Stomach cancer and occupational exposure to asbestos: a meta-analysis of occupational cohort studies

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Background: A recent Monographs Working Group of the International Agency for Research on Cancer concluded that there is limited evidence for a causal association between exposure to asbestos and stomach cancer.

Methods: We performed a meta-analysis to quantitatively evaluate this association. Random effects models were used to summarise the relative risks across studies. Sources of heterogeneity were explored through subgroup analyses and meta-regression.

Results: We identified 40 mortality cohort studies from 37 separate papers, and cancer incidence data were extracted for 15 separate cohorts from 14 papers. The overall meta-SMR for stomach cancer for total cohort was 1.15 (95% confidence interval 1.03–1.27), with heterogeneous results across studies. Statistically significant excesses were observed in North America and Australia but not in Europe, and for generic asbestos workers and insulators. Meta-SMRs were larger for cohorts reporting a SMR for lung cancer above 2 and cohort sizes below 1000.

Conclusions: Our results support the conclusion by IARC that exposure to asbestos is associated with a moderate increased risk of stomach cancer.

The most recent IARC monograph on asbestos (Straif et al, 2009; IARC, 2011) concluded that all forms of asbestos (chrysotile, crocidolite, amosite, tremolite, actinolite and anthophyllite) are carcinogenic to humans (Group 1). They concluded that asbestos causes mesothelioma and cancer of the lung, larynx and ovary (Group 1), and note that positive associations have been observed between asbestos and cancer of the pharynx, stomach and colorectum (group 2A). However, no quantitative estimates of these associations were carried out, except for ovarian cancer (Camargo et al, 2011).

We conducted a meta-analysis of the results on stomach cancer of cohort studies of workers exposed to asbestos, as part of our work estimating the burden of occupational cancer in the United Kingdom (Rushton et al, 2010). The present analysis was built on the US IOM report published in 2006 (IOM, 2006); we have updated their results and extended the analyses by gender and subcategory (geography, industry and type of asbestos).

MATERIALS AND METHODS

Literature search. A search of the literature was performed to find all published reports of asbestos-exposed cohorts according to the MOOSE guideline (Stroup et al, 2000). As stomach cancer was not generally the primary disease of concern in those studies, each paper was read and those reporting mortality from or incidence of cancer of the stomach were selected. Searches of Medline and Embase were conducted for papers published worldwide in English between 1964 and 2010. Only cohorts of workers with predominant exposure to asbestos were included. For example, although...
workers in the rubber industry are exposed to asbestos, the causal role of this specific carcinogen cannot be established (IARC, 1998). When several publications relating to the same cohort were available, we used the most recent report. References of identified papers were examined for additional relevant publications, and a check was made with previous reviews to ensure all cohorts were identified.

For each study, we extracted the following data (when the information was available): observed and expected numbers of cases due to stomach cancer and/or the SMR/SIR and its associated confidence interval (CI), the total number of cases, the lung cancer SMR/SIR, the dates when the study was carried out, inclusion and exclusion criteria, the comparison population, the percentage of men, the average duration of employment, the geographical area, the industry sector, the type of asbestos. For the studies that reported results based on latency period, latency periods were defined as the time since the first exposure or employment. We extracted both sets of results with and without latency.

Methods for quantitative syntheses. Overall pooled estimates of the SMR/SIR (meta-SMR/SIR) with associated 95% CI were obtained using random- and fixed-effects methods (Sutton et al., 2000). When not provided, 95% CI of SMR/SIR were obtained via Byar’s approximation (Breslow and Day, 1987). For studies in which there were zero observed cases, 1 was added to both observed and expected cases. Sensitivity analyses to this approach were undertaken in which either studies with zero observed case were excluded from the analysis or the observed number of cases was set to equal the expected number of cases (Alder et al., 2006).

A test for heterogeneity between study results was performed as a χ²-test with degrees of freedom equal to the number of studies minus one and associated P-value was reported. As this test is susceptible to the number of studies included in the meta-analysis, Higgins and Thompson (2002) developed an alternative approach that quantifies the effect of heterogeneity, providing a measure of the degree of inconsistency in the studies’ results. This quantity I² describes the proportion of total variation in study estimates that is due to heterogeneity. Negative values of I² are put equal to zero so that I² lies between 0 and 100%. A value of 0% indicates no observed heterogeneity and larger values show increasing heterogeneity. This quantity was also reported with its associated 95% CI; a value > 50% was considered to indicate substantial heterogeneity (Higgins et al., 2003).

The influence of individual studies on the overall meta-SMR was assessed visually via radial plots, by re-estimating the overall effect omitting each study in turn. In addition, we used common influence diagnostics to highlight outlying influential studies (Viechtbauer and Cheung, 2010). Meta-regression techniques and stratified analyses were used to explore the influence of cohort and study characteristics. Publication bias was also assessed graphically with a funnel plot and by using Egger's test (Egger et al., 1997).

Analyses were performed separately for men and women, and for both genders combined. We also analysed the data according to the latency, that is, the time since the first exposure: studies were categorised as to whether they had carried out a lagged analysis or not, with the definition of a lagged category being an exposure lag of at least 10 years after the first exposure/employment. Separate subgroup analyses were carried out by geography (Europe, North America and Australia, China and Russia together) and by occupation/industry. The latter contained six categories as defined in the IOM reports (IOM, 2006): insulators, generic asbestos workers (where no occupation or industry was specified), textile asbestos workers, cement asbestos workers, miners and other occupations with substantial exposure to asbestos (such as shipyard workers). We also provided a pooled estimated by type of asbestos, sample size and publication year.

To analyse the dose–response effect of asbestos exposure, we used two different methods. The first one was based on the RR for the highest category of exposure, as the categories for the dose–response relationships were not comparable. In the second approach, studies were divided according to the magnitude of the lung cancer SMR (below or above 2), corresponding to low and high occupational exposure to asbestos. Lung cancer mortality/ incidence was used as a substitute for the exposure measurements, because of the clear relationship between asbestos exposure and lung cancer (IARC, 2011).

All the analyses described above were carried out using the Metafor package (Viechtbauer, 2010) for R software.

RESULTS

Characteristics of the studies. The literature search identified 70 references that contained potentially relevant information for the meta-analysis. Mortality was the outcome in most of the cohort studies reviewed. Data on mortality were extracted for 40 cohorts from 37 separate papers, and data on cancer incidence were extracted for 15 separate cohorts from 14 papers. Table 1 summarises the study characteristics. Unique cohorts are numbered 1–55.

Mortality cohort studies have been carried out mainly in Europe (23 studies, 58%) and North America (12 studies, 30%). Three mortality cohorts were Chinese, one was Russian and one was Australian. Study mortality cohorts ranged in size between 145 and 52 387 workers. Thirteen (33%) of the mortality cohorts included women, although in most women were a small proportion of the total. Four studies involved only women (Acheson et al., 1982; Peto et al., 1985; Germani et al., 1999), and four reported results for the total cohort (Gardner et al., 1986; Zhu and Wang, 1993; Frost et al., 2008; Harding et al., 2009). The most common occupations were insulators (20%), generic asbestos workers (20%), textile asbestos workers (15%), cement asbestos workers (13%) and miners (10%). The latency (exposure lag) ranged between 10 and 20 years. The earliest follow-up period started in 1941 and the latest ended in 2007. The average length of follow-up was 29.9 years (range = 9–49). The largest overall cohort RRs were among the earliest insulation workers (Selikoff et al., 1979) with a RR of 3.52 (Figure 1), and among two sets of workers in Chinese asbestos factories (Zhu and Wang, 1993; Pang et al., 1997): RRs were 4.4 and 2.2, respectively. Two studies carried out in Canada (Liddell et al., 1997) and the United Kingdom (Harding et al., 2009), involving 183 and 322 deaths from stomach cancer, showed consistent RR estimates with narrow 95% CI (1.24 and 1.66, respectively).

Incidence studies have been carried out in Northern Europe (11 studies, 73%), in France (2 studies), in Lithuania (1 study) and in Australia (1 study) and included fewer than 900 subjects to over 24 200. Half of the studies included women, in a small proportion of the total cohort. The largest overall cohort RR was among Danish asbestos cement workers (Raffin et al., 1989) with a RR of 1.43 (95% CI 1.03–1.93). All the other studies reported RRs close to one.

Quantitative synthesis. Table 2 summarises all the meta-SMRs and meta-SIRs obtained for men and women separately, and by consideration of an exposure lag or not. The meta-SIR for stomach cancer incidence was 1.09 (95% CI 0.94–1.26; 14 studies) and 1.10 (95% CI 0.52–2.33; 6 studies) for men and women, respectively, with homogenous results (P = 0.16 and 0.99, respectively).

The pooled analysis for stomach cancer mortality yielded a meta-SMR of 1.16 (95% CI 1.00–1.34; 30 studies) for men, with large heterogeneity of results (P < 0.001; I² = 63.5%); a meta-SMR of 0.93 (95% CI 0.67–1.30, 13 studies) was found for women, with homogeneous results across studies (P = 0.90). For the total cohort,
| ID | Reference (related papers) | O  | Year  | Country | Industry | Asbestos type | Gender | Employment | End of follow-up | No of subjects |
|----|-----------------------------|----|-------|---------|----------|---------------|--------|------------|-----------------|---------------|
| 1  | Selikoff 1979 (Selikoff et al, 1979) (Selikoff et al, 1964; Selikoff and Seidman, 1991; Selikoff et al, 1980) | M  | 1979  | USA     | Insulation workers (union) | Ch, Am | Men       | Union before 1943 | 1976          | 632           |
| 2  | Acheson 1982 I (Acheson et al, 1982) | M  | 1982  | UK     | Manufacture of gas masks | Ch     | Women    | From 1939 | 1980          | 570           |
| 3  | Acheson 1982 II (Acheson et al, 1982) | M  | 1982  | UK     | Manufacture of gas masks | Cr     | Women    | From 1939 | 1980          | 757           |
| 4  | Acheson 1984 (Acheson et al, 1984) | M  | 1984  | UK     | Manufacture of insulation board | Am     | Men      | 1947–1978 | 1980          | 5969          |
| 5  | Olhson 1984 (Olhson et al, 1984) | M  | 1984  | Sweden | Railroad shop | Mixed | Men       | 1939–1980 | 1980          | 3442          |
| 6  | Peto 1985 I (Peto et al, 1985) | M  | 1985  | UK     | Asbestos textile workers | Ch, Cr | Men      | 1916–1983 | 1983          | 145           |
| 7  | Peto 1985 II (Peto et al, 1985) | M  | 1985  | UK     | Asbestos textile workers | Ch, Cr | Women    | 1916–1983 | 1983          | 283           |
| 8  | Peto 1985 III (Peto et al, 1985) | M  | 1985  | UK     | Asbestos textile workers | Ch, Cr | Men      | 1916–1983 | 1983          | 3211          |
| 9  | Gardner 1986 (Gardner et al, 1986) | M  | 1986  | UK     | asbestos cement factory | Ch     | Men and women | 1941–1983 | 1984          | 2167          |
| 10 | Seidman 1986 (Seidman et al, 1986) | M  | 1986  | USA    | Insulation workers | Am     | Men       | 1941–1945 | 1985          | 820           |
| 11 | Amandus 1987 (Amandus and Wheeler, 1987) | M  | 1987  | USA    | Vermiculite miners and millers | Tr-Ac | Men      | Until 1970 | 1981          | 575           |
| 12 | Enterline 1987 (Enterline et al, 1987) | M  | 1987  | USA    | Asbestos products company | Ch, Cr, Am | Men      | 1941–1967 | 1980          | 1074          |
| 13 | Hughes 1987 (Hughes et al, 1987) | M  | 1987  | USA    | Asbestos cement factory | Ch, Cr, Am | Men      | Until 1970 | 1982          | 6931          |
| 14 | Sanden 1987 (Sanden and Järnholm, 1987) | I  | 1987  | Sweden | Shipyard workers | Ch     | Men      | 1977–1979 | 1983          | 3787          |
| 15 | Tola 1988 (Tola et al, 1988) | I  | 1988  | Finland | Shipyard workers | Mixed | Men      | 1945–1960 | 1981          | 7775          |
| 16 | Melkiå 1989 (Melkiå et al, 1989) | I  | 1989  | Norway | Shipyard workers | Ch     | Men      | 1946–1977 | 1986          | 4778          |
| 17 | Raffn 1989 (Raffn et al, 1989) | I  | 1989  | Denmark | Asbestos cement factory | Mixed | Men      | 1928–1984 | 1984          | 7996          |
| 18 | Neuberger 1990 (Neuberger and Kundi, 1990) | M  | 1990  | Austria | Asbestos cement factory | Ch, Cr | Men and women | 1950–1981 | 1987          | 2816          |
| 19 | Botta 1991 (Botta et al, 1991) | M  | 1991  | Italy  | Asbestos cement factory | Ch, Cr | Men and women | 1950–1980 | 1986          | 3367          |
| 20 | Selikoff 1991 (Selikoff and Seidman, 1991) (Selikoff et al, 1964; Selikoff et al, 1979; Selikoff et al, 1980) | M  | 1991  | USA/Canada | Insulation workers (union) | Ch, Am | Men      | In union 1967 | 1987          | 17800         |
| 21 | Cheng 1992 (Cheng and Kong, 1992) | M  | 1992  | China  | Chrysotile asbestos products workers | Ch     | Men and women | Present in 1972 | 1987          | 1172          |
| 22 | Sanden 1992 (Sanden et al, 1992) | M  | 1992  | Sweden | Shipyard workers | Ch     | Men      | 1977–1979 | 1987          | 3893          |
| 23 | Danielsen 1993 (Danielsen et al, 1993) | I  | 1993  | Norway | Shipyard production workers | Ch     | Men      | 1940–1979 | –            | 4571          |
| 24 | Kogan 1993 (Kogan et al, 1993) | M  | 1993  | Russia | Friction products | Ch     | Men and women | –            | 1988          | 2834          |
| 25 | Zhu 1993 (Zhu and Wang, 1993) | M  | 1993  | China  | Asbestos factory | Ch     | Men and women | –            | 1986          | 5893          |
| 26 | Meurman 1994 (Meurman et al, 1994) | I  | 1994  | Finland | Asbestos miners | An     | Men and women | 1953–1967 | 1991          | 903           |
| 27 | Lidell 1997 (Lidell et al, 1997) (McDonald et al, 1993; McDonald et al, 1980) | M  | 1997  | Canada | Miners and millers | Ch     | Men       | Until 1972 | 1994          | 530           |
| 28 | Pang 1997 (Pang et al, 1997) | M  | 1997  | China  | Asbestos factory | Ch     | Men and women | –            | 1992          | 9780          |
| ID | Reference (related papers) | Gender | Year | Country | Industry | Asbestos type | Employment | End of follow-up | No of subjects |
|----|-----------------------------|--------|------|---------|----------|---------------|------------|-----------------|---------------|
| 29 | Levin et al. (1998)         | Men    | 1998 | USA     | Manufacture of asbestos pipe insulation | Am, Cr, Asbestos | Men and women | Alive in 1994   | 1/21          |
| 30 | Battista et al. (1999)      | Men    | 1999 | Italy   | Rail carriage construction and repair | Cr, Ch, Asbestos | Men and women | Alive in 1945–1964 | 1998          |
| 31 | Germani et al. (1999)       | Men    | 1999 | Italy   | Women compensated for asbestosis | Cr, Ch, Asbestos | Men and women | Alive in 1979   | 1998          |
| 32 | Karjalainen et al. (1999)   | Men    | 1999 | Finland | Patients with asbestos-related pulmonary disease | Mixed | Men and women | 1964–1995 | 2000          |
| 33 | Karjalainen et al. (1999)   | Men    | 1999 | Finland | Patients with pleural fibrosis | Mixed | Men and women | 1964–1995 | 1999          |
| 34 | Berry et al. (2000)         | Men    | 2000 | UK      | Asbestos factory | Cr, Ch, Asbestos | Mixed | 1933–1964 | 1980          |
| 35 | Szeszenia et al. (2000)     | Men    | 2000 | Poland  | Asbestos cement factory | Mixed | Men and women | Until 1980 | 1991          |
| 36 | Puntoni et al. (2001)       | Men    | 2001 | Italy   | Shipyard workers | Mixed | Men and women | Until 1978 | 1996          |
| 37 | De La Provoste et al. (2002)| Men    | 2002 | France  | Crocidolite miners and millers | Mixed | Men and women | Until 1978 | 1997          |
| 38 | Ulvestad et al. (2002)      | Men    | 2002 | Norway  | Shipyard workers | Mixed | Men and women | 1942–1976 | 1999          |
| 39 | Smailyte et al. (2004)      | Men    | 2004 | Lithuania | Asbestos textile workers | Mixed | Men and women | 1942–1972 | 1999          |
| 40 | Finkelstein et al. (2005)   | Men    | 2005 | USA     | Shipyard production workers | Mixed | Men and women | 1942–1972 | 2000          |
| 41 | Reid et al. (2005)          | Men    | 2005 | GB      | Asbestos textile workers | Mixed | Men and women | 1942–1964 | 1999          |
| 42 | Smailyte et al. (2006)      | Men    | 2006 | Lithuania | Asbestos textile workers | Mixed | Men and women | 1942–1964 | 2000          |
| 43 | Frost et al. (2008)         | Men    | 2008 | GB      | Asbestos textile workers | Mixed | Men and women | 1942–1964 | 2000          |
| 44 | Wilczynska et al. (2008)    | Men    | 2008 | Lithuania | Asbestos textile workers | Mixed | Men and women | 1942–1964 | 2000          |
| 45 | Wilczynska et al. (2008)    | Men    | 2008 | Lithuania | Asbestos textile workers | Mixed | Men and women | 1942–1964 | 2000          |
| 46 | Wilczynska et al. (2008)    | Men    | 2008 | Lithuania | Asbestos textile workers | Mixed | Men and women | 1942–1964 | 2000          |
| 47 | Wilczynska et al. (2008)    | Men    | 2008 | Lithuania | Asbestos textile workers | Mixed | Men and women | 1942–1964 | 2000          |
| 48 | Wilczynska et al. (2008)    | Men    | 2008 | Lithuania | Asbestos textile workers | Mixed | Men and women | 1942–1964 | 2000          |
| 49 | Wilczynska et al. (2008)    | Men    | 2008 | Lithuania | Asbestos textile workers | Mixed | Men and women | 1942–1964 | 2000          |
the meta-SMR was similar to that found for men only (meta-
SMR = 1.17, 95% CI 1.03–1.33, 40 studies).

Because mortality is a relatively accurate measure of disease
incidence as stomach cancer has a low survival rate, and because
of the very limited numbers of primary studies in which incidence
data were reported, pooled analyses are also reported using
mortality and incidence combined. In this situation, the meta-
SMRs were similar to those found using only mortality data, with
a slight reduction in heterogeneity ($I^2 = 54.7\%$). Figure 1 presents
the individual study results and the overall meta-SMR for total
cohort.

As the meta-SMRs from studies reporting results with exposure
lag did not differ substantially from the overall results, the meta-
SMRs below are reported for all exposure lag group and for
mortality and incidence combined, unless specified otherwise.

**Between study heterogeneity and influence of individual
studies.** Table 2 also shows the heterogeneity ($P$-value) for each
analysis. There was no evidence of heterogeneity in women but
some in men. A few specific studies contributed to this
heterogeneity, as illustrated by outlying points in the radial plot
for stomach cancer for men (Figure 2): cohort 1 (Selikoff et al,
1979) was conducted in the earliest period, cohort 5 (Ohlson et al,
1984) was the only study to find a significant decrease in risk,
and cohort 28 (Pang et al, 1997) was carried out in China. For the
total cohort, another cohort in China, cohort 25 (Zhu and Wang, 1993)
also contributed to the heterogeneity.

The covariates listed in the Methods section were explored as
potential sources of heterogeneity using meta-regression methods.
Table 3 gives the meta-SMR by subgroup for men and women. No
significant predictor of the meta-SMR for women was found. Apart
for type of asbestos and publication year, all the variables were
a significant predictor for men, with some heterogeneity.

The meta-SMRs for men showed elevated risks in the United
States and Australia (meta-SMR = 1.30, 95% CI 1.10–1.55), and
China and Russia (meta-SMR = 1.91, 95% CI 1.03–3.56).
The pooled analysis within occupational strata demonstrated the
highest meta-SMR for stomach cancer among generic asbestos
workers (meta-SMR = 1.41, 95% CI 1.10–1.82), followed by
insulators (meta-SMR = 1.27, 95% CI 1.05–1.53). Meta-regression
also showed positive associations for stomach cancer for the cohort
sizes below 1000 compared with cohort size above 1000. Similar
results were found for the total cohort (Supplementary Table 1).

Figure 3 shows, for men, the investigation of the influence of
individual studies via systematic ‘leave one out’ exclusion.
The studies appearing to contribute to heterogeneity also influence
the meta-SMR. Using the other diagnostics, only Selikoff et al
(1979) and Ohlson et al (1984) were influential (Supplementary
Figure 1). The meta-SMR for stomach cancer excluding these 2
studies was 1.13 (95% CI 1.05–1.22), relatively similar to the one
found with all the studies for men. The exclusion of the 3
influential studies (Selikoff et al,1979; Ohlson et al, 1984;
Pang et al, 1997) led to a meta-SMR of 1.12 (95% CI 1.04–1.20)
and eliminated completely the heterogeneity ($P = 0.59$, $I^2 = 7.3\%$)
as well as the residual heterogeneity in the meta-regressions
($P > 0.44$). The associations were generally attenuated
(Supplementary Table 2), except for the miners (meta-SMR = 1.21,
95% CI 1.07–1.36) compared with the other occupations.

**Dose–response associations.** Estimates of cumulative or duration
of exposure among asbestos-exposed workers were reported for
only 11 studies (Supplementary Table 3). The pooled SMR estimate
of stomach cancer for men was 1.40 (95% CI 0.81–2.40), with
a large degree of heterogeneity ($I^2 = 67.7\%$). Using a low/high
exposure categorisation based on the lung cancer SMR, cohorts that reported a lung cancer SMR above 2.0
had higher meta-SMRs (SMR = 1.46; 95% CI 1.22–1.77) compared
with other cohorts (SMR = 1.02; 95% CI 0.91–1.15).
The association between asbestos and stomach cancer has been estimated in a meta-analysis of studies of workers in which a major portion of the cohort is presumed to have been exposed to asbestos. Our results demonstrated an increase in the pooled estimate in men (meta-SMR = 1.13, 95% CI 1.02–1.26) for stomach cancer in relation to exposure to asbestos. Our meta-analysis provided an update of studies, compared with previous reviews and quantitative estimates and also thoroughly explored heterogeneity and publication bias.

The magnitude of the association in our meta-analysis was similar to that reported in the IOM report that included 42 cohorts (meta-SMR = 1.17, 95% CI 1.07–1.28). More recently, Gamble (2008) reported that point estimates for cancer of the stomach mortality trended towards 1, with an overall RR estimate of 1.01 (95% CI 0.94–1.08), results more similar to those obtained by Goodman et al (1999).

Our analysis addressed heterogeneity and was based on studies included in the published meta-analyses and more recent publications. The observed overall heterogeneity among studies seemed to be explained by four cohorts. The cohort by Selikoff et al (1979) considered an early exposure period (up to 1962). Ohlson et al (1984) were the only ones to find a significant decrease in risk (SMR = 0.57, 95% CI 0.42–0.79). Two studies (Zhu and Wang, 1993; Pang et al, 1997) were conducted in China, where asbestos production and exposure can be very high (LaDou, 2004).

We carried out meta-regression to investigate the influence of several variables. Positive and statistically significant associations were observed for non-European cohorts, generic asbestos workers, cohorts reporting a SMR for lung cancer above 2, and cohort size below 1000.

**Assessment of publication bias.** For men and women, there was no evidence of publication bias from plots and statistical tests. However, for the total cohort, there is an evidence of publication bias (funnel plot in Supplementary Figure 2), with a suggestive lack of studies in the top right-hand corner of the plot, that is, large cohorts with large associations.

**Zero cases.** Four studies reported no deaths from stomach cancer for women; (Cheng and Kong, 1992; Pang et al, 1997; Hein et al, 2007; Krstev et al, 2017) only one study with men was concerned with this issue (Levin et al, 1998) Therefore, the investigation of the influence of approaches to handling zero cases was carried out only for women. Both excluding studies for which observed cases are zero and setting observed equal to expected values resulted in an increase in meta-SMRs and a slight widening of the confidence intervals compared with the default method of adding 1 to both observed and expected values. Whatever the latency, the meta-SMRs were 1.00 (95% CI 0.73–1.36) and 1.03 (95% CI 0.77–1.39) with the exclusion approach and imputation method, respectively, compared with a meta-SMR of 0.96 (95% CI 0.71–1.30) with the default method.
Our meta-analysis mainly represented studies conducted in developed geographical areas, particularly among European populations. It is possible that studies conducted in other geographic regions (e.g., developing countries) may be available through other biomedical literature databases. The meta-analysis (da Sun et al, 2008) published in Chinese with an abstract in English, which searched Chinese literature as well, found a meta-SMR of 1.20 ($P<0.01$) among workers exposed to chrysotile alone or mixed asbestos. The stomach cancer SMR was significantly increased in the asbestos cement workers, the former Soviet Union where asbestos use is increasing and the former Soviet Union and several asbestos exposure variables, adjusted for age and family history of gastric cancer, although, with the exception of long duration at high exposure, these associations tended to disappear after adjusting for smoking (Offermans et al, 2014).

Increases in stomach cancer have also been associated with work in a variety of dusty industries and from exposure to fumes and metal particles, for example, in foundry, steel and mining work (Cocco et al, 1996; JI and Hemminki, 2006). A study in Swedish construction workers found exposure to silica exposure, but not asbestos, was significantly related to stomach cancer (Sjoedhal et al, 2007). However, in our meta-analysis we restricted our studies to only those where the dominant exposure was asbestos.

We found a suggestive but nonsignificant association between asbestos type and the stomach cancer meta-SMR. Cohorts exposed to mixed asbestos showed larger SMRs than those exposed only to chrysotile asbestos. A meta-analysis by Li et al (2004) of 15 studies published before 2003 of workers exposed only to chrysotile found also a nonsignificant association (meta-SMR = 1.24; 95% CI 0.95–1.62). Our risk estimate was slightly smaller as we did not include four cohorts, as they were published in Chinese. There has been a considerable controversy over the potency of asbestos fibre types with the risks of lung cancer and mesothelioma. As discussed in the review by Hodgson and Darnton (2000) some studies showed no difference in risk between these cancers and asbestos fibre types, while others have claimed a reduced potency for chrysotile, leading to a substantial heterogeneity in the findings. Our results tend to support a reduced risk for chrysotile and stomach cancer compared with the risk associated with other asbestos types.

In summary our results support the conclusion by IARC that exposure to asbestos is associated with a moderate increased risk of stomach cancer. Given the large number of workers exposed to asbestos worldwide, this may contribute to a substantial burden of mortality and morbidity.
Figure 2. Radial plot for SMRs in a meta-analysis of stomach cancer mortality and incidence for total cohort, all exposure lags.

Table 3. Stratification of cohort studies by subgroups, for men and women, mortality and incidence combined, all exposure lags (random effects model)

| Geography          | Men | Women |
|--------------------|-----|-------|
|                    | n a | SMR   | 95% CI     | \(t^2\) b | \(P_{QE}\) c | \(P_{QM}\) d | n a | SMR   | 95% CI     | \(t^2\) b | \(P_{QE}\) c | \(P_{QM}\) d |
| Europe             | 28  | 1.03  | (0.91–1.16)| 0.042     | <0.001       | <0.001       | 14  | 1.1   | (0.77–1.57) | 0.046     | <0.001       | <0.001       |
| North America + A  | 13  | 1.3   | (1.10–1.55)| 0.028     | <0.001       | <0.001       | 7   | 0.37  | (0.04–3.13) | 0.56      | <0.001       | <0.001       |
| China + Russia     | 3   | 1.91  | (1.03–3.56)|           |              |              | 3   | 0.69  | (0.38–1.28) |           |              |              |
|                    |     |       |           |           |              |              |     |       |           |           |              |              |
| Occupation         |     |       |           |           |              |              |     |       |           |           |              |              |
| Cement asbestos workers | 6  | 1.12  | (0.88–1.42)|           |              |              | 2   | 1.27  | (0.59–2.72) |           |              |              |
| Generic asbestos workers | 7  | 1.41  | (1.10–1.82)|           |              |              | 5   | 0.87  | (0.44–1.73) |           |              |              |
| Insulators         | 10  | 1.27  | (1.05–1.53)|           |              |              | 1   | 0.63  | (0.03–12.89)|           |              |              |
| Miners             | 6   | 1.18  | (0.95–1.47)|           |              |              | 1   | 0.67  | (0.05–9.13) |           |              |              |
| Textile asbestos workers | 4  | 1.15  | (0.83–1.61)|           |              |              | 3   | 1.22  | (0.53–2.79) |           |              |              |
| Other occupation   | 11  | 0.87  | (0.73–1.04)|           |              |              | 7   | 0.87  | (0.56–1.34) |           |              |              |
|                    |     |       |           |           |              |              |     |       |           |           |              |              |
| SMR for lung cancer|     |       |           |           |              |              |     |       |           |           |              |              |
| \(\leq 2\)         | 25  | 1.02  | (0.91–1.15)| 0.039     | <0.001       | <0.001       | 5   | 0.88  | (0.54–1.42) | 0.039     | <0.001       | <0.001       |
| \(> 2\)            | 17  | 1.46  | (1.22–1.77)|           |              |              | 13  | 1.02  | (0.69–1.64) | 0.039     | <0.001       | <0.001       |
|                    |     |       |           |           |              |              |     |       |           |           |              |              |
| Type of asbestos   |     |       |           |           |              |              |     |       |           |           |              |              |
| Asbestosite        | 3   | 1.25  | (0.64–2.44)| 0.058     | <0.001       | 0.32         | –   | –     | –          | 0.058     | <0.001       | 0.32         |
| Chrysotile         | 11  | 1.09  | (0.87–1.37)|           |              |              | 1   | 1.14  | (0.42–3.06) |           |              |              |
| Crocidolite        | 2   | 1.14  | (0.75–1.74)|           |              |              | 11  | 1.05  | (0.68–1.64) |           |              |              |
| Mixed              | 27  | 1.13  | (0.99–1.29)|           |              |              |     |       |           |           |              |              |
|                    |     |       |           |           |              |              |     |       |           |           |              |              |
| Sample size        |     |       |           |           |              |              |     |       |           |           |              |              |
| \(< 1000\)         | 12  | 1.68  | (1.32–2.15)| 0.034     | <0.001       | <0.001       | 15  | 1.15  | (0.77–1.71) | 0.034     | <0.001       | <0.001       |
| 1000–1500          | 6   | 1.19  | (0.88–1.61)| 0.001     | <0.001       | <0.001       | 3   | 0.79  | (0.38–1.62) | 0.001     | <0.001       | <0.001       |
| \(> 1500\)         | 26  | 1.04  | (0.93–1.16)|           |              |              | 1   | 0.7   | (0.37–1.33) |           |              |              |
|                    |     |       |           |           |              |              |     |       |           |           |              |              |
| Publication year   |     |       |           |           |              |              |     |       |           |           |              |              |
| Before 1999        | 26  | 1.16  | (1.00–1.34)| 0.057     | <0.001       | 0.07        | 11  | 0.94  | (0.63–1.40) | 0.057     | <0.001       | 0.07        |
| After 1999         | 18  | 1.1   | (0.94–1.29)|           |              |              | 8   | 0.99  | (0.62–1.59) |           |              |              |

Abbreviations: – = not applicable; CI = confidence interval.  

* Number of cohorts included.  

b Residual variance (residual amount of heterogeneity).  

c-P-value for the residual heterogeneity test.  

d-P-value for the test of moderators (if the SMRs are different or not within the subgroup).
This work was supported by the UK Health and Safety Executive (Grant JN3117). We thank Sally Hutchings for her valuable comments.

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

This work was supported by the UK Health and Safety Executive (Grant JN3117). We thank Sally Hutchings for her valuable comments.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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