Supplementary information

Health effects associated with vegetable consumption: a Burden of Proof study

In the format provided by the authors and unedited
Supplementary Information: supplementary methods, data sources, and results for “Health effects associated with vegetable consumption: a Burden of Proof study”

This appendix provides detailed information on input data sources, and presents supplementary results—particularly sensitivity analysis results—for “Health effects associated with vegetable consumption: a Burden of Proof study.”
Section 1: Data source identification and assessment

The data used for this study can be categorized into the following types: prospective cohort and case-cohort. Underlying data and citations are available for download using the “download” button on each risk curve page at https://vizhub.healthdata.org/burden-of-proof/.

Section 1.1: Literature identification

We conducted literature searches to obtain input data from prospective studies evaluating the relationship between vegetable consumption and ischemic heart disease (IHD), ischemic stroke, hemorrhagic stroke, type 2 diabetes, and esophageal cancer in our analysis.

A search string was developed to identify the most recent PRISMA-compliant meta-analyses which examined the effect of vegetable consumption and IHD, ischemic stroke, hemorrhagic stroke, and type 2 diabetes. Then the citation of the selected meta-analysis was searched. After selecting a meta-analysis for each outcome, another search string was developed to identify sources published after the period covered in the identified most recent PRISMA-compliant meta-analysis for each outcome of interest. For each of the outcome of interests, we searched PubMed, EMBASE, and Web of Science from the last date of the identified meta-analysis through May 31, 2022. We also searched the global health data exchange (GHDx) databases. For vegetable consumption and esophageal cancer, we conducted a full systematic review with no date constraint because we did not find a meta-analysis that meets our selection criteria. A full description of the search strings and searching strategy is presented below.

Ischemic Heart diseases: We developed PubMed strings to identify the most recent PRISMA complaint meta-analysis on vegetable consumption and IHD. The most recent PRISMA complaint meta-analysis that met our definition of exposure (i.e., vegetable consumption) and outcome (i.e., Ischemic heart diseases) was a study published by Bechtold et al in 2019. From this study meta-analysis, we identified 32 citations, with 11 studies meeting the inclusion criteria to be included in the final analysis. We found three additional studies from the global health data exchange (GHDx) database but only two studies met our inclusion criteria.

| Search strings for ischemic heart diseases                                                                 | Identified meta-analysis                                                                 |
|-----------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| ("Vegetables"[Mesh] OR Vegetables [Title/Abstract] OR "green leafy vegetables" OR "Cruciferous vegetables" OR Fruits and Vegetables" [Title/Abstract]) AND ("systematic review" [Publication Type] OR "systematic review" [Title/Abstract] OR "Meta-Analysis" [Publication Type] OR "meta-analysis" OR "Dose-Response"[Title/Abstract]) AND ("Myocardial Ischemia" [Mesh] OR "Coronary Artery Disease" [Mesh] OR "Angina, Stable" [Mesh] OR "Acute Coronary Syndrome" [Mesh] OR "ischemic heart disease" [tiab] OR "ischaemic heart disease" [tiab] OR "coronary artery disease" [tiab] OR "coronary heart disease" [tiab] OR "myocardial ischemia" [tiab] OR "myocardial ischaemia" [tiab] OR "myocardial infarction" [tiab] OR "angina" [tiab] OR "acute coronary syndrome") | Angela Bechthold, Heiner Boeing, Carolina Schwedhelm, Georg Hoffmann, Sven Knüppel, Khalid Iqbal, Stefaan De Henauw, Nathalie Michels, Brecht Devleesschauwer, Sabrina Schlesinger & Lukas Schwingshackl (2019) Food groups and risk of coronary heart disease, stroke and heart failure: A systematic review and dose-response meta-analysis of prospective studies, Critical Reviews in Food Science and Nutrition, 59:7, 1071-1090. |

A search string was developed to identify sources published after the period covered in Bechtold (March 1, 2017 to May 31, 2022). PubMed, EMBASE, and Web of Science were searched on May 31, 2022. The searches returned 473 total citations. Duplicates between the search results were identified by DOI and PubMed, then the remaining records were screened by title and abstract for possible retrieval. As a sensitivity test, 20% of each reviewer’s exclusions were independently verified by the other reviewer. The full text of included studies was retrieved and evaluated for extraction. Each full-text exclusion was verified by both reviewers. No discrepancies occurred.
between the 2 reviewers. Each exclusion reason source count is depicted in the Vegetable-IHD PRISMA diagram (Extended Data Figure 2).

Search Strings:

("Vegetables"[Mesh] OR "Vegetables" [Title/Abstract] OR "green leafy vegetables" OR "leafy vegetables" OR "Cruciferous vegetables" OR "Fruits and Vegetables" [Title/Abstract])
AND ("Cohort" [Publication type] OR "Prospective cohort" [Title/Abstract] OR "case-cohort" OR "Follow-up" OR "Longitudinal" [Title/Abstract])
AND ("Myocardial Ischemia" [Mesh] OR "Coronary Artery Disease" [Mesh] OR "Angina, Stable" [Mesh] OR "Acute Coronary Syndrome" [Mesh] OR "ischemic heart disease" [tiab] OR "ischaemic heart disease" [tiab] OR "coronary artery disease" [tiab] OR "coronary heart disease" [tiab] OR "myocardial ischemia" [tiab] OR "myocardial ischaemia" [tiab] OR "myocardial infarction" [tiab] OR "angina" [tiab] OR "acute coronary syndrome")

Stroke subtypes (Ischemic and hemorrhagic stroke). We developed search strings for both stroke subtypes (i.e. hemorrhagic stroke and ischemic strokes) to identify the most recent PRISMA complaint meta-analyses that fulfilled our definition of exposure (total vegetable consumption) and outcomes (stroke subtypes: Ischemic and hemorrhagic stroke). The meta-analysis used for IHD (Bechtold et al 2019) was determined to be the best source available for stroke citations as well. Due to the substantial overlap among studies on ischemic and hemorrhagic stroke, sources were screened simultaneously for data on either outcome. A total of 38 citations were identified in the citations of this meta-analysis and screened. From a total of 38 citations, only eight studies (all eight studies included ischemic stroke while 5 of them included hemorrhagic stroke only) were eligible to be included in the final analysis. From the GHDX database, we identified three studies and only two of these studies met our inclusion criteria (reported both ischemic and hemorrhagic stroke).

| Search strings for hemorrhagic stroke                                                                 | Identified meta-analysis                                                                 |
|-------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| ("Vegetables"[Mesh] OR Vegetables [Title/Abstract] OR "green leafy vegetables" OR "Cruciferous vegetables" OR "Fruits and Vegetables" [Title/Abstract]) AND ("Systematic Review" [Publication Type] OR "systematic review" [Title/Abstract] OR "meta-analysis" [Title/Abstract] OR "Dose-Response"[Title/Abstract]) AND ("Hemorrhagic Stroke" [Mesh] OR ("subarachnoid" [Title/Abstract] AND ("hemorrhage" [Title/Abstract] OR "haemorrhage" [Title/Abstract])) OR "stroke" [Title/Abstract]) | Angela Bechthold, Heiner Boeing, Carolina Schwedhelm, Georg Hoffmann, Sven Knüppel, Khalid Iqbal, Steffaan De Henauw, Nathalie Michels, Brecht Devleesschauwer, Sabrina Schlesinger & Lukas Schwingshackl (2019) Food groups and risk of coronary heart disease, stroke and heart failure: A systematic review and dose-response meta-analysis of prospective studies, Critical Reviews in Food Science and Nutrition, 59:7, 1071-1090. |

| Search strings for ischemic stroke                                                                 | Identified meta-analysis                                                                 |
|-------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| ("Vegetables"[Mesh] OR Vegetables [Title/Abstract] OR "green leafy vegetables" OR "Cruciferous vegetables" OR "Fruits and Vegetables" [Title/Abstract]) AND ("Systematic Review" [Publication Type] OR "systematic review" [Title/Abstract] OR "meta-analysis" [Title/Abstract] OR "Dose-Response"[Title/Abstract]) AND ("Ischemic Stroke" [Mesh] OR "ischemic stroke" [Title/Abstract] OR "ischaemic stroke" [Title/Abstract] OR "cerebral infarction" [Title/Abstract] OR "unspecified stroke" [Title/Abstract] OR "stroke" [Title/Abstract]) | Angela Bechthold, Heiner Boeing, Carolina Schwedhelm, Georg Hoffmann, Sven Knüppel, Khalid Iqbal, Stefaan De Henauw, Nathalie Michels, Brecht Devleesschauwer, Sabrina Schlesinger & Lukas Schwingshackl (2019) Food groups and risk of coronary heart disease, stroke and heart failure: A systematic review and dose-response meta-analysis of prospective studies, Critical Reviews in Food Science and Nutrition, 59:7, 1071-1090. |
A search string was developed to identify sources published after the period covered in Bechtold et al 2019 study. PubMed, EMBASE, and Web of Science were searched on May 31, 2022. The search was filtered for publication dates beginning March 01, 2017, the cutoff date for the search in Bechtold et al 2019 study. The search string included terms for each stroke subtype, and sources were screened simultaneously for both stroke subtypes of interest. The searches returned 356 total citations, of which 2 records were ultimately extracted and included in the model. As described in the section on IHD, search results were deduplicated and screened by two reviewers, with each reviewer verifying the other’s exclusions for both the title-abstract and full-text screening steps.

Search strings for stroke subtypes:

("Vegetables"[MeSH Terms] OR "Vegetable*"[Title/Abstract] OR "green leafy vegetable*"[All Fields] OR "leafy vegetable*"[All Fields] OR "Cruciferous vegetables"[All Fields] OR "Fruits and Vegetables"[Title/Abstract] OR "Fruit and Vegetable"[Title/Abstract])
AND ("Cohort studies" [Mesh] OR "Prospective cohort" [Title/Abstract] OR "case-cohort" OR "Follow-up" OR "Longitudinal" [Title/Abstract])
AND ("Ischemic Stroke" [Mesh] OR "ischemic stroke" [Title/Abstract] OR "ischaemic stroke" [Title/Abstract] OR "cerebral infarction" [Title/Abstract] OR "unspecified stroke" [Title/Abstract] OR "stroke" [Title/Abstract])
AND ("Hemorrhagic Stroke" [Mesh] OR "Intracranial Hemorrhages"[Mesh] OR "intracerebral hemorrhage"[Title/Abstract] OR "intracerebral haemorrhage"[Title/Abstract] OR "hemorrhagic stroke"[Title/Abstract] OR "haemorrhagic stroke"[Title/Abstract] OR ("subarachnoid" [Title/Abstract] AND "hemorrhage" [Title/Abstract] OR "haemorrhage" [Title/Abstract]))).

**Diabetes:** We developed a PubMed search string to identify the most recent PRISMA complaint meta-analysis on vegetable consumption and type 2 diabetes. The meta-analysis identified that fulfills our criteria of exposure definition (total vegetables consumption), outcome definition (Type 2 diabetes) and PRISMA complaint was Halvorsen et al 2021. A total of 51 citations of this meta-analysis were identified and screened. From this meta-analysis, we included a total of 13 studies in the final analysis. The last date this meta-analysis covered was October 20, 2020.

| Search strings for diabetes                                                                 | Identified meta-analysis                                                                 |
|-------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| "Vegetables"[Mesh] OR Vegetables [Title/Abstract] OR "green leafy vegetables "OR" Cruciferous vegetables "OR" Fruits and Vegetables" [Title/Abstract] AND ("Systematic Review" [Publication Type] OR "systematic review" [Title/Abstract] OR "Meta-Analysis" [Publication Type] OR "meta-analysis" OR "Dose-Response"[Title/Abstract]) AND ("Diabetes Mellitus, Type 2" [Mesh] OR "diabetes mellitus type 2" [Title/Abstract] OR "Gestational diabetes" OR "diabetes type 2" [Title/Abstract] OR "type 2 diabetes mellitus" [Title/Abstract] OR "type 2 diabetes" [Title/Abstract] OR "non-insulin dependent diabetes" [Title/Abstract] OR "adult-onset diabetes" [Title/Abstract].) | Rine Elise Halvorsen, Mathilde Elvestad, Marianne Molin, Dagfinn Aune. Fruit and vegetable consumption and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of prospective studies. BMJ Nutr Prev Health. 2021 Jul 2;4(2):519-531. doi: 10.1136/bmjnph-2020-000218. |

Another search string was developed to identify sources published after the period covered in Halvorsen et al 2021. PubMed, EMBASE, and Web of Science and searched on May 31, 2022. The searches from the three databases returned 262 total hits, of which 3 studies were ultimately extracted and included in the model. As with the other risk-outcome reviews, after deduplication, two reviewers screened the results independently, with all full-text exclusions and 20% of title-abstract exclusions verified by both reviewers. The exclusion reasons by source count were reported in the PRISMA diagram (Extended Data Figure 4). We also searched the global health data exchange database to identify studies not caught from the searching of citation of the selected meta-analysis and the three databases.

Search strings:
Esophageal cancer: We conducted a full systematic review with no date constraint because we did not find a meta-
analysis that fulfilled our selection criteria (i.e. PRISMA complaint and matching our definition of exposure and outcome). A search string was developed to identify all sources published with no date constraint. PubMed,
EMBASE, and Web of Science were searched on June 16, 2022. The searches returned 214 citations, and after
deduplication by DOI and PMID, there were 151 unique records. Each record was screened on title and abstract by
one reviewer, finding 20 inclusions. As a sensitivity check, 20% of the 133 exclusions were validated by a second
reviewer. 1 discrepancy was found and was settled by moving to full-text review for additional evaluation. During
the full text review of the 20 sources, 6 met inclusion criteria and 14 were excluded. Each full-text exclusion was
verified by both reviewers. Exclusion reasons by source count described in the PRISMA flow chart (Extended Data
Figure 3).

Vegetable and esophageal cancer search strings:

("Vegetables"[Mesh] OR "Vegetables" [Title/Abstract] OR "green leafy vegetables" OR "leafy vegetables" OR
"Cruciferous vegetables" OR "Fruits and Vegetables" [Title/Abstract])

AND ("Cohort" [Publication type] OR "Prospective cohort" [Title/Abstract] OR "case-cohort" OR "Follow-up" OR
"Longitudinal" [Title/Abstract])

AND ("Diabetes Mellitus, Type 2" [Mesh] OR "diabetes mellitus type 2" [Title/Abstract] OR "diabetes type 2"
[Title/Abstract] OR "type 2 diabetes mellitus" [Title/Abstract] OR "type 2 diabetes" [Title/Abstract] OR "non-
insulin dependent diabetes" [Title/Abstract] OR "adult-onset diabetes" OR "Diabetes Mellitus" OR
"T2D"[Title/Abstract])

Section 1.2: Assessing data source eligibility

See Extended Data Figures 1-4 for details on identifying, screening, and assessing eligibility for records identified
through our search.

Inclusion criteria

- Reported a relative risk of total vegetable consumption and at least one of the five outcomes
- Included a measure of uncertainty for the effect size measure
- Quantified the amount of vegetable consumption in the reference and alternate group
- Prospective cohort study or Nested case-control or case cohort study

Exclusion criteria

- Were an aggregate study: meta-analysis or pooled cohort
- Wrong study type: not a cohort study or case-cohort study
- Duplicate study: cohort reported in paper was also reported elsewhere
- Unmeasurable exposure: reported vegetable consumption without grams or servings equivalent, such as in aggregated “diet scores”
- No measure of interest: reported RR for change in vegetable consumption or does not report RR
- No exposure of interest: did not report any vegetable exposure or only reported a specific vegetable subtype
- No outcome of interest: reported on all-cause-mortality or an outcome outside of the five outcomes of interest studied in this paper. This includes outcomes lacking specificity such as total stroke or cardiovascular disease
- Not in English
- Non-general population: study population defined by comorbidity or other traits that could interact with exposure and affect outcome
For reports that met the inclusion criteria, data were extracted for the variables listed in Supplemental Table 4.

Section 2. PRISMA checklists

Supplementary Table 1. PRISMA 2020 checklist

| Section and Topic | Item # | Checklist Item                                                                 | Location where item is reported                                                                 |
|-------------------|--------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| TITLE             | Title  | Identify the report as a systematic review.                                   | Per the journal's request, the title does not include "systematic review". It is, however, in the title of the methods section, "conducting systematic reviews". |
|                   |        |                                                                                |                                                                                                  |
| ABSTRACT          | Abstract | See the PRISMA 2020 for Abstracts checklist.                                  | See PRISMA 2020 for Abstracts Checklist below (Supplementary Table 2)                             |
|                   |        |                                                                                |                                                                                                  |
| INTRODUCTION      | Rationale | Describe the rationale for the review in the context of existing knowledge. | "Main" (intro) paragraphs 1–3                                                                  |
|                   | Objectives | Provide an explicit statement of the objective(s) or question(s) the review  | "Main" (intro) paragraph 4                                                                     |
|                   |        | addresses.                                                                     |                                                                                                  |
| METHODS           | Eligibility criteria | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Criteria summarized in Methods section "data"; full inclusion and exclusion criteria listed in SI section 1.2; reasons for exclusion and number of studies excluded also provided in PRISMA flow diagram for each pair (Extended Data Figures 1-4) |
|                   | Information sources | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Methods section “conducting systematic reviews”; paragraph 2; SI section 1.1 |
|                   | Search strategy | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Methods section "conducting systematic reviews": paragraph 2; SI section 1.1 |
|                   | Selection process | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Methods section "conducting systematic reviews" paragraph 2-3 |
|                   | Data collection process | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Methods section “conducting systematic reviews” paragraph 2-3 |
|                   | Data items | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Methods section "conducting systematic reviews" |
|                   | Study risk of bias assessment | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Methods section “testing and adjusting for biases across study designs and characteristics” |
|                   | Effect measures | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Method sections "overview" paragraph 2; “estimating the burden of proof risk function” |
| Synthesis methods | Synthesis methods | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | Methods section “data” |
| Section | Description | Methods section(s) |
|---------|-------------|-------------------|
| 13b     | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | “conducting systematic reviews” |
| 13c     | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | “conducting systematic reviews,” “estimating the shape of the risk-outcome relationship” |
| 13d     | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | “estimating the shape of the risk-outcome relationship,” “estimating the TMREL/minimum risk exposure level,” and “estimating the burden of proof risk function”. Software packages described in “code availability” section of the manuscript |
| 13e     | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | “evaluating between-study heterogeneity, uncertainty, and small numbers of studies” |
| 13f     | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | “sensitivity analyses”; SI section 8 |
| 14      | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Methods for detecting publication or reporting bias found in methods section “evaluating potential for publication or reporting bias” |
| 15      | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | “evaluating between-study heterogeneity, uncertainty, and small numbers of studies” |

**RESULTS**

| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | PRISMA flow diagram for each risk-outcome pair (Extended Data Figures 1–4); first paragraph of each risk-outcome pair results section + the results “overview” |
| Study characteristics | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | N/A |

**Risk of bias in studies**

| 18 | Present assessments of risk of bias for each included study. | Supplemental Table 6 |
| 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Supplemental Table 7 |

**Results of individual studies**

| 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | First paragraph and last sentence of each risk-outcome pair results section |
| 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Second paragraph of each risk-outcome pair results section + section titled “minimum risk level of vegetable intake;” Figures 1–5 |
| 20c | Present results of all investigations of possible causes of heterogeneity among study results. | All uncertainty intervals presented everywhere in the manuscript and appendices reflect between-study heterogeneity (unless specified otherwise); BPRFs, ROSs, and star-ratings for each risk-outcome pair also reflect between-study heterogeneity |
| 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | Supplemental Figures 1-6 |

**Reporting biases**

| 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | Last sentence of each risk-outcome pair results section; funnel plots (figures 1C–5C) |

**Certainty of evidence**

| 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | All estimates are presented with 95% uncertainty intervals. UI values are given alongside all mean estimates in the Results and Discussion sections; all risk curve figures (Figures 1–5) include shading to depict UI curves (both with and without between-study heterogeneity) |
Supplementary Table 2. PRISMA 2020 abstract checklist

| Section and Topic | Item # | Checklist item | Reported (Yes/No) |
|-------------------|--------|----------------|-------------------|
| **TITLE**         |        |                |                   |
| Title             | 1      | Identify the report as a systematic review. | Per the journal's request, the title does not include "systematic review". It is, however, in the title of the methods section, "conducting systematic reviews". |
| **BACKGROUND**    |        |                |                   |
| Objectives        | 2      | Provide an explicit statement of the main objective(s) or question(s) the review addresses. | Yes |
| **METHODS**       |        |                |                   |
| Eligibility criteria | 3 | Specify the inclusion and exclusion criteria for the review. | Not in abstract, just main text (given word count limitations by the journal) |
| Information sources | 4 | Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched. | Not in abstract, just main text (given word count limitations by the journal) |
| Risk of bias      | 5      | Specify the methods used to assess risk of bias in the included studies. | Not in abstract, just main text (given word count limitations by the journal) |
| Synthesis of results | 6 | Specify the methods used to present and synthesise results. | Yes |
| **RESULTS**       |        |                |                   |
| Included studies  | 7      | Give the total number of included studies and participants and summarise relevant characteristics of studies. | Not in abstract, just main text (given word count limitations by the journal) |
| Synthesis of results | 8 | Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured). | Yes, though number of included studies and participants only reported in the main text |
| **DISCUSSION**    |        |                |                   |
| Limitations of evidence | 9 | Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision). | Not in abstract, just main text (given word count limitations by the journal) |
| Interpretation    | 10     | Provide a general interpretation of the results and important implications. | Yes |
| **OTHER**         |        |                |                   |
| Funding           | 11     | Specify the primary source of funding for the review. | Not in abstract, just main text (given word count limitations by the journal) |
| Registration      | 12     | Provide the register name and registration number. | No |
Section 3: Study characteristics

In Supplementary Table 3 we provide characteristics for each of the studies identified and used in this meta-analysis.

**Supplementary Table 3. Studies characteristics**

| Author         | Year | Study name                                   | Population                                                                                                                                                                                                 | Location           | Study design     | Sex  | Follow-up | Age start | Age end | Exposure assessment | Endpoint   | Disease ascertainment | Events | Sample size | Outcomes            |
|----------------|------|----------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|------------------|------|------------|-----------|---------|----------------------|------------|----------------------|---------|--------------|----------------------|
| Barouti        | 2022 | Stockholm Diabetes Prevention Program       | Residents aged 35-56 years from five municipalities in Stockholm County.                                                                                                                                | Sweden             | Prospective cohort | Male | 20         | 35        | 56      | FFQ                  | Incidence  | Biomarker           | 531     | 2046         | Diabetes mellitus    |
| Barouti        | 2022 | Stockholm Diabetes Prevention Program       | Residents aged 35-56 years from five municipalities in Stockholm County.                                                                                                                                | Sweden             | Prospective cohort | Female| 20        | 35        | 56      | FFQ                  | Incidence  | Biomarker           | 493     | 4315         | Diabetes mellitus    |
| Bazzano        | 2008 | Nurses' Health Study                        | US female registered nurses                                                                                                                                                                               | United States      | Prospective cohort | Female| 18        | 30        | 55      | FFQ                  | Incidence  | Physician diagnosis | 4529    | 71346        | Diabetes mellitus    |
| Chen           | 2018 | Singapore Chinese Health Study              | Chinese permanent residents of government-built housing estates in Singapore                                                                                                                             | Singapore          | Prospective cohort | Both  | 10.9      | 45        | 74      | FFQ                  | Incidence  | Physician diagnosis | 5207    | 45411        | Diabetes mellitus    |
| Cooper         | 2012 | EPIC-InterAct study                         | Sampled participants from 8 countries: France, Germany, Netherlands, UK, Italy, Sweden, Denmark, and Spain                                                                                             | Denmark, France,   | Case-cohort       | Both  | 11        | 34.5      | 70.1    | 24-hr recall         | Incidence  | Administrative medical records or disease registries | 10821   | 14800        | Diabetes mellitus    |
| Hodge          | 2004 | Melbourne Collaborative Cohort study        | Migrants from Italy and from Greece or Macedonia in Melbourne, Australia                                                                                                                             | Australia          | Prospective cohort | Both  | 4         | 40        | 69      | FFQ                  | Incidence  | Self-report          | 365     | 31641        | Diabetes mellitus    |
| Kurotani       | 2013 | Japan Public Health Center-based study      | Residents aged 40-59 years in five Japanese public health center areas (Iwate, Akita, Nagano, Okinawa and Tokyo); the participants of cohort II included residents aged 40-69 | Japan              | Prospective cohort | Female| 10        | 40        | 69      | FFQ                  | Incidence  | Self-report          | 366     | 27168        | Diabetes mellitus    |
| Year | Study Name | Country | Study Design | Gender | Age Range | Method | Incidence | Reporting Method | Observers | Number of Observers |
|------|------------|---------|--------------|--------|-----------|--------|------------|-------------------|-----------|--------------------|
| 2013 | Japan Public Health Center-based study | Japan | Prospective cohort | Male | 40-69 | FFQ | Incidence | Self-report | 530 | 21269 |
| 2021 | China Health and Nutrition Survey | China | Prospective cohort | Both | 40-69 | 24-hr dietary recalls | Incidence | Self-report | 1080 | 16117 |
| 2004 | Womens Health study | United States | Prospective cohort | Female | 45-72 | FFQ | Incidence | Self-report | 1614 | 38018 |
| 2017 | NIH-AARP Diet and Health study | United States | Prospective cohort | Both | 50-72 | FFQ | Incidence | Self-report | 25916 | 401909 |
| 2017 | EPIC-Elderly study | Greece, The Netherlands, Spain, Sweden | Prospective cohort | Both | 50-72 | FFQ | Incidence | Self-report | 25916 | 20629 |
| 2000 | Iowa Womens Health study | United States | Prospective cohort | Female | 55-69 | FFQ | Incidence | Self-report | 1141 | 5988 |
| 2005 | Finnish Mobile Clinic Health Examination survey | Finland | Prospective cohort | Both | 23-69 | FFQ | Incidence | Administrative medical records or disease registries | 383 | 4304 |

Further details for each study are as follows:

- **Kurotani (2013)**: Japan Public Health Center-based study. Residents aged 40-59 years in five Japanese public health center areas (Iwate, Akita, Nagano, Okinawa, and Tokyo); the participants of cohort II included residents aged 40-69 years in six public health center areas (Ibaraki, Niigata, Kochi, Nagasaki, Okinawa, and Osaka).

- **Liu (2021)**: China Health and Nutrition Survey (CHNS), an ongoing multipurpose, longitudinal open cohort study initiated in 1989 in China and followed up every 2-4 years.

- **Liu (2004)**: Womens Health study. Female health professionals who were free of heart disease, stroke, or cancer at baseline.

- **Mamluk (2017)**: NIH-AARP Diet and Health study. 65,000 retired civilians.

- **Mamluk (2017)**: EPIC-Elderly study. Elderly individuals from Spain, Greece, The Netherlands, and Sweden.

- **Meyer (2000)**: Iowa Womens Health study. Postmenopausal women.

- **Montonen (2005)**: Finnish Mobile Clinic Health Examination survey. 30 communities from different parts of Finland.
| Author   | Year | Study Name                                      | Country                      | Women/Men | Born Between | Follow-up | Method       | Incidence Measure | Follow-up Time (years) | Incidence Location | Disease Type          |
|----------|------|------------------------------------------------|------------------------------|-----------|--------------|-----------|--------------|-------------------|-----------------------|----------------------|---------------------|
| Olsson   | 2021 | Malmö Diet and Cancer Study                    | Sweden                       | Male 18.4 | 1923 and 1950 | 73        | FFQ          | Incidence         | 1936                  | 10315                | Diabetes mellitus    |
| Olsson   | 2021 | Malmö Diet and Cancer Study                    | Sweden                       | Female 18.4| 1923 and 1950| 73        | FFQ          | Incidence         | 2110                  | 16307                | Diabetes mellitus    |
| Qiao     | 2014 | Women's Health Initiative study                | United States                | Female 7.6 | 1923 and 1950| 79        | FFQ          | Incidence         | 10285                 | 154493               | Diabetes mellitus    |
| Villegas | 2008 | Shanghai Women's Health Study                  | China                        | Female 4.6 | 1923 and 1950| 70        | FFQ          | Incidence         | 1608                  | 64227                | Diabetes mellitus    |
| Ahmed    | 2020 | Stockholm Public Health Cohort                 | Sweden                       | Male 4    | 1923 and 1950| 84        | Dietary recall| Incidence         | 167                   | 14718                | Diabetes mellitus    |
| Ahmed    | 2020 | Stockholm Public Health Cohort                 | Sweden                       | Female 4  | 1923 and 1950| 84        | Dietary recall| Incidence         | 152                   | 20589                | Diabetes mellitus    |
| Rayner   | 2020 | Australian Longitudinal Study on Women's Health| Australia                    | Female 20 | 1923 and 1950| 75        | FFQ          | Incidence         | 959                   | 9689                 | Diabetes mellitus    |
| Freedman | 2007 | NIH-AARP Diet and Health study                 | United States                | Both 5    | 1923 and 1950| 61.6      | FFQ          | Incidence         | 103                   | 98160                | Esophageal cancer    |
| González | 2006 | EPIC- EURGAST                                  | Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, | Both 6.5 | 1923 and 1950| 70        | FFQ          | Incidence & Mortality | 65                   | 481518               | Esophageal cancer    |
| Study Reference | Cohort Name and Details | Participants | Methodology | Follow-up Period | Diet Assessment | Incidence & Mortality | Mortality | Incidence | Disease Type |
|-----------------|-------------------------|--------------|-------------|----------------|----------------|----------------------|----------|-----------|--------------|
| Sheikh 2019 | Golestan Cohort Study | Residents aged 40-75 years from Golest an province in north eastern Iran | Prospective cohort | Both | 10, 40, 75 | FFQ and 24-h dietary recall. | Incidence & Mortality | Self-report | 317, 49155 | Esophageal cancer |
| Steevens 2011 | Netherlands Cohort Study on Diet and Cancer | Randomly sampled from Dutch municipal registries | Prospective cohort | Both | 16.3, 55, 69 | FFQ | Incidence | Administrative medical records or disease registries | 101, 120852 | Esophageal cancer |
| Tran 2005 | Linxian General Population Trial | Individuals with no history of cancer or debilitating disease at baseline from the general population of Linxian. | Prospective cohort | Both | 15, 40, 69 | FFQ | Incidence | Physician diagnosis | 1958, 29584 | Esophageal cancer |
| Yamaji 2008 | Japan Public Health Center-based Prospective Study | All male registered Japanese inhabitants in 11 public health center (PHC) areas, aged 40-59 years in Cohort I and 40-69 years in Cohort II. Study subjects were identified using population registries maintained by the local municipalities. Excluded 2 public health center areas (Tokyo and Osaka) | Prospective cohort | Male | 7.7, 40, 59 | FFQ | Incidence & Mortality | Administrative medical records or disease registries | 116, 38790 | Esophageal cancer |
| Larsson 2009 | ATBC study | Male smokers residing in southwestern Finland | Prospective cohort | Male | 13.6, 50, 69 | FFQ | Incidence | Administrative medical records or disease registries | 383, 26556 | Hemorrhagic stroke |
| Study                  | Year | Population Description                                                                 | Country      | Study Type                  | Gender | Age Range | Dietary Assessment | Exposure | Cases | Incidence/Survival | Cause of Death | Methods                                                                 |
|-----------------------|------|----------------------------------------------------------------------------------------|--------------|-----------------------------|--------|------------|-------------------|----------|-------|--------------------|----------------|-------------------------------------------------------------------------|
| Larsson               | 2013 | Men and women from central Sweden                                                       | Sweden       | Prospective cohort          | Both   | 10.2-45    | FFQ               | Incidence | 583   | 74961             | Hemorrhagic stroke | Administrative medical records or disease registries                      |
| Mizrahi               | 2009 | Finnish Mobile Clinic Health Examination Survey                                          | Finland      | Prospective cohort          | Male   | 24-40     | FFQ               | Incidence | 65    | 2051              | Hemorrhagic stroke   | Administrative medical records or disease registries                      |
| Nagura                | 2009 | Japan Collaborative Cohort Study                                                        | Japan        | Prospective cohort          | Both   | 13-40     | FFQ               | Mortality | 393   | 59485             | Hemorrhagic stroke   | Administrative medical records or disease registries                      |
| Pham                  | 2007 | Miyako Study                                                                            | Japan        | Prospective cohort          | Both   | 13.8-40   | 78.6 Self-administered questionnaire survey | Mortality | 47    | 9651              | Hemorrhagic stroke   | Death certificates                                                                 |
| Yokoyama              | 2000 | The Shibata Study                                                                       | Japan        | Prospective cohort          | Female | 20-40     | 99 FFQ           | Incidence | 18    | 870               | Hemorrhagic stroke   | Self-report                                                             |
| Yokoyama              | 2000 | The Shibata Study                                                                       | Japan        | Prospective cohort          | Male   | 20-40     | 99 FFQ           | Incidence | 36    | 1251              | Hemorrhagic stroke   | Self-report                                                             |
| Zhang                 | 2011 | Participants of cross-sectional population surveys performed in 6 geographic areas of Finland in 1982, 1987, 1992, 1997, and 2002 | Finland      | Prospective cohort          | Both   | 13.7-25   | 64 FFQ           | Incidence & Mortality | 311   | 36686             | Hemorrhagic stroke   | Administrative medical records or disease registries                      |
| Bhupathiraju         | 2013 | Nurses' Health Study                                                                    | US female registered nurses | Prospective cohort | Female | 24-30     | 55 FFQ           | Incidence | 2582  | 113276            | Ischemic heart disease | Administrative medical records or disease registries                      |
| Bhupathiraju         | 2013 | Health Professionals Follow-Up study                                                    | US male health professionals | Prospective cohort | Male   | 22-40     | 75 FFQ           | Incidence | 3607  | 113276            | Ischemic heart disease | Administrative medical records or disease registries                      |
| Study            | Year  | Study Design | Participants                                                                 | Nationality          | Study Type | Cohort | FFQ | Incidence & Mortality | Data Source | Incidence & Mortality | Disease |
|------------------|-------|--------------|-------------------------------------------------------------------------------|----------------------|------------|--------|-----|-----------------------|-------------|-----------------------|---------|
| Dauchet 2010     | PRIME study | Four WHO-MONICA centers in Belfast (UK), Lille (Northern France), Strasbourg (Eastern France) and Toulouse (Southwestern France). | Male 50-59            | FFQ               | Administrative medical records or disease registries | 367     | 2297 | Ischemic heart disease |
| Hansen 2010      | Danish Diet, Cancer, and Health Study | All men and women aged 50 to 64 years, born in Denmark, living in the greater areas of Aarhus or Copenhagen, and with no previous cancer diagnosis in the Danish Cancer Registry were invited | Female 50-64         | FFQ               | Administrative medical records or disease registries | 820     | 25065 | Ischemic heart disease |
| Hansen 2010      | Danish Diet, Cancer, and Health Study | All men and women aged 50 to 64 years, born in Denmark, living in the greater areas of Aarhus or Copenhagen, and with no previous cancer diagnosis in the Danish Cancer Registry were invited | Male 50-59            | FFQ               | Administrative medical records or disease registries | 255     | 28318 | Ischemic heart disease |
| Name                  | Year | Study Details                                                                 | Countries/Regions                                                                 | FFQ    | Incidence & Mortality | Administrative Medical Records or Disease Registries | Total Follow-Up | Total Cases | Incidence & Mortality | Administrative Medical Records or Disease Registries |
|-----------------------|------|--------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|--------|-----------------------|---------------------------------------------------|----------------|--------------|-----------------------|---------------------------------------------------|
| Knekt 1994            | Finnish Mobile Health Clinic | Adult men and women from rural, urban, and industrial communities in Finland | Finland                                                                               | Prospective cohort | Female | 14 30 69 | FFQ | Mortality | Death certificates | 244 2385 | Ischemic heart disease |
| Knekt 1994            | Finnish Mobile Health Clinic | Adult men and women from rural, urban, and industrial communities in Finland | Finland                                                                               | Prospective cohort | Male   | 14 30 69 | FFQ | Mortality | Death certificates | 244 2748 | Ischemic heart disease |
| Kobylecki 2015        | CGPS and the Copenhagen City Heart Study | Individuals aged 20–100 y were invited randomly from the Danish Civil Registration System | Denmark                                                                                | Prospective cohort | Both   | 21 20 100 | FFQ | Incidence | Administrative medical records or disease registries | 2823 97203 | Ischemic heart disease |
| Liu 2000              | Womens' Health Study      | Female health professionals who were without heart disease, stroke, or cancer (other than nonmelanoma skin cancer) at baseline. | United States                                                                         | Prospective cohort | Female | 5 40 68  | FFQ | Incidence & Mortality | Self-report | 126 39876 | Ischemic heart disease |
| Miller 2017           | PURE | 613 communities in 18 low-income, middle-income, and high-income countries (HIC) in seven geographical regions: North America and Europe, South America, the Middle East, south Asia, China, southeast Asia, and Africa. | United Arab Emirates, Canada, Sweden, Poland, Argentina, Chile, Malaysia, Turkey, Iran, Occupied Palestinian territory, Brazil, South Africa, Columbia, China, India, Pakistan, Bangladesh, Zimbabwe | Prospective cohort | Both   | 7.4 35 70 | FFQ | Incidence | Physician diagnosis | 2143 135335 | Ischemic heart disease |
| Perez-Cornago 2021    | European Prospective Investigation into Cancer and Nutrition | Men and women recruited through 23 centers in 10 European countries (Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, ...) | Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, ...                     | Prospective cohort | Female | 12.6 35 70 | FFQ | Incidence & Mortality | Administrative medical records or disease registries | 8504 490311 | Ischemic heart disease |
| Study                     | Year | Design                  | Country/Region                                                                 | Gender | Age Range | Recruitment | Study Type | FFQ | Disease Endpoint | Data Source                                                          | Cases |对照 | Disease                        |
|--------------------------|------|-------------------------|--------------------------------------------------------------------------------|--------|------------|-------------|------------|-----|-----------------|-----------------------------------------------------------------------|-------|-----|-----------------------------|
| Pietinen 1996 Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study | 1996 | Male smokers recruited from 14 geographic areas in southwestern Finland       | Finland                                       | Male   | 6.1-50-69  | Prospective cohort | Male     | FFQ | Incidence & Mortality | Administrative medical records or disease registries                | 1399  | 29133 | Ischemic heart disease     |
| Rebello 2014 Singapore Chinese Health Study                      | 2014 | Singapore citizens or permanent residents aged between 45-74 y who were residing at public housing estates | Singapore                                      | Female | 15-45-74   | Prospective cohort | Female   | FFQ | Mortality          | Administrative medical records or disease registries                | 638   | 29968 | Ischemic heart disease     |
| Rebello 2014 Singapore Chinese Health Study                      | 2014 | Singapore citizens or permanent residents aged between 45-74 y who were residing at public housing estates | Singapore                                      | Male   | 15-45-74   | Prospective cohort | Male     | FFQ | Mortality          | Administrative medical records or disease registries                | 1022  | 23501 | Ischemic heart disease     |
| Sharma 2014 MEC study                                            | 2014 | Large representative samples of five ethnic groups in the United States; Caucasian, African American, Native Hawaiian, Japanese American, and Latino. | United States                                  | Male   | 8-45-75    | Prospective cohort | Male     | FFQ | Mortality          | Administrative medical records or disease registries                | 1140  | 72866 | Ischemic heart disease     |
| Sharma 2014 MEC study                                            | 2014 | Large representative samples of five ethnic groups in the United States; Caucasian, African American, Native Hawaiian, Japanese American, and Latino. | United States                                  | Female | 8-45-75    | Prospective cohort | Female   | FFQ | Mortality          | Administrative medical records or disease registries                | 811   | 91940 | Ischemic heart disease     |
| Sonestedt 2015 Malmö Diet and Cancer Study                       | 2015 | All men born between 1923 and 1945 and women born between 1923 and 1950 that live in Malmö were invited via personal letters and advertisements in the local newspaper and | Sweden                                          | Both   | 14-44-74   | 7-day diet history | Both     | FFQ | Incidence & Mortality | Administrative medical records or disease registries                | 2921  | 26445 | Ischemic heart disease     |
| Author     | Year | Study Name                          | Countries/Regions                                      | Study Design          | Follow-up (Year) | Method of Measurement | Cause of Death                          | Participants (Sex) | Participants (Total) |
|------------|------|-------------------------------------|--------------------------------------------------------|-----------------------|------------------|-----------------------|-----------------------------------------|-------------------|---------------------|
| Stefler    | 2016 | HAPIEE study                        | Czech Republic, Poland and Russia, Novosibirsk (Russia) and six cities of the Czech Republic | Prospective cohort    | Both             | FFQ                   | Mortality, Administrative medical records or disease registries | 226               | 19333               |
| Tognon     | 2014 | MONICA                              | Denmark                                                | Prospective cohort    | Both             | 7d food record, Incidence & Mortality | Administrative medical records or disease registries | 161               | 1849                |
| Yoshizaki  | 2020 | Japan Public Health Center-Based Prospective Study | Residents of the Okinawa Prefecture (two PHC areas: Chubu from Cohort I and Miyako from Cohort II) | Japan Prospective cohort Male | 74               | FFQ                   | Incidence & Mortality, Administrative medical records or disease registries | 147               | 7726                |
| Yoshizaki  | 2020 | Japan Public Health Center-Based Prospective Study | Residents of the Okinawa Prefecture (two PHC areas: Chubu from Cohort I and Miyako from Cohort II) | Japan Prospective cohort Female | 74               | FFQ                   | Incidence & Mortality, Administrative medical records or disease registries | 32                | 8772                |
| Yu         | 2014 | Shanghai Women's Health Study (SWHS) | Participants from the Shanghai Women’s Health Study (SWHS) and the Shanghai Men’s Health Study (SMHS) | China Prospective cohort Female | 70               | FFQ                   | Incidence, Physician diagnosis | 148               | 67211               |
| Yu         | 2014 | Shanghai Men's Health Study (SMHS)   | Participants from the Shanghai Women’s Health Study (SWHS) and the Shanghai Men’s Health Study (SMHS) | China Prospective cohort Male | 74               | FFQ                   | Incidence, Physician diagnosis | 217               | 55474               |
| Yu         | 2014 | Shanghai Women's Health Study (SWHS) | Participants from the Shanghai Women’s Health Study (SWHS) and the Shanghai Men’s Health Study (SMHS) | China Prospective cohort Female | 70               | FFQ                   | Incidence, Physician diagnosis | 148               | 67211               |
| First Name | Year | Study | Description | Country | Region | Age | Gender | FFQ/Mortality | Incidence | Administrative Medical Records | Ischemic Heart Disease |
|------------|------|-------|-------------|---------|--------|------|--------|--------------|-----------|-------------------------------|---------------------|
| Zhang      | 2021 | UK Biobank study | CVD-free participants aged 40-69y | United Kingdom | Prospective cohort | Female | 11.2 | FFQ | 40 | 69 | Incidence | Administrative medical records or disease registries | 11161 | 462155 | Ischemic heart disease |
| Johnsen    | 2003 | Diet, Cancer, and Health study | Persons living in the Copenhagen and Aarhus areas | Denmark | Prospective cohort | Both | 3.1 | FFQ | 50 | 64 | Incidence & Mortality | Administrative medical records or disease registries | 266 | 57053 | Ischemic stroke |
| Joshipura  | 1999 | Nurses' Health Study | US female registered nurses | United States | Prospective cohort | Female | 14 | FFQ | 34 | 59 | Incidence & Mortality | Administrative medical records or disease registries | 366 | 75596 | Ischemic stroke |
| Joshipura  | 1999 | Health Professionals Follow-Up Study | US male health professionals | United States | Prospective cohort | Male | 8 | FFQ | 40 | 75 | Incidence & Mortality | Administrative medical records or disease registries | 204 | 38683 | Ischemic stroke |
| Larsson    | 2009 | ATBC study | Male smokers residing in southwestern Finland | Finland | Prospective cohort | Male | 13.6 | FFQ | 50 | 69 | Incidence | Administrative medical records or disease registries | 2702 | 26556 | Ischemic stroke |
| Larsson    | 2013 | | Men and women from central Sweden | Sweden | Prospective cohort | Both | 10.2 | FFQ | 45 | 83 | Incidence | Administrative medical records or disease registries | 3159 | 74961 | Ischemic stroke |
| Mizrahi    | 2009 | Finnish Mobile Clinic Health Examination Survey | 40-74 years of age and free of cardiovascular diseases at baseline. | Finland | Prospective cohort | Male | 24 | FFQ | 40 | 74 | Incidence | Administrative medical records or disease registries | 342 | 2051 | Ischemic stroke |
| Nagura     | 2009 | Japan Collaborative Cohort Study | aged 40–79 years living in forty-five communities across Japan participated in municipal health screening examinations | Japan | Prospective cohort | Both | 13 | FFQ | 40 | 79 | Incidence | Administrative medical records or disease registries | 362 | 59485 | Ischemic stroke |
| Pham       | 2007 | Miyako Study | Four selected districts in Fukoka Prefecture, Japan | Japan | Prospective cohort | Both | 13.8 | FFQ | 40 | 78.6 | Self-administered questionnaire survey | Death certificates | 109 | 9651 | Ischemic stroke |
| Steffen    | 2003 | ARIC study | African American and white, men and women residents from Forsyth County, NC; Jackson, MS; selected suburbs of | United States | Prospective cohort | Both | 11 | FFQ | 45 | 64 | Incidence | Administrative medical records or disease registries | 214 | 11940 | Ischemic stroke |
| Study | Year | Dataset | Design | Country | Sex | Age | FFQ | Incidence & Mortality | Follow-Up | Participants | Outcome |
|-------|------|---------|--------|---------|-----|-----|-----|-----------------------|-----------|-------------|---------|
| Tong | 2020 | EPIC | Prospective cohort | Denmark, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden, and the UK | Both | 12–70 | FFQ | Incidence & Mortality | Administrative medical records or disease registries | 4281 | 418329 | Ischemic stroke |
| Yokoyama | 2000 | The Shibata Study | Prospective cohort | Japan | Male | 20–99 | FFQ | Incidence | Self-report | 58 | 870 | Ischemic stroke |
| Yokoyama | 2000 | The Shibata Study | Prospective cohort | Japan | Female | 20–99 | FFQ | Incidence | Self-report | 51 | 1251 | Ischemic stroke |
| Yoshizaki | 2020 | JPHC | Prospective cohort | Japan | Male | 13.2–74 | FFQ | Incidence & Mortality | Administrative medical records or disease registries | 298 | 7726 | Ischemic stroke |
| Yoshizaki | 2020 | JPHC | Prospective cohort | Japan | Female | 13.2–74 | FFQ | Incidence & Mortality | Administrative medical records or disease registries | 168 | 8772 | Ischemic stroke |
| Zhang | 2011 | | Prospective cohort | Finland | Both | 13.7–64 | FFQ | Incidence & Mortality | Administrative medical records or disease registries | 1167 | 36686 | Ischemic stroke |
| Author  | Year | Study | Participants | Country | Study Design | Exposure | Age | Duration | Method | Event Type |
|---------|------|-------|--------------|---------|--------------|----------|-----|----------|--------|------------|
| Tong    | 2020 | EPIC  | Men and women from 22 centres in nine European countries (Denmark, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden, and the UK) | Denmark, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden, and the UK | Prospective cohort | Both | 12.7 | 35 | 70 | FFQ | Incidence & Mortality | Administrative medical records or disease registries | 1430 | 418329 | Hemorrhagic stroke |
| Yoshizaki | 2020 | JPHC  | Adults from Okinawa Prefecture (two PHC areas: Chubu from Cohort I and Miyako from Cohort II) | Japan | Prospective cohort | Male | 13.2 | 45 | 74 | FFQ | Incidence & Mortality | Administrative medical records or disease registries | 159 | 7726 | Hemorrhagic stroke |
| Yoshizaki | 2020 | JPHC  | Adults from Okinawa Prefecture (two PHC areas: Chubu from Cohort I and Miyako from Cohort II) | Japan | Prospective cohort | Female | 13.2 | 45 | 74 | FFQ | Incidence & Mortality | Administrative medical records or disease registries | 132 | 8772 | Hemorrhagic stroke |
**Supplementary Table 4. GATHER checklist**

| Item # | Checklist item                                                                 | Reported on page #                                |
|--------|--------------------------------------------------------------------------------|---------------------------------------------------|
|        | **Objectives and funding**                                                      |                                                   |
| 1      | Define the indicator(s), populations (including age, sex, and geographic entities), and time period(s) for which estimates were made. | Main text methods overview, paragraph 2           |
| 2      | List the funding sources for the work.                                          | Main text acknowledgement section                 |
|        | **Data Inputs**                                                                 |                                                   |
|        | For all data inputs from multiple sources that are synthesized as part of the study: |                                                   |
| 3      | Describe how the data were identified and how the data were accessed.          | Main text methods section “conducting systematic reviews” |
| 4      | Specify the inclusion and exclusion criteria. Identify all ad-hoc exclusions.    | Main text methods section “conducting systematic reviews”; reasons for exclusion and number of studies excluded also provided in PRISMA flow diagram (Extended Data Figures 1–4) |
| 5      | Provide information on all included data sources and their main characteristics. For each data source used, report reference information or contact name/institution, population represented, data collection method, year(s) of data collection, sex and age range, diagnostic criteria or measurement method, and sample size, as relevant. | SI section 3, Supplemental Table 3 (“study characteristics”); citations also available for download from the online viz tools: [https://vizhub.healthdata.org/burden-of-proof/](https://vizhub.healthdata.org/burden-of-proof/) |
| 6      | Identify and describe any categories of input data that have potentially important biases (e.g., based on characteristics listed in item 5). | Main text methods section “testing and adjusting for biases across study designs and characteristics” and “evaluating potential for publication or reporting bias” |
|        | **For data inputs that contribute to the analysis but were not synthesized as part of the study:** |                                                   |
| 7      | Describe and give sources for any other data inputs.                           | N/A                                               |
|        | **For all data inputs:**                                                       |                                                   |
| 8      | Provide all data inputs in a file format from which data can be efficiently extracted (e.g., a spreadsheet rather than a PDF), including all relevant meta-data listed in item 5. For any data inputs that cannot be shared because of ethical or legal reasons, such as third-party ownership, provide a contact name or the name of the institution that retains the right to the data. | As stated in the Data Availability Statement, data inputs in excel format available for download from the online viz tools: [https://vizhub.healthdata.org/burden-of-proof/](https://vizhub.healthdata.org/burden-of-proof/) |
| 9      | Provide a conceptual overview of the data analysis method. A diagram may be helpful. | Main text methods overview, paragraph 1           |
| 10     | Provide a detailed description of all steps of the analysis, including mathematical formulae. This description should cover, as relevant, data cleaning, data pre-processing, data adjustments and weighting of data sources, and mathematical or statistical model(s). | Main text methods                                          |
| 11     | Describe how candidate models were evaluated and how the final model(s) were selected. | Main text methods “estimating the shape of the exposure-relative risk relationship” paragraph 2 |
| 12     | Provide the results of an evaluation of model performance, if done, as well as the results of any relevant sensitivity analysis. | Main text methods “sensitivity analyses” section; Supplemental Figures 1–6 |
| 13     | Describe methods for calculating uncertainty of the estimates. State which sources of uncertainty were, and were not, accounted for in the uncertainty analysis. | Main text methods “evaluating between-study heterogeneity, uncertainty, and small numbers of studies” |
| 14     | State how analytic or statistical source code used to generate estimates can be accessed. | Code availability statement in the main text       |
|        | **Results and Discussion**                                                      |                                                   |
| 15     | Provide published estimates in a file format from which data can be efficiently extracted. | Available at: [https://vizhub.healthdata.org/burden-of-proof/](https://vizhub.healthdata.org/burden-of-proof/) |
| 16     | Report a quantitative measure of the uncertainty of the estimates (e.g. uncertainty intervals). | ULs given for all findings, including in the text, figures, and tables in the main text and SI; online viz tools (see information above) |
| 17     | Interpret results in light of existing evidence. If updating a previous set of estimates, describe the reasons for changes in estimates. | Main text discussion paragraphs 2, 6, & 7          |
| 18     | Discuss limitations of the estimates. Include a discussion of any modelling assumptions or data limitations that affect interpretation of the estimates. | Main text discussion paragraph 5                   |
For reports that met the inclusion criteria, data were extracted for the variables listed in Supplemental Table 5.

**Supplementary Table 5. Causal criteria extraction template**

| Category     | Variable            | Definition                                                                                                                                                                                                 |
|--------------|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Source       | seq                 |                                                                                                                                                                                                          |
|              | underlying_nid      | Underlying NID: Enter the underlying NID of the study (if applicable). Always talk to a data indexer if you don't know if an underlying NID is needed. They may be used for meta-analyses, certain database sources, and in some other specific cases. |
|              | nid                 | Found in GHDx, created through the epi form, or created by Data Indexer.                                                                                                                                     |
|              | field_citation_value| IHME Zotero format or if source has NID, citation info from GHDx.                                                                                                                                           |
|              | file_path           | Optional, full file path of article; Only needed if source doesn't have NID, to facilitate NID creation.                                                                                                   |
| R-O pair     | risk                | Risk: Select the risk factor, if not listed here, contact the causal criteria team.                                                                                                                          |
|              | risk_mapping        | the relationship between study definition of risk and GBD definition of risk for a particular effect size                                                                                               |
|              | outcome             | Outcome: Select the outcome.                                                                                                                                                                               |
|              | outcome_mapping     | the relationship between study definition of outcome and GBD definition of outcome for a particular effect size                                                                                           |
| Location     | location_name       | location name (from locations tab). Do a fast double-click in this field to get the drop-down menu, then start typing the location_name. For location names with special characters, you may need to use the scroll bar. |
|              | location_id         | autopopulated from location_name                                                                                                                                                                          |
|              | rep_geography       | Were the study participants representative of the geography? 1=yes, 0=no                                                                                                                                 |
|              | rep_selection_criteria| If rep_geography is 0, please specify the selection criteria of the study that is used in the analysis.                                                                                                     |
|              | rep_prevalent_disease| Is the study aiming to evaluate the risk or mortality of people who have already developed the outcome? 1=yes 0=no (i.e. yes if for SBP-IHD paper, all participants have IHD at baseline and the paper is looking at mortality due to SBP, no if for SBP-IHD paper the participants have other prevalent diseases) |
| Study        | year_start_study    | year the study was started. If not specified, leave blank                                                                                                                                                |
| Population   | year_end_study      | year the study was finished (including most recent follow up). If not specified, leave blank                                                                                                                |
|              | age_start           | ages from 1 and above must be entered as an integer. Ages <1 can be entered as decimal values, e.g., 3 days = 3/365.                                                                                       |
|              | age_end             | ages from 1 and above must be entered as an integer. Ages <1 can be entered as decimal values, e.g., 3 days = 3/365.                                                                                       |
|              | age_mean            | Mean age                                                                                                                                                                                                  |
|              | age_sd              | SD of age                                                                                                                                                                                                 |
|              | age_issue           | 0 = no issue flagged; 1 = issue flagged for modeler; always include explanatory notes the note SR column                                                                                                   |
|              | percent_male        | what percent of the population is male (0-1), if pop is all female then it would be 0                                                                                                                     |
| Study        | design              | Study design: Specify the design of the study                                                                                                                                                            |
| Design       | study_name          | Study Name: Enter the name of the study (e.g., Nurses' Health Study), if provided. Do not enter the title of the article.                                                                                 |
| Exposure     | exp_assess_level    | Level of exposure assessment: The exposure was assessed…                                                                                                                                                 |
|              | exp_instrument      | Exposure assessment instrument: Specify the name of the exposure assessment instrument. For self-reported exposures, please specify the name of the questionnaire e.g., International Physical Activity Questionnaire (IPAQ). If more than one instrument specify all |
|              | exp_assess_period   | What was the frequency of exposure assessment?                                                                                                                                                            |
|              | exp_assess_num      | If multiple, specify the number of times that exposure was assessed (excluding baseline)                                                                                                                  |
|              | exp_method_1        | Please specify the method of exposure assessment. If there are more than 1, please add in the next columns labeled "exp_method_2".                                                                      |
|              | exp_method_2        | Please specify the method of exposure assessment. If there are more than 2, please add in the next columns labeled "exp_method_3".                                                                      |
|              | exp_method_3        | Please specify the method of exposure assessment.                                                                                                                                                         |
| Field                                      | Description                                                                                                                                                                                                 |
|--------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| exp_recall_period                         | This field describes the unit of exposure recall used in data collection ONLY for self-report. Select the correct option from the drop-down menu. If the unit is days, weeks, months, or years, please enter the number in exp_recall_period_value (next column). If the unit is 'lifetime', nothing needs to be entered in exp_recall_period_value. For example, if the study said the recall period was 4 weeks, enter 4 in exp_recall_period_value, and 'weeks' in the field exp_recall_period. If 'other' is selected, please describe in exp_recall_period_other. |
| exp_recall_period_value                   | If you entered days, weeks, months, or years in the field exp_recall_period, please enter the corresponding integer in this field. For example, if the study said the recall period was 4 weeks, enter 4 in exp_recall_period_value, and 'weeks' in the field exp_recall_period. |
| exp_recall_period_other                   | If 'other' was selected in exp_recall_period, please describe the exposure recall period that the study specified (e.g., recall of exposure from 12 to 18 years). |
| exp_type                                  | Which form of the exposure was included in relative risk estimation analysis?                                                                                                                                    |
| outcome_def                               | Outcome definition: Provide a brief description of the outcome as reported in the study.                                                                                                                     |
| outcome_type                              | Outcome type: please specify if the outcome definition included incidence of or mortality from a disease endpoint                                                                                             |
| outcome_assess_1                          | Method of outcome assessment: Specify the method of assessment of the study outcome. If more than 1 are appropriate, enter additional methods in the next column labeled "outcome_assess_2" |
| outcome_assess_2                          | Method of outcome assessment: Specify the method of assessment of the study outcome. If more than 2 are appropriate, enter additional methods in the next column labeled "outcome_assess_3" |
| outcome_assess_3                          | Method of outcome assessment: Specify the method of assessment of the study outcome.                                                                                                                         |
| duration_fup_measure                      | Type of follow up measure (i.e. mean, median, max, min)                                                                                                                                                       |
| duration_fup_units                        | Units of follow up duration                                                                                                                                                                                  |
| value_of_duration_fup                     | Enter the length of participant follow-up.                                                                                                                                                                   |
| confounders_age                           | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_sex                           | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_education                     | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_income                        | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_smoking                       | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_alcohol_use                   | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_physical_activity             | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_dietary_activity              | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_bmi                           | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_hypertension                  | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_diabetes                      | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_hypercholesterolemia          | if controlled for in the relative risk estimation analysis, mark 1 for yes. Mark 0 for no                                                                                                                                 |
| confounders_other                         | For other confounders that not listed, list here                                                                                                                                                             |
| page_num_effect_size                      | Page number (where you found effect_size) from literature, or survey question where you found effect size; Use page number(s) of article, not page # of pdf                                                                 |
| effect_size_measure                       | Effect size measure: Specify the measure of effect size                                                                                                                                                      |
| effect_size                               | Effect size estimate: Provide the effect size estimate                                                                                                                                                        |
| lower                                     | Provide the lower limit of the confidence interval. Enter on a "per 1" basis. (If the CI is reported as a percent, you must convert to a decimal.) These 3 fields must all be filled in if any of them are filled in: lower, upper, uncertainty_type_value. |
| Field                          | Description                                                                                                                                                                                                 |
|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| upper                         | Provide the upper limit of the confidence interval. Enter on a "per 1" basis. (If the CI is reported as a percent, you must convert to a decimal.) These 3 fields must all be filled in if any of them are filled in: lower, upper, uncertainty_type_value. |
| CI_uncertainty_type_value     | This field is required if 'lower' & 'upper' are entered. This column represents the confidence level which is reported at (Eg. 95, 90, 99). These 3 fields must all be filled in if any of them are filled in: lower, upper, uncertainty_type_value.                   |
| nonCI_uncertainty_value       | Numerical value of the nonCI_uncertainty_type entered in that column. For example, if SD=5.3, you'd put 5.3 in this column, and choose SD from the drop down menu in nonCI_uncertainty_type.                                   |
| nonCI_uncertainty_type        | Enter SE or SD if appropriate. For example, if SD=5.3, you'd put 5.3 in nonCI_uncertainty_value, and choose SD from the drop down menu in this column (nonCI_uncertainty_type).                                                   |
| uncertainty_issue             | Mark with a 1 if no uncertainty is reported, if some sort of uncertainty is reported, mark 0                                                                                                               |
| subgroup_analysis             | 1 if RR is from main analysis (all participants), 0 if sub-analysis (only males, or among a specific age group, etc.)                                                                                         |
| subgroup_analysis_free_text   | If a sub-analysis, describe it (i.e. age, sex, etc.)                                                                                                                                                          |
| effect_size_multi_location    | 1 if the reported effect size is from a multi-country study and only one effect size has been reported for all locations, otherwise 0                                                                       |
| effect_size_multi_location Specify | which geography level is the RR for                                                                                                                                   |
| pooled_cohort                 | 1 if the reported effect size is from a pooled analysis and only pooled effect size has been reported, otherwise 0                                                                                           |
| dose_response                 | Does the study support a dose-response relationship between the exposure and the outcome? (1= yes, 0= no)                                                                                                       |
| dose_response_detail          | If "1" was specified in the dose_response field, please specify in this field the type of evidence supporting the dose-response relationship. For example, "statistically significant p value for linear trend".                 |
| cohorts                       | Please specify the person years of follow up in the exposed group                                                                                                                                              |
| cohort_person_years_exp       | Please specify the person years of follow up in the exposed group                                                                                                                                              |
| cohort_person_years_unexp     | Please specify the person years of follow up in the unexposed group                                                                                                                                              |
| cohort_person_years_total     | Enter the total person-years of follow-up if person-years of follow up in exposed and unexposed not reported                                                                                                    |
| cohort_number_events_exp      | Please specify the number of events in the exposed group                                                                                                                                                        |
| cohort_number_events_unexp    | Please specify the number of events in the unexposed group                                                                                                                                                      |
| cohort_number_events_total    | Enter the total number of events/cases if number of events in exposed and unexposed not reported                                                                                                                 |
| cohort_sample_size_exp        | Please specify the number of people in the exposed group if person-years of follow up in exposed not reported                                                                                               |
| cohort_sample_size_unexp      | Please specify the number of people in the unexposed group if person-years of follow up in unexposed not reported                                                                                             |
| cohort_sample_size_total      | Please specify the number of people included in the analysis if total person-years of follow up in not reported                                                                                             |
| cohort_dropout_rate           | Dropout rate: Specify the dropout rate (%) at the end of the study. Enter on a "per 1" basis. For example: 23% is entered as .23.                                                                           |
| cohort_dropout_assess         | Specify how dropout rate was defined in the study.                                                                                                                                                           |
| cohort_exposed_def            | exposed group definition: Provide a brief description of the exposed group (i.e., the comparison group) as used in estimation of the relative risk (e.g., never smokers)                                           |
| cohort_exp_unit_rr            | Exposure unit (for continuous risks): Specify the unit of exposure (e.g., grams/day).                                                                                                                         |
| cohort_exp_level_rr           | Exposure level in the exposed group (for continuous risks): Specify the mean/median level of exposure in the exposed group.                                                                                |
| cohort_unexp_def              | unexposed group definition: Provide a brief description of the unexposed group (i.e., the comparison group) as used in estimation of the relative risk (e.g., never smokers)                                 |
| cohort_unexp_unit_rr          | Exposure unit (for continuous risks): Specify the unit of exposure (e.g., grams/day) for the unexposed group                                                                                                  |
| cohort_unexp_level_rr         | Exposure level in the unexposed group (for continuous risks): Specify the mean/median level of exposure in the unexposed group.                                                                             |
| cohort_exp_level_dr           | Exposure level in for dose-repose RRs (for continuous risks): If the study reports dose-repose RR, please specify the level of exposure for the reported RR                                                                |
| Case-control                  | Were the controls selected from the community? 1 = yes, 0= no                                                                                                                                                |
| cc_community                  | Number of cases                                                                                                                                                                                             |
| Field | Description |
|-------|-------------|
| cc_control | Number of controls |
| cc_exposed_def | Exposed group definition: Provide a brief description of the exposed group for which the relative risk is reported (e.g., current smokers) |
| cc_exp_unit_rr | Exposure unit (for continuous risks): Specify the unit of exposure (e.g., grams/day) |
| cc_exp_level_rr | Exposure level in the exposed group (for continuous risks): Specify the mean/median level of exposure in the exposed group |
| cc_unexposed_def | Unexposed group definition: Provide a brief description of the unexposed group (i.e., the comparison group) as used in estimation of the relative risk (e.g., never smokers) |
| cc_unexp_unit_rr | Exposure level in the unexposed group (for continuous risks): Specify the mean/median level of exposure in the unexposed group |
| int_intervention_description | Intervention definition: Provide a brief description of the intervention as reported in the study |
| int_control_description | Control definition: Provide a brief description of the control as reported in the study |
| int_intervention_multi_rf | Does this intervention simultaneously target more than one risk? (1=yes, 0=no) |
| int_intervention_multi_rf_specify | Specify the risks that are targeted by the intervention |
| int_intervention_level | Level of intervention: The intervention was implemented ... |
| int_adhere_assess | Specify how adherence was defined in the study |
| int_adhere_rate_intervention | Adherence rate in the intervention group; Enter on a "per 1" basis. For example: 23% is entered as .23 |
| int_adhere_rate_control | Adherence rate in the control group; Enter on a "per 1" basis. For example: 23% is entered as .23 |
| int_dropout_rate_intervention | Dropout rate in the intervention group: Specify the dropout rate (%) at the end of the study. Enter on a "per 1" basis. For example: 23% is entered as .23 |
| int_dropout_rate_control | Dropout rate in the control group: Specify the dropout rate (%) at the end of the study. Enter on a "per 1" basis. For example: 23% is entered as .23 |
| int_dropout_assess | Specify how dropout rate was defined in the study |
| int_blinding | For interventional studies. Blinding: The trial was ... (select 1) |
| int_exp_unit | For trials, specify the unit of exposure (e.g., mmol/l) |
| int_baseline_exp_int | For trials, specify the exposure level in the intervention group at baseline |
| int_baseline_exp_comp | For trials, specify the exposure level in the comparison group at baseline |
| int_fup_exp_int | For trials, specify the exposure level in the intervention group at the end of the follow-up time |
| int_fup_exp_comp | For trials, specify the exposure level in the comparison group at the end of follow-up time |
| int_fup_exp_int_difference | For trials, please specify the difference of exposure level between baseline and follow-up time for the intervention group |
| int_fup_exp_comp_difference | For trials, please specify the difference of exposure level between baseline and follow-up time for the comparison group |
| int_person_years_int | Please specify the number of person years of follow up for the intervention group |
| int_person_years_comp | Please specify the number of person years of follow up in the comparison group |
| int_number_events_int | For trials, specify the number of cases in the intervention group at the end of follow up |
| int_number_events_comp | For trials, specify the number of cases in the control group at the end of follow up |
| int_sample_size_int_group_baseline | For trials, specify the sample size in the intervention group at baseline |
| int_sample_size_comparison_group_baseline | For trials, specify the sample size in the comparison group at baseline |
| int_sample_size_int_group_follow_up | For trials, specify the sample size in the intervention group at the end of follow-up time |
| int_sample_size_comparison_group_follow_up | For trials, specify the sample size in the comparison group at the end of follow-up time |

**Other**
- note_modeler: for modelers only, audience is modeler, not for correspondence
- note_sr: notes related to extraction, including assumptions, data adjustment, problems with source, any other notes that may be relevant, etc.
| extractor | uwnet id of person who extracted the data |
|-----------|------------------------------------------|
| custom_exp_meas_num | If the exposure level was assessed multiple times at a given time point (e.g., systolic blood pressure), specify the number of measurements at each time point. |
| custom_exp_biomarker | If the exposure level was assessed via a biomarker, specify the full name of the biomarker. |
| custom_exp_kilometer | Specify the geographical unit of measurement in kilometer (if applicable, e.g., satellite data). |
| custom_exp_level_lower | If don't have a mean/midpoint exposure level can use this column in conjecture with the custom_exp_level_upper to enter in a range |
| custom_exp_level_upper | If don't have a mean/midpoint exposure level can use this column in conjecture with the custom_exp_level_lower to enter in a range |
| custom_unexp_level_lower | If don't have a mean/midpoint exposure level can use this column in conjecture with the custom_outcome_level_upper to enter in a range |
| custom_unexp_level_upper | If don't have a mean/midpoint exposure level can use this column in conjecture with the custom_outcome_level_lower to enter in a range |
| custom_prospective_lag | Specify lag time between exposure assessment and outcome |
| custom_age_demographer | A binary flag to identify if ages are presented in demographer notation or not in the source. This value is currently not used to adjust any age_start or age_end values, but in the future, that is the intention; 0 = article does not use demographer notation (4 = 4.00 not 4.99); 1 = article uses demographer notation (4=4.99 not 4.00) |
| custom_bmi_menopause_free_text | Free text field for bmi team |
| custom_cvd_outcome | Used for mapping cvd outcomes, free text field |
| custom_dm_type | Used for documenting diabetes type |
| custom_dm_case_defn | Used for documenting diabetes definitions, free text |
| custom_pmid | To document Pubmed id |
| custom_cvd_rep_high_risk | Cvd specific, binary, if the study only includes people at high risk for CVD (1 for example if it is only among diabetics) |
| custom_drug_class | Class of drug being used in intervention, free text |
| custom_outcome_primary | Outcome is the primary outcome of RCT (1=yes, 0=no) |
| custom_outcome_prespecified | Outcome is the prespecified outcome of RCT (1=yes, 0=no) |
| custom_multipollutant | Are any other pollutants controlled for in the model? 0=no, 1=yes |
| custom_pollutants_controlled | If custom_multipollutant=1, list the pollutants controlled for |
| custom_PM2.5_model_type | Describe the model used for exposure |
| custom_assign_method | How do researchers assign participants to exp? (ex: by home address, by city, nearest zipcode centroid, etc.) |
| custom_PM2.5_def | What metric are they using to measure PM2.5 (ex: mean of annual PM2.5 averages for 35-1 year prior to study) |
| custom_lag | Do the authors take into account lag? If so, how? |
| custom_PM2.5_min | All of these have to do with the spread of the PM2.5 exposure covered by the study. Minimum |
| custom_PM2.5_5th | 5-percentile |
| custom_PM2.5_25th | 25-percentile |
| custom_PM2.5_50th | Median/50-percentile |
| custom_PM2.5_75th | 75-percentile |
| custom_PM2.5_95th | 95-percentile |
| custom_PM2.5_max | Maximum |
| custom_PM2.5_mean | Mean |
| custom_PM2.5_stddev | Standard Deviation |
| custom_PM2.5_other_measure | Any other measures of the distribution of PM2.5 amongst participants? |
| custom_PM2.5_other_measure_description | If so, what are they? (ex: 10-, 90-, IQR) |
Section 6: Study quality and risk of bias assessment

For each study that met the inclusion criteria, two reviewers assessed several indicators of bias during the extraction process. The full list of bias covariates assessed across all studies can be found in the extraction template (Supplementary Table 5).

To assist with a broad sense of data quality, we calculated a quality score for each study used in this analysis based on four study characteristics that were most applicable and likely to introduce bias (see supplementary Table 6). The overall score assessment was measured from 0 to 5, where 0 indicated the least bias and 5 indicated the most bias.

Supplementary Table 6. Study quality for every study used in the models
In this presentation of the data, there is one row per study/outcome pair

| Author   | Year | Outcome            | Exposure Measurement Score (multiple-0, single-1) | Exposure Assessment Score (objective-0 vs self-report-1) | Outcome Assessment Score (objective-0 vs self-report-1) | Confounders Score (age,sex,smoking,income,education-0; age,sex,smoking-1; age,sex-2) | Quality Score (best-0, worst-5) |
|----------|------|--------------------|--------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|----------------------------------------------------------------------------------|--------------------------------|
| Barouti  | 2022 | Diabetes mellitus   | 0                                                | 1                                                        | 0                                                      | 0                                                                                | 1                               |
| Barouti  | 2022 | Diabetes mellitus   | 0                                                | 1                                                        | 0                                                      | 0                                                                                | 1                               |
| Bazzano  | 2008 | Diabetes mellitus   | 0                                                | 1                                                        | 0                                                      | 2                                                                                | 3                               |
| Chen     | 2018 | Diabetes mellitus   | 1                                                | 1                                                        | 0                                                      | 1                                                                                | 3                               |
| Cooper   | 2012 | Diabetes mellitus   | 1                                                | 1                                                        | 0                                                      | 1                                                                                | 3                               |
| Hodge    | 2004 | Diabetes mellitus   | 1                                                | 1                                                        | 1                                                      | 2                                                                                | 5                               |
| Kurotani | 2013 | Diabetes mellitus   | 0                                                | 1                                                        | 1                                                      | 2                                                                                | 4                               |
| Liu      | 2021 | Diabetes mellitus   | 1                                                | 1                                                        | 1                                                      | 0                                                                                | 3                               |
| Liu      | 2004 | Diabetes mellitus   | 1                                                | 1                                                        | 1                                                      | 2                                                                                | 5                               |
| Mamluk   | 2017 | Diabetes mellitus   | 1                                                | 1                                                        | 1                                                      | 1                                                                                | 4                               |
| Meyer    | 2000 | Diabetes mellitus   | 1                                                | 1                                                        | 1                                                      | 2                                                                                | 5                               |
| Montonen | 2005 | Diabetes mellitus   | 1                                                | 1                                                        | 0                                                      | 1                                                                                | 3                               |
| Olsson   | 2021 | Diabetes mellitus   | 1                                                | 1                                                        | 0                                                      | 1                                                                                | 3                               |
| Qiao     | 2014 | Diabetes mellitus   | 1                                                | 1                                                        | 1                                                      | 2                                                                                | 5                               |
| Villegas | 2008 | Diabetes mellitus   | 0                                                | 1                                                        | 1                                                      | 2                                                                                | 4                               |
| Ahmed    | 2020 | Diabetes mellitus   | 0                                                | 1                                                        | 1                                                      | 1                                                                                | 3                               |
| Rayner   | 2020 | Diabetes mellitus   | 0                                                | 1                                                        | 1                                                      | 2                                                                                | 4                               |
| Freedman | 2007 | Esophageal cancer   | 1                                                | 1                                                        | 0                                                      | 1                                                                                | 3                               |
| Author         | Year | Disease Description       | Year | Month | Disease Description       | Year | Month | Disease Description       | Year | Month | Disease Description       | Year | Month | Disease Description       |
|---------------|------|---------------------------|------|-------|---------------------------|------|-------|---------------------------|------|-------|---------------------------|------|-------|---------------------------|------|-------|---------------------------|
| González      | 2006 | Esophageal cancer         |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Sheikh       | 2019 | Esophageal cancer         |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Steevens     | 2011 | Esophageal cancer         |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Tran         | 2005 | Esophageal cancer         |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Yamaji       | 2008 | Esophageal cancer         |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Larsson      | 2009 | Hemorrhagic stroke        |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Larsson      | 2013 | Hemorrhagic stroke        |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Mizrahi      | 2009 | Hemorrhagic stroke        |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Nagura       | 2009 | Hemorrhagic stroke        |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Pham         | 2007 | Hemorrhagic stroke        |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Yokoyama     | 2000 | Hemorrhagic stroke        |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Zhang        | 2011 | Hemorrhagic stroke        |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Bhupathiraju | 2013 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Dauchet      | 2010 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Hansen       | 2010 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Knekt        | 1994 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Kobylecki    | 2015 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Liu          | 2000 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Miller       | 2017 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Perez-       | 2021 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Cornago      |      |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Pietinen     | 1996 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Rebello      | 2014 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Sharma       | 2014 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Sonestedt    | 2015 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Stefler      | 2016 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Tognon       | 2014 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Yoshizaki    | 2020 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Yu           | 2014 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Zhang        | 2021 | Ischemic heart disease    |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
| Johnsen      | 2003 | Ischemic stroke           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |      |       |                           |
Section 7: Results from individual studies

The health outcome, reference group exposure, alternative group exposure, log effect size, and log effect size SE identified from each report are provided in Supplementary Table 7.

Supplementary Table 7. Summary results from input studies

| Outcome          | Alternative group exposure | Reference group exposure | Log effect size | Log effect size standard error | Study          |
|------------------|----------------------------|--------------------------|-----------------|--------------------------------|----------------|
| Diabetes mellitus| 0 - 41 grams               | 42 - 78 grams            | -0.29           | 0.15                           | Montonen 2005  |
| Diabetes mellitus| 0 - 41 grams               | 131 - 182 grams          | -0.26           | 0.15                           | Montonen 2005  |
| Diabetes mellitus| 0 - 41 grams               | 79 - 130 grams           | -0.07           | 0.14                           | Montonen 2005  |
| Diabetes mellitus| 0 - 146 grams              | 146 - 203 grams          | 0               | 0.05                           | Bazzano 2008   |
| Diabetes mellitus| 0 - 146 grams              | 203 - 257 grams          | 0.02            | 0.05                           | Bazzano 2008   |
| Diabetes mellitus| 0 - 146 grams              | 341 - 425 grams          | 0.05            | 0.05                           | Bazzano 2008   |
| Diabetes mellitus| 0 - 146 grams              | 257 - 341 grams          | 0.08            | 0.05                           | Bazzano 2008   |
| Diabetes mellitus| 0 - 152 grams              | 213 - 274 grams          | -0.01           | 0.1                            | Meyer 2000     |
| Diabetes mellitus| 0 - 152 grams              | 153 - 212 grams          | 0.03            | 0.1                            | Meyer 2000     |
| Diabetes mellitus| 0 - 152 grams              | 368 - 460 grams          | 0.07            | 0.11                           | Meyer 2000     |
| Diabetes mellitus| 0 - 152 grams              | 275 - 367 grams          | 0.09            | 0.1                            | Meyer 2000     |
| Diabetes mellitus| 0 - 152 grams              | 226 - 306 grams          | -0.02           | 0.09                           | Liu 2004       |
| Diabetes mellitus| 0 - 152 grams              | 306 - 438 grams          | -0.01           | 0.09                           | Liu 2004       |
| Diabetes mellitus | 0 - 152 grams | 152 - 226 grams | 0.01 | 0.08 | Liu 2004 |
|-------------------|---------------|-----------------|------|------|----------|
| Diabetes mellitus | 0 - 152 grams | 438 - 569 grams | 0.03 | 0.09 | Liu 2004 |
| Diabetes mellitus | 0 - 212 grams | 300 - 387 grams | -0.39 | 0.08 | Villegas 2008 |
| Diabetes mellitus | 0 - 212 grams | 387 - 517 grams | -0.33 | 0.08 | Villegas 2008 |
| Diabetes mellitus | 0 - 212 grams | 517 - 646 grams | -0.33 | 0.08 | Villegas 2008 |
| Diabetes mellitus | 0 - 212 grams | 212 - 300 grams | -0.3 | 0.08 | Villegas 2008 |
| Diabetes mellitus | 0 - 138 grams | 209 - 312 grams | -0.27 | 0.18 | Kurotani 2013 |
| Diabetes mellitus | 0 - 110 grams | 267 - 358 grams | -0.21 | 0.17 | Kurotani 2013 |
| Diabetes mellitus | 0 - 110 grams | 175 - 267 grams | -0.08 | 0.14 | Kurotani 2013 |
| Diabetes mellitus | 0 - 110 grams | 110 - 175 grams | -0.07 | 0.12 | Kurotani 2013 |
| Diabetes mellitus | 0 - 138 grams | 312 - 415 grams | -0.01 | 0.2 | Kurotani 2013 |
| Diabetes mellitus | 0 - 138 grams | 138 - 209 grams | 0.04 | 0.15 | Kurotani 2013 |
| Diabetes mellitus | 0 - 222 grams | 536 - 682 grams | -0.13 | 0.19 | Hodge 2004 |
| Diabetes mellitus | 0 - 222 grams | 383 - 529 grams | -0.03 | 0.18 | Hodge 2004 |
| Diabetes mellitus | 0 - 222 grams | 230 - 375 grams | 0.09 | 0.17 | Hodge 2004 |
| Diabetes mellitus | 0 - 230 grams | 231 - 460 grams | 0.1 | 0.07 | Qiao 2014 |
| Diabetes mellitus | 0 - 100 grams | 100 - 155 grams | -0.08 | 0.05 | Cooper 2012 |
| Diabetes mellitus | 0 - 100 grams | 155 - 238 grams | -0.07 | 0.06 | Cooper 2012 |
| Diabetes mellitus | 0 - 112 grams | 238 - 320 grams | -0.06 | 0.06 | Cooper 2012 |
| Diabetes mellitus | 0 - 112 grams | 200 - 312 grams | -0.13 | 0.03 | Mamluk 2017 |
| Diabetes mellitus | 0 - 112 grams | 120 - 192 grams | -0.08 | 0.03 | Mamluk 2017 |
| Diabetes mellitus | 0 - 112 grams | 320 - 432 grams | -0.08 | 0.03 | Mamluk 2017 |
| Diabetes mellitus | 0 - 112 grams | 120 - 192 grams | -0.01 | 0.12 | Mamluk 2017 |
| Diabetes mellitus | 0 - 112 grams | 320 - 432 grams | 0.05 | 0.14 | Mamluk 2017 |
| Diabetes mellitus | 0 - 112 grams | 200 - 312 grams | 0.1 | 0.13 | Mamluk 2017 |
| Diabetes mellitus | 0 - 102 grams | 102 - 142 grams | -0.08 | 0.07 | Olsson 2021 |
| Diabetes mellitus | 0 - 102 grams | 142 - 184 grams | -0.12 | 0.07 | Olsson 2021 |
| Diabetes mellitus | 0 - 102 grams | 184 - 246 grams | -0.06 | 0.07 | Olsson 2021 |
| Diabetes mellitus | 0 - 102 grams | 246 - 1177 grams | -0.16 | 0.08 | Olsson 2021 |
| Diabetes mellitus | 0 - 102 grams | 102 - 142 grams | -0.05 | 0.07 | Olsson 2021 |
| Diabetes mellitus | 0 - 102 grams | 142 - 184 grams | -0.11 | 0.07 | Olsson 2021 |
| Diabetes mellitus | 0 - 102 grams | 184 - 246 grams | 0.02 | 0.07 | Olsson 2021 |
| Diabetes mellitus | 0 - 102 grams | 246 - 1177 grams | 0.05 | 0.07 | Olsson 2021 |
| Diabetes mellitus | 0 - 167 grams | 167 - 205 grams | -0.37 | 0.16 | Liu 2021 |
| Diabetes mellitus | 0 - 71 grams | 71 - 138 grams | -0.21 | 0.11 | Barouti 2022 |
| Diabetes mellitus | 0 - 71 grams | 138 - 216 grams | -0.19 | 0.11 | Barouti 2022 |
| Diabetes mellitus | 0 - 100 grams | 100 - 181 grams | 0.02 | 0.12 | Barouti 2022 |
| Diabetes mellitus | 0 - 100 grams | 181 - 279 grams | 0.13 | 0.12 | Barouti 2022 |
| Diabetes mellitus | 0 - 90 grams | 90 - 120 grams | 0.15 | 0.04 | Chen 2018 |
| Diabetes mellitus | 0 - 90 grams | 120 - 152 grams | -0.02 | 0.05 | Chen 2018 |
| Diabetes mellitus | 0 - 90 grams | 152 - 202 grams | 0.02 | 0.05 | Chen 2018 |
| Condition                  | Amount Range | Weight Range | Value 1 | Value 2 | Year      |
|---------------------------|--------------|--------------|---------|---------|-----------|
| Diabetes mellitus         | 0 - 90 grams | 202 - 268 grams | 0.08   | 0.05   | Chen 2018 |
| Diabetes mellitus         | 0 - 154 grams | 154 - 308 grams | 0.48   | 0.24   | Ahmed 2020 |
| Diabetes mellitus         | 0 - 154 grams | 154 - 308 grams | 0.17   | 0.19   | Ahmed 2020 |
| Diabetes mellitus         | 3 - 3 grams  | 1 - 1 grams  | 0.03   | 0.1    | Rayner 2020 |
| Diabetes mellitus         | 3 - 3 grams  | 2 - 2 grams  | 0.02   | 0.11   | Rayner 2020 |
| Ischemic heart disease    | 0 - 77 grams | 78 - 137 grams | -0.87  | 0.36   | Knekt 1994 |
| Ischemic heart disease    | 0 - 61 grams | 117 - 172 grams | -0.42  | 0.19   | Knekt 1994 |
| Ischemic heart disease    | 0 - 77 grams | 137 - 196 grams | -0.42  | 0.32   | Knekt 1994 |
| Ischemic heart disease    | 0 - 61 grams | 62 - 115 grams | -0.17  | 0.17   | Knekt 1994 |
| Ischemic heart disease    | 0 - 38 grams | 38 - 77 grams  | -0.12  | 0.07   | Kobylecki 2015 |
| Ischemic heart disease    | 0 - 38 grams | 77 - 115 grams | -0.19  | 0.07   | Kobylecki 2015 |
| Ischemic heart disease    | 0 - 38 grams | 153 - 230 grams | -0.13  | 0.08   | Kobylecki 2015 |
| Ischemic heart disease    | 0 - 143 grams | 197 - 252 grams | -0.24  | 0.06   | Bhupathiraju 2013 |
| Ischemic heart disease    | 0 - 143 grams | 252 - 338 grams | -0.17  | 0.07   | Bhupathiraju 2013 |
| Ischemic heart disease    | 0 - 143 grams | 338 - 424 grams | -0.16  | 0.07   | Bhupathiraju 2013 |
| Ischemic heart disease    | 0 - 143 grams | 143 - 197 grams | -0.12  | 0.06   | Bhupathiraju 2013 |
| Ischemic heart disease    | 0 - 134 grams | 189 - 247 grams | -0.04  | 0.05   | Bhupathiraju 2013 |
| Ischemic heart disease    | 0 - 134 grams | 247 - 340 grams | -0.04  | 0.06   | Bhupathiraju 2013 |
| Ischemic heart disease    | 0 - 134 grams | 134 - 189 grams | -0.01  | 0.05   | Bhupathiraju 2013 |
| Ischemic heart disease    | 0 - 37 grams  | 127 - 169 grams | -0.51  | 0.14   | Pietinen 1996 |
| Ischemic heart disease    | 0 - 37 grams  | 59 - 85 grams  | -0.37  | 0.13   | Pietinen 1996 |
| Ischemic heart disease    | 0 - 37 grams  | 85 - 127 grams | -0.26  | 0.13   | Pietinen 1996 |
| Ischemic heart disease    | 0 - 37 grams  | 37 - 59 grams  | 0.03   | 0.11   | Pietinen 1996 |
| Ischemic heart disease    | 0 - 176 grams | 506 - 659 grams | -0.31  | 0.12   | Sharma 2014 |
| Ischemic heart disease    | 0 - 176 grams | 261 - 352 grams | -0.27  | 0.1    | Sharma 2014 |
| Ischemic heart disease    | 0 - 176 grams | 261 - 352 grams | -0.27  | 0.12   | Sharma 2014 |
| Ischemic heart disease    | 0 - 176 grams | 352 - 506 grams | -0.26  | 0.13   | Sharma 2014 |
| Ischemic heart disease    | 0 - 176 grams | 352 - 506 grams | -0.2   | 0.1    | Sharma 2014 |
| Ischemic heart disease    | 0 - 176 grams | 176 - 261 grams | -0.07  | 0.09   | Sharma 2014 |
| Ischemic heart disease    | 0 - 176 grams | 506 - 659 grams | -0.05  | 0.14   | Sharma 2014 |
| Ischemic heart disease    | 0 - 176 grams | 176 - 261 grams | -0.01  | 0.11   | Sharma 2014 |
| Ischemic heart disease    | 0 - 153 grams | 226 - 306 grams | -0.6   | 0.33   | Liu 2000   |
| Ischemic heart disease    | 0 - 153 grams | 306 - 441 grams | -0.14  | 0.29   | Liu 2000   |
| Ischemic heart disease    | 0 - 153 grams | 441 - 575 grams | -0.13  | 0.29   | Liu 2000   |
| Ischemic heart disease    | 0 - 153 grams | 153 - 226 grams | -0.06  | 0.28   | Liu 2000   |
| Ischemic heart disease    | 0 - 61 grams  | 77 - 99 grams  | -0.43  | 0.2    | Dauchet 2010 |
| Ischemic heart disease    | 0 - 61 grams  | 77 - 99 grams  | -0.34  | 0.29   | Dauchet 2010 |
| Ischemic heart disease    | 0 - 61 grams  | 115 - 137 grams | -0.33  | 0.24   | Dauchet 2010 |
| Ischemic heart disease    | 0 - 61 grams  | 77 - 99 grams  | -0.05  | 0.22   | Dauchet 2010 |
| Ischemic heart disease | 0 - 61 grams | 115 - 137 grams | 0.22 | 0.27 | Dauchet 2010 |
|------------------------|-------------|-----------------|------|------|--------------|
| Ischemic heart disease | 0 - 61 grams | 115 - 137 grams | 0.25 | 0.21 | Dauchet 2010 |
| Ischemic heart disease | 80 - 162 grams | 183 - 318 grams | -0.2 | 0.2 | Stefler 2016 |
| Ischemic heart disease | 80 - 162 grams | 138 - 234 grams | -0.06 | 0.18 | Stefler 2016 |
| Ischemic heart disease | 80 - 162 grams | 263 - 495 grams | 0 | 0.21 | Stefler 2016 |
| Ischemic heart disease | 0 - 48 grams | 99 - 797 grams | -0.37 | 0.15 | Rebello 2014 |
| Ischemic heart disease | 0 - 48 grams | 62 - 77 grams | -0.22 | 0.1 | Rebello 2014 |
| Ischemic heart disease | 0 - 48 grams | 99 - 668 grams | -0.17 | 0.11 | Rebello 2014 |
| Ischemic heart disease | 0 - 48 grams | 62 - 77 grams | -0.17 | 0.13 | Rebello 2014 |
| Ischemic heart disease | 0 - 48 grams | 77 - 99 grams | -0.15 | 0.13 | Rebello 2014 |
| Ischemic heart disease | 0 - 48 grams | 77 - 99 grams | -0.14 | 0.1 | Rebello 2014 |
| Ischemic heart disease | 0 - 48 grams | 48 - 62 grams | -0.07 | 0.13 | Rebello 2014 |
| Ischemic heart disease | 0 - 192 grams | 192 - 384 grams | -0.31 | 0.16 | Tognon 2014 |
| Ischemic heart disease | 0 - 175 grams | 175 - 252 grams | 0.14 | 0.22 | Yu 2014 |
| Ischemic heart disease | 0 - 175 grams | 252 - 360 grams | -0.26 | 0.24 | Yu 2014 |
| Ischemic heart disease | 0 - 175 grams | 360 - 498 grams | -0.19 | 0.24 | Yu 2014 |
| Ischemic heart disease | 0 - 206 grams | 206 - 298 grams | 0.05 | 0.19 | Yu 2014 |
| Ischemic heart disease | 0 - 206 grams | 298 - 423 grams | -0.39 | 0.21 | Yu 2014 |
| Ischemic heart disease | 0 - 206 grams | 423 - 581 grams | 0.02 | 0.19 | Yu 2014 |
| Ischemic heart disease | 0 - 77 grams | 77 - 154 grams | 0.06 | 0.07 | Miller 2017 |
| Ischemic heart disease | 0 - 77 grams | 154 - 231 grams | 0.12 | 0.07 | Miller 2017 |
| Ischemic heart disease | 0 - 77 grams | 231 - 308 grams | -0.07 | 0.09 | Miller 2017 |
| Ischemic heart disease | 0 - 98 grams | 98 - 144 grams | -0.05 | 0.07 | Sonestedt 2015 |
| Ischemic heart disease | 0 - 98 grams | 144 - 188 grams | -0.01 | 0.07 | Sonestedt 2015 |
| Ischemic heart disease | 0 - 98 grams | 188 - 272 grams | -0.02 | 0.07 | Sonestedt 2015 |
| Ischemic heart disease | 0 - 98 grams | 272 - 392 grams | -0.01 | 0.08 | Sonestedt 2015 |
| Ischemic heart disease | 0 - 143 grams | 143 - 254 grams | 0.17 | 0.21 | Yoshizaki 2020 |
| Ischemic heart disease | 0 - 143 grams | 254 - 386 grams | 0.04 | 0.24 | Yoshizaki 2020 |
| Ischemic heart disease | 0 - 169 grams | 169 - 285 grams | 0.22 | 0.38 | Yoshizaki 2020 |
| Ischemic heart disease | 0 - 169 grams | 285 - 422 grams | 0.17 | 0.41 | Yoshizaki 2020 |
| Ischemic heart disease | 0 - 154 grams | 154 - 231 grams | -0.04 | 0.02 | Zhang 2021 |
| Ischemic heart disease | 0 - 154 grams | 231 - 308 grams | -0.01 | 0.02 | Zhang 2021 |
| Ischemic heart disease | 0 - 154 grams | 308 - 385 grams | -0.05 | 0.02 | Zhang 2021 |
| Ischemic heart disease | 0 - 116 grams | 116 - 192 grams | 0.01 | 0.03 | Perez-Cornago 2021 |
| Ischemic heart disease | 0 - 116 grams | 192 - 308 grams | -0.07 | 0.04 | Perez-Cornago 2021 |
| Ischemic heart disease | 0 - 116 grams | 308 - 424 grams | -0.04 | 0.05 | Perez-Cornago 2021 |
| Ischemic heart disease | 0 - 96 grams | 96 - 148 grams | 0.06 | 0.1 | Hansen 2010 |
| Ischemic heart disease | 0 - 96 grams | 148 - 211 grams | 0.03 | 0.1 | Hansen 2010 |
| Ischemic heart disease | 0 - 96 grams | 211 - 274 grams | -0.07 | 0.11 | Hansen 2010 |
| Ischemic heart disease | 0 - 110 grams | 110 - 167 grams | 0.14 | 0.16 | Hansen 2010 |
| Condition            | Weight Range | Mean | SD  | Reference     |
|----------------------|--------------|------|-----|---------------|
| Ischemic heart disease | 0 - 110 grams | 167 - 237 grams | -0.13 | 0.19          | Hansen 2010 |
| Ischemic stroke      | 0 - 110 grams | 237 - 307 grams | 0.09  | 0.2           | Hansen 2010 |
| Ischemic stroke      | 0 - 19 grams  | 19 - 31 grams   | -0.14 | 0.16          | Nagura 2009 |
| Ischemic stroke      | 0 - 19 grams  | 45 - 66 grams   | 0.03  | 0.17          | Nagura 2009 |
| Ischemic stroke      | 0 - 19 grams  | 31 - 45 grams   | 0.22  | 0.16          | Nagura 2009 |
| Ischemic stroke      | 0 - 44 grams  | 45 - 84 grams   | -0.36 | 0.15          | Mizrahi 2009|
| Ischemic stroke      | 0 - 56 grams  | 57 - 95 grams   | -0.36 | 0.15          | Mizrahi 2009|
| Ischemic stroke      | 0 - 44 grams  | 85 - 137 grams  | -0.25 | 0.15          | Mizrahi 2009|
| Ischemic stroke      | 0 - 11 grams  | 138 - 535 grams | -0.08 | 0.16          | Mizrahi 2009|
| Ischemic stroke      | 0 - 11 grams  | 33 - 66 grams   | -0.17 | 0.09          | Zhang 2011  |
| Ischemic stroke      | 0 - 11 grams  | 77 - 109 grams  | -0.17 | 0.11          | Zhang 2011  |
| Ischemic stroke      | 0 - 157 grams | 310 - 421 grams | -0.27 | 0.18          | Joshipura 1999|
| Ischemic stroke      | 0 - 134 grams | 188 - 264 grams | -0.27 | 0.23          | Joshipura 1999|
| Ischemic stroke      | 0 - 134 grams | 264 - 364 grams | -0.21 | 0.23          | Joshipura 1999|
| Ischemic stroke      | 0 - 157 grams | 222 - 310 grams | -0.13 | 0.17          | Joshipura 1999|
| Ischemic stroke      | 0 - 157 grams | 421 - 533 grams | -0.12 | 0.18          | Joshipura 1999|
| Ischemic stroke      | 0 - 134 grams | 364 - 464 grams | -0.11 | 0.23          | Joshipura 1999|
| Ischemic stroke      | 0 - 134 grams | 134 - 188 grams | -0.01 | 0.22          | Joshipura 1999|
| Ischemic stroke      | 0 - 157 grams | 157 - 222 grams | 0.21  | 0.15          | Joshipura 1999|
| Ischemic stroke      | 0 - 92 grams  | 264 - 338 grams | -0.16 | 0.2           | Johnsen 2003|
| Ischemic stroke      | 0 - 92 grams  | 92 - 140 grams  | -0.09 | 0.18          | Johnsen 2003|
| Ischemic stroke      | 0 - 92 grams  | 140 - 188 grams | -0.07 | 0.18          | Johnsen 2003|
| Ischemic stroke      | 0 - 92 grams  | 188 - 264 grams | -0.03 | 0.19          | Johnsen 2003|
| Ischemic stroke      | 0 - 37 grams  | 126 - 168 grams | -0.29 | 0.06          | Larsson 2009 |
| Ischemic stroke      | 0 - 37 grams  | 59 - 84 grams   | -0.11 | 0.06          | Larsson 2009 |
| Ischemic stroke      | 0 - 37 grams  | 84 - 126 grams  | -0.09 | 0.06          | Larsson 2009 |
| Ischemic stroke      | 0 - 37 grams  | 37 - 59 grams   | -0.06 | 0.06          | Larsson 2009 |
| Ischemic stroke      | 0 - 153 grams | 479 - 632 grams | -0.06 | 0.28          | Steffen 2003 |
| Ischemic stroke      | 0 - 153 grams | 326 - 479 grams | 0.04  | 0.25          | Steffen 2003 |
| Ischemic stroke      | 0 - 153 grams | 230 - 326 grams | 0.1   | 0.24          | Steffen 2003 |
| Ischemic stroke      | 0 - 153 grams | 153 - 230 grams | 0.44  | 0.22          | Steffen 2003 |
| Ischemic stroke      | 0 - 103 grams | 165 - 226 grams | -0.13 | 0.06          | Larsson 2013 |
| Ischemic stroke      | 0 - 103 grams | 326 - 425 grams | -0.13 | 0.07          | Larsson 2013 |
| Ischemic stroke      | 0 - 103 grams | 226 - 326 grams | -0.06 | 0.06          | Larsson 2013 |
| Ischemic stroke      | 0 - 103 grams | 103 - 165 grams | -0.05 | 0.06          | Larsson 2013 |
| Ischemic stroke      | 0 - 77 grams  | 77 - 115 grams  | 0.18  | 0.2           | Pham 2007   |
| Ischemic stroke      | 0 - 22 grams  | 66 - 77 grams   | -0.71 | 0.61          | Yokoyama 2000|
| Ischemic stroke      | 0 - 22 grams  | 66 - 77 grams   | -0.19 | 1.03          | Yokoyama 2000|
| Ischemic stroke      | 0 - 22 grams  | 33 - 55 grams   | -0.16 | 1.27          | Yokoyama 2000|
| Ischemic stroke      | 0 - 22 grams  | 22 - 55 grams   | -0.04 | 0.75          | Yokoyama 2000|
| Condition              | Range         | Mean | SD   | Year       |
|------------------------|---------------|------|------|------------|
| Esophageal cancer      | 0 - 125 grams | 0.58 | 0.36 | Steevens 2011 |
| Hemorrhagic stroke     | 0 - 19 grams  | 0.13 | 0.16 | Nagura 2009 |
| Ischemic stroke        | 0 - 286 grams | 0.14 | 0.06 | Tong 2020  |
| Ischemic stroke        | 0 - 136 grams | 0.13 | 0.05 | Tong 2020  |
| Ischemic stroke        | 0 - 286 grams | 0.13 | 0.05 | Tong 2020  |
| Ischemic stroke        | 0 - 254 grams | 0.14 | 0.06 | Tong 2020  |
| Ischemic stroke        | 0 - 143 grams | 0.13 | 0.05 | Tong 2020  |
| Ischemic stroke        | 0 - 380 grams | 0.14 | 0.06 | Tong 2020  |
| Ischemic stroke        | 0 - 254 grams | 0.13 | 0.05 | Tong 2020  |
| Hemorrhagic stroke     | 0 - 422 grams | 0.13 | 0.16 | Nagura 2009 |
| Hemorrhagic stroke     | 0 - 31 grams  | 0.09 | 0.15 | Nagura 2009 |
| Hemorrhagic stroke     | 0 - 84 grams  | 0.04 | 0.39 | Mizrahi 2009 |
| Hemorrhagic stroke     | 0 - 57 grams  | 0.04 | 0.39 | Mizrahi 2009 |
| Hemorrhagic stroke     | 0 - 137 grams | 0.37 | 0.36 | Mizrahi 2009 |
| Hemorrhagic stroke     | 0 - 535 grams | 0.37 | 0.38 | Mizrahi 2009 |
| Hemorrhagic stroke     | 0 - 109 grams | 0.34 | 0.22 | Zhang 2011  |
| Hemorrhagic stroke     | 0 - 66 grams  | 0.22 | 0.19 | Zhang 2011  |
| Hemorrhagic stroke     | 0 - 22 grams  | 0.15 | 0.17 | Zhang 2011  |
| Hemorrhagic stroke     | 0 - 168 grams | 0.48 | 0.23 | Larsson 2009 |
| Hemorrhagic stroke     | 0 - 126 grams | 0.31 | 0.17 | Larsson 2009 |
| Hemorrhagic stroke     | 0 - 59 grams  | 0.09 | 0.15 | Larsson 2009 |
| Hemorrhagic stroke     | 0 - 84 grams  | 0.03 | 0.15 | Larsson 2009 |
| Hemorrhagic stroke     | 0 - 425 grams | 0.13 | 0.18 | Larsson 2013 |
| Hemorrhagic stroke     | 0 - 165 grams | 0.05 | 0.14 | Larsson 2013 |
| Hemorrhagic stroke     | 0 - 226 grams | 0.04 | 0.16 | Larsson 2013 |
| Hemorrhagic stroke     | 0 - 326 grams | 0.02 | 0.17 | Larsson 2013 |
| Hemorrhagic stroke     | 0 - 77 grams  | 0.1  | 0.31 | Pham 2007   |
| Hemorrhagic stroke     | 0 - 77 grams  | 0.1  | 0.31 | Pham 2007   |
| Hemorrhagic stroke     | 0 - 66 grams  | 0.62 | 1.04 | Yokoyama 2000 |
| Hemorrhagic stroke     | 0 - 66 grams  | 0.4  | 1.09 | Yokoyama 2000 |
| Hemorrhagic stroke     | 0 - 35 grams  | 0.23 | 1.29 | Yokoyama 2000 |
| Hemorrhagic stroke     | 0 - 92 grams  | 0.03 | 0.08 | Tong 2020  |
| Hemorrhagic stroke     | 0 - 136 grams | 0.19 | 0.09 | Tong 2020  |
| Hemorrhagic stroke     | 0 - 192 grams | 0.03 | 0.08 | Tong 2020  |
| Hemorrhagic stroke     | 0 - 286 grams | 0.15 | 0.09 | Tong 2020  |
| Hemorrhagic stroke     | 0 - 286 grams | 0.15 | 0.09 | Tong 2020  |
| Hemorrhagic stroke     | 0 - 143 grams | 0.39 | 0.21 | Yoshizaki 2020 |
| Hemorrhagic stroke     | 0 - 254 grams | 0.39 | 0.21 | Yoshizaki 2020 |
| Hemorrhagic stroke     | 0 - 169 grams | 0.58 | 0.23 | Yoshizaki 2020 |
| Hemorrhagic stroke     | 0 - 286 grams | 0.12 | 0.24 | Yoshizaki 2020 |
| Hemorrhagic stroke     | 0 - 285 grams | 0.12 | 0.24 | Yoshizaki 2020 |

This table summarizes the blood flow rates for different types of strokes, with the range, mean, standard deviation, and the year of publication for each study.
| Esophageal cancer | 0 - 125 grams | 260 - 318 grams | -0.53 | 0.3 | Steevens 2011 |
| Esophageal cancer | 0 - 125 grams | 164 - 202 grams | -0.49 | 0.28 | Steevens 2011 |
| Esophageal cancer | 0 - 125 grams | 260 - 318 grams | -0.49 | 0.39 | Steevens 2011 |
| Esophageal cancer | 0 - 125 grams | 125 - 164 grams | -0.34 | 0.27 | Steevens 2011 |
| Esophageal cancer | 0 - 125 grams | 125 - 164 grams | -0.3 | 0.34 | Steevens 2011 |
| Esophageal cancer | 0 - 125 grams | 202 - 260 grams | -0.19 | 0.26 | Steevens 2011 |
| Esophageal cancer | 0 - 125 grams | 202 - 260 grams | 0.31 | 0.3 | Steevens 2011 |
| Esophageal cancer | 0 - 139 grams | 321 - 381 grams | -0.56 | 0.37 | Freedman 2007 |
| Esophageal cancer | 0 - 139 grams | 236 - 321 grams | -0.45 | 0.33 | Freedman 2007 |
| Esophageal cancer | 0 - 139 grams | 186 - 236 grams | -0.36 | 0.3 | Freedman 2007 |
| Esophageal cancer | 0 - 139 grams | 139 - 186 grams | -0.25 | 0.27 | Freedman 2007 |
| Esophageal cancer | 0 - 139 grams | 321 - 381 grams | -0.08 | 0.25 | Freedman 2007 |
| Esophageal cancer | 0 - 139 grams | 236 - 321 grams | -0.04 | 0.22 | Freedman 2007 |
| Esophageal cancer | 0 - 139 grams | 186 - 236 grams | 0.08 | 0.21 | Freedman 2007 |
| Esophageal cancer | 0 - 139 grams | 139 - 186 grams | 0.16 | 0.2 | Freedman 2007 |
| Esophageal cancer | 0 - 126 grams | 226 - 324 grams | -0.39 | 0.25 | Yamaji 2008 |
| Esophageal cancer | 0 - 126 grams | 126 - 226 grams | -0.22 | 0.22 | Yamaji 2008 |
| Esophageal cancer | 0 - 115 grams | 115 - 154 grams | -0.07 | 0.06 | Tran 2005 |
| Esophageal cancer | 0 - 115 grams | 154 - 192 grams | 0.01 | 0.06 | Tran 2005 |
| Esophageal cancer | 0 - 115 grams | 192 - 231 grams | 0.02 | 0.08 | Tran 2005 |
| Esophageal cancer | 240 - 320 grams | 80 - 160 grams | 0.46 | 0.12 | Sheikh 2019 |
| Esophageal cancer | 240 - 320 grams | 40 - 80 grams | 0.48 | 0.23 | Sheikh 2019 |
| Esophageal cancer | 0 - 136 grams | 136 - 243 grams | -0.13 | 0.31 | González 2006 |
Section 8: Sensitivity results

Supplementary Figure 1: Vegetable consumption and ischemic stroke: Non-trimmed data.

\[ a, \text{log-relative risk function} \]
\[ b, \text{relative risk function} \]
\[ c, \text{A modified funnel plot showing the residuals (relative to 0) on the x-axis and the estimated standard deviation (SD) that includes reported SD and between-study heterogeneity on the y-axis} \]

Supplementary Figure 2: Vegetable consumption and ischemic heart disease: Non-trimmed data.

\[ a, \text{log-relative risk function} \]
\[ b, \text{relative risk function} \]
\[ c, \text{A modified funnel plot showing the residuals (relative to 0) on the x-axis and the estimated standard deviation (SD) that includes reported SD and between-study heterogeneity on the y-axis} \]
Supplementary Figure 3: Vegetable consumption and hemorrhagic stroke: Non-trimmed data.

a, log-relative risk function  
b, relative risk function  
c, A modified funnel plot showing the residuals (relative to 0) on the x-axis and the estimated standard deviation (SD) that includes reported SD and between-study heterogeneity on the y-axis

Supplementary Figure 4: Vegetable consumption and esophageal cancer: Non-trimmed data.

a, log-relative risk function  
b, relative risk function  
c, A modified funnel plot showing the residuals (relative to 0) on the x-axis and the estimated standard deviation (SD) that includes reported SD and between-study heterogeneity on the y-axis
Supplementary Figure 5: Vegetable consumption and type 2 diabetes: Non-trimmed data.

- **a**, log-relative risk function
- **b**, relative risk function
- **c**, A modified funnel plot showing the residuals (relative to 0) on the x-axis and the estimated standard deviation (SD) that includes reported SD and between-study heterogeneity on the y-axis
Supplementary Figure 6: caloric adjusted vs unadjusted

Sensitivity analysis results comparing calorie adjusted (pink) and calorie intake unadjusted (Turquoise) models for vegetables and five health outcomes (ischemic stroke, ischemic heart diseases, hemorrhagic stroke and esophageal cancer, diabetes mellitus type 2).