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| Is there a Risk of Lymphoma Associated With Anti-tumor Necrosis       | Ferraro, Sara; Leonardi, Luca; Convertino, Irma; Blandizzi, Corrado;    | 2019 | 10     | 10154| 247   | https://dx.doi.org/10.3389/fonc |                                          |
| Factor Drugs in Patients With Inflammatory Bowel Disease? A Systematic| Tuccori, Marco                                                            |      |        |       |       |     | Ferraro 2019     | Exclusion reason: Incorrect indication |
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| Is there an increased risk of cancer among spouses of patients with   | Mirghani, Hailham; Sturgis, Erin M; Auperin, Anne; Monsonego, Joseph;   | 2017 | 67     | 97091| 138-145| https://dx.doi.org/10.1016/j.          |                                           |
| an HPV-related cancer: A systematic review.                          | Blanchard, Pierre                                                        |      |        |       |       |     | Mirghani 2017    | Exclusion reason: Incorrect indication |
| Late onset post transplantation lymphoproliferative disorders:       | Khedmat, Hossein; Taheri, Saeed                                        | 2009 | 14     |       | 40-5  | https://dx.doi.org/10.1045/kh     |                                          |
| analysis of international data                                       |                                                                 |      |        |       |       |     | Khedmat 2009    | Exclusion reason: Incorrect indication |
| Leisure time physical activity and cancer risk: evaluation of the    | Liu, Li; Shi, Yun; Li; Tingtong; Qin; Yin; Jieyun; Pang; Shuo; Nie;    | 2016 | 50     | 6     | 372-8 | https://dx.doi.org/10.1136/bli     |                                          |
| WHO’s recommendation based on 126 high-quality epidemiologic studies.| Shaoa; Wei; Sheng                                                         |      |        |       |       |     | Liu 2016        | Exclusion reason: Incorrect indication |
| Light Alcohol Drinking and Risk of Cancer: A Meta-Analysis of Cohort | Choi, Yoon-Jung; Myung, Seung-Kwon; Lee, J-H                             | 2016 | 50     | 2     | 474-487| https://dx.doi.org/10.4143/          |                                          |
| Studies.                                                             |                                                                 |      |        |       |       |     | Choi 2016       | Exclusion reason: Incorrect indication |
| Linoleic acid intake and cancer risk: a review and meta-analysis.    | Zock, P L; Katan, M B                                                   | 1998 | 68     |       | 142-53| https://dx.doi.org/10.1898/     | Exclusion reason: Incorrect indication |
| Literature review of cancer mortality and incidence among dentists.  | Simming, Adam; van Wijngaarden, Edwin                                   | 2007 | 84     |       | 432-8 | https://dx.doi.org/10.1043/si     | Exclusion reason: Incorrect indication |
| Long term hormone therapy for perimenopausal and postmenopausal     | Farquhar, Cindy; Marjoribanks, Jane; Lethaby, Anne; Suckling, Jane A;  | 2009 | 2      | 10022| 141-146| https://dx.doi.org/10.1002/jn     | Exclusion reason: Incorrect indication |
| women.                                                               | Lamberts, Quirine                                                       |      |        |       |       |     | Farquhar 2009    | Exclusion reason: Incorrect indication |
| Mediterranean diet and cancer.                                       | La Vecchia, Carlo                                                       | 2004 | 7      |       | 966-8 | https://dx.doi.org/10.1080/     | Exclusion reason: Incorrect indication |
| Mediterranean diet and cancer risk: an open issue.                   | O’Alessandro, Annunziata; De Pergola, Giovanni; Silvestris, Franco      | 2016 | 67     |       | 593-606| https://dx.doi.org/10.1080/og      | Exclusion reason: Incorrect indication |
| Mediterranean diet and health status: an updated meta-analysis and a  | Sofi, Francesco; Macchi, Claudio; Abbate, Rossana; Gensis, Gian Franco; | 2014 | 17     | 12    | 2769-82| https://dx.doi.org/10.1017/st1    | Exclusion reason: Incorrect indication |
| proposal for a literature-based adherence score.                     | Casini, Alessandro                                                      |      |        |       |       |     | Sofi 2014        | Exclusion reason: Incorrect indication |
| Meta-analyses of studies on the association between electromagnetic   | Meinter, R; Michaelis, J                                                | 1996 | 35     | 1     | 8-Nov | https://dx.doi.org/10.1186/jenbi   | Exclusion reason: Incorrect indication |
| fields and childhood cancer.                                         |                                                                      |      |        |       |       |     | Meinter 1996    | Exclusion reason: Incorrect indication |
| Meta-analysis of extremely low frequency electromagnetic fields and   | Zhang, Yemao; Lai; Jinsheng; Ruan; Guoran; Chen; Wang; Dao Wen          | 2016 | 88     | 78072| 38-43 | https://dx.doi.org/10.1016/j radiation and environmental biophysics | Exclusion reason: Incorrect indication |
| cancer risk: a pooled analysis of epidemiologic studies.             |                                                                      |      |        |       |       |     | Zhang 2016      | Exclusion reason: Incorrect indication |
| Meta-analysis of risk of malignancy with immunosuppressive drugs in  | Masunaga, Yukari; Ohno, Keiko; Ogawa, Ryuchi; Hashiguchi, Masayuki;     | 2007 | 41     | 1     | 21-8  | https://dx.doi.org/10.1111/j.1365-3 | Exclusion reason: Incorrect indication |
| inflammatory bowel disease.                                          | Echizen, Hiroto; Ogata, Hiroyasu                                        |      |        |       |       |     | Masunaga 2007   | Exclusion reason: Incorrect indication |
| Meta-analysis of the association of dermatomyositis and polymyositis | Wang, J; Guo, G; Chen, G; Wu, B; Lu, L; Bao, L                          | 2013 | 169    | 4     | 638-47| https://dx.doi.org/10.1111/j.         |                                          |
| with cancer.                                                         |                                                                      |      |        |       |       |     | Wang 2013      | Exclusion reason: Incorrect indication |
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| Meta-analysis on the possible association between in vitro fertilization and cancer risk. | Li, Li L; Zhou, Jun; Qian, Xia Jing; Chen, Yi; Ding                      | 2013 | International Journal of Gynecological Cancer: official journal of the International Gynecological Cancer Society | Exclusion reason: Incorrect indication |
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| Review of the evidence for an association between infant feeding and childhood cancer. | Davis, M K                                                              | 1998 | [International journal of cancer. Supplement = Journal international du cancer. Supplement](https://doi.org/10.1002/1097-0246(199805)91:5<29:aid-ijc27>3.0.co;2-4) 11 5 29-33 (Davis 1998) |
| Pesticides and childhood cancer: an update.                           | Nasterlack, Michael                                                    | 2007 | [International journal of hygiene and environmental health](https://doi.org/10.1080/00207510701383165) 210 5 644-57 (Nasterlack 2007) |
| A review of the infection-associated cancers in North African countries | Hussein, W. M.; Anwar, W. A.; Alateeb, M.; Mazini, L.; Forsti, A.; Thinhitas, R. D.; Khyatt, M. | 2018 | [Infectious Agents and Cancer](https://doi.org/10.1089/inf.2017.0662) 11 12 10.1186/s13027-016-0083-8 (Hussein 2018) |
| Antibody induction therapy in renal transplant patients receiving calcineurin-inhibitor immunosuppressive regimens: A comparative review. | Nashan, B.                                                              | 2005 | [Biodrugs](https://doi.org/10.2165/00063030-200505000-00006) 19 1 39-46 (Nashan 2005) |
| Avoiding Rash Decision Making: Skin Cancer Screening of Patients With Inflammatory Bowel Disease | Siao, D.; Velayos, F.                                                   | 2014 | [Clinical Gastroenterology and Hepatology](https://doi.org/10.1016/j.cgh.2013.10.018) 12 2 274-276 (Siao 2014) |
| Genetically Determined Height and Risk of Non-Hodgkin Lymphoma         | Moore, A.; Kane, E.; Wang, Z. M.; Paragotou, O. A.; Teras, L. R.; Monnereau, A.; Doo, N. W.; Machida, M. J.; Skiboda, C. F.; Slager, S. L.; Salles, G.; Camp, N. J.; Bracci, P. M.; Nieters, A.; Vermeulen, R. C. H.; Vijai, J.; Smadby, K. E.; Zhang, Y. W.; Vajdic, C. M.; Cozen, W.; Spinelli, J. | 2020 | [Frontiers in Oncology](https://doi.org/10.3389/fonc.2019.01539) 9 8 10.3389/fonc.2019.01539 (Moore 2020) |
| Title                                                                 | Authors                                                                 | publication Year | Volume/Issue/Start Page | PubMed/DOI                                                                 | Exclusion reason                                                                 |
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| Leukemia in petroleum refinery workers: a review of recent studies   | Clapp, R. W.; Coogan, P. F.                                              | 1999             | 9                        | 457-587; 10.2190/METL-UD49-01YH-Clapp 1999                                    |                                                                                 |
| Meflornin: Risk-benefit profile with a focus on cancer                | Provinciali, N.; Lazerooni, M.; Cazzaniga, M.; Gorliro, F.; Dunn, B. K.; Decensi, A. | 2015             | 14                       | 1573-1580; http://dx.doi.org/10.1517/14740338.2015.102                       | Exclusion reason: Incorrect study design                                         |
| Physical activity, sedentary behaviors, and risk of cancer           | Moore, S. C.; Matthews, C. E.; Keadie, S.; Patel, A. V.; Lee, I. M.       | 2017             | 14                       | 577-394; 10.1093/uso/078019002866-Moore 2017                                | Exclusion reason: Incorrect study design                                         |
| Psoriasis and skin cancer                                            | Yin, L.; Hu, Y. Y.; Bin Jameel, A. A.; Xu, J. L.; Yin, Z. Q.              | 2017             | 28                       | 2111-2113; Yin 2017                                                          | Exclusion reason: Incorrect study design                                         |
| Safety of infliximab for the treatment of inflammatory bowel disease: Current understanding of the potential for serious adverse events | Khanna, R.; Feagan, B. G.                                              | 2015             | 14                       | 987-999; 10.1517/14740338.2015.102; Khanna 2015                          | Exclusion reason: Incorrect study design                                         |
| ABO-Mismatched Allogeneic Hematopoietic Stem Cell Transplantation     | Wore, N.                                                                | 2016             | 43                       | 1-12-March; http://dx.doi.org/10.1158/0000-0000-Wore 2016                    | Exclusion reason: Incorrect study design                                         |
| Adverse effects of immunosuppression in pediatric solid organ transplantation | Schonder, K. S.; Mazariagos, G. V.; Weber, R. J.                        | 2010             | 12                       | 35-49; 10.2165/11316180-00000000-Schonder 2010                           | Exclusion reason: Incorrect study design                                         |
| Decolonization of Staphylococcus aureus in Healthcare: A Dermatology Perspective | Kuraltis, D.; Williams, L.                                               | 2016             | 2018                     | 2382050; http://dx.doi.org/10.1155/2018-Kuraltis 2018                      | Exclusion reason: Incorrect study design                                         |
| Excess Weight as a Risk Factor Common to Many Cancer Sites: Words of Caution when Interpreting Meta-analytic Evidence. | Arnold, Melina; Renehan, Andrew G; Colditz, Graham A                     | 2017             | 26                       | 5663-666; https://dx.doi.org/10.1158/1078-0432-Armold 2017                  | Exclusion reason: Incorrect study design                                         |
| A review of epidemiologic studies of tizaine herbicides and cancer    | Sathiaikumar, N.; Delzeil, E.                                           | 1997             | 27                       | 599-612; 10.3109/1040844079088440-Sathiai-kumar 1997                      | Exclusion reason: Incorrect study design                                         |
| Alcoholic beverages, obesity physical activity and other nutritional factors, and cancer risk: A review of the evidence. | Latino-Martel, Paule; Cottel, Vanessa; Druesne-Picollo, Nathalie; Pierre, Fabrice H F; Touilaud, Marina; Touvier, Mathilde; Vaussion, Marie-Paule; Deschasaux, Melanie; Le Mery, Julie; Barrandon, Emilie; Ancelin, Raphaelle | 2018             | 99-100                    | 308-23; https://dx.doi.org/10.1016/j.latino-martel 2016                   | Exclusion reason: Incorrect study design                                         |
| Body mass index and 20 specific cancers: re-analyses of dose-response meta-analyses of observational studies. | Choi, E K; Park, H B; Lee, K H; Park, J H; Eisenhut, M; van der Vliet, H J; Kim, G; Shin, J I | 2018             | 29                       | 749-757; https://dx.doi.org/10.1093/analsci/ Choi 2018                    | Exclusion reason: Incorrect study design                                         |
| Endometriosis: a high-risk population for major chronic diseases?.   | Kvasnakoff, Marina; Mu, Fan; Terry, Kathryn L; Harris, Holly R; Poole, Elizabeth M; Farland, Leslie; Misser, Stacey | 2015             | 21                       | 4500-16; https://dx.doi.org/10.1093/humrep/kv 2015                         | Exclusion reason: Incorrect study design                                         |
| Cancer risks after solid organ transplantation and after long-term dialysis | Hortlund, M.; Muhr, L B A.; Storm, H.; Engholm, G.; Dillner, J.; Bzhalava, D. | 2017             | 140                      | 1091-1110; 10.1002/jc.30531; Hortlund 2017                               | Exclusion reason: Incorrect study design                                         |
| Title                                                                                                                                                                                                 | Year of Publication | Journal Name                                      | Volume | Pages                                      | Digital Object Identifier                                                                 | Exclusion reason         |
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| Epidemiology and etiology of mantle cell lymphoma and other non-Hodgkin lymphoma subtypes.                                                                                                                 | 2011                | Seminars in Cancer Biology                        | 21     | 5293-5298                                  | 10.1016/j.semcancer.2011.06.015                                                         | Smedby 2011              |
| Metabolic factors and blood cancers among 578,000 adults in the metabolic syndrome and cancer project (Me-Can).                                                                                             | 2012                | Annals of Hematology                              | 91     | 1519-153                                   | 10.1007/s00277-012-1489-z                                                               | Nagel 2012               |
| Plasma levels of polychlorinated biphenyls, non-Hodgkin lymphoma, and causation.                                                                                                                        | 2012                | Journal of Environmental and public health        | 2012   | 256981                                     | https://dx.doi.org/10.1159/000417656                                                   | Freema 2012              |
| Ranking occupational contexts associated with risk of non-Hodgkin lymphoma.                                                                                                                            | 2016                | American Journal of Industrial Medicine           | 59     | 561-574                                    | 10.1002/ajim.22004                                                                        | Reutort 2016             |
| Risk of cancer among firefighters: A quantitative review of selected malignancies.                                                                                                                     | 2006                | Archives of Environmental & Occupational Health  | 61     | 223-231                                    | https://dx.doi.org/10.1016/j.aeoeh.2006                                                | Youakim 2006             |
| ABO blood group and cancer risk.                                                                                                                                                                         | 2010                | European journal of cancer (Oxford, England : 1990) | 46     | 18345-18350                                | https://dx.doi.org/10.1016/j.ejca.2010                                                  | Iodice 2010              |
| The challenge of AIDS-related malignancies in sub-Saharan Africa.                                                                                                                                       | 2010                | PLoS one                                         | 5      | 1e8621                                     | https://dx.doi.org/10.1371/journal.pone.0008621                                         | Sasco 2010               |
| Risk of lymphoma in women with breast implants: analysis of clinical studies.                                                                                                                           | 2012                | European Journal of Cancer Prevention            | 21     | 274-280                                    | 10.1097/CEJ.0b013e326350                                                                   | Larget 2012             |
| Anti-TNF therapy in inflammatory bowel diseases.                                                                                                                                                           | 2010                | Clinical Update on Inflammatory Disorders of the Gastrointestinal Tract | 26     | 95-107                                     | http://dx.doi.org/10.1159/000417656                                                      | Fiorino 2010             |
| A critical review of perfluorooctanoate and perfluorooctanesulfonate exposure and cancer risk in humans.                                                                                                  | 2014                | Critical Reviews in Toxicology                   | 44     | S1                                         | http://dx.doi.org/10.3106/1047686                                                      | Chang 2014               |
| Reproductive factors and non-Hodgkin lymphoma: a systematic review.                                                                                                                                     | 2014                | Critical reviews in oncology/hematology          | 92     | 181-193                                    | https://dx.doi.org/10.1016/j.crot.2014                                                  | Costas 2014              |
| Statin use is associated with a lower risk of diffuse large B-cell lymphoma: A systematic review and meta-analysis.                                                                                       | 2020                | J. Clin. Oncol.                                   | 38     | 15                                         | 10.1200/jco.2020.38.15_supplement                                                      | Ponvila 2020             |
| Occupational exposure to formaldehyde and risk of non-Hodgkin lymphoma: a meta-analysis.                                                                                                                  | 2019                | BMC cancer                                       | 19     | 1240                                       | https://dx.doi.org/10.1186/s12885-019-0651                                               | Catalan 2019             |
| Tooth loss and cancer risk: A dose-response meta-analysis of prospective cohort studies.                                                                                                                 | 2018                | Oncotarget                                       | 9      | 15090-15100                                | 10.18632/oncotarget.23850                                                               | Shi 2018                |
| The risk of developing a second primary cancer in melanoma patients: a comprehensive review of the literature and meta-analysis.                                                                         | 2014                | Journal of dermatological science              | 75     | 1                                         | 9-Mar                                                                                   | Cai 2014             |
| Study Title                                                                 | Authors                                                                 | Year | Journal                                                                 | Page(s) | DOI Link                                                                 | Exclusion Reason                                      |
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| Health effects of occupational exposure to uranium: Do physicochemical properties matter? | Zhivin, S.; Launier, D.; Guseva Gamu, I. | 2014 | International Journal of Radiation Biology                               | 90      | 1104-11 http://dx.doi.org/10.3109/09993993.2014.929234 | Exclusion reason: Incorrect study focus; |
| Inflammatory myopathies and lymphoma                                       | Stuigen, J. P.                                                         | 2016 | Journal of the Neurological Sciences                                    | 369     | 377-389 http://dx.doi.org/10.1016/j.jnns.2016.06.018                   | Exclusion reason: Incorrect study focus; |
| THE INCIDENCE OF NON-HODGKIN LYMPHOMA IN IRAN: A SYSTEMATIC REVIEW AND META-ANALYSIS | Fouladseresht, H.; Ghobari, M.; Hassanpour, S.; Dastmohseni, A.; Mohseni, S.; Abbate, Rosanna; Abbate, Rosanna; Gensini, Gian Franco; Casini, Alessandro | 2019 | World Cancer Research Journal                                           | 6       | 7 http://dx.doi.org/10.1002/wcr.20101001 | Exclusion reason: Incorrect study focus; |
| Is Banning Texturized Implants to Prevent Breast Implant-Associated Anaplastic Large Cell Lymphoma a Rational Decision? A Meta-Analysis and Cost-Effectiveness Study | Danilla, Stefan V.; Jara, Rocio P.; Miranda, Felipe; Aparicio, A.; Aguilera, E.; Rioja, S.; Mohammadian-Hafshejani, A.; Salehi-Rouhi, H. | 2020 | Aesthetic Surgery Journal                                               | 40      | 7 121-731 https://dx.doi.org/10.1093/apt/faz180 | Exclusion reason: Incorrect study focus; |
| A Systematic Review of Factors That Contribute to Hepatosplenic T-Cell Lymphoma in Patients With Inflammatory Bowel Disease | Kolyar, D. S.; Osterman, M. T.; Diamond, R. H.; Porter, D.; Blonski, W. C.; Wasik, M.; Sampaio, S.; Mendizabal, M.; Lin, M. V.; Lichtenstein, G. R. | 2011 | Clinical Gastroenterology and Hepatology                               | 9       | 1 10164.ghg.2010.09.016 Kolyar 2011 | Exclusion reason: Incorrect study focus; |
| A systematic review of the incidence and prevalence of cancer in multiple sclerosis. | Mairie, Ruth Ann; Reider, Nadia; Cohen, Jeffrey; Steve, Olaf; Trojano, Maria; Sorensen, Per; Soelberg, Reingold, Stephen C; Cutter, Gary | 2015 | Multiple sclerosis (Houndmills, Basingstoke, England)                   | 21      | 3 294-304 https://dx.doi.org/10.1177/1345915615578060 | Exclusion reason: Incorrect study focus; |
| Ethylene oxide: an assessment of the epidemiological evidence on carcinogenicity. | Shore, R. E; Gardner, M J; Pannett, B                                  | 1993 | British Journal of Industrial Medicine                                  | 50      | 11 971-97 Shore 1993                                                    | Exclusion reason: Incorrect study focus; |
| HLA-haploidentical vs matched-sibling hematopoietic cell transplantation: A systematic review and meta-analysis | Meybodi, M. A.; Cao, W.; Luznik, L.; Bashey, A.; Zhang, X.; Romee, R.; Saber, W.; Hamadian, M.; Weisdorf, D. J.; Chu, H.; Rashid, A. | 2019 | Blood Advances                                                        | 3       | 17 2561-2587 https://dx.doi.org/10.1182/blood.2018-819430 Meybodi 2019 | Exclusion reason: Incorrect study focus; |
| Weight loss as a predictor of cancer in primary care: a systematic review and meta-analysis. | Nicholson, Bnian B; Hamilton, William; O’Sullivan, Jack; Aveyard, Paul; Hobbs, Fd Richard | 2013 | The British journal of general practice : the journal of the Royal College of General Practitioners | 68      | 670 431-432 https://dx.doi.org/10.3399/bjgp18X708961 Nicholson 2018 | Exclusion reason: Incorrect study focus; |
| Obesity and Other Cancers.                                                 | Yang, Lin; Drake, Betina F; Coolitz, Graham A                          | 2016 | Journal of clinical oncology : official journal of the American Society of Clinical Oncology | 34      | 35 4231-4237 Yang 2016                                                   | Exclusion reason: Incorrect study focus; |
| Adherence to Mediterranean diet and health status: meta-analysis.          | Solfi, Francesco; Cesari, Francesco; Abbate, Rosanna; Gensini, Gian Franco; Casini, Alessandro | 2008 | BMJ (Clinical research ed.)                                             | 337     | 3800488, bm1344 https://dx.doi.org/10.1136/bmj.3800488, bm1344 Solfi 2008 | Exclusion reason: Insufficient data for analysis; |
| Acrylonitrile and cancer: a review of the epidemiology.                    | Cole, Philip; Mandel, Jack S; Collins, James J                         | 2008 | Regulatory toxicology and pharmacology : RTP                           | 52      | 3 342-51 https://dx.doi.org/10.1016/j.yrtp.2008.04.007 Cole 2008       | Exclusion reason: Insufficient data for analysis; |
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| Adherence to Diet and Physical Activity Cancer Prevention Guidelines and Cancer Outcomes: A Systematic Review. | Kohler, Lindsay N; Garcia, David D; Harris, Robin B; Oren, Eyad; Roe, Denise J; Jacobs, Elizabeth T | 2016 | 25     | 7     | 1016-28 | https://dx.doi.org/10.1158/1058-8840.CAN-16-0063 (Kohler 2016)       | Insufficient data for analysis;                        |
| Active Commuting and Multiple Health Outcomes: A Systematic Review and Meta-Analysis. | Dinu, Monica; Pagliai, Giuditta; Macchi, Claudio; Sofi, Francesco        | 2019 | 49     | 3     | 437-452 | https://dx.doi.org/10.1007/s10555-019-00806-5 (Dinu 2019)            | Insufficient data for analysis;                        |
| Pentachlorophenol and cancer risk: focusing the lens on specific chlorophenols and contaminants. | Cooper, Glenis; Jones, Samantha                                         | 2008 | 116    | 8     | 1001-8  | https://dx.doi.org/10.1289/ehp.1104711 (Cooper 2008)                 | Insufficient data for analysis;                        |
| Comparison of anthropometric measurements of adiposity in relation to cancer risk: a systematic review of prospective studies. | De Ridder, Josefine; Julian-Almarcegui, Cristina; Mullée, Amy; Rinaldi, Sabina; Van Herck, Koen; Vicente-Rodriguez, German; Huybrechts, Inge | 2016 | 27     | 3     | 291-300 | https://dx.doi.org/10.1007/s10555-016-0287-z (DeRidder 2016)         | Insufficient data for analysis;                        |
| Associations between aspirin use and the risk of cancers: a meta-analysis of observational studies. | Qiao, Tian; Yang, Tingting; Gan, Yong; Li, Wenzhen; Wang, Chao; Gong, Yanhong; Liu, Zuxun | 2018 | 18     | 1     | 286    | https://dx.doi.org/10.1289/ehp.208295 (Qiao 2018)                    | Insufficient data for analysis;                        |
| Nut Consumption and Risk of Cancer: A Meta-Analysis of Prospective Studies | Long, Jieyi; Ji, Zhi; Yuan, Peihong; Long, Tingting; Liu, Ke; Li, Jiaoyuan; Cheng, Liming | 2020 | 29     | 3     | 565-573 | https://dx.doi.org/10.1158/1058-8840.CAN-20-0267 (Long 2020)         | Insufficient data for analysis;                        |
| Relationship between exposure to mixtures of persistent, bioaccumulative, and toxic chemicals and cancer risk: A systematic review | Fernandez-Martinez, Nicolas Francisco; Ching-Lopez, Ana; Oly de Labry Lima, Antonio; Salamanca-Fernandez, Elena; Perez-Gomez, Beatriz; Jimenez-Moleen, Jose Juan; Sanchez, Maria Jose; Rodriguez-Barranco, Miguel | 2020 | 18     | 1     | 109787 | https://dx.doi.org/10.1016/j.envres.2020.109787 (Fernandez-Martinez 2020) | Insufficient data for analysis;                        |
| Maternal exposure to pesticides and risk of childhood lymphoma in France: A pooled analysis of the ESCALE and ESTELLE studies (SFCE). | Mavounou, Sandra; Rios, Paula; Pacquement, Helene; Nolla, Marie; Rigaud, Charlotte; Simonin, Mathieu; Bertrand, Yves; Lambillotte, Anne; Faure, Laure; Orsi, Laurent; Clavel, Jacqueline; Bonaventure, Audrey | 2020 | 68     | 4     | 101797 | https://dx.doi.org/10.1016/j.envres.2020.101797 (Mavounou 2020)      | Insufficient data for analysis;                        |
| Muscle-strengthening activities and cancer incidence and mortality: a systematic review and meta-analysis of observational studies | Nascimento, Wilson; Ferrari, Gerson; Martini, Camila Berlinki; Rey-Lopez, Juan Pablo; Izquierdo, Mikel; Lee, Dong Hoon; Giovannucci, Edward L; Rezende, Leandro M | 2021 | 18     | 1     | 69     | https://dx.doi.org/10.1186/s11767-021-01831-2 (Nascimento 2021)      | Insufficient data for analysis;                        |
| Consumption of Sweet Beverages and Cancer Risk: A Systematic Review and Meta-Analysis of Observational Studies | Llaha, Fjorida; Gil-Lespinard, Mercedes; Unal, Pelin; de Villante, Izar; Castaneda, Jazmin; Zamora-Ros, Raul | 2021 | 13     | 2     | 3390-3612 | https://dx.doi.org/10.3390/nutrients130303390 (Llaha 2021) | Insufficient data for analysis;                        |
| Title                                                                 | Authors                                                                                       | Year | Volume | Pages   | Journal                                                                 | Date       | Exclusion reason                          |
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| Cellular Phone Use and Risk of Tumors: Systematic Review and Meta-Analysis | Cho, Yoon-Jung; Moskowitz, Joel M.; Myung, Seung-Kwon; Lee, Yi-Ryong; Hong, Yun-Chul            | 2020 | 75     | 1-8     | International Journal of environmental research and public health         | Choi 2020 | Insufficient data for analysis;          |
| Exposure to permethrin and cancer risk: a systematic review.         | Boffetta, Paolo; Desai, Vini                                                                 | 2018 | 33     | 4-12    | Critical Reviews in Toxicology                                            | Boffetta 2018 | Insufficient data for analysis;          |
| Is periodontitis a risk indicator for cancer? A meta-analysis.        | Corbella, Stefano; Veronesi, Paolo; Galimberti, Viviana; Weinstein, Roberto; Del Fabbro, Massimo; Francetti, Luca | 2018 | 23     | 4-12    | PloS One                                                               | Corbella 2018 | Insufficient data for analysis;          |
| Consumption of whole grains and cereal fiber in relation to cancer risk: a systematic review of longitudinal studies. | Makarem, Nour; Nicholson, Joseph M; Bandera, Elisa V; McGowan, Nicola M; Parekh, Niyaati        | 2018 | 33     | 1-8     | Nutrition Reviews                                                        | Makarem 2016 | Insufficient data for analysis;          |
| Thiazolidinedione use and diabetes: a systematic review and meta-analysis. | Colmers, J N; Bowker, S L; Johnson, J A                                                   | 2012 | 138    | 1-8     | Diabetes & Metabolism                                                    | Colmer 2012 | Insufficient data for analysis;          |
| Risk of lymphoma associated with combination anti-tumor necrosis factor and immunomodulator therapy for the treatment of Crohn’s disease: a meta-analysis. | Siegel, Corey A; Marden, Sadie M; Persing, Sarah M; Larson, Robin J; Sands, Bruce E          | 2009 | 33     | 1-8     | Clinical Gastroenterology and Hepatology: the official clinical practice journal of the American Gastroenterology Association | Siegel 2009 | Insufficient data for analysis;          |
| The comparative efficacy and safety of biologics for the treatment of rheumatoid arthritis: A systematic review and meta-analysis. | Gartlehner, G.; Hansen, R. A.; Jonas, B. L.; Thieda, P.; Loehr, K. N.                           | 2005 | 12     | 1-8     | Journal of Rheumatology                                                  | Garthe 2006 | Insufficient data for analysis;          |
| Comorbidities in polymyalgia rheumatica: a systematic review.        | Parington, Richard; Heilwell, Toby; Muller, Sara; Abdul Sultan, Alyshah; Mallen, Christian     | 2016 | 23     | 1-8     | Arthritis Research & Therapy                                             | Paringt 2016 | Insufficient data for analysis;          |
| Dietary total antioxidant capacity and risk of cancer: a systematic review and meta-analysis on observational studies. | Paro, Mohammad; Sadeghi, Ali; Khatri, Seyed Reza; Nasir, Morteza; Milajerdi, Ali; Khosadost, Mahmoud; Sadeghi, Omid | 2019 | 23     | 1-8     | Critical Reviews in Oncology/Hematology                                  | Paroha 2019 | Insufficient data for analysis;          |
| A review and meta-analysis of cancer risks in relation to Portland cement exposure. | Cohen, Sarah S; Sadoff, Margaret M; Jiang, Xiaohui; Fryzek, Jon P; Garabrant, David H           | 2014 | 37     | 1-8     | Occupational and Environmental Medicine                                  | Cohen 2014  | Insufficient data for analysis;          |
| Systemic sclerosis (scleroderma) and cancer risk: systematic review and meta-analysis of observational studies. | Bonfazi, Marina; Tramacere, Irene; Pomponio, Giovanni; Gabrielli, Barbara; Avvedimento, Enrico V; La Vecchia, Carlo; Negri, Eva; Gabrielli, Armando | 2013 | 24     | 1-8     | Rheumatology (Oxford, England)                                            | Bonfazi 2013 | Insufficient data for analysis;          |
| Sex Differences in the Association between Night Shift Work and the Risk of Cancers: A Meta-Analysis of 57 Articles. | Liu, Wen; Zhou, Zhong; Han, Dong; Chen, Jun; Zhang, Guiming                               | 2018 | 35     | 1-8     | Disease Markers                                                          | Liu 2018   | Insufficient data for analysis;          |
| Dietary factors and risk of chronic lymphocytic leukemia and small lymphocytic lymphoma: a pooled analysis of two prospective studies. | Tsai, Hue-Ting; Cross, Amanda J; Graubard, Barry I; Oken, Martin; Moskowitz, Joel; Barnett, Neil E | 2010 | 33     | 1-8     | Cancer Epidemiology, Biomarkers & Prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society for Preventive Oncology | Tsai 2010   | Insufficient data for analysis;          |
| Title                                                                 | Authors                                                                 | Year | Volume | Pages   | Journal                                      | DOI                                    | Exclusion reason                                                                 |
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| Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: pooled analysis of two Swedish case-control studies. | Hardell, Lennart; Eriksson, Mikael; Nordstrom, Marie                    | 2002 | 43     | 1045-9 | Leukemia & lymphoma                          | https://dx.doi.org/10.1043-9           | Hardev 2002                                                                 |
| Sweetened carbonated beverage consumption and cancer risk: meta-analysis and review. | Boyle, Peter; Koechlin, Alice; Aulier, Philippe                          | 2014 | European Journal of cancer prevention: the official journal of the European Cancer Prevention Organisation (ECP) | 23   | 5       | 481-90                                      | https://dx.doi.org/10.1097/CEJ      | Boyle 2014                                                                    |
| Risk of lymphoma in patients with inflammatory bowel disease treated with azathioprine and 6-mercaptopurine: a meta-analysis. | Koltyar, David S; Lewis, James D; Beaugerite, Laurent; Tiemey, Ann; Brenninger, Colleen M; Gisbert, Javier P; Loftus, Edward V Jr; Peyrin-Biroulet, Laurent; Blonski, Wojciech C; Van Domselaar, Manuel; Chaparro, Maria; Sandiyya, Sandipani; Bewtra, Meenakshi; Beigel, Florian; | 2015 | Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association | 13   | 5       | 847-50                                      | https://dx.doi.org/10.1016/j.cge  | Koltyar 2015                                                                   |
| Hepatitis C infection and lymphoproliferative disease: accidental comorbidities?. | Khoury, Fawik; Chen, Shmuel; Adar, Tomer; Jacob, E; Otteh, Mizrati, Meir; | 2014 | World Journal of gastroenterology | 20   | 43      | 16197-20                                     | https://dx.doi.org/10.3748/wjm   | Khoury 2014                                                                    |
| Association Between Marijuana Use and Risk of Cancer: A Systematic Review and Meta-analysis. | Ghasemiesfe, Mehrnaz; Barlow, Brooke; Leonard, Samuel; Keyhani, Salomeh; Kerenstein, Deborah; | 2019 | JAMA network open | 2    | 11      | e191631                                     | https://dx.doi.org/10.1001/jama  | Ghasemiesfe 2019                                                                |
| Cancer Risk Following Bariatric Surgery: Systematic Review and Meta-analysis of National Population-Based Cohort Studies. | Wiggins, Tom; Antonowicz, Stefan S; Marker, Sheraz R; | 2019 | Obesity surgery | 29   | 3       | 1031-106                                     | https://dx.doi.org/10.1007/s10561  | Wiggins 2019                                                                   |
| Effect of bariatric surgery on oncologic outcomes: a systematic review and meta-analysis. | Tee, May C; Cao, Yin; Warnock, Garth L; Hu, Frank B; Chavarro, Jorge E; | 2013 | Surgical endoscopy | 27   | 12      | 4449-56                                     | https://dx.doi.org/10.1001/jam  | Tee 2013                                                                       |
| Exposure to Secondhand Smoke and Risk of Cancer in Never Smokers: A Meta-Analysis of Epidemiologic Studies. | Kim, A-Sol; Ko, Hae-Jin; Kwon, Jin-Hyun; Lee, Jong-Mying; | 2018 | International Journal of environmental research and public health | 15   | 9       |                                             | https://dx.doi.org/10.3390/ijer  | Kim 2018                                                                       |
| The association between acid suppressive agent use and the risk of cancer: a systematic review and meta-analysis. | Song, Hyun Jin; Jeon, Nakyung; Squires, Patrick; | 2020 | European Journal of Clinical Pharmacology | 106  | 2       | 650-656                                     | https://dx.doi.org/10.1007/s00239  | Song 2020                                                                      |
| Dietary fat intake and risk of non-Hodgkin lymphoma in 2 large prospective cohorts. | Bertrand, Kimberly A; Giovannucci, Edward; Rosner, Bernard A; Zhang, Shummi M; Laden, Francine; Birmann, Brenda M; | 2017 | The American Journal of clinical nutrition | 14   | 11      | 863-872                                     | https://dx.doi.org/10.3945/ajcn  | Bertrand 2017                                                                  |
| Cancer risk in asphalt workers and roofers: review and meta-analysis of epidemiologic studies. | Partanen, T; Boffetta, P; | 1994 | American Journal of industrial medicine | 28   | 6       | 721-40                                      | https://dx.doi.org/10.1080/15  | Partanen 1994                                                                   |
| Exposure to benzene in a pooled analysis of petroleum industry case-control studies. | Glass, D C; Schnatter, A R; Tang, G; Armstrong, T W; Rushion, L; | 2017 | Journal of occupational and environmental hygiene | 14   | 11      | 863-872                                     | https://dx.doi.org/10.1080/15  | Glass 2017                                                                     |
| Mobile phone use and risk of tumors: a meta-analysis. | Myung, Seung-Kwon; Ju, Woong; McDonnell, Diana D; Lee, Yeon Ji; Kazinets, Gene; Cheng, Chih-Tao; Moskowitz, Joel M; | 2000 | Journal of clinical oncology official journal of the American Society of Clinical Oncology | 27   | 33      | 5565-72                                     | https://dx.doi.org/10.1200/jco  | Myung 2009                                                                      |
| Title                                                                 | Authors                                                                 | Year | PMID  | URL | Exclusion reason |
|----------------------------------------------------------------------|-------------------------------------------------------------------------|------|-------|-----|-----------------|
| A prospective analysis of body size during childhood, adolescence, and adulthood and risk of non-Hodgkin lymphoma.  | Bertrand, Kimberly A; Giovannucci, Edward; Zhang, Shumin M; Laden, Francine; Rosner, Bernard; Birnbaum, Brenda M | 2013 | 2064-73 | https://dx.doi.org/10.1158/1940-6288.CAN-12-0426 | Bertran d 2013 |
| Proximity of industries and occupational populations to petrochemical industries and hematological malignancies: Systematic review and meta-analysis of available epidemiological studies | Lefranc, Agnes | 2020 | 6 Envir. Risques et Sante | https://dx.doi.org/10.1684/ERS.2020.1495 | Exclusion reason: Non-English |
| Influence of food or food groups intake on the occurrence and/or protection of different types of cancer: systematic review | Contreras Garcia, Enrique; Zaragoza-Martí, Ana | 2020 | 169-192 | https://dx.doi.org/10.20960/nEnviron. Risques et Sante | Exclusion reason: Non-English |
| Risk of cancer in occupational exposure to radar radiation: A systematic review | Zaroushani, V.; Vanani, A. S.; Ahmadi, S. | 2019 | 46-58 | http://dx.doi.org/10.1684/ERS.2019.1190 | Exclusion reason: Non-English |
| Meta-analysis of case-control studies on risk factors of malignant lymphoma in China | Wang, L.; Xie, X. H.; Chen, Y. J. | 2010 | 4477-480 | http://dx.doi.org/10.1007/s10388-010-0736-9 | Wang 2010 |
| Pills and cancer risk: Contraindication versus chemoprevention | Schmidmayr, M.; Siefer, Klaus; Klauss, V.; Kiechle, M. | 2014 | 1583-143 | http://dx.doi.org/10.1007/s10388-010-0736-9 | Exclusion reason: Non-English |
| Documented and suspected risk factors for childhood cancer aetiology | Magnani, C.; Miligi, L.; Parodi, S. | 2018 | 16-Oct | http://dx.doi.org/10.1007/s10388-010-0736-9 | Exclusion reason: Non-English |
| Does the bariatric surgery allow a decrease of oncologic risk in obese subject? | Vanderingen, M.; Waraumont, M.; Ciazzo, R.; Pigeyre, M. | 2014 | 214-220 | http://dx.doi.org/10.1007/s10388-010-0736-9 | Exclusion reason: Non-English |
| Domestic waste management: State of current knowledge and health effects assessment in general and occupational populations | Anzivino-Viricel, L.; Falette, N.; Carrelier, J.; Montestruq, L.; Guye, O.; Philip, T.; Fervers, B. | 2012 | 360-377 | http://dx.doi.org/10.1684/ers.2012.1478 | Exclusion reason: Non-English |
| Parental tobacco smoke and childhood cancer | Ferris, I.; Tortajada J.; Ortega Garcia, J. A.; Lopez Andreu, J. A.; Berbel Tomero, O.; Marco Macian, A.; Garcia, I.; Castell J. | 2004 | 226-236 | http://dx.doi.org/10.1684/ers.2012.1478 | Exclusion reason: Non-English |
| Research progress on the correlation between obesity, exercise and tumor | Qi, G.; Feng, L. Y.; Liang, H. | 2018 | 1611-1614 | http://dx.doi.org/10.1684/ers.2018.1183 | Exclusion reason: Non-English |
| Correlation between obstructive sleep apnea syndrome and tumor: A Meta-analysis | Sun, Y.; Wang, W.; Kang, J. | 2019 | 1394-143 | http://dx.doi.org/10.1158/1940-6288.CAN-18-1119 | Sun 2019 |
| Environmental health of European children: Priorities recommended by the PINCHE network | Zuurberg, M.; Salines, G.; Moshhammer, H.; Stansfeld, S.; Lundqvist, C.; Hanke, W.; Van den Hazel, P.; Bistrup, M.; Babisch, W. | 2007 | 143-56 | http://dx.doi.org/10.1007/s10388-010-0736-9 | Exclusion reason: Non-English |
| Pesticide exposure and cancers in children: Meta-analysis of recent studies | Nicolle-Mir, L. | 2012 | 191-192 | http://dx.doi.org/10.1684/ers.2012.1478 | Exclusion reason: Non-English |
| Title                                                                 | Authors                                           | Year | Journal                           | Volume | Pages  | DOI                                  | Exclusion reason                      |
|---------------------------------------------------------------------|---------------------------------------------------|------|-----------------------------------|--------|--------|--------------------------------------|---------------------------------------|
| HCV-associated mixed cryoglobulinemia and b-cell non-Hodgkin's lymphoma - pathogenetically related problems | Milovanova, S. Y.; Lysenko, L. V.; Milovanova, L. Y.; Mykhlin, N. N.; Russikh, A. V.; Muchin, N. A. | 2018 | Terapevticheskii Arkhiv           | 90     | 6      | 112-120                              | Milovanova 2018                        |
| Childhood cancer of occupations origin: Leukemia and lymphomas      | Lopez Duenas, A.; Aldea Romero, A. E.; Sanz Anquela, J. M.; Jimenez Bustos, J. M. | 2012 | Revista Española de Pediatría     | 68     | 1      | 59-64                                | LopezDuenas 2012                       |
| Non-Hodgkin’s lymphoma and pesticides                               | Lasfargues, G.                                    | 2017 | Bulletin De L’Academie Nationale De Medecine | 201    | 9-Jun  | 1161-1161                            | Lasfargues 2017                        |
| Risk of cancer associated with the use of antidepressants            | Boaventura, C. S.; Guimaraes, A. N.; Soares, G. R.; Fraga, A. M. B. F.; Neves, F. B. C. S.; Fonse, M. P. | 2007 | Revista de Psiquiatria do Rio Grande do Sul | 29     | 1      | 163-169                              | Boaventura 2007                        |
| Overweight, obesity and cancer risks                                 | Ancelin, R.; Bessette, D.                          | 2013 | Oncologie                         | 15     | 4-Mar  | 193-201                              | Ancelin 2013                           |
| Depression and cancer: Challenging the myth through epidemiology    | Lemogne, C.; Consoli, S. M.                        | 2010 | Psycho-Oncologie                  | 4      | 1      | 22-27                                | Lemogne 2010                           |

Exclusion reason: Non-English;
| Topic                                                                 | Year   | Type of Review            |
|----------------------------------------------------------------------|--------|---------------------------|
| Hepatitis C virus and risk of lymphoma and other lymphoid neoplasms: a meta-analysis of epidemiologic studies | DalMaso 2006 | meta-analysis of summary level data |
| Hazardous waste and health impact: a systematic review of the scientific literature | Fazzo 2017 | systematic review |
| Effects of omega-3 fatty acids on cancer risk: a systematic review | MacLean 2006 | systematic review |
| Anaplastic Large Cell Lymphoma and Breast Implants: A Systematic Review | Kim 2011 | systematic review |
| Malignancies and monoclonal gammopathy in Gaucher disease: a systematic review of the literature | Arends 2013 | systematic review |
| Systematic review of the relationship between artificial sweetener consumption and cancer in humans: analysis of 999,741 participants | Mishra 2015 | systematic review |
| Consumption of Sugars, Sugary Foods, and Sugary Beverages in Relation to Cancer Risk: A Systematic Review of Longitudinal Studies | Makarem 2018 | systematic review |
| Are pre- or postnatal diagnostic X-rays a risk factor for childhood cancer? A systematic review | Schulze-Rath 2008 | systematic review |
| Cancer risk in children and young adults born preterm: A systematic review and meta-analysis | Paquette 2019 | systematic review |
| Rating | Topic                                                                 | Author year | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 | Item 10 | Item 11 | Item 12 | Item 13 | Item 14 | Item 15 | Item 16 |
|-------|----------------------------------------------------------------------|-------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| eTable 3: AMSTAR 2 evaluation | | | | | | | | | | | | | | | | | | |
| Dietary factors | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
|----------------|------------------------|--------------------|--------------|---------------|-----------------------|-------------|--------------|------------------------------------|------------------------------------------|
| Meat           | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Fish           | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Fruits and vegetables | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Legumes        | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Coffee and tea | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Condiments     | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Dietary fat    | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Dietary fibre  | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Alcoholic drink | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Breastfeeding  | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| High-risk lymphomas | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Non-steroidal anti-inflammatory drugs | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Contraception  | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Smoking        | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |
| Alcohol        | Nutritional risk factor | Level of comparison | Outcome type | Follow-up type | No. of primary studies | No. of cases | Effect measure | Relative effects summary effect size | P-value of strength of reported association |

**Table 5: Environmental factors for NHL, reported in reanalysis of summary level data with suggestive (Class III), weak (Class IV) and nonsignificant evidence (Class V) of an association with NHL.**

*RR*: relative risk; *OR*: odds ratio; *CI*: confidence interval; *NS*: nonsignificant; *IV*: informative value; *b*: baseline value; *b-l*: baseline level; *b-h*: baseline high level.
| Outcome | Group 1 | Group 2 | Reference | OR/RR | 95% CI | P value | Methodology |
|--------|--------|--------|-----------|-------|--------|----------|-------------|
| | | | | | | | |
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**Notes:**
- OR/RR: Odds ratio/relative risk.
- CI: Confidence interval.
- P: Probability.
- Methodology: IV = Inverse variance, NS = Not significant.
A P value for summary effect estimates using a random-effects DerSimonian and Laird estimator.

b Strength of association using the criteria listed in Table 1.

c These studies considered NHL incidence and mortality.

d Summary effect estimates were calculated using a fixed effect estimator.

e Not using inverse variance weighting.
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BMJ Medicine

eTable 5: Nominally significant associations from meta-analysis of individual participant data

Study
Kane 2013
Kane 2013
Kane 2013
Kane 2013
Kane 2013
Kane 2013
Kane 2013
Kane 2013
Kane 2013
Kane 2013
Kane 2013

Outcome
NHL
NHL
NHL
NHL
NHL
NHL
DLBCL
DLBCL
DLBCL
DLBCL
FL

Exposure
Hormone therapy (ever vs. never)
Hormone therapy age first used (50-54 years vs. never used)
Hormone therapy age first used (55+ years vs. never used)
Hormone therapy years used (<2 years vs. never used)
Hormone therapy years used (5 to <10 years vs. never used)
Hormone therapy years since last used (current vs. never used)
Hormone therapy (ever vs. never)
Hormone therapy age first used (50-54 years vs. never used)
Hormone therapy years used (5 to <10 years vs. never used)
Hormone therapy years since last used (current vs. never used)
Hormone therapy years since last used (current vs. never used)

Number of cases
2094
1987
1987
2094
2094
2035
675
637
675
552
418

Cocco 2013

DLBCL

0.4 (0.2-1.0)

Weak

DLBCL

1251

0.6 (0.4-1.0)

Weak

Cocco 2013

FL

Duration trichloroethylene exposure (30-39 years vs. unexposed)
Frequency trichloroethylene exposure (<=5% work time vs.
unexposed)
Frequency trichloroethylene exposure (31%+ work time vs.
unexposed)

1251

Cocco 2013

639

1.8 (1.1-2.9)

Weak

Cocco 2013
Willet 2008
Willet 2008
Willet 2008
Willet 2008
Willet 2008
Willet 2008
Willet 2008
Slager 2014
Slager 2014
Slager 2014
Slager 2014

FL
NHL
FL
CLL/SLL
Other BCL
Other BCL
DLBCL
BL
CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL

639
5731
1047
625
228
174
6285
90
2345
2182
1168
1168

2.2 (1.1-4.2)
1.19 (1.06-1.34)
1.47 (1.18-1.84)
0.72 (0.56-0.93)
1.71 (1.14-2.58)
1.87 (1.14-3.05)
1.80 (1.23-2.62)
3.13 (1.19-8.25)
0.86 (0.78-0.95)
0.87 (0.77-0.98)
0.79 (0.66-0.94)
0.81 (0.66-0.99)

Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak

Slager 2014

CLL/SLL

1168

0.71 (0.55-0.92)

Weak

Slager 2014
Slager 2014
Slager 2014
Slager 2014
Slager 2014
Slager 2014
Slager 2014
Slager 2014
Slager 2014
Slager 2014
Slager 2014
Slager 2014
Slager 2014

CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL

1168
1794
1794
994
1595
1042
1042
1013
1042
685
1301
1301
2191

0.68 (0.49-0.94)
1.23 (1.05-1.44)
1.10 (1.02-1.19)
1.99 (1.16-3.41)
1.21 (1.07-1.36)
1.20 (1.06-1.35)
0.64 (0.43-0.96)
1.32 (1.08-1.61)
1.77 (1.05-3.01)
0.75 (0.59-0.96)
0.80(0.69-0.94)
0.81 (0.68-0.96)
0.90 (0.81-0.99)

Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak

Slager 2014
Slager 2014
Slager 2014

CLL/SLL
CLL/SLL
CLL/SLL

2191
2191
2191

0.82 (0.71-0.94)
0.87 (0.76-0.99)
0.83 (0.71-0.98)

Weak
Weak
Weak

Slager 2014
Slager 2014

CLL/SLL
CLL/SLL

2191
2191

0.72 (0.57-0.90)
0.82 (0.71-0.96)

Weak
Weak

Slager 2014
Slager 2014
Slager 2014
Slager 2014
Morton 2014
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CLL/SLL
CLL/SLL
CLL/SLL
CLL/SLL
NHL
MZL
LPL/WM
DLBCL
NHL
DLBCL
MZL
DLBCL
NHL
MZL
LPL/WM
DLBCL
FL
NHL
MF/SS
PTCL
MZL
LPL/WM
DLBCL
MF/SS
PTCL
NHL
PTCL
DLBCL
PTCL
MF/SS
HCL
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MZL
LPL/WM
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CLL/SLL
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17471

2.54 (1.53-4.21)
0.84 (0.72-0.98)
0.82 (0.70-0.95)
1.51 (1.09-2.10)
1.96 (1.60-2.40)
5.46 (3.81-7.83)
2.61 (1.34-5.08)
2.45 (1.91-3.16)
2.24 (1.03-4.87)
2.72 (1.13-6.57)
3.45 (1.07-11.15)
1.94 (1.35-2.79)
7.52 (3.68-15.36)
38.07 (16.94-85.55)
12.14 (3.16-46.58)
8.77 (3.94-19.54)
3.23 (1.19-8.80)
2.83 (1.82-4.41)
5.03 (1.16-21.57)
3.90 (1.24-12.30)
6.54 (3.10-13.82)
8.41 (2.81-25.20)
2.49 (1.42-4.37)
1.66 (1.00-2.75)
1.95 (1.37-2.77)
1.77 (1.05-2.99)
14.82 (7.27-30.19)
2.09 (1.04-4.18)
2.05 (1.23-3.42)
8.87 (1.11-71.25)
12.74 (1.49-108.84)
1.81 (1.39-2.37)
3.04 (1.65-5.60)
2.70 (1.11-6.56)
2.33 (1.71-3.19)
2.08 (1.23-3.49)
1.56 (1.21-2.03)
0.86 (0.81-0.92)
0.82 (0.74-0.90)
0.87 (0.77-0.98)
0.88 (0.79-0.98)
0.63 (0.48-0.82)
0.79 (0.63-0.98)
0.83 (0.74-0.92)
0.87 (0.77-0.98)
0.77 (0.65-0.91)
0.79 (0.67-0.94)
0.82 (0.77-0.88)
20.16 (2.44-166.28)
0.64 (0.44-0.95)
0.70 (0.52-0.96)
0.78 (0.70-0.86)
0.85 (0.74-0.97)
0.82 (0.73-0.91)
0.83 (0.77-0.91)
0.84 (0.75-0.95)
0.79 (0.66-0.94)
0.78 (0.68-0.89)
0.21 (0.05-0.86)
0.80 (0.71-0.90)
0.83 (0.70-0.97)
0.73 (0.56-0.96)
0.76 (0.63-0.92)
0.10 (0.01-0.93)
0.72 (0.61-0.85)

Suggestive
Weak
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HIghly suggestive
Highly suggestive
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Suggestive
HIghly suggestive
Highly suggestive
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Highly suggestive
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Suggestive
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Suggestive
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Suggestive
Suggestive
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Highly suggestive
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Suggestive
Suggestive
Suggestive
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Suggestive
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Weak
Suggestive

Intensity of trichloroethylene exposure (>150 ppm vs. unexposed)
Male height (100% vs. 60%)
Male height (100% vs. 60%)
Female height (20% vs. 60%)
Male height (100% vs. 60%)
Female height (80% vs. 60%)
Weight (Grade 3 obese vs. normal weight)
Weight (Underweight vs. normal weight)
Any atopic disease (yes vs. no)
Allergy (yes vs. no)
Blood transfusion (yes vs. no)
Total number of transfusions (1 vs none)
Number of years from first transfusion to date of diagnosis (<20
years vs. no transfusion)
Transfusion before 1990 (Transfusion 1990+ vs. No transfusion)
Adult height (Q4 vs Q1)
Adult height (continuous, 10 cm)
HCV
Ever lived or worked on a farm (yes vs. no)
Farmer (yes vs. no)
Animal farmer (yes vs. no)
Mixed animal and crop farmer (yes vs. no)
Hairdresser (yes vs. no)
Total sun exposure (quartile 4 (high) vs. 1 (low))
Recreational sun exposure (Quartile 4 (high) vs 1 (low))
Recreational sun exposure (Quartile 2 vs. 1)
Hisotry of cigarette smoking (yes vs. no)
Smoking status as of ~1 year before diagnosis/interview (current
vs.nonsmoker)
Age started smoking cigarettes (14-<18 years)
Age started smoking cigarettes (18-<20 years)
Frequency of cigarette smoking (30+ cigarettes/day vs.
nonsmoker)
Duration of cigarette smoking (30-39 years vs. nonsmoker)
Years since quitting cigarette smoking (former smoker unknown
when quit vs. nonsmoker)
Lifetime cigarette exposure (>20-35 plac-years vs. nonsmoker)
Lifetime cigarette exposure (>35 plack-years vs. nonsmoker)
Frequency of hair dye use (12+ times/year vs. never hair dye)
History of B-cell activating autoimmune disease (any vs. none)
History of B-cell activating autoimmune disease (any vs. none)
History of B-cell activating autoimmune disease (any vs. none)
History of B-cell activating autoimmune disease (any vs. none)
Hemolytic anemia (any vs. non)
Hemolytic anemia (any vs. non)
Pernicious anemia
Rheumatoid arthritis (any vs. none)
Sjogren's syndrome (any vs. none)
Sjogren's syndrome (any vs. none)
Sjogren's syndrome (any vs. none)
Sjogren's syndrome (any vs. none)
Sjogren's syndrome (any vs. none)
Systemic lupus erythematosus (any vs. none)
Systemic lupus erythematosus (any vs. none)
Systemic lupus erythematosus (any vs. none)
Systemic lupus erythematosus (any vs. none)
Systemic lupus erythematosus (any vs. none)
Systemic lupus erythematosus (any vs. none)
History of T-cell activating autoimmune disease
History of T-cell activating autoimmune disease
Celiac disease (any vs. none)
Celiac disease (any vs. none)
Celiac disease (any vs. none)
Psoriasis (any vs. none)
Systemic sclerosis/scleroderma
Systemic sclerosis/scleroderma
Hepatitis C virus seropositivity
Hepatitis C virus seropositivity
HCV
HCV
HCV
Peptic ulcer
Allergy
Allergy
Allergy
Allergy
Hay fever
Allergy
Food allergy
Asthma
Food allergy
Food allergy
Hay fever
Systemic sclerosis/scleroderma
Hay fever
Hay fever
Hay fever
Asthma
Hay fever
History of blood transfusion (any vs. none)
History of blood transfusion (any vs. none)
History of blood transfusion (any vs. none)
History of blood transfusion (any vs. none)
History of blood transfusion (any vs. none)
Age at least transfusion (%>40 years)
Age at least transfusion (%>40 years)
Age at least transfusion (%>40 years)
Age at least transfusion (%>40 years)
Age at least transfusion (%>40 years)
No. transfusions (% 2+)

Effect estimate (95% CI)
0.79 (0.69-0.90)
0.74 (0.61-0.91)
0.78 (0.62-0.98)
0.78 (0.62-0.98)
0.72 (0.57-0.91)
0.70 (0.54-0.90)
0.66 (0.54-0.80)
0.58 (0.42-0.80)
0.59 (0.40-0.86)
0.57 (0.44-0.74)
0.76 (0.58-0.99)

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Classification of evidence
Suggestive
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak
Weak


Any beer 17471 0.90 (0.84-0.97) Weak
Any liquor 324 0.66 (0.47-0.92) Weak
Frequency (%>14 servings/week) alcohol 3530 0.82 (0.69-0.96) Weak
Lifetime (%>200 kg) alcohol 295 0.28 (0.12-0.70) Weak
HCL
BL
Any liquor 17471 0.84 (0.78-0.91) Suggestive
Height (% Q3-Q4) 3530 1.20 (1.02-1.40) Weak
Frequency (%>14 servings/week) beer 4667 0.67 (0.55-0.83) Suggestive
Lifetime (%>200 kg) alcohol 4667 0.64 (0.52-0.79) Suggestive
Years since quitting (%>15 years) cigarette smoking 374 1.37 (1.01-1.85) Weak
Packyears (%>20) cigarette smoking 3530 1.13 (1.01-1.27) Weak
Any alcohol 17471 0.87 (0.81-0.93) Suggestive
PTCL
BL
NHL
HCL
FL
Frequency (%>14 servings/week) beer 3530 0.78 (0.61-0.99) Weak
Lifetime (%>200 kg) beer 4667 0.64 (0.46-0.87) Weak
History of cigarette smoking (any vs. none) 2440 0.90 (0.81-0.99) Weak
Young adult BMI (% 25 kg/m^2+) 4667 3.02 (2.13-4.37) Highly suggestive
LPL/WM
Any wine 584 0.67 (0.52-0.86) Weak
Frequency (%>-12 times/year) personal hairdye use 1052 1.55 (1.05-2.29) Weak
Years since quitting (%>15 years) 2440 0.82 (0.72-0.94) Weak
LPL/WM
MF/SS
HCL
History of cigarette smoking (any vs. none) 154 0.51 (0.37-0.71) Weak
Any wine 4667 0.81 (0.73-0.89) Suggestive
Ever used HRT 17471 0.84 (0.73-0.96) Weak
FL
BL
CLL/SLL
HCL
BL
Duration of hairdye use (%>=20 years) 17471 1.18 (1.02-1.35) Weak
Any alcohol 3530 0.86 (0.77-0.96) Weak
PTCL
Status (% current) 17471 0.86 (0.78-0.94) Weak
Height (% Q3-Q4) 295 2.43 (1.37-4.31) Weak
DLBCL
Any wine 1052 0.64 (0.53-0.78) Suggestive
Usual adult BMI (% 25 kg/m^2+) 324 1.95 (1.10-3.46) Weak
Ever used HRT 4667 0.78 (0.65-0.94) Weak
DLBCL
Year first Ocs use (%<1970) 4667 0.74 (0.59-0.93) Weak
FL
Any wine 3530 0.85 (0.76-0.95) Weak
No. transfusions (% 2+) 4667 0.70 (0.56-0.88) Weak
Frequency (%>=14 servings/week) wine 1052 0.45 (0.30-0.69) Suggestive
FL
NHL
CLL/SLL
HCL
BL
Age at initiation (% <20 years) alcohol 4667 0.73 (0.62-0.86) Suggestive
Frequency (%>14 servings/week) beer 584 0.49 (0.27-0.88) Weak
LPL/WM
NHL
MZL
BL
DLBCL
HCL
LPL/WM
Age at initiation (%<19 years) alcohol 4667 0.72 (0.60-0.87) Suggestive
Frequency (%>=14 servings/week) wine 4667 0.67 (0.57-0.80) Suggestive
Frequency (%>14 servings/week) 1052 0.61 (0.45-0.84) Weak
DLBCL
BL
DLBCL
MZL
HCL
LPL/WM
Frequency (%>20) cigarette smoking 2440 0.78 (0.66-0.93) Weak
Duration (%>30 years) alcohol 4667 0.73 (0.62-0.86) Suggestive
NHL
FL
PTCL
Blood transfusion <1991 4667 0.78 (0.65-0.94) Weak
DLBCL
NHL
CLL/SLL
PTCL
Duration (%>20 years) cigarette smoking 374 1.50 (1.10-2.04) Weak
NHL
NHL
CLL/SLL
PTCL
Blood transfusion <1994 154 0.06 (0.00-0.82) Weak
NHL
NHL
NHL
Frequency (%>=23 servings/week) any liquor 3530 1.70 (1.15-2.52) Weak
PTCL
Usual adult BMI (% 25 kg/m^2+) 4667 1.32 (1.11-1.57) Weak
Packyears (%>20) cigarette smoking 584 1.67 (1.28-2.18) Weak
Years since quitting (%>15 years) cigarette smoking 154 0.40 (0.26-0.61) Weak
Lifetime (%>200 kg) any liquor 4667 0.57 (0.41-0.79) Suggestive
Frequency (%>=14 servings/week) 1052 0.61 (0.45-0.84) Weak
DLBCL
NHL
CLL/SLL
PTCL
Duration (%>30 years) alcohol 4667 0.73 (0.62-0.86) Suggestive
NHL
FL
LPL/WM
DLBCL
Blood transfusion <1991 4667 0.78 (0.65-0.94) Weak
DLBCL
Frequency (%>14 servings/week) any liquor 17471 2.21 (1.71-2.86) Highly suggestive
Any liquor 3530 0.86 (0.76-0.97) Weak
Height (% Q3-Q4) 4667 1.16 (1.01-1.33) Weak
LPL/WM
NHL
DLBCL
Frequency (%>=23 servings/week) any liquor 3530 1.70 (1.15-2.52) Weak
Frequency (%>14 servings/week) wine 1052 0.61 (0.45-0.84) Weak
Frequency (%>14 servings/week) 1052 0.61 (0.45-0.84) Weak
DLBCL
NHL
CLL/SLL
PTCL
Frequency (%>14 servings/week) any liquor 17471 2.21 (1.71-2.86) Highly suggestive
Any liquor 3530 0.86 (0.76-0.97) Weak
Height (% Q3-Q4) 4667 1.16 (1.01-1.33) Weak
LPL/WM
NHL
DLBCL
Frequency (%>=23 servings/week) any liquor 3530 1.70 (1.15-2.52) Weak
Frequency (%>14 servings/week) wine 4667 0.67 (0.57-0.80) Suggestive
Frequency (%>14 servings/week) wine 584 0.61 (0.39-0.95) Weak
DLBCL
NHL
CLL/SLL
PTCL
| Condition                  | OR     | 95% CI            | Evidence Level |
|----------------------------|--------|------------------|----------------|
| **CLL/SLL**                |        |                  |                |
| Recreational sun exposure (%Q3-Q4 hours/week) | 17471  | 0.74 (0.66-0.83) | Highly suggestive |
| **DLBCL**                  |        |                  |                |
| Sjogren's syndrome (any vs. none) | 1801  | 3.91 (1.39-11.0) | Weak           |
| Intensity (21-30 cigarettes/d) | 6393  | 1.19 (1.04-1.36) | Weak           |
| General unspecified laborer | 3530  | 1.28 (1.06-1.55) | Weak           |
| **FL**                     |        |                  |                |
| Women's hairdresser        | 17471  | 1.42 (1.07-1.89) | Weak           |
| Status (% current) cigarette smoking | 10351 | 1.10 (1.00-1.20) | Weak           |
| **HCL**                    |        |                  |                |
| Leather worker             | 152    | 3.89 (1.34-11.33) | Weak           |
| **MF/SS**                  |        |                  |                |
| Recreational sun exposure (%Q3-Q4 hours/week) | 3530  | 0.70 (0.58-0.84) | Suggestive     |
| **NHL**                    |        |                  |                |
| Frequency (>=28 servings per week vs. none) | 6492  | 0.87 (0.76-0.99) | Weak           |
| Ever vs. non-drinker       | 2126   | 0.75 (0.66-0.84) | Suggestive     |
| Frequency (>=28 servings per week vs. none) drinking | 2126  | 0.73 (0.60-0.90) | Weak           |
| Age of 1st transfusion (31-40 years vs. none) white men | 4599  | 0.71 (0.51-0.97) | Weak           |
| Duration (14-27 servings per week vs. none) drinking | 2126  | 0.73 (0.61-0.86) | Suggestive     |
| **PTCL**                   |        |                  |                |
| Painter                    | 324    | 3.42 (1.81-6.47) | Weak           |
| Lifetime liquor (%>200 kg) | 324    | 3.18 (1.44-7.05) | Weak           |
| Duration (21-30 years) drinking | 2126 | 0.74 (0.57-0.94) | Weak           |
| **DLBCL**                  |        |                  |                |
| Hairdresser                | 17471  | 1.34 (1.05-1.72) | Weak           |
| **NHL**                    |        |                  |                |
| MZL                        |        |                  |                |
| Age at initiation (% >-20 years) cigarette smoking | 1452 | 1.24 (1.05-1.46) | Weak           |
| DLBCL                      |        |                  |                |
| Type 1 diabetes            | 1813   | 1.97 (1.00-3.88) | Weak           |
| **DLBCL**                  |        |                  |                |
| NHL                        |        |                  |                |
| MZL                        |        |                  |                |
| Farmland any type          | 2440   | 1.23 (1.04-1.45) | Weak           |
| **Socioeconomic status (% low)** | 17471 | 0.88 (0.83-0.93) | Suggestive     |
| **Primary sjorgen's syndrom** | 2356   | 6.57 (2.12-20.3) | Weak           |
| **Beer, wine, and liquor** | 6492   | 0.76 (0.68-0.84) | Highly suggestive |
| **Sjogren's syndrome (any vs. none)** | 8230  | 6.56 (3.10-13.9) | Suggestive     |
| **Field crop/vegetable farmer** | 324   | 2.80 (1.38-5.68) | Weak           |
| **NHL**                    |        |                  |                |
| MZL                        |        |                  |                |
| Age at initiation (18-19 years vs. nonsmoker) | 89    | 0.34 (0.12-0.96) | Weak           |
| **DLBCL**                  |        |                  |                |
| Duration (>=41 years) drinking | 2126 | 0.67 (0.53-0.85) | Suggestive     |
| **MF/SS**                  |        |                  |                |
| Women's hairdresser        | 2440   | 2.46 (1.31-4.62) | Weak           |
| **NHL**                    |        |                  |                |
| Duration (>=36 years) cigarette smoking | 6570  | 1.16 (1.05-1.28) | Weak           |
| Pack-years (>=36) cigarette smoking | 6373  | 1.21 (1.09-1.34) | Weak           |
| **CLL/SLL**                |        |                  |                |
| Number of blood transfusions (One vs none) white men | 4571  | 0.70 (0.60-0.81) | Suggestive     |
| **NHL**                    |        |                  |                |
| History of living or working on a farm | 584   | 0.73 (0.56-0.99) | Weak           |
| **PTCL**                   |        |                  |                |
| Age of 1st transfusion (1970s) white men | 4501  | 0.58 (0.42-0.79) | Suggestive     |
| Era first transfusion (1990+) white men | 4501  | 0.66 (0.52-0.84) | Suggestive     |
| **Baker/miller**           |        |                  |                |
| History of living or working on a farm | 584   | 0.73 (0.55-0.95) | Weak           |
| **BL**                     |        |                  |                |
| NHL                        |        |                  |                |
| History of living or working on a farm | 4599  | 0.61 (0.45-0.82) | Weak           |
| **ALL**                    |        |                  |                |
| MZL                        |        |                  |                |
| Women's hairdresser        | 4667   | 1.63 (1.15-2.31) | Weak           |
| **NHL**                    |        |                  |                |
| **Systemic lupus erythematosus (any vs. none)** | 3364  | 2.74 (1.47-5.11) | Weak           |
| **NHL**                    |        |                  |                |
| **MCL**                    |        |                  |                |
| **PTCL**                   |        |                  |                |
| History of living or working on a farm | 4501  | 0.73 (0.55-0.95) | Weak           |
| Year | Study | Exposure | Outcomes | HR (95% CI) | Grade |
|------|-------|----------|----------|-------------|--------|
| 2014 | Wang  | NMZL     | B-cell activation | 1.07 (1.01-1.13) | Weak |
| 2014 | Wang  | NMZL     | Asthma with or without atopy | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | PTCL-NOS | 1.04 (1.00-1.09) | Weak |
| 2014 | Wang  | NMZL     | Mycosis fungoides and Sézary syndrome | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Intensity (21-30 cigarettes/d) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Textile worker | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Any type of alcohol (Q1 vs non-drinkers) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Sjogren's syndrome (any vs. none) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Any type of alcohol (Q4 vs non-drinkers) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Adult infectious mononucleosis | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Electrical fitters | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | History of eczema | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Duration of cigarette smoking (40+ years) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Adult infectious mononucleosis | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Any type of alcohol (Q1 vs non-drinkers) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Angioimmunoblastic lymphoma | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Duration of employment as cleaner (1-10 years vs. never) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Smoker, duration unknown | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | PTCL | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | MZL | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | EMZL | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | General carpenter | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Duration (21-35 years) of cigarette smoking | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Wine (Q3 vs non-drinkers) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | HCV (>=50 years) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | MZL | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | ALCL | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | PTCL-Cutaneous NOS | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | African carpenter | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Duration of employment as cleaner (1-10 years vs. never) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Smoker, duration unknown | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | PTCL | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | MZL | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | EMZL | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | General carpenter | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Duration (21-35 years) of cigarette smoking | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | Wine (Q3 vs non-drinkers) | 1.03 (1.00-1.07) | Weak |
| 2014 | Wang  | NMZL     | HCV (>=50 years) | 1.03 (1.00-1.07) | Weak |
| Description                                                                 | Odds Ratio | 95% CI     | P-value | Interpretation       |
|----------------------------------------------------------------------------|------------|------------|---------|----------------------|
| Lifetime alcohol consumption (101-200 kg vs nondrinker)                   | 0.68       | 0.51-0.91  | 0.016   | Weak                 |
| LPL/WM                                                                     |            |            |         |                      |
| Usual adult weight (Q4 vs Q1)                                             | 1.20       | 1.07-1.33  | 0.002   | Weak                 |
| Hay fever                                                                  | 0.73       | 0.44-0.99  | 0.032   | Weak                 |
| Recreational sun exposure (Q4 vs Q1 hours/week), Female                   | 0.70       | 0.58-0.85  | 0.003   | Suggestive           |
| Status (% current) cigarette smoking                                       | 1.19       | 1.07-1.32  | 0.002   | Weak                 |
| LPL/WM                                                                     |            |            |         |                      |
| Allergy and asthma, hay fever, or eczema                                  | 0.68       | 0.52-0.88  | 0.003   | Weak                 |
| Color of hairdye used (women only; light vs. never)                       | 9.69       | 2.12-44.34 | 0.001   | Weak                 |
| History of cigarette smoking (any vs. none), Female                       | 1.22       | 1.09-1.37  | 0.002   | Suggestive           |
| Duration (>=40 years) cigarette smoking                                   | 1.18       | 1.04-1.35  | 0.009   | Weak                 |
| Physical activity (Mild), Female                                          | 1.53       | 1.02-2.30  | 0.038   | Weak                 |
| Transfusions before 1990                                                   | 0.87       | 0.76-0.99  | 0.016   | Weak                 |
| Blood transfusion, Female                                                 | 0.80       | 0.68-0.95  | 0.005   | Weak                 |
| Metal worker                                                               | 3.56       | 1.67-7.58  | 0.001   | Weak                 |
| Age started smoking cigarettes regularly (14-17 years)                   | 1.12       | 1.01-1.25  | 0.038   | Weak                 |
| Grams of ethanol per week as an adult (Q4 vs nondrinker)                 | 0.79       | 0.66-0.94  | 0.005   | Weak                 |
| Blood transfusion                                                          | 0.78       | 0.68-0.89  | 0.001   | Suggestive           |
| Any atopic disorder                                                        | 0.74       | 0.61-0.89  | 0.001   | Weak                 |
| Asthma no other atopy                                                      | 2.28       | 1.23-4.23  | 0.008   | Weak                 |
| BMI as young adult (25-<30 kg/m²)                                          | 1.49       | 1.21-1.83  | 0.001   | Suggestive           |
| Total number of blood transfusions (2+ vs none)                           | 0.70       | 0.53-0.92  | 0.011   | Weak                 |
| University and higher education teachers, Male                            | 0.53       | 0.31-0.90  | 0.024   | Weak                 |
| Total sun exposure (Q4 vs Q1 hours/week)                                  | 0.82       | 0.69-0.99  | 0.030   | Weak                 |
| Color of hairdye used (women only; dark vs. never)                        | 5.30       | 1.19-23.66 | 0.031   | Weak                 |
| Duration of alcohol consumption (Drinker duration unknown vs. nondrinker) | 1.45       | 1.04-2.00  | 0.026   | Weak                 |
| Usual adult height (Q4 vs Q1)                                              | 1.12       | 1.01-1.25  | 0.033   | Weak                 |
| Duration of alcohol consumption (Drinker duration unknown vs. nondrinker) | 1.46       | 1.04-2.05  | 0.026   | Weak                 |
| Atelectasis                                                                | 0.85       | 0.75-0.97  | 0.002   | Weak                 |
| History of chronic obstructive lung disease                               | 1.17       | 1.01-1.35  | 0.041   | Weak                 |
| University and higher education teachers, Female                          | 0.53       | 0.31-0.90  | 0.024   | Weak                 |
| Total sun exposure (Q4 vs Q1 hours/week), Female                          | 0.77       | 0.63-0.95  | 0.006   | Weak                 |
| University and higher education teachers, Female                          | 0.53       | 0.31-0.90  | 0.024   | Weak                 |
| Blood transfusion                                                          | 0.79       | 0.63-0.98  | 0.021   | Weak                 |
| Age started smoking cigarettes regularly (>=20 years vs. nonsmoker)       | 1.45       | 1.04-2.00  | 0.026   | Weak                 |
| Usual adult body mass index (15-<18.5 vs. 18.5-<22.5)                     | 0.60       | 0.41-0.88  | 0.008   | Weak                 |
| Total sun exposure (Q4 vs Q1 hours/week), Female                          | 0.77       | 0.63-0.95  | 0.006   | Weak                 |
| Electrical and electronics workers                                         | 1.63       | 1.09-2.44  | 0.020   | Weak                 |
| Hay fever and asthma, allergy, or eczema                                  | 0.66       | 0.49-0.89  | 0.008   | Weak                 |
| Celiac disease (any vs. none)                                              | 2.14       | 1.07-4.28  | 0.030   | Weak                 |
| Metal worker                                                               | 3.56       | 1.67-7.58  | 0.001   | Weak                 |
| History of chronic obstructive lung disease                               | 1.17       | 1.01-1.35  | 0.041   | Weak                 |
| History of chronic obstructive lung disease                               | 1.17       | 1.01-1.35  | 0.041   | Weak                 |
| University and higher education teachers, Male                            | 0.53       | 0.31-0.90  | 0.024   | Weak                 |
| Total sun exposure (Q4 vs Q1 hours/week), Female                          | 0.77       | 0.63-0.95  | 0.006   | Weak                 |
| University and higher education teachers, Female                          | 0.53       | 0.31-0.90  | 0.024   | Weak                 |
| Year   | Code | Description                      | N | Ratio   | 95% CI           | P Value |
|--------|------|----------------------------------|---|---------|------------------|---------|
| Mannetje 2016 | NHL | Secondary education teachers     | 10046 | 0.82    | 0.69-0.98        | Weak    |
| Mannetje 2016 | NHL | Head teacher                     | 10046 | 2.16    | 1.15-4.06        | Weak    |
| Mannetje 2016 | NHL | Other teachers                   | 10046 | 0.63    | 0.40-0.98        | Weak    |
| Mannetje 2016 | NHL | Milliners and hatmakers          | 10046 | 2.46    | 1.28-4.74        | Weak    |
| Mannetje 2016 | NHL | Carpenter, general               | 10046 | 1.42    | 1.14-1.79        | Weak    |
| Mannetje 2016 | DLBCL | Charworkers, cleaners and related | 10046 | 1.50    | 1.16-1.99        | Weak    |
| Mannetje 2016 | DLBCL | Field crop farmer general        | 10046 | 1.38    | 1.04-1.85        | Weak    |
| Mannetje 2016 | DLBCL | Milliners                       | 10046 | 4.17    | 1.19-14.32       | Weak    |
| Mannetje 2016 | DLBCL | Sewer and embroiderer           | 10046 | 2.30    | 0.90-6.06        | Weak    |
| Mannetje 2016 | DLBCL | Field workers                    | 10046 | 1.14    | 0.95-1.37        | Weak    |
| Mannetje 2016 | DLBCL | Field crop farm worker general   | 10046 | 1.48    | 1.01-2.17        | Weak    |
| Mannetje 2016 | DLBCL | Carpenter, general               | 10046 | 2.10    | 1.08-4.09        | Weak    |
| Mannetje 2016 | DLBCL | Printers                         | 10046 | 1.80    | 1.14-2.84        | Weak    |
| Mannetje 2016 | DLBCL | Spinners, weavers, knitters, dye | 10046 | 1.85    | 1.21-2.83        | Weak    |
| Mannetje 2016 | DLBCL | Wood workers                     | 10046 | 1.54    | 1.04-2.27        | Weak    |
| Mannetje 2016 | DLBCL | Cabinetmakers                    | 10046 | 2.41    | 1.22-4.74        | Weak    |
| Mannetje 2016 | PTCL | Electric fitters                 | 652  | 2.02    | 1.03-3.97        | Weak    |
| Mannetje 2016 | PTCL | Metal workers                    | 652  | 0.66    | 0.45-0.99        | Weak    |
| Mannetje 2016 | PTCL | Painters                         | 652  | 1.80    | 1.14-2.84        | Weak    |
| Mannetje 2016 | PTCL | Textile worker                   | 652  | 1.60    | 1.18-2.17        | Weak    |
| Mannetje 2016 | PTCL | Spinners, weavers, knitters, dye | 652  | 1.85    | 1.21-2.83        | Weak    |
| Mannetje 2016 | PTCL | Wood workers                     | 652  | 1.54    | 1.04-2.27        | Weak    |
| Mannetje 2016 | PTCL | Cabinetmakers                    | 652  | 2.41    | 1.22-4.74        | Weak    |
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| Mannetje 2016 | PTCL | Wood workers                     | 652  | 1.54    | 1.04-2.27        | Weak    |

**Note:** The table shows odds ratios (OR) with 95% confidence intervals (CI) and p-values for different occupations, indicating the association with increased risk of certain diseases.
| Condition                        | OR (95% CI) | Strength of association | Concordance |
|---------------------------------|-------------|-------------------------|-------------|
| Hepatitis C virus [FL]           | 0.57 (0.30, 1.10) | No                      | Both        |
| Meat worker [NHL]                | 1.08 (0.81, 1.42) | No                      | Both        |
| Any alcohol [TCL]                | 0.68 (0.53, 0.87) | Yes                     | Both        |
| Petroleum workers [NHL]          | 0.79 (0.38, 1.67) | Yes                     | Neither     |
| Firefighter [NHL]                | 0.76 (0.53, 1.09) | No                      | Both        |
| Any alcohol [DLBCL]              | 0.81 (0.73, 0.89) | Yes                     | Both        |
| Any smoking [DLBCL]              | 1.01 (0.94, 1.08) | Yes                     | Neither     |
| Sarcoidosis [NHL]                | 0.71 (0.39, 1.29) | No                      | Neither     |
| Herpes Zoster [NHL]              | 2.26 (1.82, 2.81) | NS                      | II          |
| Tuberculosis [NHL]               | 1.37 (0.80, 2.19) | Yes                     | None        |
| Psoriasis [NHL]                  | 1.72 (1.27, 2.32) | III                     | Adult Shingles |
| celiac disease [CLL/SLL]         | 0.60 (0.14, 2.61) | Yes                     | None        |
| celiac disease [DLBCL]           | 2.09 (1.04, 4.18) | Yes                     | Both        |
| celiac disease [TCL]             | 14.82 (7.27, 30.19) | Yes                   | Both        |
| Type 1 diabetes [NHL]            | 1.15 (0.80, 1.66) | Yes                     | None        |
| Rheumatoid arthritis [NHL]       | 5.40 (3.75, 7.77) | II                      |         |
| Primary Sjogren's syndrome [NHL] | 13.76 (8.53, 18.99) | II                     |         |
| Ever drinking [CLL/SLL]          | 1.32 (0.99, 1.77) | Yes                     | None        |
| Ever drinking [FL]               | 0.89 (0.66, 1.22) | No                      | None        |
| Ever drinking [DLBCL]            | 2.83 (1.81, 4.11) | Yes                     | Both        |
| Ever drinking [TCL]              | 1.77 (1.02, 3.09) | Yes                     | Both        |
| Ever smoking [TCL]               | 1.32 (0.99, 1.77) | Yes                     | None        |
| Ever smoking [CLL/SLL]           | 1.32 (0.99, 1.77) | Yes                     | None        |
| Ever smoking [DLBCL]             | 1.32 (0.99, 1.77) | Yes                     | None        |
| Ever smoking [NHL]               | 1.81 (1.39, 2.37) | Yes                     | None        |
| Red blood cell transfusion [FL]   | 0.9 (0.71, 1.14)  | No                      | None        |
| Red blood cell transfusion [CLL/SLL] | 0.9 (0.71, 1.14) | No                      | None        |
| Red blood cell transfusion [NHL]  | 0.9 (0.71, 1.14)  | No                      | None        |

**Footnotes**

- [FL]: Hepatitis C virus
- [CLL/SLL]: Chronic lymphocytic leukemia/small lymphocytic lymphoma
- [DLBCL]: Diffuse large B-cell lymphoma
- [TCL]: T-cell lymphoma
- [NHL]: Non-Hodgkin lymphoma
- OR: Odds ratio
- CI: Confidence interval
- RR: Risk ratio
- SIR: Standardized incidence ratio
- MA: Meta-analysis
- NS: Not significant