Influence of Alternative Exposure Estimates in the Diesel Exhaust Miners Study: Diesel Exhaust and Lung Cancer

Kenny S. Crump, \(^1\)* Cynthia Van Landingham, \(^2\) and Roger O. McClellan \(^3\)

The landmark Diesel Exhaust in Miners Study (DEMS) studied the relationship between diesel exhaust exposure (DEE) and lung cancer mortality of workers at eight nonmetal mines who were followed from beginning of dieselization of the mines (1947-1967) through December 31, 1997. The original analyses quantified DEE exposures using exposure to respirable elemental carbon (REC) to represent DEE, and CO as a surrogate for REC. However, this use of CO data, and the CO data themselves, have numerous shortcomings. We developed new estimates of REC exposures using historical data on use of diesel equipment, diesel engine horsepower (HP), mine ventilation rates, and the documented reduction in particulate matter emissions per HP in diesel engines from 1975 through 1995. These new REC estimates were applied in a conditional logistic regression of the DEMS nested case-control data very similar to the one applied in the original DEMS analyses. None of the trend slopes calculated using the new REC estimates were statistically significant (\(p > 0.05\)). Moreover, these trend slopes were smaller by roughly factors of five without control for radon exposure and factors of 12 with control for radon exposure compared to those estimated in the original DEMS analyses. Also, the 95% confidence intervals for these trend slopes had only minimal overlap with those for the slopes in the original DEMS analyses. These results underscore the uncertainty in estimates of the potency of diesel exhaust in causing lung cancer based on analysis of the DEMS data due to uncertainty in estimates of exposures to diesel exhaust.

**KEY WORDS:** DEMS study; diesel exhaust exposure; lung cancer

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1. INTRODUCTION

The Diesel Exhaust in Miners Study (DEMS) of workers at eight nonmetal mines in the United States is one of the most substantial studies conducted of the association between exposure to diesel exhaust emissions and lung cancer. Some basic characteristics of the eight mines are shown in Table I. The DEMS involved three distinct activities: an exposure analysis that developed estimates of the exposures of mine workers to respirable elemental carbon (REC), the indicator selected to represent diesel exhaust exposure (DEE),\(^{1-5}\) a cohort analysis by Attfield et al.,\(^6\) and a nested case-control study by Silverman et al.,\(^7,8\) that controlled for smoking and other covariables. DEMS was conducted by scientists at the National Institute of Occupational Safety and Health (NIOSH) and the National Cancer Institute (NCI), the agencies that funded DEMS. Results from DEMS had a major role in the deliberations of the International Agency for Research on Cancer that led to an upgrade of the classification of exposure to diesel exhaust from a probable human carcinogen to a known human carcinogen.\(^9\)

During 1998-2001, DEMS investigators conducted an exposure survey that collected samples of personal and area REC air concentrations within seven of the eight mines. These data were used to estimate REC exposures for different jobs and mine lo-
<table>
<thead>
<tr>
<th>Mine</th>
<th>State</th>
<th>Ore</th>
<th>Ventilation</th>
<th>Year of First Diesel Use</th>
<th>Primary Mode of Operation</th>
<th>CO</th>
<th>Radon</th>
<th>CFM/min (in thousands)</th>
<th>Diesel (Adj HP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Missouri</td>
<td>Limestone</td>
<td>Natural</td>
<td>1947</td>
<td>Cv/H</td>
<td>248</td>
<td>37</td>
<td>70</td>
<td>18</td>
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<tr>
<td>B</td>
<td>New Mexico</td>
<td>Potash</td>
<td>Mechanical</td>
<td>1964</td>
<td>Cv/Con, Ct</td>
<td>447</td>
<td>62</td>
<td>18</td>
<td>44</td>
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<tr>
<td>D</td>
<td>New Mexico</td>
<td>Potash</td>
<td>Mechanical</td>
<td>1950</td>
<td>Cv/H, Cv/Con, Ct</td>
<td>323</td>
<td>54</td>
<td>61</td>
<td>39</td>
</tr>
<tr>
<td>J</td>
<td>New Mexico</td>
<td>Potash</td>
<td>Mechanical</td>
<td>1952</td>
<td>Cv/H, Cv/Con, Ct</td>
<td>175</td>
<td>52</td>
<td>13</td>
<td>38</td>
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<tr>
<td>E</td>
<td>Ohio</td>
<td>Salt</td>
<td>Mechanical</td>
<td>1959</td>
<td>Cv/H</td>
<td>207</td>
<td>52</td>
<td>24</td>
<td>70</td>
</tr>
<tr>
<td>G</td>
<td>Wyoming</td>
<td>Trona</td>
<td>Mechanical</td>
<td>1962</td>
<td>Cv/Con, Ct</td>
<td>276</td>
<td>50</td>
<td>17</td>
<td>24</td>
</tr>
<tr>
<td>H</td>
<td>Wyoming</td>
<td>Trona</td>
<td>Vlechanica</td>
<td>1967</td>
<td>Cv/Con, L.W, Ct</td>
<td>2,263</td>
<td>39</td>
<td>40</td>
<td>15</td>
</tr>
<tr>
<td>I</td>
<td>Wyoming</td>
<td>Trona</td>
<td>Mechanical</td>
<td>1956</td>
<td>Cv/Con, Ct, L.W</td>
<td>2,000</td>
<td>54</td>
<td>54</td>
<td>20</td>
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<td>Total</td>
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<td>6,040</td>
<td>50</td>
<td>279</td>
<td>42</td>
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</table>

Notice: The above data were compiled from Stewart et al.(1) and the substantial DEMS data files. Primary Mode of Operation: Cv/H, conventional with truck haulage; Cv/Con, conventional with conveyor belts; Ct, continuous with conveyor belts; and L.W, long wall with conveyor belts. Specific data for ventilation rates and HP are shown for 1982 for illustrative purposes, as 1982 was the last year of effective exposure for workers, assuming a 15-year lag, as follow-up ended in 1997.
Influence of Alternative Exposure Estimates in DEMS cations during that time period. There were no REC measurements available at earlier times, although historical measurements of other air contaminants were available. From these several contaminants, variation in CO levels was selected to represent variation in REC levels, and four estimates of REC exposures were developed by DEMS investigators, each of which used CO as a surrogate for REC.\(^{1-5}\)

The DEMS cohort study\(^6\) involved 12,315 miners, 4,008 who only worked on the surface, 4,080 who only worked underground, and 4,227 who worked both underground and aboveground. Workers were followed through December 31, 1997. Two hundred deaths from lung cancer were identified in the cohort. A subset of 198 of these lung cancers were selected for a case-control study\(^7,8\) in which up to four controls were matched to each case by age, sex, race, mining facility, and birth cohort. Information on demographics, smoking habits, occupational and medical histories, etc. was collected using interviews. Both the cohort study\(^6\) and the case-control study\(^7,8\) found that lung cancer was positively associated with all four REC estimates.

Because of the evident strengths of the DEMS (e.g., long follow-up, large number of lung cancers, and high exposures to DEE in comparison to other studies) and its role in IARC's decision, the DEMS has attracted substantial interest from multiple parties interested in the issue of the cancer-causing potential of diesel engine exhaust exposure for workers and the general public. With funding from a coalition created by the Engine Manufacturers Association, we applied to NIOSH and NCI for access to the DEMS data in order to replicate the original findings and conduct additional analyses. We eventually obtained access to the DEMS data we needed for our analyses, although we were restricted to conducting analyses that involved alternative REC exposure estimates at the Research Data Center (RDC) of the National Center for Health Statistics (NCHS). Results of our earlier analyses of these data are provided in three publications.\(^{10-12}\)

A major motivation for this work relates to the potential use of the DEMS data for quantitative risk assessment: Are the DEMS data and associated analyses sufficiently robust for use in deriving quantitative estimates of the potency of DEE for causing lung cancer and, if so, what are the uncertainties in such potency estimates? A panel of the Health Effects Institute (HEI)\(^13\) is currently addressing this question and at a meeting on May 4, 2015, provided a progress report on its findings.

A rigorous evaluation of the utility of the DEMS data for quantitative risk assessment requires careful consideration of three key elements of an epidemiological investigation: (i) the exposure component, (ii) the vital data component, and (iii) the statistical methods utilized to evaluate the association between exposure and health outcome, in this case lung cancer. This article focuses on the exposure component of DEMS and extends the work of the original investigators of DEMS by applying an alternative exposure metric and control for radon.

Using DEMS exposure data provided by the DEMS investigators, Crump and Van Landingham\(^10\) evaluated the REC exposure estimates developed by DEMS investigators. Moolgavkar et al.\(^11\) reported on analyses that replicated the findings of the DEMS cohort study, and on extended analyses using biologically-based models. Crump et al.\(^12\) replicated the findings of the DEMS case-control study\(^7\) and, using the NCHS/RDC facilities, conducted analyses using alternative REC exposure estimates and control for radon exposure.

This article is an extension of Crump et al.\(^12\) and reports analyses using an alternative approach to estimating the REC exposure of mine workers. As noted earlier, all four REC estimates developed by the DEMS investigators relied upon using CO as a surrogate for REC. These estimates also took into account the rate (CFM) of mine air ventilation. However, there are a number of shortcomings both with the use of CO as a surrogate for REC, and with the CO data themselves.\(^10\) Specifically:

1. There are large uncertainties concerning the assumption of a consistent CO-REC relationship across engines and over time. The period of exposure of the DEMS cohort, 1947 through 1997, was a period of substantial changes in diesel technology and emissions.\(^14-16\) This included introduction of direct oxidation catalyst (DOC) technology that converts CO in the exhaust stream to CO\(_2\). Consequently, the improvements in diesel technology during the period of exposure of the DEMS cohort affected the relationship between CO and REC. However, the methodology used to estimate REC exposures in the DEMS cohort and case-control analyses assumed a fixed relation between CO and REC throughout most of the exposure period of DEMS.
(2) There are also large uncertainties in the assumed HP-CO relationship in the DEMS analyses (e.g., Fig. 1). CO data were only available from 1976 onward, whereas diesel use in the various mines began in 1947 in one mine, in the 1950s in four mines, and in the 1960s in the remaining three mines (Table I). Consequently, there were no CO data for predicting REC levels in most of the years of interest. The REC exposures used in the DEMS analyses assumed a consistent HP-CO relationship across engines and over time, through 1990. However, the improvements to diesel exhaust technology prior to 1990, including the use of DOCs, would have affected the relationship between HP and CO during this period. However, there was no accounting for these changes in the HP-CO relationship over time in the REC estimates used in the cohort and case-control analyses.

(3) A substantial portion (50%) of the CO measurements were below the detection limit (LOD) (Table I). Moreover, the fraction of CO samples below the LOD in the eight mines was quite variable, from 30% to 61%. Thus, a statistical approach was needed to impute CO concentrations for these samples.

These assumptions used in developing the DEMS REC exposure estimates used in cohort and case-control analyses regarding the HP-CO relationship and the CO-REC relationship imply that the HP-REC relationship did not vary with year prior to 1990. However, Fig. 2, which shows the relationship between HP and PM in exhaust of diesel engines built between 1975 and 1995, from data compiled by the U.S. Environmental Protection Agency, shows that this assumption is not valid. Instead, REC emissions per brake HP, which presumably are closely related to total PM emissions per brake HP, decreased precipitously between 1975 and 1995. This, coupled with the limitations in the CO data themselves, led us to conclude that more defensible estimates of REC could be obtained using yearly HP and CFM values, along with the documented reduction in PM emissions per HP in diesel engines over time (Fig. 2), to estimate REC levels (without using the CO data). This approach automatically takes into account improvements in diesel technology over time. (As an aside, there is evidence that PM emissions per brake HP were even higher for pre-1975 engines.) The alternative approach used here extends an approach used in our earlier publication, and was also discussed when the Health Effects Institute (HEI) Epidemiology Panel presented a preliminary report on the use of analyses of the DEMS data for quantitative risk analysis at the HEI Conference in Philadelphia, PA on May 4, 2015.

2. METHODS

We developed new REC exposures that used the detailed yearly HP and CFM information available for each of the eight mines. Thus, our estimates do not depend upon the CO data, which had 50% nondetects, or the relationship of CO levels to either HP or REC levels. This approach took account of the substantial differences in the total HP of diesel equipment used and ventilation rates in the various mines (Table I). Most notably, the approach took account of the reduction in PM emissions per HP in diesel engines manufactured between 1975 and 1995 (Fig. 2). The data points in Fig. 2 are reproduced from Fig. 2-20 in the EPA report, which was a plot of transient test results from multiple studies. The transient test cycles studied used a variable engine load as the exhaust emissions of a range of heavy-duty engines were evaluated. Some of the engines tested were manufactured by the same companies and were the same model and year as engines used in the mines. In extrapolating from the data in the EPA report to the mines, it is assumed that the PM emissions per HP in the tests are similar to the emissions of the diesel engines used in the mines from 1975 through 1995.

The REC exposure estimates used in the cohort and case-control analyses adjusted for possible differences in CO output per HP from engines purchased before and after 1990, which would also translate into differences in REC estimates. However this adjustment was not applied to REC estimates for two of the mines, and the amount of the adjustment came from fitting the CO data to the DEMS HP-CO statistical model and was not based on any external data on the reduction in CO per HP over time.

In the new REC exposures developed herein, the REC exposure of a worker in department d, job j, mine m, and year y was computed, following the general approach used by the original DEMS investigators, as:
Influence of Alternative Exposure Estimates in DEMS

Fig. 1. Graph of data from Yanowitz et al.\(^{(17)}\) of individual diesel engines of Ln(CO) versus Ln(HP) with regression line showing a barely statistically significant relationship and a great deal of scatter \((p = 0.05, r^2 = 0.01)\). This graph illustrates the uncertainty involved in assuming there is a consistent quantitative relationship between CO and HP, as assumed in REC estimates used in Silverman et al.\(^{(16)}\) (Figure from Crump and Van Landingham,\(^{(10)}\) permission requested.)

Fig. 2. Plot showing diesel engine certification for engine PM emissions in grams per brake horsepower-hour (g/bhp-h) as a function of model year. Reproduced from Ref. 14 (Table 2-8 and Figure 2-20). The sloping portion of the black line is the regression line \((y = 77.7053 - 0.0389x)\). The entire black line was used to estimate PM emissions as a function of model year. The regression line was not extrapolated beyond the data. Consequently, PM emissions per bhp-h were assumed to remain constant for model years before 1975 and also for model years after 1995.

\[
REC_{djm} = R_{ym} \times REF_{.REC}_{djm},
\]

where \(REF_{.REC}_{djm}\) is the estimate of REC exposure calculated by the DEMS investigators using the data obtained from the DEMS survey of mines conducted during 1998–2001,\(^{(4)}\) and

\[
R_{ym} = \frac{\sum_{i,eym} adj_{HP_{im}}H(e_i)}{\sum_{i,eym} adj_{HP_{im}}}/CFM_{ym},
\]

where \(i\) indexes engines, \(i,eym\) indicates the sum is over all engines operating in mine \(m\) during year \(y\), \(R_{ym}\) is the reference year for mine \(m\) (year the DEMS survey in mine \(m\) was conducted: 1998 for mines A, D, E, and H, 1999 for mines G and I, and 2001 for mine B), \(adj_{HP_{im}}\) is adjusted HP (adjusted to account for the fraction of time the engine was operating),\(^{(1,4)}\) \(e_i\) is the model year for engine \(i\), and \(H(y)\) is the PM output per brake HP-h for engines manufactured in year \(y\) defined by the graph in Fig. 2. Mine A (limestone) did not use forced ventilation and, following the approach in the original analysis,\(^{(4)}\) the \(REF_{.REC}\) values for mine B (also a potash mine) were used to calculate REC estimates for mine J.

The information available for calculating the ratio \(R_{ym}\) consisted of (1) the horsepower of each diesel engine used at each mine, along with the year the engine was presumed purchased, the first and last year the engine operated in the mine, the estimate percent of a shift the engine was used, and the number of shifts per day (out of three), (2) the yearly ventilation rate for each mine, and (3) the PM emissions per HP for each model year obtained from the graph in Fig. 2. The model year for an engine in the mines was assumed to be the year the engine was presumed to have been purchased (if not missing and no larger than the first year the engine was operated) and otherwise the first year the engine was operated.\(^{(4)}\) If the

\(^{(4)}\)The first year an engine was operated was not missing for any engine. The year an engine was presumed to have been purchased
last year an engine was operated in a mine was missing (4.1% of engines), the first year the engine was operated plus 7.6 years (the average duration of use in one of the mines) was used for the missing value. An engine was assumed to be operating in a mine in a given year if the year was between the first year and last year of operation, inclusive. Following Vermeulen et al.,\(^{(6)}\) adjHP was calculated as HP \(\times \text{fraction of a shift engine was operated)} \times \text{(number of shifts operated)/3.}

The resulting mine-specific yearly estimates of REC ("HP-CFM” estimates) for workers with the job of “mine operator,” compared to the primary REC estimates relied on in both the DEMS cohort study\(^{(6)}\) and the case-control study,\(^{(7)}\) are shown in Fig. 3. The differences between these REC estimates appear large enough possibly to make an important quantitative difference in the REC-lung cancer association. The magnitudes of the differences between two sets of REC estimates appear to roughly correspond to the adjHP-weighted average ages of the engines in operation in the mines in the mine-specific reference years (mine A: 5.6 years, mine B: 7.7 years, mine D: 10.7 years, mine E: 5.7 years, mine G: 5.2 years, mine H: 7.1 years, mine I: 9.7 years), with the closest correspondence coming in the mines with the oldest equipment. For example, the two sets of estimates appear to be in closest agreement for mines D and I (Fig. 3), which also had the oldest equipment. We note that the ages of the diesel engines operating in a mine during the reference year affect the denominator of the expression above for \(R_{\text{sym}}\), and thus play a pivot role in the REC estimates for a mine. Estimating the REC exposures in a given year for a mine using a ratio of an expression involving data in the given year to the corresponding expression involving the data in the reference year, multiplied by the REC estimate for the reference year, is necessary because REC samples were only available in the reference year for a mine.

These newly derived HP-CFM REC estimates were applied in a conditional logistic regression very similar to that of the original DEMS case-control analysis.\(^{(7)}\) Details are described in Crump et al.\(^{(12)}\) Cut points for exposure were selected to achieve approximately equal numbers of cases in each of four quartiles. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated for each quartile by conditional logistic regression. A trend test was conducted that applied the average exposure in a quartile to each member of the quartile. Two sets of potential confounders were controlled: one (“without radon”) did not include radon exposure (a known human lung carcinogen that was not controlled for in the original DEMS analyses),\(^{(7,8)}\) but included smoking status, body mass, respiratory disease status, and smokers in childhood residence, and a second set (“with radon”) included variables previously mentioned plus cumulative radon exposure, family history of lung cancer, and work in a high-risk job. It is noteworthy that radon levels, as reflected by the percentage of radon samples above limits of detection, were quite variable across the eight mines (Table I). This reflects differences in the presence of radon in the particular geologic structures being mined and differences in the ventilation rates among the mines.

3. RESULTS

Table II compares results from Silverman et al.,\(^{(7)}\) which used CO-based REC estimates with results obtained using the HP-CFM REC estimates. Results using the exposure metric cumulative REC exposure lagged 15 years are presented, as this metric showed the strongest association with lung cancer in earlier analyses of both cohort and case-control data.\(^{(6-8)}\) The trend tests are the same as used by Silverman et al.\(^{(7)}\) (with the minor exception that Silverman et al. assigned the median exposure in a quartile to every member of the quartile, whereas we assigned the average exposure). Results obtained by Silverman et al.\(^{(7)}\) are very similar to results obtained using the same REC values and “without radon” controls,\(^{(12)}\) indicating that the different controls used in the two analyses made little difference as long as radon was not included. None of the trend tests based on the new HP-CFM REC estimates reached statistical significance, although some ORs for the highest exposure groups were significantly increased when radon was not controlled. Trend tests were also conducted using the individual estimated HP-CFM REC values, rather than quartile averages. Results from these tests (not shown) had very similar interpretations to those in Table II, which assigned the average HP-CFM REC to all members of a quartile. ORs based on HP-CFM REC and restricted to subjects who only worked underground show monotone trends, but were nonsignificant (possibly due to the reduced sample sizes). However, it is important to note that the (nonsignificant) trend slopes...
Fig. 3. Graphs of mine-specific yearly estimates of REC for mine operators (load operators for mine A) used by Silverman et al. (7) based on using CO as a surrogate for REC, compared with corresponding REC estimates (labeled "HP-CFM") developed herein using diesel engine horsepower by year for each mine, the relationship between model year and PM emissions per HP shown in Fig. 2, and mine-specific ventilation rates by year, and which do not rely upon CO data.
### Table II. Comparison of Original Conditional Logistic Regression Results (Silverman\(^7\)) with Results of Similar Analyses Except Based on New REC Estimates Defined Using HP and CFM

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Quartiles of Cumulative REC, Lagged 15 Years (µg/m(^3)-yr)</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95% CI)</th>
<th>(P_{\text{trend}})</th>
<th>95% CI</th>
<th>Slope (µg/m(^3)-yr)(^{-1})</th>
</tr>
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<tbody>
<tr>
<td><strong>All Subjects</strong></td>
<td></td>
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<tr>
<td>Silverman et al(^7) &amp; REC estimates from Silverman et al(^7) &amp; “without radon” controls &amp; HP-CFM REC estimates and “with radon” controls</td>
<td>0 to &lt;3 &amp; 0 to &lt;3 &amp; 0 to &lt;6.6 &amp; 0 to &lt;6.6</td>
<td>49 &amp; 49 &amp; 49 &amp; 49</td>
<td>158 &amp; 158 &amp; 172 &amp; 172</td>
<td>0.74 (0.40-1.38) &amp; 1.0 (referent) &amp; 1.0 (referent) &amp; 1.0 (referent)</td>
<td>0.0016 &amp; 0.0006</td>
<td>0.00073* &amp; 0.00065*</td>
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<tr>
<td>3 to &lt;7 &amp; 3 to &lt;7 &amp; 6.6 to &lt;12 &amp; 6.6 to &lt;12</td>
<td>50 &amp; 50 &amp; 50 &amp; 50</td>
<td>228 &amp; 228 &amp; 191 &amp; 191</td>
<td>1.54 (0.74-3.20) &amp; 1.54 (0.74-3.20) &amp; 1.05 (0.58-1.93) &amp; 1.60 (0.79-3.24)</td>
<td>0.00006 &amp; 0.00006 &amp; (-0.000012, 0.00003) &amp; 0.06</td>
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<td>≥536 &amp; ≥536 &amp; ≥891 &amp; ≥891</td>
<td>50 &amp; 50 &amp; 50 &amp; 50</td>
<td>123 &amp; 123 &amp; 135 &amp; 135</td>
<td>2.83 (1.28-6.26) &amp; 1.62 (0.75-3.49) &amp; 2.37 (1.02-5.50) &amp; 1.60 (0.79-3.24)</td>
<td>0.00062 &amp; 0.00062 &amp; (-0.000012, 0.00003) &amp; 0.06</td>
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<tr>
<td><strong>All Subjects Who Ever Worked Underground</strong></td>
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<td>Silverman et al(^7) &amp; REC estimates from Silverman et al(^7) &amp; “without radon” controls &amp; HP-CFM REC estimates and “with radon” controls</td>
<td>0 to &lt;31 &amp; 0 to &lt;97 &amp; 0 to &lt;130 &amp; 0 to &lt;130</td>
<td>29 &amp; 31 &amp; 31 &amp; 31</td>
<td>92 &amp; 158 &amp; 158 &amp; 158</td>
<td>2.46 (1.01-6.01) &amp; 1.0 (referent) &amp; 0.0073 &amp; 1.0 (referent)</td>
<td>0.004 &amp; 0.01 &amp; 0.63</td>
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<tr>
<td>81 to &lt;325 &amp; 97 to &lt;384 &amp; 130 to &lt;331 &amp; 0 to &lt;130</td>
<td>29 &amp; 31 &amp; 31 &amp; 31</td>
<td>52 &amp; 90 &amp; 99 &amp; 144</td>
<td>2.41 (1.00-5.82) &amp; 1.90 (0.78-4.63) &amp; 2.03 (0.83-4.96) &amp; 3.45 (1.27-9.41)</td>
<td>0.00028 &amp; 0.00022 &amp; (-0.000052, 0.00003) &amp; 0.16</td>
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<tr>
<td>≥325 &amp; ≥891 &amp; ≥2,149 &amp; ≥2,149</td>
<td>29 &amp; 31 &amp; 31 &amp; 31</td>
<td>69 &amp; 80 &amp; 70 &amp; 70</td>
<td>5.10 (1.88-13.87) &amp; 2.73 (1.08-6.88) &amp; 3.84 (1.07-13.74) &amp; 3.84 (1.07-13.74)</td>
<td>0.69 &amp; 0.69 &amp; 0.69 &amp; 0.69</td>
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<tr>
<td><strong>All Subjects Who Only Worked Underground</strong></td>
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<tr>
<td>HP-CFM REC estimates and “without radon” controls &amp; HP-CFM REC estimates and “with radon” controls &amp; HP-CFM REC estimates and “without radon” controls &amp; HP-CFM REC estimates and “with radon” controls</td>
<td>0 to &lt;106 &amp; 0 to &lt;106 &amp; 0 to &lt;106 &amp; 0 to &lt;106</td>
<td>14 &amp; 14 &amp; 14 &amp; 14</td>
<td>26 &amp; 26 &amp; 26 &amp; 26</td>
<td>1.0 (referent) &amp; 1.0 (referent) &amp; 1.0 (referent) &amp; 1.0 (referent)</td>
<td>0.27 &amp; 0.36 &amp; 0.27 &amp; 0.27</td>
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<tr>
<td>106 to &lt;410 &amp; 130 to &lt;331 &amp; 130 to &lt;331 &amp; 130 to &lt;331</td>
<td>15 &amp; 31 &amp; 31 &amp; 31</td>
<td>28 &amp; 99 &amp; 99 &amp; 99</td>
<td>1.89 (0.4-9.07) &amp; 1.83 (0.73-4.61) &amp; 1.83 (0.73-4.61) &amp; 2.47 (0.79-7.73)</td>
<td>(-0.0000179, 0.00007) &amp; (-0.000020, 0.000030) &amp; (-0.0000179, 0.00007) &amp; (-0.000020, 0.000030)</td>
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<tr>
<td>410 to &lt;1,486 &amp; 531 to &lt;2,149 &amp; 531 to &lt;2,149 &amp; 531 to &lt;2,149</td>
<td>14 &amp; 31 &amp; 31 &amp; 31</td>
<td>17 &amp; 99 &amp; 99 &amp; 99</td>
<td>3.15 (0.47-21.05) &amp; 3.45 (1.27-9.41) &amp; 3.45 (1.27-9.41) &amp; 2.47 (0.79-7.73)</td>
<td>3.15 (0.47-21.05) &amp; 3.45 (1.27-9.41) &amp; 3.45 (1.27-9.41) &amp; 2.47 (0.79-7.73)</td>
<td></td>
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<tr>
<td>≥1,486 &amp; ≥2,149 &amp; ≥2,149 &amp; ≥2,149</td>
<td>15 &amp; 31 &amp; 31 &amp; 31</td>
<td>26 &amp; 70 &amp; 70 &amp; 70</td>
<td>4.73 (0.38-38.84) &amp; 3.84 (1.07-13.74) &amp; 3.84 (1.07-13.74) &amp; 2.5 (0.49-12.79)</td>
<td>4.73 (0.38-38.84) &amp; 3.84 (1.07-13.74) &amp; 3.84 (1.07-13.74) &amp; 2.5 (0.49-12.79)</td>
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*Calculated by us after reproducing Silverman et al\(^7\) results.
based on HP-CFM REC estimates are about fivefold smaller than the comparable ones calculated by Silverman et al. when radon is not controlled, about 12-fold smaller when radon is controlled, and the 95% CIs on the trend slopes only barely overlap.

4. DISCUSSION

The original DEMS investigators examined the robustness of their conclusions by considering four measures of REC. All four of these measures used CO as a surrogate for REC. As noted in this article, this use of the CO data, and the CO data themselves, involve a great deal of uncertainty. Herein we developed and applied REC estimates that did not require use of the CO data, but used yearly data on the horsepower of diesel equipment used in a mine, mine ventilation rates, and the documented reduction in PM output per brake HP of diesel engines manufactured between 1975 and 1995 (Fig. 2). In applying the test data in Fig. 2 to the engines used in the mines it is assumed that the relative reductions in PM emissions per HP between an engine manufactured in a given year and 1995 in the tested engines and those used in the mines are similar.

Analyses of the DEMS case-control data using these new REC estimates resulted in weaker and statistically nonsignificant associations between REC exposures and lung cancer. Moreover, trend slope estimates based on the new REC estimates were smaller, by factors of around 5 if exposure to radon was not controlled and factors of around 12 if radon exposure was controlled, than estimates made in the original DEMS case-control analysis. Statistically, the trend slopes based on the new REC estimates were only very marginally compatible with comparable estimates made in the original DEMS case-control analysis (i.e., the 95% CIs on the slopes derived using the new REC estimates barely intersected the 95% CIs on the slopes developed in the original DEMS analysis). These results demonstrate the uncertainty in quantitative estimates of the potency of diesel exhaust from the DEMS data stemming from uncertainty in the estimates of exposures to diesel exhaust. This uncertainty needs to be taken into account in any attempt to use the DEMS data to make quantitative estimates of the lung cancer risk from exposure to DEE.

The analyses described in this article were possible because the DEMS data were made available for these analyses by NIOSH and NCI through the NCHS. We appreciate the cooperation of the original DEMS investigators and the NCHS in making these data available to us. We believe such access to data should be commonplace. Whenever a complex study such as DEMS is to be used to inform or establish public policy, it is prudent to allow multiple investigators to have access to the data to evaluate the robustness of the original conclusions.

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The analyses reported herein were based upon data provided to us by the DEMS team, and we thank them for their cooperation in providing us access to these data. To address confidentiality issues, we were restricted to conducting statistical work involving alternative exposure estimates at the Research Data Center (RDC) at the National Center for Health Statistics. We express appreciation to Dr. Frances McCarty of the RDC for her assistance in conducting the analyses reported herein. The findings and conclusions in this article are those of the authors and do not necessarily represent the views of the funding organizations, or of the RDC, the National Center for Health Statistics, or the Centers for Disease Control and Prevention.

REFERENCES


