Diesel Exhaust Exposure and Lung Cancer
Rajiv Bhatia,1 Peggy Lopipero,2 and Allan H. Smith2

We evaluated the relation between occupational exposure to diesel exhaust and cancer of the lung in a meta-analysis of 29 published cohort and case-control studies. Twenty-one of the 23 studies meeting the inclusion criteria had observed relative risk estimates greater than one. Pooled effect measures weighted by study precision indicated an increased relative risk (RR) for lung cancer from occupational exposure to diesel exhaust [RR = 1.33; 95% confidence interval (CI) = 1.24–1.44]. Subanalysis of case-control (RR = 1.33; 95% CI = 1.18–1.55) vs. cohort studies (RR = 1.33; 95% CI = 1.21–1.47) and of studies that controlled for smoking (RR = 1.35; 95% CI = 1.20–1.52) vs. those that did not (RR = 1.33; 95% CI = 1.20–1.47) produced results that did not differ from those of the overall analysis. On the other hand, cohort studies using internal comparisons (RR = 1.43; 95% CI = 1.29–1.58) showed higher relative risks than those using external comparisons (RR = 1.22; 95% CI = 1.04–1.44). Heterogeneity between studies was reduced when we stratified studies by the occupational setting in which exposure occurred. A positive duration-response relation was evident in those studies that were stratified by employment duration. This meta-analysis supports a causal association between increased risks for lung cancer and exposure to diesel exhaust. (Epidemiology 1998;9:84–91)

Keywords: lung cancer, diesel exhaust, meta-analysis.

Studies of exposure to diesel exhaust and lung cancer have included diverse occupational groups and research methods. Few of these studies have had the benefit of individual-level exposure estimation; relative risk estimates are generally less than two. Such studies are particularly susceptible to biases, including confounding. Given these recognized limitations, the interpretation of these studies has been challenging and controversial. In 1989, the International Agency for Research on Cancer classified the evidence for the human carcinogenicity of diesel exhaust as limited.1 In this article, we combine results from published data of lung cancer mortality among workers with potential exposure to diesel exhaust fumes. The objective of this analysis is to evaluate quantitatively the epidemiologic evidence that exposure to diesel exhaust is a cause of lung cancer. We attempt to answer the following questions: (1) Are the risks of lung cancer in these observational studies likely to be due to chance? (2) Is confounding due to smoking a likely explanation for the increased observed risks? (3) Do differences in study methods or exposure settings explain differences in observed risks?

Methods
We followed the general principles of meta-analysis, such as those outlined by L’Abbe et al.2 as well as those discussed by Greenland.3 We searched the epidemiologic literature for all studies concerning lung cancer and occupational diesel exhaust exposure. Within most of these studies, exposure was defined as work in an occupation or industry in which diesel engines and equipment were in use; however, a few of the studies benefited from quantitative exposure measures. In addition to looking for primary references using resources such as Medline, we surveyed reviews on the subject for secondary references. We included only studies reported in peer-reviewed journals.

Although the use of diesel engines in the coal and metal mining industries is common, we chose to exclude occupational studies of miners because of the potential role of multiple occupational carcinogens, including radon and silica. When different updates of a study had been published in more than one journal, we used the most recent report. Similarly, when a study population had been followed for different time intervals, we used the analysis based on the longest period of follow-up.

We extracted effect measures [relative risks (RRs), odds ratios, and standardized mortality ratios (SMRs)] and their confidence intervals (CI) for lung cancer mortality among diesel exhaust-exposed workers from each.
study. We estimated missing confidence intervals by
Byar's approximation for the cohort studies, or by cal-
culating the variance of the log of the odds ratio using
unadjusted data for the case-control studies. If infor-
mation on lung cancer mortality was not provided, we used
the data on total respiratory cancer mortality.

We reviewed studies for inclusion into a pooled anal-
ysis, based on their validity. We excluded (1) studies in
which inadequate latency for lung cancer after exposure
to diesel exhaust was likely; and (2) studies in which
work with diesel equipment or engines could not be
confirmed or reliably inferred.

We chose a period of 10 years as a minimum inter-
val time from first exposure to end of follow-up. If studies
were conducted at or near the time of transition to
diesel fuels in an industry, we defined the time of potential first
exposure as the midpoint between the year when diesel
fuels were introduced and the year that the transition to
diesel was completed. If a study did not provide sufficient
information to estimate latency for the entire cohort, yet
it was apparent that at least some of the subjects had
been followed for 10 years after first exposure, we in-
cluded these studies in the analysis.

If a study presented risk estimates for more than one
specific occupational category of diesel exhaust-exposed
workers, we used the subgroup risk estimates in the
meta-analysis. If a study considered data on duration of
exposure or employment, we used the risk estimates from
the longest exposure stratum. If more than one stratum
represented 20 or more years of diesel exposure, these
strata were combined. In cohort studies in which both
national and regional populations were used to calculate
the expected deaths, we used results based on the re-

gional rates in the meta-analysis. We always used smoking-
adjusted effect measures when present.

We used the method of weighting by precision to
calculate the pooled estimates. We calculated the
weight or inverse variance \( w = 1/[\text{SE}]^2 \) of each study
using a standard error equal to the natural log of the ratio
of the upper to lower 95% confidence intervals divided by
3.92 \( \text{SE} = \ln(\text{RR}_{\text{upper}}/\text{RR}_{\text{lower}})/3.92 \). The value 3.29
replaced 3.92 in the formula if 90% confidence intervals
were presented. For each study, the weight \( w \) was
multiplied by the natural log of the effect measure \( \beta = \log \text{RR} \) to give a summary measure \( \omega \beta \) for the ith
study. We calculated a weighted mean or pooled sum-
mary estimate \( \beta \) by dividing the weighted sum of the
results by the sum of the weights \( \beta = \Sigma \omega \beta / \Sigma \omega \).

The variance of this pooled estimate is simply \( 1/\Sigma \omega \).

We estimated pooled summaries for all studies com-
bined and separately for cohort studies and case-control
studies. We further subdivided cohort studies into those
that used internal reference populations and those that
did not. We also calculated pooled estimates for studies
that statistically adjusted for smoking and for those that
did not have available smoking data. We estimated
summaries for occupational categories when more than
two studies in that category met the criteria for inclu-
sion. We converted all pooled estimates into rate ratios
(\( RR = \exp B \)) with 95% confidence intervals.

We evaluated heterogeneity among studies with the
statistic \( \chi^2 = \omega (B - \beta)^2 \), with degrees of freedom (df)
equal to one less than the number of studies combined.
Where evidence for heterogeneity was present, it was
reflected in the confidence interval by adjusting the
variance of the pooled relative risk estimate using a
factor derived from the heterogeneity test. The method
used was originally suggested by Armitage and described
by Shore et al. The variance of the log of the relative
risk estimate is adjusted by multiplying it by the ratio of
the heterogeneity \( \chi^2 \) to its degrees of freedom (\( \text{Var}_{\text{adj}} = \text{Var} \times \chi^2/df \) when \( \chi^2 > df \)). The adjusted variance is
then used to calculate the adjusted confidence interval.

In cohort studies that used external reference popula-
tions, we examined potential bias from the healthy
worker by a simple adjustment of the lung cancer SMR
by the SMR for all causes excluding lung cancer in those
studies in which data were available. Briefly, we recal-
culated the SMR for all causes of death after removing
observed and expected cases of lung cancer. Then, we
adjusted the expected number of lung cancer deaths by
multiplying the general population expected number by
the SMR for all causes excluding lung cancer. We then
calculated an adjusted lung cancer SMR with the ob-
erved lung cancer deaths and the adjusted expected
number of deaths.

To assess the studies for evidence of dose-response
relations, we examined those studies that had data for
exposure duration and which used internal reference
groups. As exposure duration categories were defined
differently in the various studies, we were not able to
pool the risk estimates by duration of exposure.

Results

We found 35 studies in the published literature with
data concerning exposure to diesel exhaust and lung
cancer. Six pairs of studies represented analyses of the
same study population. Burns and Swanson, Hall and
Wynder, Schenker et al., and Damber and Larsson10
presented preliminary results of data later re-analyzed by
Swanson et al., Boffetta et al., Garshick et al.,13 and
Damber and Larsson.14 We used the later publications
in the meta-analysis. The paper by Siemiatycki15 was a
re-analysis of a 1988 publication; however, we used the
earlier study, since the later analysis presented only a
subset of the earlier data. Emmelink et al.16 presented a
nested case-control analysis of the cohort studied by
Gustafsson et al17; we used the original cohort study
owing to uncertainty in the methods of exposure catego-
rization in the later analysis.

The study of Hayes et al.18 presented a secondary
analysis of three pooled case-control studies of lung
cancer examining the effect of occupation in diesel
exhaust-exposed trades. The original studies were case-
control studies of lung cancer that had not focused on
diesel exhaust exposure.19-21 The data we used in the
pooled analysis were derived from the analysis presented
by Hayes et al.

We excluded two case-control studies because of un-
certain exposure to diesel exhaust. These included the
<table>
<thead>
<tr>
<th>Authors and Year</th>
<th>Type*</th>
<th>Smoking Adjusted</th>
<th>Occupation</th>
<th>Exposure or Duration Category</th>
<th>Cases</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahlberg et al.²⁰ 1981</td>
<td>RC</td>
<td>No</td>
<td>Truck driver</td>
<td>161</td>
<td>1.3</td>
<td>1.1-1.6</td>
<td></td>
</tr>
<tr>
<td>Boffetta et al.²³ 1988</td>
<td>PC</td>
<td>Yes</td>
<td>Truck driver</td>
<td>48</td>
<td>1.24</td>
<td>0.93-1.66</td>
<td></td>
</tr>
<tr>
<td>Boffetta et al.²¹ 1990</td>
<td>CC</td>
<td>Yes</td>
<td>Equipment operator</td>
<td>5</td>
<td>2.6</td>
<td>1.12-6.06</td>
<td></td>
</tr>
<tr>
<td>Coggon et al.²² 1984</td>
<td>CC</td>
<td>No</td>
<td>Railroad worker</td>
<td>14</td>
<td>1.59</td>
<td>0.94-2.69</td>
<td></td>
</tr>
<tr>
<td>Damber &amp; Larsson,²⁴ 1987</td>
<td>CC</td>
<td>Yes</td>
<td>Professional driver</td>
<td>172</td>
<td>1.3</td>
<td>0.72-3.11</td>
<td></td>
</tr>
<tr>
<td>Edling et al.²⁵ 1987</td>
<td>RC</td>
<td>No</td>
<td>Bus worker</td>
<td>37</td>
<td>1.2</td>
<td>0.6-2.2</td>
<td></td>
</tr>
<tr>
<td>Garshick et al.²⁶ 1987</td>
<td>CC</td>
<td>Yes</td>
<td>Railroad worker</td>
<td>6</td>
<td>0.67</td>
<td>0.24-1.46</td>
<td></td>
</tr>
<tr>
<td>Garshick et al.²⁶ 1988</td>
<td>RC</td>
<td>No</td>
<td>Railroad worker</td>
<td>117</td>
<td>1.64</td>
<td>1.18-2.20</td>
<td></td>
</tr>
<tr>
<td>Gustafsson et al.²⁷ 1986</td>
<td>RC</td>
<td>No</td>
<td>Dock worker</td>
<td>70</td>
<td>1.52</td>
<td>1.05-2.16</td>
<td></td>
</tr>
<tr>
<td>Gustavsson et al.²⁸ 1990</td>
<td>RC</td>
<td>No</td>
<td>Bus garage worker</td>
<td>12</td>
<td>2.0</td>
<td>1.43-2.81</td>
<td></td>
</tr>
<tr>
<td>Hansen,²⁹ 1993</td>
<td>CC</td>
<td>Yes</td>
<td>Truck driver</td>
<td>76</td>
<td>1.6</td>
<td>1.26-2.0</td>
<td></td>
</tr>
<tr>
<td>Hayes et al.²⁹ 1989</td>
<td>RC</td>
<td>No</td>
<td>Bus garage worker</td>
<td>38</td>
<td>1.6</td>
<td>0.9-2.8</td>
<td></td>
</tr>
<tr>
<td>Howel et al.³⁰ 1983</td>
<td>RC</td>
<td>No</td>
<td>Truck driver</td>
<td>147</td>
<td>1.5</td>
<td>1.1-1.9</td>
<td></td>
</tr>
<tr>
<td>Lerchen et al.³¹ 1987</td>
<td>RC</td>
<td>No</td>
<td>Equipment operator</td>
<td>14</td>
<td>1.3</td>
<td>0.6-3.1</td>
<td></td>
</tr>
<tr>
<td>Merck &amp; Henderson,³² 1976</td>
<td>RC</td>
<td>No</td>
<td>Truck driver</td>
<td>108</td>
<td>1.65</td>
<td>1.35-1.99</td>
<td></td>
</tr>
<tr>
<td>Raffle,³³ 1957</td>
<td>RC</td>
<td>No</td>
<td>Bus &amp; trolley worker</td>
<td>30</td>
<td>1.4</td>
<td>0.94-2.01</td>
<td></td>
</tr>
<tr>
<td>Ransonn &amp; Gunnarsson,³⁴ 1991</td>
<td>RC</td>
<td>No</td>
<td>Truck driver</td>
<td>24</td>
<td>2.32</td>
<td>0.85-5.04</td>
<td></td>
</tr>
<tr>
<td>Rushon et al.³⁵ 1983</td>
<td>RC</td>
<td>No</td>
<td>Truck driver</td>
<td>102</td>
<td>1.0</td>
<td>0.82-1.22</td>
<td></td>
</tr>
<tr>
<td>Siemiatycki et al.³⁶ 1988</td>
<td>CC</td>
<td>Yes</td>
<td>Diesel truck driver</td>
<td>76</td>
<td>1.08</td>
<td>0.92-1.27</td>
<td></td>
</tr>
<tr>
<td>Steenland et al.³⁷ 1990</td>
<td>CC</td>
<td>Yes</td>
<td>Diesel truck driver</td>
<td>128</td>
<td>1.60</td>
<td>1.2-2.3</td>
<td></td>
</tr>
<tr>
<td>Swanson et al.³⁸ 1993</td>
<td>CC</td>
<td>Yes</td>
<td>Truck driver</td>
<td>121</td>
<td>2.44</td>
<td>1.45-4.16</td>
<td></td>
</tr>
<tr>
<td>Williams et al.³⁹ 1977</td>
<td>CC</td>
<td>Yes</td>
<td>Railroad worker</td>
<td>40</td>
<td>2.46</td>
<td>1.24-4.87</td>
<td></td>
</tr>
<tr>
<td>Wong et al.⁰ 1985</td>
<td>RC</td>
<td>No</td>
<td>Equipment operator</td>
<td>63</td>
<td>1.07</td>
<td>0.91-1.24</td>
<td></td>
</tr>
</tbody>
</table>

* RC = retrospective cohort study; PC = prospective cohort study; CC = case-control study.
† Confidence intervals are calculated from the published data as described in Methods.
‡ N/A = not available.

studies by Benhamou et al.²² and Buiatti et al.,²³ who studied professional drivers and transportation workers, respectively, but did not provide information on vehicle or engine types. We included, however, the case-control study of professional drivers by Damber and Larsson,²⁴ as a majority of the lung cancer deaths were among truck drivers who would have been exposed to diesel exhaust.

We excluded two studies because the follow-up period would not allow for a 10-year latency interval. Kaplan¹⁴ studied a cohort of railroad workers from 1953 to 1958. The midpoint for transition to diesel fuels in the United States was 1952, and the transition was complete in 1959.¹³ Milne et al.²⁵ looked at occupations and lung cancer in Alameda County, CA, from 1958 to 1962. Risk estimates were provided for truck drivers, yet diesel trucks were not introduced until the late 1950s.²⁶

We included several studies with possibly adequate latency. Raffle²⁷ followed a cohort of bus company employees from 1950 to 1954. Diesel buses were introduced in England in the mid-1930s, and 85% of buses were using diesel by the end of World War II. It is likely that many of these workers would have been exposed for at least 10 years. In the Rushon et al.³⁸ cohort of bus garage maintenance workers, the follow-up averaged about 6 years, but no data on duration of employment were available. The Coggon et al.³⁹ case-control study of lung cancer restricted cases to men under 40 years of age and did not provide any data on duration of employment. The case-control studies of Lerchen et al.,³¹ Siemiatycki et al.³¹ and Williams et al.²² also did not provide sufficient data to make a good estimate of latency, but in each of these studies, subjects were ascertained well after the transitions to diesel fuels were completed.

We excluded the studies of Waller³³ and Luepker and Smith,³⁴ because of the selection bias that would likely result from restricting the cohort to actively employed workers. We included the study of Williams et al.,³² although it had only a 57% response rate to questionnaires.¹ The authors note that the response rate among cancer subjects with the more aggressive sites including lung, pancreas, and esophagus was slightly lower than the rate among subjects with the less aggressive cancers; still, as all other cancers were used as the controls for the lung cancer cases, we considered a large selection bias to be unlikely.

The 23 studies that we included in the pooled analysis are presented in Table 1, and those that we excluded are presented in Table 2. The tables include information on occupation, whether statistical adjustment for smoking was done, effect measures, and confidence intervals. Missing confidence intervals have been calculated for several studies.³²,³⁵,³⁶,³⁷,³⁸,³⁹,⁴⁰,⁴¹

In some cases, we found it necessary to pool data reported within an individual study. Siemiatycki et al.³⁶ presented odds ratios for four histologic categories of lung cancer separately; we combined these estimates into a single odds ratio using the weighting by precision technique described in the Methods. For
Swanson et al., 11 we pooled the race-stratified odds ratios for white men and black men. For Steenland et al., 39 we combined the odds ratios for the strata 25-34 and ≥35 years employment, and for the nested case-control study of Gustavson et al., 40 we combined the strata for cumulative exposure indices of 20-30 and ≥30.

The case-control study of Garshick et al., 41 stratified the analysis by age, as they demonstrated a lower prevalence of diesel exposure in employees older than 64 years. The data shown in Table 1 and used in the pooled analysis are for workers less than 64 years old.

The studies done by Williams et al., 32 Boffetta et al., 42 and Swanson et al., 11 included data for more than one occupational group; we used the effect measures for each group in the pooled analysis. Although the case-control study of Boffetta et al., 32 presented a separate analysis for truck drivers, no separate result for any other occupational group was presented. In the analysis, we use the data for all "probably exposed" occupations.

We observed relative risks of less than one in only two of the 23 studies meeting our inclusion criteria. These studies by Edding et al., 36 and Lerchen et al., 37 were also the two smallest studies, each with less than 10 lung cancer cases. No study that included more than 10 lung cancer cases had relative risks of less than one.

We conducted pooled analyses for the following subgroups of studies: (1) all included studies; (2) case-control studies; (3) cohort studies; (4) cohort studies using internal reference populations; (5) cohort studies making external comparisons; (6) studies adjusted for smoking; (7) studies not adjusted for smoking; and (8) studies by occupational groups.

The results of the pooled analyses are presented in Table 3 and in Figure 1. Statistical tests for heterogeneity and adjusted and unadjusted confidence intervals are also presented in Table 3. The pooled relative risk estimate for lung cancer from exposure to diesel exhaust using all studies was 1.33 (95% CI = 1.24-1.44). Subanalyses of studies stratified on study methods showed similar results. Stratification of studies by exposure setting showed greater effects among railroad workers (RR = 1.44; 95% CI = 1.30-1.60) and truck drivers (RR = 1.49; 95% CI = 1.36-1.65) than equipment operators (RR = 1.11; 95% CI = 0.89-1.38) and bus workers (RR = 1.24; 95% CI = 0.93-1.64).

Statistical evidence for heterogeneity was present among all studies combined, case-control studies, cohort studies, studies adjusted and not adjusted for smoking, and studies of bus employees (Table 3). Cohort studies and studies not adjusted for smoking showed relatively more heterogeneity than did the case-control and smoking-adjusted studies. When we subdivided cohort studies by comparison population, studies using external comparisons accounted for a larger proportion of the heterogeneity than those using internal comparisons. There was little statistical evidence of heterogeneity for the studies of railroad workers, equipment operators, and truck drivers.

Seven studies included in our analysis presented standard mortality rate based on external comparison populations. 32,37,38,39,41 Four of the seven studies presented sufficient information to adjust the lung cancer mortality for the healthy worker effect, as described in the Methods. The calculations and results for the four studies with available data are presented in Table 4. For the four adjusted studies, the pooled RR before adjustment was 1.09 (95% CI = 0.98-1.22; heterogeneity \( \chi^2 = 4.42, df = 3, P = 0.22 \)) and after adjustment was 1.33 (95% CI = 1.19-1.48; heterogeneity \( \chi^2 = 2.66, df = 3, P = 0.45 \)).

Nine studies included in the pooled analysis presented data for years of exposure or for years of employment.

---

**TABLE 2. Studies Excluded From Pooled Analysis**

<table>
<thead>
<tr>
<th>Authors and Year</th>
<th>Type*</th>
<th>Smoking Adjusted</th>
<th>Occupation</th>
<th>Cases</th>
<th>RR</th>
<th>95% CI</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benhamou et al., 32 1988</td>
<td>CC</td>
<td>Yes</td>
<td>Professional driver</td>
<td>128</td>
<td>1.42</td>
<td>1.07-1.89</td>
<td>Uncertain exposure</td>
</tr>
<tr>
<td>Buatari et al., 33 1985</td>
<td>CC</td>
<td>Yes</td>
<td>Transportation</td>
<td>45</td>
<td>1.1</td>
<td>0.7-1.6</td>
<td>Uncertain exposure</td>
</tr>
<tr>
<td>Kaplan, 34 1959</td>
<td>RC</td>
<td>No</td>
<td>Railroad worker</td>
<td>49</td>
<td>0.88</td>
<td>0.65-1.16</td>
<td>Inadequate latency</td>
</tr>
<tr>
<td>Leupker &amp; Smith, 35 1978</td>
<td>RC</td>
<td>No</td>
<td>Truck driver</td>
<td>34</td>
<td>1.21</td>
<td>0.84-1.69</td>
<td>Excluded retirees</td>
</tr>
<tr>
<td>Milne et al., 36 1983</td>
<td>CC</td>
<td>No</td>
<td>Truck driver</td>
<td>36</td>
<td>1.6</td>
<td>0.97-2.62</td>
<td>Inadequate latency</td>
</tr>
<tr>
<td>Waller, 37 1981</td>
<td>RC</td>
<td>No</td>
<td>Company worker</td>
<td>677</td>
<td>0.79</td>
<td>0.73-0.85</td>
<td>Excluded retirees</td>
</tr>
</tbody>
</table>

* RC = retrospective cohort study; PC = prospective cohort study; CC = case-control study.
† Confidence intervals are calculated from the published data as described in Methods.

---

**TABLE 3. Summary of Pooled Relative Risks**

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>RR</th>
<th>95% CI</th>
<th>( \chi^2 ) Heterogeneity</th>
<th>Adjusted 95% CI*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All studies</td>
<td>29</td>
<td>1.33</td>
<td>1.27-1.40</td>
<td>58.0</td>
<td>1.24-1.44</td>
</tr>
<tr>
<td>Case-control studies</td>
<td>14</td>
<td>1.33</td>
<td>1.21-1.47</td>
<td>20.5</td>
<td>1.18-1.51</td>
</tr>
<tr>
<td>Cohort studies</td>
<td>15</td>
<td>1.33</td>
<td>1.26-1.42</td>
<td>37.5</td>
<td>1.21-1.47</td>
</tr>
<tr>
<td>Internal comparison group</td>
<td>8</td>
<td>1.43</td>
<td>1.32-1.55</td>
<td>11.0</td>
<td>1.29-1.58</td>
</tr>
<tr>
<td>External comparison group</td>
<td>7</td>
<td>1.22</td>
<td>1.12-1.34</td>
<td>20.0</td>
<td>1.04-1.44</td>
</tr>
<tr>
<td>Smoking adjusted</td>
<td>16</td>
<td>1.35</td>
<td>1.22-1.49</td>
<td>23.4</td>
<td>1.20-1.52</td>
</tr>
<tr>
<td>Smoking not adjusted</td>
<td>13</td>
<td>1.33</td>
<td>1.25-1.41</td>
<td>34.5</td>
<td>1.20-1.47</td>
</tr>
<tr>
<td>Subanalysis by occupation</td>
<td>24</td>
<td>1.37</td>
<td>1.30-1.46</td>
<td>48.4</td>
<td>1.27-1.49</td>
</tr>
<tr>
<td>Railroad workers</td>
<td>6</td>
<td>1.44</td>
<td>1.30-1.59</td>
<td>5.6</td>
<td>1.30-1.60</td>
</tr>
<tr>
<td>Equipment operators</td>
<td>3</td>
<td>1.11</td>
<td>0.95-1.29</td>
<td>4.3</td>
<td>0.89-1.38</td>
</tr>
<tr>
<td>Truck drivers</td>
<td>10</td>
<td>1.49</td>
<td>1.36-1.64</td>
<td>9.8</td>
<td>1.36-1.65</td>
</tr>
<tr>
<td>Bus workers</td>
<td>5</td>
<td>1.24</td>
<td>1.07-1.43</td>
<td>14.8</td>
<td>0.93-1.64</td>
</tr>
</tbody>
</table>

* Heterogeneity-adjusted confidence intervals using method described by Shor et al.*
In 10 of the studies included in our pooled analysis, statistical adjustment for confounding from smoking was done. Three of these studies used continuous measures of smoking in the analysis,\textsuperscript{11,13,14} and five reduced the data to categories of cigarette consumption.\textsuperscript{14,16,30,39,41} The form of the smoking covariate was not presented in the study of Siemiatycki et al\textsuperscript{16} or the study of Williams et al.\textsuperscript{18} In Table 6, we present the forms of the smoking data used for statistical adjustment in 5 of the 10 studies that presented both smoking-adjusted and -unadjusted risk estimates for diesel exhaust. (Smoking-adjusted RRs presented in Table 6 are not necessarily the same as those presented in Table 1, as the unadjusted RRs presented in the papers did not always correspond to the exposure categories selected for the pooled analysis.)

**Discussion**

This analysis shows a small but consistent increase in the risk for lung cancer among workers with exposure to diesel exhaust. Of the 23 publications included in our analysis, only two present relative risks of less than one, and both of these were very small studies. Such a finding is extremely unlikely to be due to chance.

The pooled relative risk estimates center around 1.33 (95% CI = 1.24–1.44). Given the low relative risks observed in these studies, bias from known causes of lung cancer, such as smoking, is an important concern. In the pooled analyses, we found that the studies that adjusted for smoking had a similar pooled relative risk estimate (RR = 1.35) as the studies that did not control for smoking (RR = 1.33) (Table 3). This result gives some assurance that smoking does not explain the observed increased risks for diesel exhaust. A preferred method to assess confounding from a covariate is to compare crude and adjusted risk estimates within studies.\textsuperscript{44} As shown in Table 6, in four of five studies in which data on adjusted and unadjusted risk were presented, adjustment for smoking resulted in a decrease in the observed relative risk. In these five studies, the pooled smoking-unadjusted RR for all occupation and exposure duration categories was 1.34 (95% CI = 1.24–1.44; heterogeneity $\chi^2 = 1.39, df = 4, P = 0.84$), and the smoking-adjusted pooled RR was 1.26 (95% CI = 1.12–1.41; heterogeneity $\chi^2 = 10.87, df = 4, P = 0.03$). This small reduction in the pooled RR estimates would not be consistent with a major effect from residual confounding.

The study by Garshick et al\textsuperscript{14} found little difference in the lung cancer risk estimate due to diesel exhaust exposure in models treating smoking as pack-years as a continuous and categorical variable, cigarettes per day, years of smoking, or pack-years categories considering years since quitting smoking, showing that the classification scheme for smoking did not

---

**FIGURE 1.** Pooled relative risk estimates and heterogeneity-adjusted 95% confidence intervals for all studies and subgroups of studies included in the meta-analysis.

The employment duration-stratified data from seven of these studies that used internal reference groups are presented in Table 5. Except in the subanalysis of equipment operators by Hayes et al,\textsuperscript{18} the relative risk estimates consistently increase with duration of exposure.

**TABLE 4. Adjustment of Studies with External Reference Populations for the Healthy Worker Effect**

<table>
<thead>
<tr>
<th>Study</th>
<th>Cause of Death</th>
<th>Observed</th>
<th>Expected</th>
<th>SMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edling et al\textsuperscript{16} 1987</td>
<td>All causes</td>
<td>195</td>
<td>237.0</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>All causes excluding lung cancer</td>
<td>189</td>
<td>228.0</td>
<td>0.83</td>
</tr>
<tr>
<td></td>
<td>Lung cancer</td>
<td>6</td>
<td>9.0</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>Lung cancer (adjusted)</td>
<td>6</td>
<td>7.5</td>
<td>0.80</td>
</tr>
<tr>
<td>Gustafsson et al\textsuperscript{17} 1986</td>
<td>All causes</td>
<td>1,077</td>
<td>1,201.5</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>All causes excluding lung cancer</td>
<td>991</td>
<td>1,135.4</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>Lung cancer</td>
<td>71</td>
<td>55.1</td>
<td>1.29</td>
</tr>
<tr>
<td></td>
<td>Lung cancer (adjusted)</td>
<td>71</td>
<td>48.1</td>
<td>1.48</td>
</tr>
<tr>
<td>Rushton et al\textsuperscript{18} 1983</td>
<td>All causes</td>
<td>705</td>
<td>836.6</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>All causes excluding lung cancer</td>
<td>603</td>
<td>735.3</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>Lung cancer</td>
<td>102</td>
<td>101.3</td>
<td>1.01</td>
</tr>
<tr>
<td></td>
<td>Lung cancer (adjusted)</td>
<td>102</td>
<td>83.1</td>
<td>1.23</td>
</tr>
<tr>
<td>Wong et al\textsuperscript{17} 1985*</td>
<td>All causes</td>
<td>1,526</td>
<td>1,855.7</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>All causes excluding lung cancer</td>
<td>1,363</td>
<td>1,703.8</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>Lung cancer</td>
<td>163</td>
<td>151.9</td>
<td>1.07</td>
</tr>
<tr>
<td></td>
<td>Lung cancer (adjusted)</td>
<td>163</td>
<td>121.5</td>
<td>1.34</td>
</tr>
</tbody>
</table>

* Adjustments using data from >20 years employment duration.
change estimates of main effects. In this study, the lung cancer relative risk was 1.39 before and 1.41 after adjusting for smoking using a pack-year measure (Table 6). Other studies did not include such detailed consideration of smoking.

For the eight cohort studies that had internal comparison populations, the pooled RR was 1.43 (95% CI = 1.29–1.58; heterogeneity $\chi^2 = 11.0, df = 7, P = 0.14$). Although the use of an internal comparison group does not eliminate the potential for confounding bias from smoking, smoking prevalence is more likely to be similar among individuals within an industry or occupation.

Thus, we note three reasons why it is unlikely that the increased risks observed in these studies are due to smoking: (1) The pooled RR for studies adjusted for smoking was the same as for those studies not adjusted for smoking. (2) In those studies giving both smoking-unadjusted and -adjusted risk estimates, there was only a small reduction in the pooled RR from diesel exhaust exposure. (3) In studies with internal comparison populations, in which confounding is less likely, the pooled RR estimate was 1.43.

Lack of exposure data is another limitation of this meta-analysis. Only three of the studies included in the pooled analysis examined quantified exposure measures, and none of these had access to historical exposure measures. The studies of Coggon et al. and Gustavsson et al. made use of job-exposure matrices to evaluate exposure. In the remainder of studies considered in this report, occupation or industry of work is used as a surrogate measure of exposure to diesel exhaust. In cohort studies using general population comparison groups and in population-based case-control studies, a classification scheme based on occupation alone is likely to include those not exposed to diesel exhaust along with those exposed and thus may dilute the observed effect. In all of the studies, nondifferential exposure misclassification due to crude exposure definitions would also likely dilute any observed effects. Thus, although measures of exposure in these studies are limited, bias from exposure misclassification is unlikely to create an observed effect artificially.

A healthy worker effect for cancer has been observed in a number of studies. In re-analysis of lung cancer risk in an occupational cohort exposed to arsenic, Arrighi and Hertz-Picciotto showed that diverse methods for the control of the healthy worker effect enhanced the observed effect of exposure. Although the data available within the published reports included in this meta-analysis only allowed us to use a simple method to account for the health worker effect, we felt it important to demonstrate the potential magnitude and direction of this bias in our analysis.

For instance, the pooled analysis was heavily weighted by the study of Wong et al. in which the low all-cause SMR of 0.81 indicated the presence of a healthy worker effect. Although the lung cancer SMR for the longest duration of union membership was only 1.07, a trend was evident for
increasing lung cancer risk both by duration of union membership and by latency period. As shown in Table 4, in the Wong et al study, adjustment of the lung cancer SMR for >20 years of employment (SMR = 1.07) by the SMR for all causes (SMR = 0.82) produces an adjusted lung cancer SMR of 1.34 that is consistent with the pooled estimate using all studies. Thus, the healthy worker effect is a potential source of bias that would tend to underestimate the risks of diesel exhaust exposure in cohort studies with external comparison populations.

We did not find large differences in the pooled relative risk estimates after stratification of the studies on their design, on occupations studied, or on control for a smoking covariate. Heterogeneity was present, however, between studies in many of the pooled analyses. Studies stratified by industry or occupation tended to have less evidence for heterogeneity than either all studies or those stratified by study design. Differences in exposure to diesel exhaust are likely to explain some of the differences in results among studies. Studies of truck drivers and railroad workers were relatively homogeneous, but studies among bus company workers found dissimilar effects. The studies of bus company workers included several occupational categories, including mechanics, drivers, and other service workers.

Fixed effects methods as used in this analysis weight the studies on the within-study variance, which is primarily determined by study size. We did not attempt to account for the heterogeneity among studies with a random effects model, as described by DerSimonian and Laird. Such methods have been used to account for interstudy variation in the pooling of summary statistics and generally produce wider confidence intervals than the fixed effects model used in this analysis. Random effects models postulate that interstudy variation can be estimated by a single value and have been criticized for the assumption that studies are representative of a hypothetical population of studies. We felt that major sources of heterogeneity could be predicted from the study methods and populations. Thus, the underlying assumption that interstudy variance was constant was unlikely to be met. Furthermore, since the component of interstudy variation is assumed constant for all studies, smaller studies would be given a relatively larger weight than they would receive by fixed effects methods. Given these issues, we chose to use a model in which studies were weighted primarily on precision.

Publication bias is another potential limitation to meta-analysis. The tendency to not publish negative or null results is of particular concern and is thought to be more likely for small studies. Several small studies were included in our analysis. In the review by Steenland, we identified several studies of lung cancer among truck drivers that were presented as agency reports or documents. These unpublished studies were not included in our analysis; however, the risk ratios of these studies are similar to the those in published studies among truck drivers.

Funnel plots can be used to estimate whether a publication bias exists. The risk estimates are plotted against a measure of the study precision, such as the logarithm of the standard error. The scattering of the point estimates should decrease as the precision of the studies increases. A publication bias is suggested when larger studies having greater precision observe no effect. In Figure 2, we present a funnel plot of all studies included in the analysis. As study precision increases, the point estimates appear to congregate just below 1.5. Overall, the funnel plot supports our overall finding of an average relative risk estimate around 1.3 and does not indicate publication bias.

The possible causal association between exposure to diesel exhaust and lung cancer is an important public health question. Animal evidence has indicated that inhaled diesel exhaust may produce tumors of the lung in rats. The interpretation of occupational epidemiology in this field has been limited by the lack of quantitative exposure data in many of the studies and the potential for confounding from smoking given the relatively low risk estimates. This quantitative analysis of pub-

![Figure 2](image-url) Figure 2. Plot of observed relative risks of studies included in the meta-analysis against the standard error of the natural logarithm of the relative risk. Studies with available data are adjusted for the healthy worker effect.
lished occupational studies indicates that although the risk estimates for diesel exhaust exposure are small, they are consistently above one and are, in aggregate, unlikely to be due to chance. Confounding from smoking is also unlikely to explain all of the increased risks among diesel exhaust-exposed workers. The heterogeneity in observed relative risk estimates may be explained by differences between studies in methods, in populations studied and comparison groups used, in latency intervals, in intensity and duration of exposure, and in the chemical and physical characteristics of diesel exhaust.

References


