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Mesothelioma and Lung Cancer Among Motor Vehicle Mechanics: a Meta-analysis

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We conducted a systematic review and analysis of the epidemiological literature that examines the risk of lung cancer and mesothelioma among motor vehicle mechanics who may have been engaged in brake repair and, thus, were potentially exposed to asbestos. All relevant studies were classified into three tiers according to their quality. Tier III (lowest quality) studies were cited for completeness, but were not included in the meta-analysis. Meta relative risks (meta-RRs) were calculated for mesothelioma and lung cancer using both fixed and random effects models for Tiers I and II, separately, followed by stratified analyses based on study design or exposure characterization (garage workers versus brake workers) and, for lung cancer studies, based on adequate adjustment for smoking. The meta-analysis for Tier I (higher quality) and Tier II (lower quality) studies of mesothelioma yielded RR estimates of 0.92 (95% CI 0.55–1.56) and 0.81 (95% CI 0.52–1.28), respectively. Further stratification according to exposure characterization did not affect the results. The meta-analysis for lung cancer produced RR estimates of 1.07 (95% CI 0.88–1.31) for Tier I and 1.17 (95% CI 1.01–1.36) for Tier II. When the lung cancer analysis was limited to studies that used adequate control for smoking, the resulting RR estimate was 1.09 (95% CI 0.92–1.28). Based on these findings, we conclude that employment as a motor vehicle mechanic does not increase the risk of developing mesothelioma. Although some studies showed a small increase in risk of lung cancer among motor vehicle mechanics, the data on balance do not support a conclusion that lung cancer risk in this occupational group is related to asbestos exposure.

Keywords: asbestos; brakes; epidemiology; lung cancer; mesothelioma; meta-analysis; motor vehicle mechanics

INTRODUCTION

The causal association between inhaled asbestos fibers and the development of lung cancer is well established. While the causal role of amphibole asbestos in the development of mesothelioma is also clear, there is still disagreement regarding the dose–response relationship between chrysotile asbestos and mesothelioma and the role of amphibole contaminants in that relationship (Hodgson and Darnton, 2000). Excess risk of these two cancers has not been found in all settings where there is potential exposure to asbestos. Recent attention has shifted from highly exposed occupational groups such as insulators and shipyard workers to those with asbestos exposures that could be both qualitatively and quantitatively different. One such occupation is motor vehicle repair, where exposure to short chrysotile fibers can occur during installation and repair of asbestos-containing brakes. (In North America, automobile

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brakes typically contained chrysotile asbestos embedded in a solid binder.) The process of brake replacement involves two potential opportunities for release of asbestos fibers: (i) small amounts of chrysotile asbestos (usually less than 1%) that may be present in the brake wear debris and (ii) asbestos that can be released during grinding and beveling of new asbestos brake linings or pads.

Some authors (Lorimer *et al.*, 1976), regulatory agencies (EPA, 1986c) and trade organizations (World Trade Organization, 2000) have opined in the past that motor vehicle mechanics are likely to be at increased risk of developing asbestos-related disease, most notably mesothelioma. These opinions have been based primarily on the fact that asbestos exposures can occur during brake work and cases of mesothelioma have been reported among workers who had done brake repair (EPA, 1986a,b,c).

When the EPA conducted its evaluation (EPA, 1986b,c) the epidemiological information on mesothelioma among vehicle mechanics was limited to only three studies (McDonald and McDonald, 1980; Teta *et al.*, 1983; Spirtas *et al.*, 1985). However, in more recent years a number of additional epidemiological studies have examined the risk of mesothelioma and/or lung cancer among motor vehicle mechanics or specifically among brake workers. These studies are preferable to case reports and case series in assessing associations between exposure and disease.

We conducted a systematic review of the epidemiological literature examining the relative risks of mesothelioma and lung cancer among workers engaged in motor vehicle repair and, when possible, among workers occupationally exposed to brake dust. A previous review of the literature examined six case–control studies of mesothelioma among garage mechanics (Wong, 2001). However, we felt that these analyses could be enhanced by including additional published and unpublished studies and by including a re-analysis of one of the original data sets. In addition, we expanded the scope of our review beyond mesothelioma to include studies of lung cancer.

This issue is of growing scientific, public health and societal importance (Schneider and Smith, 2000; Truby, 2002). Large numbers of people have been exposed to brake dust over the last several decades (Lorimer *et al.*, 1976; Nicholson *et al.*, 1984; Huncharek, 1990) and an increased risk of asbestos-related cancers among these workers could translate into a substantial burden of disease.

METHODS

Study selection

A number of electronic literature databases were searched using a variety of search strategies and multiple combinations of keywords such as 'asbestos', 'brakes', 'mesothelioma', 'lung cancer', 'cancer', 'garage mechanics', 'automobile mechanics', 'motor mechanics', 'mechanics', etc. Copies of the articles were obtained, including those from foreign language journals, which were translated into English. Reference lists of identified articles were examined to locate additional studies.

Internet and literature searches were also conducted to identify relevant studies that were not published in the peer-reviewed literature. Of particular interest were government documents and book chapters. When information was missing from published reports, attempts were made to contact the authors to obtain the missing information.

In order to be included in the review, studies were required to meet all of the following criteria:

- outcomes of interest included mesothelioma and/or lung cancer;
- relative risk estimates and associated variance measures were either reported by the authors or could be calculated based on the data obtained from the authors or reported in the papers;
- the exposed population was involved in motor vehicle repair, excluding general mechanics.

After this initial study selection, the meta-analysis included two steps: (i) a review and quality scoring of each study and (ii) a quantitative analysis of the pooled measures of association from studies that met the inclusion criteria.

Review of the literature

All potentially relevant studies underwent a formal evaluation and were assigned a quality score according to their methodological strengths and weaknesses. The general approach involved awarding each study a point (+1) for each methodological strength and penalizing with a negative score (–1) for each evident shortcoming. The quality scoring was conducted according to the following criteria.

- Overall study design: proportionate mortality/incidence ratio (PMR/PIR) studies or death certificate-based standardized mortality odds ratio (SMOR) studies = –1; else (cohort or case–control studies) = 0.
- Asbestos exposure: non-specific = 0 (e.g. 'car mechanic'); specific = 1 [e.g. 'brake repairmen' or industrial hygiene (IH) based].
- Age adjustment: no = –1; yes = 0.
- Confounding by other occupational exposure: likely = –1 (e.g. studies where motor vehicle mechanics with other multiple occupations were compared with persons with no history of any at-risk occupations); possible but not clearly evident = 0; unlikely/addressed = 1 (e.g. studies that

accounted for other known at-risk occupations in the analysis).
- Exposure–response analysis: no = 0; yes = 1.
- Analysis by latency: no = 0; yes = 1.
- For case–control studies: response rate <80% or not reported = –1; >90% = 1; else = 0.
- For cohort studies: follow-up: <10 years = –1; >20 years = 1; else = 0.
- Reporting bias: likely = –1 (e.g. interview-based case–control studies with clear differences in terms of sources of information between cases and controls); possible but not clearly evident = 0; unlikely/addressed = 1 (e.g. in case–control studies using recorded occupational histories).
- Selection bias: likely = –1 (e.g. due to reliance on referral of cases to a clinic or using inappropriate controls); possible but not clearly evident = 0 (e.g. in hospital-based case–control studies); unlikely/addressed = 1 (e.g. in cohort studies or population-based case–control studies).

In addition to the above criteria, mesothelioma studies were evaluated based on whether or not the diagnoses were confirmed by a pathology review (i.e. +1 if yes, 0 if no). Lung cancer studies were also evaluated based on their ability to adjust results for smoking habit. Studies that did not control for smoking received a negative score (–1), studies that adequately controlled for both smoking status (current, former or never) and intensity (duration and/or number of cigarettes per day) received a positive score (+1) and studies that had only partial control for smoking (e.g. using only ever–never categories, only pack-years or using blue collar/internal reference groups) were neither penalized nor rewarded.

The scoring was used as a formal approach to classify all studies into three tiers. Tier III included studies that had an overall negative score (i.e. less than 0) and were considered unreliable. These studies were only mentioned for completeness and were not included in the meta-analysis. Those studies that had scores of zero or above were divided into two approximately equal groups. Studies with the higher (above median) total score were included in Tier I and considered most informative. Tier II included the remaining studies that received a total score of ≥0 but were considered less useful due to methodological shortcomings.

Statistical analysis

We calculated a meta relative risk (meta-RR) for Tiers I and II separately, followed by stratified analyses of both tiers combined, based on study design or exposure characterization and, for lung cancer studies, based on adequate adjustment for smoking. The necessary input from each study included (i) an RR estimate and (ii) the associated measure of variance, which usually can be derived from the 95% confidence interval (95% CI).

When case–control studies did not report the results in terms of RRs but did provide information necessary to reconstruct the two-by-two tables, the odds ratios (ORs) and 95% CIs were calculated using Epi Info software (CDC, 2001). Some cohort studies did not report 95% CIs, but did provide information on the numbers of observed and expected cases. In those instances, 95% CIs were calculated based on the Poisson distribution, as recommended by Breslow and Day (1987).

In one study (Morabia *et al.*, 1992), the information needed to calculate 95% CIs was not provided. However, we were able to calculate the standard deviation based on the information that there were 39 exposed controls (1.2% of all controls) and the statistical power to detect an OR of 1.5 was 0.41, as reported by the authors.

There are two general approaches for combining the data in a meta-analysis: a fixed effects model or a random effects model. The fixed effects method assumes no heterogeneity among studies and attributes all observed variations among results to sampling error alone (Sutton *et al.*, 1998). The random effects model assumes that the study-specific effect sizes arise from a random distribution of effect sizes with a certain mean and variance.

All analyses involved a test for heterogeneity. However, the interpretation of the test for heterogeneity is problematic because of the wide variation in study designs, study populations and reference groups. Therefore, we used both the fixed and random effects models for each analysis. Where the variability among studies was negligible (high level of homogeneity), the random effects model reduced to a fixed effects model (Sutton *et al.*, 1998). The details of calculations for both models are provided in the Appendix.

RESULTS

Mesothelioma

Overview of the literature. Relative risk estimates could not be calculated for three cohort studies of motor vehicle mechanics (two from Sweden and one from Denmark) that provided information on mesothelioma (Jarvholm and Brisman, 1988; Hansen, 1989; Gustavsson *et al.*, 1990). For this reason, these studies could not be included in the meta-analysis. These three cohort studies combined reported three observed cases of mesothelioma and one case of ‘pleural cancer’. All three mesothelioma cases had other potential occupational asbestos exposures. For the remaining case of pleural cancer, information regarding other exposures was not provided.

There were 11 studies that reported (or permitted calculations of) the relative risk estimates for mesothelioma. These studies underwent formal evaluation and scoring. The results of scoring for each study are presented in Table 1. Four studies were included in Tier III (Coggon *et al.*, 1995; Hodgson *et al.*, 1997; Milham and Ossiander, 2001; NIOSH, personal communication, 2002). Of the seven remaining studies, four studies with scores between 3 and 5 were included in Tier I (Table 2A) and three studies with scores between 0 and 2 were included in Tier II (Table 2B). All relevant studies were published in English. Two studies were conducted exclusively in the USA, one study was conducted in Canada, one combined US and Canadian data and three took place in Europe (one in Germany, one in Denmark and one in Spain). The years of publication ranged from 1980 to 2004. A more detailed discussion of each Tier I and Tier II study follows.

Tier I. McDonald and McDonald (1980). The study here compared histologically confirmed mesothelioma cases to matched controls who had pulmonary metastases from non-pulmonary malignancies. Occupational histories obtained through interviews with relatives were ranked according to their potential for asbestos exposure. Of the 156 cases and 156 controls without a recognized increase in mesothelioma risk, the occupation 'garage' was reported for 11 cases and 12 controls, from which we calculated an OR of 0.91 (95% CI 0.35–2.34).

This study had a large sample size, a high response rate and used pathologists to establish the diagnosis of mesothelioma. The use of non-pulmonary cancers as controls has both advantages and disadvantages. Hospital-based cancer cases may not be representative of the general population (i.e. possible selection bias). However, the choice of controls with other cancers may have reduced recall bias. The use of the highest asbestos exposure to characterize each participant's occupational history helped decrease potential confounding by other asbestos exposures. However, the occupational category defined as 'garage' is insufficiently specific.

Teta *et al.* (1983). After a pathology review, cases from the Connecticut Tumor Registry and from a large Veterans Administration hospital were compared with controls selected from the death certificate files of the Connecticut State Department of Health Services. Occupational histories for cases and controls were obtained from death certificates and from city directories. The OR for subjects employed in 'automobile repair and related service' was 0.65 (95% CI 0.08–5.53).

Unlike other case–control studies, Teta *et al.* (1983) relied on objective historical employment information rather than subjective reports from interviews. The choice of population controls, the high response rate and the histological confirmation of the mesothelioma diagnoses have to be considered as methodological strengths. The main shortcomings are non-specific exposure characterization and the inability to eliminate other exposures due to its small size.

Table 1. Quality scores of studies evaluating the association between mesothelioma risk and employment as a motor vehicle mechanic

Quality criteria	Study										
	1	2	3	4	5	6	7	8	9	10	11
Overall study design: PMR/PIR/SMOR = –1; else = 0	0	0	0	0	0	0	0	–1	–1	–1	–1
Asbestos exposure: non-specific (e.g. 'car mechanic') = 0; specific (e.g. brake repairman, or IH-based) = 1	0	1	1	0	0	0	1	0	0	0	0
Age adjustment: no = –1; yes = 0	0	0	0	–1	0	0	–1	0	0	0	0
Confounding by other occupational exposure: likely = –1; possible = 0; unlikely/addressed = 1	1	1	1	0	0	0	0	0	0	0	0
Exposure-response analysis: no = 0; yes = 1	0	1	0	0	0	0	0	0	0	0	0
Analysis by latency: no = 0; yes = 1	0	0	1	0	0	0	0	0	0	0	0
For case–control studies: response rate: <80% or not reported = –1; >90% = 1; else = 0	1	–1	0	1	1	1	1	0	0	0	0
For cohort studies: follow-up <10 yr = –1; >20 yr = 1; else = 0	0	0	0	0	0	0	0	0	0	0	0
Reporting bias: likely = –1; possible = 0; unlikely/addressed = 1	0	0	1	–1	1	0	0	0	0	0	0
Selection bias: likely = –1; possible = 0; unlikely/addressed = 1	0	1	0	1	1	0	0	0	0	0	0
Diagnosis of mesothelioma by pathology review: no = 0; yes = 1	1	1	1	1	1	0	1	0	0	0	0
Total score	3	4	5	1	4	1	2	–1	–1	–1	–1

1, McDonald and McDonald (1980); 2, Hessel *et al.* (2004); 3, Teschke *et al.* (1997); 4, Agudo *et al.* (2000); 5, Teta *et al.* (1983); 6, Hansen (personal comunication, 2003); 7, Woitowirz and Rödelsperger (1994); 8, Coggon *et al.* (1995); 9, Hodgson *et al.* (1997); 10, Milham and Ossiander (2001); 11, NIOSH (personal comunication, 2002).

Table 2. Summary of mesothelioma studies and corresponding RR estimates included in the meta-analysis

First author	Year	Design	Exposure definition	Source of cases	Comparison group	RR estimate (95% CI)
(A) Tier I studies						
McDonald	1980	Case–control	Garage workers	Hospital records	Non-pulmonary cancers	0.91 (0.35–2.34)
Teta	1983	Case–control	Automobile repair and related services	CT Tumor Registry	Connecticut decedents	0.65 (0.08–5.53)
Hessel	2004	Case–control	Brake lining installation or repair	NY Cancer Registry, LA County Cancer Surveillance Program, VA Hospitals	Deaths from causes other than cancer, respiratory disease, suicide or violence	1.04 (0.46–2.22)
			Other asbestos exposures controlled			0.82 (0.36–1.80)
Teschke	1997	Case–control	Vehicle mechanics	British Columbia's Cancer Registry	Randomly selected from voters lists	0.8 (0.2–2.3)
			Brake lining installation or repair			0.3 (0.0–1.4)
			Vehicle mechanics (ever employed in at risk occupations excluded)			0.4 (0.0–3.2)
(B) Tier II studies						
Hansen	2003	Case–control	Repair of motor vehicles and motorcycles	Danish Cancer Registry	All other occupations combined	0.8 (0.4–1.5)
Woitowitz	1994	Case–control	Motor vehicle repair workers	Not specified	Lung resection patients and population controls	0.87 (0.43–1.70)
			Definitely engaged in brake service			0.89 (0.31–2.47)
Agudo	2000	Case–control	Mechanics, motor vehicles	Hospital records	Patients with non-asbestos-related conditions	0.62 (0.11–2.36)

CI, confidence interval; CT, Connecticut; LA, Los Angeles; NIOSH, National Institute for Occupational Safety and Health; NY, New York; RR, estimate of relative risk; VA, Veterans Administration.

Table 3. Summary of mesothelioma studies and corresponding RR estimates not included in the meta-analysis

First author	Year	Design	RR estimate	95% CI	Reason for eclusion
Malker[a]	1985	Cohort	2.4 ($P < 0.01$)	NA	Exposure defined as 'mechanics'
Jarvholm	1988	Cohort	NA (1 case)	NA	Unable to calculate relative risk
Schiffman	1988	Case–control	0 (no cases, 2 controls)	NA	Exposure defined as 'mechanics'
Hansen	1989	Cohort	NA (1 case)	NA	Unable to calculate relative risk
Gustavsson	1990	Cohort	NA (2 cases)	NA	Unable to calculate relative risk
Coggon	1995	Proportionate mortality	0.46	NA	Total score <0; data overlapping with Hodgson *et al.* (1997)
Hodgson	1997	Proportionate mortality	0.4 approximated from figure	0.3–0.7 approximated from figure	PMR design; total score <0
Milham	2001	Proportionate mortality	0.75	0.30–1.55	PMR design; total score <0
NIOSH	2002	Proportionate mortality	0.81	0.45–1.34	PMR design; total score <0

CI, confidence interval; NIOSH, National Institute for Occupational Safety and Health; NA, not available; PMR, proportionate mortality ratio; RR, estimate of relative risk.
[a]Of the 16 mechanics with mesothelioma in this study, only one was likely to be an auto mechanic (Blot, personal communication, 2003).

National Cancer Institute study (Spirtas *et al.*, 1994, 1985; Hessel *et al.*, 2004, in press). The 1994 report of a case–control study by the National Cancer Institute (NCI) identified mesothelioma cases in the Los Angeles County Cancer Surveillance Program, the New York State Cancer Registry (excluding New York City) and 39 Veterans Administration hospitals. A pathology review was conducted in most cases. Controls included patients who died of causes other than cancer, respiratory disease, suicide or violence. The authors did not calculate ORs by occupational category because of multiple confounding exposures, preferring to discuss attributable risk of asbestos exposure in general. Among subjects engaged in ‘brake lining installation or repair’, 33% also had shipbuilding or shipyard work and 55% had performed insulation work.

In an earlier analysis of the same data, but with cases and controls matched for age, the authors did calculate the ORs for different occupational groups (Spirtas *et al.*, 1985). Brake lining installation or repair had an OR of 1.0 (95% CI 0.6–1.6).

A re-analysis of these data (Hessel *et al.*, 2004, in press) for the occupational category ‘brake installation or repair’ yielded an OR of 1.04 (95% CI 0.46–2.22). After adjusting for any of eight occupations with potential asbestos exposure, the OR was 0.82 (95% CI 0.36–1.80). When cases and controls with a history of employment in any of the eight occupations were removed from the analysis, the OR for occupational brake installation and repair was 0.62 (95% CI 0.01–4.71). These NCI data have several important features: (i) exposure was defined as brake installation and repair, (ii) confounding by other occupational exposures could be addressed, (iii) information on duration of employment allowed an exposure–response analysis and (iv) and the majority of the mesotheliomas underwent pathology review. A limitation of this data set is the relatively low (<80%) response rate.

Teschke *et al.* (1997). Teschke and colleagues compared pathology-confirmed mesothelioma cases from the British Columbia Cancer Agency data to matched controls selected among provincial voters. Occupational and exposure histories were obtained, whenever possible, directly from cases and controls. The OR for ‘vehicle mechanics’ considered as an *a priori* suspect occupational group was 0.8 (95% CI 0.2–2.3). The OR for the category ‘brake lining installation or repair’ was 0.3 (95% CI 0.0–1.4). After removing cases and controls with at-risk occupational asbestos exposures, the OR for ‘vehicle mechanics’ was 0.4 (95% CI 0.0–3.2). The results did not change after 20 years of latency. The authors also reported that, after removal of at-risk exposures, ‘brake installation and repair did not appear to be associated with mesothelioma’.

Although fairly small in size, this study is strong methodologically because it considered other asbestos exposures, specified exposure as ‘brake lining installation or repair’, relied on histologically confirmed diagnoses of mesothelioma and frequency matched next-of-kin interviews among cases and controls. Unlike other studies, the analyses in Teschke *et al.* (1997) considered latency.

Tier II studies. Olsen and Jensen (1987) and Hansen (personal communication, 2003). In 1987, Olsen and Jensen published a proportionate incidence ratio (PIR) surveillance study that linked cases from the Danish Cancer Registry with occupational histories (Olsen and Jensen, 1987). There were no cases of mesothelioma (pleural or peritoneal) for the occupational category ‘repair of motor vehicles and motorcycles’ and for the industry category ‘garage’.

We contacted the authors of this study and learned that the data had been updated in a case–control study (Hansen, personal communication, 2003). For the category ‘repair of motor vehicles and motorcycles’ the OR was 0.8 (95% CI 0.4–1.5), based on 10 cases. The weaknesses of this study are lack of histological confirmation of mesothelioma diagnosis and inability to obtain a complete work history. Its strengths include analysis by latency and a relatively large sample size.

Woitowitz and Rödelsperger (1994). This German case–control study compared occupational histories of 324 pathology confirmed mesothelioma with two groups of controls: 315 hospital controls selected among patients who underwent lung resection and 182 population controls. Sixteen cases, 16 hospital controls and 12 population controls were listed as ‘motor vehicle repair workers’. Calculations based on these data produced an OR of 0.97 (95% CI 0.45–2.12) using hospital controls and 0.74 (95% CI 0.32–1.75) using population controls. For people definitely engaged in brake service, the OR was 0.75 (95% CI 0.25–2.23) using hospital controls and 1.32 (95% CI 0.30–6.51) using population controls. When the two types of controls were combined, the OR was 0.87 (95% CI 0.43–1.70) for motor vehicle mechanics and 0.89 (95% CI 0.31–2.47) for persons definitely engaged in brake servicing. (These calculations use updated numbers provided by the authors, Prof. H.-J. Woitowitz and Dr K. Rödelsperger, of Justus-Liebig University, Germany.)

The strengths of this study are its ability to examine the association with brake repair, its high response rate and the pathology review of cases. The most important shortcomings include the lack of adjustment for age and an inadequate description of subject selection.

Agudo *et al.* (2000). This hospital-based case–control study compared pathology-confirmed cases of mesothelioma to population/hospital controls selected using a two-step procedure (Agudo and Gonzalez, 1999). The authors reported that there were three cases and 14 controls in the category 'mechanics, motor vehicle'. The non-exposed category included 51 cases and 148 controls that had never worked in any of the at-risk occupations. Based on this information, the crude OR for 'mechanics, motor vehicle' was 0.62 (95% CI 0.11–2.36). The comparison of motor vehicle mechanics who may have had other potential asbestos exposure to persons without any exposure is problematical. However, the result indicates that substantial confounding by other exposures in this study population is unlikely. Because 44% of cases and less than 1% of controls had next of kin interviews, information bias needs to be considered. The study's high response rate, novel methods of control selection and confirmation of diagnosis by pathology review are among its strengths.

Meta-analysis. The results of the meta-analysis for mesothelioma are presented in Table 4. All tests for heterogeneity produced non-significant results regardless of stratification and in all analyses the random effects model reduced to a fixed effects model. The meta-RR estimates for Tier I and Tier II studies were 0.92 (95% CI 0.55–1.56) and 0.81 (95% CI 0.52–1.28), respectively.

Analysis limited to studies evaluating the association between mesothelioma and brake repair, as opposed to motor vehicle repair, resulted in a meta-RR of 0.86 (95% CI 0.48–1.56). Inclusion of only those studies that considered other asbestos exposures resulted in a meta-RR of 0.80 (95% CI 0.46–1.40).

Lung cancer

Overview of the literature. Twenty-nine studies were identified initially. Of these, seven were eliminated because they did not meet the three initial inclusion criteria or they presented data that overlapped with other studies. The remaining 22 studies were evaluated and scored (Table 5). Thirteen studies were further excluded from the meta-analysis because they had an overall negative score. Nine studies remained, of which four (scores of 3 or 4) were included in Tier I (Table 6A) and five (scores 0–2) were included in Tier II (Table 6B). Tier I included two cohort studies (Gustavsson *et al.*, 1990; Hrubec *et al.*, 1992) and two case–control studies (Lerchen *et al.*, 1987; Benhamou *et al.*, 1988). Tier II included two cohort studies (Jarvholm and Brisman, 1988; Hansen, 1989) and three case–control studies (Williams *et al.*, 1977; Vineis *et al.*, 1988; Morabia *et al.*, 1992). Only six studies adequately controlled for smoking; of these, three were included in Tier I. Despite adequate control for smoking, three studies (Williams *et al.*, 1977; Vineis *et al.*, 1988; Morabia *et al.*, 1992) were included in Tier II due to other limitations. The earliest of the studies included in the meta-analysis was published in 1977 (Williams *et al.*, 1977) and the most recent were published in 1992 (Hrubec *et al.*, 1992; Morabia *et al.*, 1992). Notably, none of the Tier I or II studies was published in the last 10 yr. Three of the four cohort studies included in the meta-analysis were published in Europe: two in Sweden (Jarvholm and Brisman, 1988; Gustavsson *et al.*, 1990) and one in Denmark (Hansen, 1989). The fourth cohort study was published in the USA (Hrubec *et al.*, 1992, 1995) and presented in two reports, one evaluating cancer risk by occupation and one evaluating cancer risk by industry. All but one (Benhamou *et al.*, 1988) of the case–control studies were conducted in the USA.

Tier I. Lerchen *et al.* (1987). This case–control study compared lung cancer patients from the New Mexico tumor registry to matched controls selected either through random digit dialing or from the Health Care Financing Administration records. The information for roughly half of all cases and 2% of controls was available from the next of kin interviews. Smoking variables used for adjustment included smoking status (current, former or never), number of cigarettes/day and smoking duration. The non-exposed group included subjects never employed in the industry or occupation of interest. For auto mechanics the adjusted OR was 0.9 (95% CI 0.5–1.9).

Table 4. Meta-analysis results for mesothelioma

Analyses	*K*	Meta-RR	95% CI	*Q*-test
Tier I studies	4	0.92	0.55–1.56	0.97
Tier II studies	3	0.81	0.52–1.28	0.92
Studies that eliminated other exposures[a]	4	0.80	0.46–1.40	0.94
Studies that defined exposure as 'brake work'[b]	3	0.86	0.48–1.56	0.46

K, number of studies; *Q*-test, *P*-value of the test for heterogeneity; RR, an estimate of relative risk; CI, confidence interval.
[a]Agudo *et al.* (2000), McDonald and McDonald (1980), Teschke *et al.* (1997) and Hessel *et al.* (2004, in press).
[b]Woitowitz and Rödelsperger (1994), Teschke *et al.* (1997) and Hessel *et al.* (2004, in press).

Table 5. Quality scores of studies evaluating the association between lung cancer risk and employment as a motor vehicle mechanic

Quality criteria	Study																					
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Overall study design: PMR/PIR/SMOR = –1; else = 0	0	0	0	0	0	0	0	0	0	0	0	–1	0	0	0	0	–1	0	–1	–1	–1	–1
Asbestos exposure: non-specific (e.g. 'car mechanic') = 0; specific (e.g. brake repairman, or IH-based) = 1	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Age adjustment: no = –1; yes = 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Confounding by other occupational exposure: likely = –1; possible = 0; unlikely/addressed = 1	0	0	0	0	0	0	0	–1	0	0	–1	0	0	0	0	0	0	0	0	0	0	0
Exposure-response analysis: no = 0; yes =1	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Analysis by latency: no = 0; yes = 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
For case–control studies: response rate: <80% or not reported = –1; >90% = 1; else = 0	0	0	0	0	0	0	1	–1	–1	–1	–1	0	0	0	0	0	0	–1	1	0	0	0
For cohort studies: follow-up <10 yr = –1; >20 yr = 1; else = 0	–1	1	0	0	1	0	0	0	0	0	0	0	0	–1	–1	–1	–1	0	0	0	0	0
Adjustment for smoking: none = –1, partial/inadequate = 0; adequate/ detailed = 1	–1	0	–1	0	1	1	1	1	1	1	0	–1	–1	–1	–1	–1	–1	–1	–1	–1	–1	–1
Reporting bias: likely = –1; possible = 0; unlikely/addressed = 1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Selection bias: likely = –1; possible = 0; unlikely/addressed = 1	1	1	1	1	1	1	0	0	0	0	–1	0	0	1	1	1	0	0	0	0	0	0
Total score	–1	4	0	1	3	3	2	0	0	0	–2	–2	–1	–1	–1	–1	–3	–2	–1	–1	–2	–2

1, Rushton *et al.* (1983); 2, Gustavsson *et al.* (1990); 3, Jarvholm and Brisman (1988); 4, Hansen (1989); 5, Hrubec *et al.* (1992); 6, Lerchen *et al.* (1987); 7, Benhamou *et al.* (1988); 8, Vineis *et al.* (1988); 9, Williams *et al.* (1977); 10, Morabia *et al.* (1992); 11, Swanson *et al.* (1993); 12, Achwartz (1987); 13, Finkelstein (1995); 14, Enterline and McKiever (1963); 15, Menck and Henderson (1976); 16, Leigh (1996); 17, Petersen and Milham (1980); 18, Milne *et al.* (1983); 19, Dubrow and Wegman (1984); 20, Olsen and Jensen (1987); 21, Milham and Ossiander (2001); 22, NIOSH (personal communication, 2002).

Table 6. Summary of lung cancer studies and corresponding RR estimates included in the meta-analysis

First author	Year	Design	Exposure definition	Source of cases	Comparison group	RR estimate (95% CI)
(A) Tier I studies						
Lerchen	1987	Case–control	Auto mechanics	New Mexico Tumor Registry	Randomly selected residential telephone numbers or Medicare roster (age 65+)	0.9 (0.5–1.9)[a]
Benhamou	1988	Case–control	Motor vehicle mechanics	French hospitals	French hospital patients without tobacco-related disease	1.06 (0.73–1.54)[a]
Gustavsson	1990	Cohort	Bus garage mechanics, servicemen or hostlers	Swedish Cancer Registry	Occupationally active population of greater Stockholm	1.22 (0.71–1.96)
					General population of greater Stockholm	1.15 (0.67–1.84)
		Nested case–control	Highest asbestos exposure category		Lowest asbestos exposure category	1.20 (0.26–5.64)[b]
Hrubec	1992	Cohort	Automobile mechanics and repairmen (occupation)	US veterans' life insurance records	All other occupations	1.1 (0.85–1.41)[a,b,c]
	1995		Automobile repair services and garages (industry)			0.9 (0.64–1.23)[a,c]
(B) Tier II studies						
Williams	1977	Case–control	Car repair services	Third National Cancer Survey	Other cancer cases	0.85 (NR)[a]
Jarvholm	1988	Cohort	Car repair mechanic	Swedish Cancer Register	General Swedish population	1.27 (1.03–1.56)
Vineis	1988	Case–control	Automobile brake workers	Cancer registries, hospitals, or death certificates	Other hospital patients, death certificates, and drivers license records	1.2 (0.9–1.7)[a]
Hansen	1989	Cohort	Auto mechanics	Death certificates	Other skilled workers	1.01 (0.72–1.37)
Morabia	1992	Case–control	Mechanics and automobile repairmen	US hospitals	U.S. hospital patients without tobacco-related disease	0.7 (NR)[a]

CI, confidence interval; RR, estimate of relative risk.
[a]Adequately controlled for smoking.
[b]Values used in meta-analysis.
[c]95% CI recalculated, authors only reported 90% CI.

The strengths of this study are the population-based design and adequate adjustment for smoking. Conscious of the disparity in next of kin interviews, the authors evaluated the number of jobs reported for cases and controls by interview method. Surrogate interviews generally identified fewer jobs, but the difference between cases and controls was small.

Benhamou *et al.* (1988). In this French case–control study lung cancer cases were matched to controls selected from hospital patients with diseases not related to tobacco exposure. All subjects had completed a questionnaire that included a full occupational history. The non-exposed group consisted of people who had never been engaged in the particular occupation under study. Smoking variables included smoking status, age when started smoking, cigarettes per day and duration of smoking. Analyses for 'motor vehicle mechanics' yielded an adjusted OR of 1.06 (95% CI 0.73–1.54). The major strengths of this study are its very detailed adjustment for smoking and an apparently high response rate (Lubin *et al.*, 1984; Benhamou *et al.*, 1985). However, the use of hospital-based controls could be considered a limitation.

Gustavsson *et al.* (1990). Gustavsson and colleagues followed a cohort of workers who were employed in one of five Stockholm bus garages between 1945 and 1970. Exposure to asbestos was estimated by industrial hygienists based on personal sampling results. Observed mortality for the period from 1952 to 1986 was compared with mortality of the general and the 'occupationally active' population of Stockholm. The SMRs for lung cancer were 1.22 (95% CI 0.71–1.96) using occupationally active population rates and 1.15 (95% CI 0.67–1.84) using general population rates. The lung cancer SMRs by asbestos exposure index (exposure intensity × duration in years) were 0.86 for index 0–20, 1.97 for 20–40 and 1.18 for >40.

Table 7. Summary of lung cancer studies and corresponding RR estimates not included in the meta-analysis

First author	Year	Design	RR estimate	95% CI	Reason for eclusion
Enterline	1963	Cohort	1.28	NR	No control for smoking, follow up 1 yr; total score <0
Menck	1976	Cohort	1.46	NR	No control for smoking, follow up 5 yr; total score <0
Decoufle	1977	Cohort	1.12	NR	Exposure defined as 'mechanics and repairmen'
Petersen	1980	Proportionate mortality	1.23	NR	No control for smoking, follow up 3 yr; total score <0
Rushton	1983	Cohort	1.01 (workers in bus garages)	NR	No control for smoking, follow up <10 yr; total score <0
			0.92 (bus mechanics)[d]	NR	
Milne	1983	Case–control	1.2	NR	No control for smoking, does not report response rate; total score <0
Dubrow	1984	Case–control	1.38	NR	No control for smoking; total score <0
Blair	1985	Cohort	1.03	NR	Updated in Hrubec *et al.* (1992)
Olsen	1987	Proportionate incidence	1.17	0.8–1.63	PIR design, no control for smoking; total score <0
Schoenberg	1987	Case–control	1.4	0.84–2.3	Included in a larger study by Vineis *et al.* (1988)
Schwartz	1987	Proportionate mortality	1.12	0.82–1.53	PMR design, no control for smoking; total score <0
Carstensen	1988	Cohort	1.07	0.92–1.22	Exposure defined as 'mechanics and repairmen'
Zahm	1989	Case–control	1.3	1.0–1.7	Exposure defined as 'mechanics, repairers'
Burns	1991	Case–control	1.72 (mechanics, motor vehicles)	1.15–2.59	Updated in Swanson *et al.* (1993); selection bias due to use of colon or rectum cancer cases as controls, confounding by other occupations, total score <0
			1.56 (automobile repair)	0.85–2.87	
Swanson	1993	Case–control	Presented OR by number of years employed	Presented OR by number of years employed	Selection bias due to use of colon or rectum cancer cases as controls, confounding by other occupations, poor response rate; inadequate control for smoking; total score <0
Finkelstein	1995	Case–control	0.88	0.39–1.85	No control for smoking; total score <0
De Stefani	1996	Case–control	0.6	0.3–1.2	Exposure defined as 'mechanic'
Leigh	1996	Cohort	1.31	1.08–1.54	No control for smoking, follow up 3 yr, relative risk related to large occupational group (auto, bus, truck, stationary engine mechanics); total score <0
Pezzotto	1999	Case–control	1.3	0.7–2.4	Exposure defined as 'mechanics'
Milham	2001	Proportionate mortality	1.15	NR	PMR design, no control for smoking; total score <0
NIOSH	2002	Proportionate mortality	1.15	NR	PMR design, no control for smoking; total score <0

CI, confidence interval; NR, not reported; PIR, proportionate incidence ratio; PMR, proportionate mortality ratio; RR, estimate of relative risk.
[a]Adequately controlled for smoking.
[b]Values used in meta-analysis.
[c]95% CI recalculated, authors only reported 90% CI.
[d]As reported in Wong (1993, 2001).

The standardized incidence ratio for lung cancer compared with the general population rates was 1.61 (95% CI 0.94–2.57). However, in this analysis two cases of mesothelioma and one case of alveolar cell cancer were counted as 'lung cancers'.

A nested case–control analysis using logistic regression reported the following RRs: index 0–20 = 1.0 (reference); 20–40 = 1.67 (95% CI 0.50–5.60); 40–60 = 1.26 (95% CI 0.32–5.00); >60 = 1.20 (95% CI 0.26–5.64).

The limitations of this study are the potential inclusion of workers not involved in motor vehicle repair and the lack of smoking information. However, the use of internal comparisons in the nested case–control analysis potentially attenuated the confounding effect of smoking. A particularly important feature that sets this study apart from other studies is its ability to conduct IH-based dose–response analyses.

Hrubec *et al.* (1992, 1995). Hrubec and co-workers conducted a cohort study of 248 046 US veterans followed from 1954 through 1980. In addition to occupational history, the cohort members responded to questionnaires providing information on smoking habits. The response rate was 84%. The underlying cause of death was identified for 95% of the decedents. Cause-specific mortality by occupation was adjusted for smoking using information on smoking status and amount of smoking. For cancers of the respiratory system, the smoking-adjusted RR was 1.1 (90% CI 0.89–1.36) in the occupational group 'automobile mechanics and repairmen' and 0.9 (90% CI 0.69–1.17) in the industry type 'automobile repair services and garages'.

This study's strengths included its large sample size, ability to control for smoking (unusual for a cohort study) and a long follow-up period. However, its weakness was the use of the category 'respiratory cancer', which is less specific than 'lung cancer'.

Tier II. Williams *et al.* (1977). Using the data from the Third National Cancer Survey, Williams *et al.* conducted inter-cancer case–control analyses for various occupations and industries while controlling for age, sex, race, education, smoking, alcohol use and geographic location. Only 57% of the cases approached for interviews participated. The non-exposed category consisted of persons in any other known job. For the industry category 'car repair services' the lung cancer analysis showed an OR of 0.85 (confidence interval not reported). Although this study adequately controlled for tobacco, alcohol and socio-economic status in all analyses, its main weakness was the poor response rate and the use of all other cancers as controls.

Jarvholm and Brisman (1988). These authors used 1960 Swedish census records to identify men employed as 'mechanics' in the 'car repair' industry. This information was linked to the Swedish Death Register (1961–1973) and the Swedish Cancer Registry (1961–1979). There were 39 deaths from lung cancer versus 23 expected, yielding an SMR of 1.70. Ninety-three lung cancers occurred among car mechanics from 1961 to 1979, while 73.0 were expected, resulting in a standardized incidence ratio (SIR) of 1.27 (95% CI 1.03–1.56). These results are limited by the lack of adjustment for smoking and by the absence of asbestos-specific exposure information.

Vineis *et al.* (1988). Occupational data from five case–control studies from five US states were combined to determine the risk of lung cancer associated with different occupations. Cases were identified from cancer registries, hospitals or death certificates. Controls for one of the individual studies were population based and matched on vital status; the remaining studies used hospital controls or deceased controls from death certificates. The non-exposed group consisted of people without any history of exposure to established and suspected lung carcinogens. Odds ratios were calculated for ever-employment in the selected occupations and were adjusted for age, birth cohort and cigarette use. Ninety-eight cases and 90 controls were ever employed as 'automobile brake workers' (OR = 1.2, 95% CI 0.9–1.7). Among the limitations of this study is the lack of a uniform job classification scheme. The comparison of automobile brake workers who may have had other potential asbestos exposure to persons without any exposure potentially biased the results. The combined response rate was <80%. The study's advantages include a relatively large sample size, adequate control for smoking and information specific to brake repair workers.

Hansen (1989). A cohort of 21 800 male 'auto mechanics' and 52 000 male skilled workers identified from the 1970 Danish Census was followed for 10 yr. Deaths were identified through the Danish National Bureau of Statistics. The reference cohort of skilled workers included carpenters, electricians, instrument makers, dairymen, upholsterers and glaziers. There were 41 lung cancer deaths among the motor vehicle mechanics, compared to 40.7 deaths expected based on the reference rates (SMR = 1.01, 95% CI 0.72–1.37). Limitations of the study included short follow-up, inclusion of workers with potential exposure to asbestos (e.g. carpenters and electricians) in the comparison group and lack of control for smoking. However, the latter limitation may have been partially offset by the use of a comparison group of manual workers.

Morabia *et al.* (1992). This hospital-based case–control study was conducted in nine US metropolitan areas. Cases were matched (age, race, hospital, year of interview and smoking) to two types of controls (cancer and non-cancer). Participants completed standardized, in-person questionnaires. Adjustment for smoking was performed using smoking status and amount of smoking categories. The reference group (non-exposed) consisted of people who were never employed in an occupation with exposure to confirmed or suspected lung carcinogens. For the usual occupation of 'mechanics and repairmen–automobile' the adjusted OR was 0.7 (confidence interval not reported). The main strength of this study is adjustment for smoking. The comparison of automobile mechanics who may have had other potential asbestos exposure to persons without any history of at-risk exposures is a potential source of bias. Use of hospital controls and the fact that the authors did not report a response rate should also be considered as weaknesses.

Meta-analysis. The results of the summary analysis for lung cancer are presented in Table 8. All tests for heterogeneity produced non-significant results regardless of stratification, and in all analyses the random effects model reduced to a fixed effects model. Analyses of the Tier I and Tier II studies produced meta-RR estimates of 1.07 (95% CI 0.88–1.31) and 1.17 (95% CI 1.01–1.36), respectively. When the analysis was limited to studies that used adequate control for smoking regardless of tier, the resulting meta-RR estimate was 1.09 (95% CI 0.92–1.28). The analysis that was limited to case–control studies (including the nested case–control results from Gustavsson *et al.*, 1990) resulted in a meta-RR estimate of 1.08 (95%CI 0.87–1.34), while the analysis of the cohort studies produced a meta-RR of 1.16 (95% CI 1.00–1.34).

DISCUSSION

None of the individual studies that examined risk of mesothelioma among motor vehicle mechanics demonstrated increased risk and, thus, the results of the meta-analysis also showed no increased risk of mesothelioma. It is also noteworthy that the meta-analysis results remained virtually the same after the analysis was limited to studies specifically mentioning brake mechanics and did not change after the removal of those with other occupations potentially involving asbestos exposures.

Although the three potentially relevant cohort studies (Jarvholm and Brisman, 1988; Hansen, 1989; Gustavsson *et al.*, 1990) could not calculate the RR, their findings largely support the case–control and PMR/PIR surveillance studies and are consistent with the results of the meta-analysis. There were four cases in a total of ~600 000 person-yr of follow-up. For reference, the reported annual rates of mesothelioma among males in Denmark and Sweden are 1.47 and 1.1 per 100 000, respectively (Ferguson *et al.*, 1987; Parkin *et al.*, 1997).

In a Swedish study of bus garage mechanics Gustavsson *et al.* (1990) reported two cases of mesothelioma. One of these was not a mechanic but an electrician and both cases 'may have been exposed to asbestos during previous employments'. In another Swedish study Jarvholm and Brisman (1988) found 'one case of mesothelioma in the cancer register and none in the death register'. The authors noted that the person diagnosed as having mesothelioma also worked in the construction industry and concluded that their data 'indicate no increased risk of mesothelioma in car mechanics …' (Jarvholm and Brisman, 1988).

The Danish study of garage mechanics also found only one death due to cancer of the pleura (Hansen, 1989). The author interpreted the finding of a single case of pleural cancer as an indication that exposure to asbestos via brake repair 'was not negligible'. Unlike Gustavsson *et al.* (1990) and Jarvholm and Brisman (1988), Hansen (1989) did not evaluate other sources of asbestos exposure for the individual who developed pleural cancer.

The conclusion by Hansen is inconsistent with the results of another record linkage study based on the data from the Danish Cancer Registry and from the Supplementary Pension Fund and the Central Population Registry (Olsen and Jensen, 1987). In this study

Table 8. Meta-analysis results for lung cancer

Analyses	K	Meta-RR	95% CI	Q-test
Tier I studies	4	1.07	0.88–1.31	0.96
Tier II studies	5	1.17	1.01–1.36	0.64
Studies with adequate adjustment for smoking[a]	6	1.09	0.92–1.28	0.92
Case–control studies	6	1.08	0.87–1.34	0.92
Cohort studies	3	1.16	1.00–1.34	0.44

CI, confidence interval; K, number of studies; Q-test, P-value of the test for heterogeneity; RR, estimate of relative risk.
[a]Hrubec *et al.* (1992), Lerchen *et al.* (1987), Benhamou *et al.* (1988), Vineis *et al.* (1988), Williams *et al.* (1977) and Morabia *et al.* (1992).

covering nearly the same period of time as the Hansen (1989) study, there were no cases of mesothelioma (pleural or peritoneal) in the category ‘garages’ and in the category ‘repair of motor vehicles and motorcycles’. Because cancer registries typically report higher numbers of cases than are recorded on death certificates, the discrepancy between one case of pleural cancer and no cases of mesothelioma could be explained by the fact that not all pleural cancers are mesotheliomas. Another potential explanation for the discrepancy between Hansen (1989) and Olsen and Jensen (1987) is the difference in evaluating occupational exposure. Hansen relied on occupation on the day of the 1970 census, while Olsen and Jensen allocated cancer cases to the occupational group in which the person was employed for the longest period of time and with at least 10 yr of latency.

It is important to note that automobile repair is a common occupation. For example, according to the 1984 NIOSH report, ~5 000 000 persons in the USA had a history of having been formally involved in automobile repair (Nicholson *et al.*, 1984). Assuming a background rate of 1–3 cases/million/yr (McDonald, 1985; Parkin *et al.*, 1997), as reported to apply to persons without occupational asbestos exposure in North America, some cases of mesothelioma are expected to be found among motor vehicle mechanics, even in the absence of any increase in risk due to this occupation.

The pitfalls of relying on case reports/case series for causal inference were illustrated by two reports that appeared in the early 1990s. In 1991, Woitowitz and Rödelsperger described cases of mesothelioma among their clinic patients who had worked at one time as garage mechanics (Woitowitz and Rödelsperger, 1991). These patients were part of an ongoing case–control study. Based on their clinical experience, the authors concluded that there was an increased incidence of mesothelioma among car mechanics. This conclusion was criticized by Wong, based on the absence of a comparison group (Wong, 1992). Woitowitz and Rödelsperger published the results of their case–control study in 1994. The results of this study led its authors to conclude that employment as a garage mechanic, and specifically as a brake repairman, was not associated with an increased risk of mesothelioma (Woitowitz and Rödelsperger, 1994).

The lack of association between work as a motor vehicle mechanic or brake mechanic and mesothelioma may result from several factors. First, the asbestos fibers found in airborne samples are generally short (<5 µm) chrysotile fibers (Rödelsperger *et al.*, 1986). Although still the focus of debate, there appears to be increasing consensus that short fibers, particularly those <5 µm in length, are associated with little (if any) risk of lung cancer and mesothelioma (ERG, 2003). Secondly, asbestos fibers in brake pads are embedded in resin (Weir and Meraz, 2001) and therefore are less likely to become airborne. Thirdly, much of the chrysotile in brake pads is transformed to forsterite during the braking process (Anderson *et al.*, 1973). Forsterite does not appear to have asbestos fiber properties and is not considered carcinogenic in humans (Wong, 1992). More importantly, in his recent publication Langer demonstrated that chrysotile’s biological activity becomes virtually nil hundreds of degrees below the forsterite transformation temperature. Thus, complete transformation of the mineral is not required to result in loss of activity (Langer, 2003).

Further evidence in support of the epidemiological findings comes from a recent pathology study evaluating asbestos content in lung tissue of ~1500 mesothelioma cases (Roggli *et al.*, 2002). Fifty-one of those cases were employed as motor vehicle mechanics, of whom >50% had other sources of asbestos exposure. The authors reported that lung burden analyses in this occupational group either reflected background levels or, when asbestos was found above background levels, the fibers were commercial and non-commercial amphiboles (Roggli *et al.*, 2002). These observations led the authors to conclude that ‘brake dust is unlikely to cause mesothelioma’.

Unlike mesothelioma, lung cancer has several clearly identifiable occupational and lifestyle causes that, when not taken into account, could explain some of the observed associations. Motor vehicle mechanics are among the highest ranked occupational groups with respect to smoking prevalence in the USA (Leigh, 1996; Bang and Kim, 2001). Thus, adequate adjustment for smoking is particularly important in studies of lung cancer among motor vehicle mechanics because small to moderate unadjusted increases in risk can be attributable to the high prevalence of smoking habits in this occupational group.

Another important source of confounding is the history of occupational exposures other than those associated with motor vehicle repair. For example, in the case–control study by Vineis *et al.* (1988), the category ‘automobile brake repair workers’ included all individuals who ever belonged to this occupational group, regardless of other jobs held. In contrast, the unexposed group included only cases and controls without any history of known or suspected at-risk occupations. Assuming that 50% of brake workers in the Vineis study held other asbestos exposure-related jobs (e.g. insulators, pipefitters or welders) and that the average RR of lung cancer among these occupations is 1.6 (Goodman *et al.*, 1999), confounding by other asbestos exposures would result in an OR of 1.3. Because asbestos is not the only occupational carcinogen, additional confounding by other occupational exposures may further affect the results.

It is important to point out that most asbestos-exposed occupations showing a substantial increase in risk of asbestos-related lung cancer are expected to show an even higher elevated risk of mesothelioma. For this reason, it would be difficult to conclude that motor vehicle mechanics may be at risk for developing lung cancer from asbestos given the absence of any increase in risk of mesothelioma. Importantly, the only epidemiological study that used an IH-based exposure assessment (Gustavsson *et al.*, 1990), among persons employed at as bus garage, found no dose–response relationship between the level of asbestos exposure and the risk of lung cancer.

The role of meta-analyses in observational epidemiology is the focus of ongoing discussion. By combining several studies, meta-analyses have an inherent ability to show relatively small statistically significant departures from null. However, these relatively precise meta-RR estimates may not accurately reflect the magnitude of the association unless the analyses take into consideration potential sources of systematic error. It is perhaps more useful to view meta-analysis as a formal way of understanding and quantitatively describing the level of consistency and inconsistency among studies and to identify potential sources of error that may affect the result.

One source of error that warrants consideration in a meta-analysis is publication bias, which tends to occur because studies with statistically significant positive findings are more likely to be published than studies with null results (Easterbrook *et al.*, 1991). Publication bias can be evaluated through identification of unpublished research or by calculating the fail-safe *N*, defined as the number of studies with a non-significant result that would bring a statistically significant meta-RR estimate to non-significant levels (Rosenthal, 1979). However, in this case the results are essentially null and thus publication bias would not be expected to affect our findings.

The search for sources of error inevitably leads to evaluation of study quality. Several authors recommend formalizing such evaluations by using quantitative scoring of individual studies (Jenicek, 1989; Downs and Black, 1998). Others view the use of scoring schemes as somewhat arbitrary and advise against using them (Juni *et al.*, 1999). We would agree that both points of view have merit. Using a quality score as a method of weighting study results or as a variable in a regression model may introduce a subjective element into an analysis (Greenland, 1998). On the other hand, it is important to consider and take into account methodological strengths and weaknesses that are likely to affect the results. For these reasons, we feel that the use of quality tiers is justified as long as the methodology of assigning studies to a particular tier is transparent to the readers. It would be difficult to ensure such transparency without some kind of formal scoring approach. The particular scoring method used in this study reflects the consensus of its authors, but we realize that other approaches may also exist.

It is important to point out that if one were to compare the meta-analyses of all studies combined with those of individual tiers, the results would appear somewhat different. The meta-RRs for mesothelioma based on all three tiers is 0.67, with a 95% CI between 0.53 and 0.84, while the meta-RR for Tier I is 0.92 (95% CI 0.55–1.56). The corresponding results for lung cancer are 1.16 (95% CI 1.13–1.19) and 1.07 (95% CI 0.88–1.31). These comparisons indicate that the statistically significant departures from null (down for mesothelioma and up for lung cancer) in a meta-analysis of all studies combined could be explained by methodological problems of individual studies.

CONCLUSIONS

The available epidemiological data show that employment as a motor vehicle mechanic does not increase the risk of developing mesothelioma. Although some studies showed a small increase in risk of lung cancer among motor vehicle mechanics, the epidemiological data on balance do not support a conclusion that lung cancer in this occupational group is related to asbestos exposure from vehicle repair.

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APPENDIX

Meta-analysis calculations

Using the fixed effects assumption, the general formula for the weighted average effect size of *k* studies is:

$$\bar{T} = \frac{\sum_{i=1}^{k} w_i T_i}{\sum_{i=1}^{k} w_i} \quad (1)$$

where *Ti* is the effect size estimate of the *i*th study and *wi* is the weight associated with it. The weights that minimize the variance of *T.* are given by:

$$w_i = \frac{1}{v_i} \quad (2)$$

where v_i is the variance in each study. The average effect size $T.$ has a conditional variance $v.$ given by:

$$v. = \frac{1}{\sum_{i=1}^{k}\left(\frac{1}{v_i}\right)} \quad (3)$$

Equations for variance change for the random effects assumption. The total variance of an effect size estimate is given by:

$$V_i^* = \sigma^2 + v_i \quad (4)$$

where σ^2 is the random effects variance and v_i is the conditional variance given above. The random effects variance σ^2 calculated is based on a weighted sample estimate Q of the unconditional variance of T_i. In this method, the random variance is estimated by:

$$\sigma^2 = \frac{[Q-(k-1)]}{\sum_{i=1}^{k} w_i - \left[\frac{\sum_{i=1}^{k} w_i^2}{\sum_{i=1}^{k} w_i}\right]} \quad (5)$$

In the random effects model, the average effect size $T.$ and its variance $v.$ are calculated using equations 1–3 above, however, V_i^* is substituted for v_i. The random effects model will give a non-zero estimate only when Q is greater than its expected value. Otherwise, it is assumed to be zero, and the fixed effects model applies.

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