

Industrial Injuries Advisory Council Information Note

Lung cancer and diesel exhaust emissions in miners

February 2016

1. The possible carcinogenicity of diesel engine exhaust is a topic that the Industrial Injuries Advisory Council (IIAC) has had under review. In September 2015, it published an Information Note relating to lung cancer, bladder cancer and diesel exhaust emissions across a range of occupations.¹ That Information Note set aside for separate consideration the case for prescribing under the Industrial Injuries Disablement Benefit (IIDB) Scheme for lung cancer in miners exposed to diesel exhaust emissions; it is this topic which is covered by this Note.
2. The process of diesel combustion and its products are described in the earlier Note. In brief, in diesel engines, air is introduced and heated to temperatures in excess of 425°C by compression. The fuel is injected into the combustion chamber by a high-pressure injection system and is mixed with the hot air until the jet of fuel becomes sufficiently hot for auto-ignition to occur. The centre of this burning jet is very rich in fuel, leading to the formation of elemental carbon, partially burned fuel, polycyclic aromatic hydrocarbons (PAHs) and carbon monoxide. At the outer edges of the burning jet of fuel, excess air leads to high temperatures and the formation of oxides of nitrogen (International Agency for Research on Cancer (IARC), 2013).
3. Since Rudolf Diesel patented the diesel engine in 1898, the technology has found many applications including (from the 1920s onwards) in heavy goods vehicles (HGVs), buses, tracked vehicles and railway locomotives (IARC, 2013). Until the mid-1980s, a wide variety of diesel engine designs and technologies were available, but increasingly stringent regulations have led to changes in fuel composition and after-combustion treatment techniques (e.g. selective catalytic reduction or nitrogen oxide absorber-based systems and particle filtration) to reduce fuel emissions (IARC, 2013).
4. Diesel engine exhaust comprises a combination of particles, chemical molecules and gases, some of which (such as PAHs adsorbed onto particles) are hazardous and potentially carcinogenic. IARC has classified diesel engine exhaust as a 'definite' carcinogen in humans, based on epidemiological, experimental and other evidence (Benbrahim-Tallaa *et al.*, 2012; IARC, 2013).

¹ Industrial Injuries Advisory Council. Lung and Bladder Cancer and Diesel Exhaust Emissions. September 2015. <https://www.gov.uk/government/publications/lung-and-bladder-cancer-and-diesel-exhaust-emissions-iiac-information-note>

5. Reported increases in risk in IARC's monographs were most evident for lung cancer and bladder cancer, the two tumours on which the Council's previous Note¹ focussed. Various studies of lung and bladder cancer in railway workers and professional drivers of HGVs, buses and trams were considered, some of which indicated an elevated risk of lung cancer and, to a lesser extent, bladder cancer.
6. It should be noted, however, that before recommending prescription for diseases that 1) are not specific to occupation, and 2) in which cases caused by occupation cannot reliably be distinguished in the individual case from those that would arise irrespective of occupation (such as lung and bladder cancer), the Council normally seeks research evidence that the risks are more than doubled (relative risk (RR)>2) in workers with a given exposure relative to a suitable comparator. The aim is to identify circumstances in which attribution to work can be established on the balance of probabilities in the individual claimant. As previously described, the evidence did not suggest that this standard could be met in relation to lung and bladder cancer in professional drivers of HGVs, buses and trams, and railway workers, nor in relation to bladder cancer in miners.¹
7. However, interpretation of the evidence on lung cancer and diesel emissions in underground miners is complicated by the potential for co-exposure to other carcinogens found in mines, such as radon and silica, and for confounding by cigarette smoking. A further consideration with prescription in mind is to identify potentially qualifying exposures (those sufficient to at least double risks), defined in a way that would be feasible to administer within the IIDB Scheme. For these reasons further evidence has been collected on the topic.

The epidemiological evidence

8. The Council has taken the studies on lung cancer in miners contained in the IARC monograph *Diesel and gasoline engine exhausts and some nitroarenes*, 2013 (IARC 2013), as a starting point and supplemented these with a literature review. The full list of studies considered in this Note are summarised in a concluding appendix and a brief summary of them appears below.
9. In all, they represent 12 research reports (involving six studies of cohort design, two of case-control design, and one case-control analysis nested within one of the cohort populations), as well as two reports that pooled data across investigations. Data derive from North America, Europe, the Caribbean and a single British study based on coal miners in the UK. They included mine and quarry workers engaged in extracting coal and non-metal ores, metal ores, potash and various salts. Sample sizes were large, comprising in one instance an entire national population (Guo *et al.*, 2004), in another 1.1 million workers (Sritharan *et al.*, 2014), several thousand miners in certain of the cohort studies (Boffetta *et al.*, 1988; Miller *et al.* 1997; Johnston *et al.*, 1997; Nuemeyer-Gromen *et al.*, 2009; Mohner *et al.*, 2013; Attfield *et al.*, 2012; Bergdahl *et al.*, 2010), and in excess of 14,000 cases of lung cancer in a pooled case-control analysis (Taeger *et al.*, 2015). Exposures were defined variously, as mentioned below. The Council also considered a recent over-arching review by an

independent scientific panel on behalf of the Health Effects Institute, an independent non-profit research organisation (HEI, 2015) and a review on dose-response relationships (Vermeulen *et al.*, 2014).

10. A number of the studies reported risks of lung cancer that were more than doubled by assumed exposure to diesel, for subgroups defined in various ways (Boffetta *et al.*, 1988; Guo *et al.*, 2004; Nuemeyer-Gromen *et al.*, 2009; Bergdahl *et al.*, 2010; Attfield *et al.*, 2012; Taeger *et al.*, 2015). Some reports, however, did not find an increased risk (Miller *et al.* 1997; Johnson *et al.*, 1997; Richiardi *et al.*, 2006; Sritharan *et al.*, 2014).
11. Among the first group, Boffetta *et al.* found mortality from lung cancer to be elevated 2.67-fold among 2,034 miners from the US and Puerto Rico, relative to a large comparator group of non-miners. Analysis accounted for workers' smoking habits but could not exclude concurrent exposures to silica and radon in the mines and no specific data were available on exposures to diesel engine exhaust.
12. A census-linkage study (Guo *et al.*, 2004) which employed data on all economically active Finns, found a more than doubling of lung cancer incidence in men whose longest held job was in metalliferous mining or quarrying (relative risk (RR) 3.26), while RRs were increased (but not as much as doubled) for non-metal ore and unspecified mining or quarrying. However, no account could be taken of smoking habits or exposures to other known lung carcinogens and no data were available on exposures to diesel engine exhaust.
13. Mortality risks were also elevated in a cohort of German potash miners whose exposures to radon, silica, asbestos and heavy metals were considered low (Nuemeyer-Gromen *et al.*, 2009). They were more than doubled, however, only in those with more than 10 years of employment underground (RR 3.30). Partial account was taken of smoking habits in the analysis. A further re-analysis, based on estimated exposure to respirable elemental carbon (REC) found no relationship to dose when expressed in this way (Mohner *et al.*, 2013). No data were available on exposures to diesel engine exhaust.
14. In a cohort of Swedish iron ore miners (Bergdahl *et al.*, 2010), the incidence of lung cancer was elevated overall (RR 1.48), although risks were more than doubled only in one of the two mines studied, and then within the lowest band of estimated exposure (0-10 ppm-years of nitrogen dioxide as a surrogate for diesel exhaust) as well as in those most exposed. Historical exposures to radon and crystalline silica were assessed within the study, and the latter was associated with lung cancer risk, but findings for diesel emissions were unadjusted for radon and quartz.
15. A cohort study of some 12,000 blue-collar workers from the USA (Attfield *et al.*, 2012) was noteworthy because the investigated limestone, potash and salt mines were selected to minimise exposure to silica, radon and asbestos. It also provided the most detailed assessment of exposures to diesel, with estimates of REC based on personal samples at seven of the study's eight facilities, collected blind to findings on mortality. Estimates were made of cumulative exposure and average intensity of

exposure to REC, both for short- and long-term workers, with separate figures for surface-only and ever-underground workers. Comparisons were made by level of exposure. Mortality from lung cancer was elevated overall by some 21% to 33%. Under certain reasonable assumptions, RRs were more than doubled among those in the top half of cumulative exposure ($> 445 \mu\text{g}/\text{m}^3\text{-year}$ of REC) and in those with an average intensity of exposure $>51 \mu\text{g}/\text{m}^3$.

16. Attfield's mortality analysis could not allow for smoking habits. However, a nested case-control study of incident lung cancer within the same cohort (Silverman *et al.*, 2012) interviewed 198 affected cases and a sample of 562 non-cases to collect this further information. After allowance for smoking habit, RRs were more than doubled for those ever-worked in underground jobs in the top three-quarters of estimated cumulative exposure to REC (although cumulative exposure bands were defined at different cut-points than for the mortality study).
17. Several other studies found no increase in risk of lung cancer among miners. Of these, a notable investigation was that by the Institute of Occupational Medicine (IOM), of British coal miners (Miller *et al.*, 1997; Johnston *et al.*, 1997). Diesel transport was very rare in British coal mines before the early 1950s. Thereafter, diesel vehicles for transport were introduced gradually in many mines, although there were also many where such transport was unsuitable. Of 10 pits included in the IOM's study, six used diesel vehicles at various times. No data were available on the concentrations of particulate emissions from diesel engines employed in different coalmining occupations over the study period, but two surrogates of exposure were considered, estimated time spent travelling to and from pitheads on diesel-drawn vehicles and data on concentrations of oxides of nitrogen (the main sources of which were diesel vehicles and shot-firing). By the first of these metrics, most men had relatively little exposure but a few had much higher values. Deaths from lung cancer overall were less common than expected from rates in the local population (RR 0.86), a finding that was statistically significant. No evidence was found of an increase in lung cancer mortality with time spent travelling on diesel locomotives, after allowing for known confounders such as age and amount smoked; nor was the fitted model improved significantly by including estimates of diesel exposure based on oxides of nitrogen. Various sensitivity analyses were performed, but these did not alter this conclusion materially.
18. A Canadian cohort study, based on census linkage data, considered mortality in a cohort of 1.1 million working men, including 14,000 miners (Sritharan *et al.*, 2014). No excess of lung cancer was found in relation to diesel engine exhaust, although detail on the study is limited as it was reported only as a research abstract.
19. A case-control study from Turin, involving 595 incident cases of lung cancer and controls from the general population found a reduced risk in exposed miners (odds ratio (OR) 0.53). Analysis considered smoking habits and past occupational exposure to known carcinogens, but only five of the cases were miners, and the study had limited power to exclude a doubling of risks.

20. A pooled analysis of 14 other case-control studies containing over 14,000 cases of lung cancer offered greater statistical power (Taeger *et al.*, 2015). In an analysis which allowed for smoking habits, ORs were elevated for ever-working as a miner or quarryman (OR 1.55) or as a coal miner (OR 1.40), but were only as much as doubled for ever having worked as an ore miner (OR 2.34). There was no strong evidence for an exposure-response relationship based on duration of employment. Among coal miners, risks were highest after 20 or more years of employment, although they were not doubled (OR 1.73).
21. Two other general reports considered by the Council concerned exposure-response relationships to diesel more generally. A meta-analysis involving some reports on miners (but also some investigations of professional drivers) found an increased RR per unit of cumulative exposure to diesel engine exhaust, expressed as concentration of REC (Vermeulen *et al.*, 2014). A review by an expert panel for the HEI, in considering the Attfield-Silverman (Diesel Exhaust in Miners) study and a second report from the trucking industry (the Trucking Industry Particle Study), found reasonable evidence on which to develop quantitative assessments of risk, while suggesting that further work was required to characterise the risk at lower exposures (HEI, 2015).
22. In case these putative dose-response estimates could be related to actual exposures in British mines, IAC sought evidence from the Health and Safety Executive on assessed levels of diesel emissions within its hazards database. Only a very few measurements were identified of exposures expressed in terms of REC (in coal mines). These were of a relatively high magnitude, although perhaps undertaken because of safety concerns. In practice, no firm estimates were available that could be said to be representative of everyday working conditions.

Summary and discussion

23. IARC has classified diesel engine exhaust as a 'definite' carcinogen in humans, as judged by a range of evidence, including animal experiments and mechanistic studies. The epidemiological reports concerning lung cancer in miners have been considered in this report, along with some more recent epidemiological evidence.
24. Elevated risks of these cancers have been reported in many (but not all) of the studies, in keeping with IARC's assessment of the hazard. In several investigations, RRs have been more than doubled in circumstances that appear not to be explained solely by concurrent exposure to known carcinogens (e.g. tobacco smoke, silica, radon, asbestos) as opposed to diesel.
25. Not all studies carried information specifically on exposures to diesel engine exhaust. However, the high quality US Diesel Exhaust in Miners Study (Attfield *et al.*, 2012; Silverman *et al.*, 2012) suggests an exposure-response relationship with estimated REC. Although this was not confirmed in the analysis by Mohner *et al.* (2013), reports such as that by Vermeulen *et al.* (2014) also point in this direction.

26. While diesel emissions are likely to be carcinogenic, and on this evidence may be carcinogenic in some circumstances within the mining industry, one challenge posed to the Council in prescribing for such circumstances lies in identifying a practical metric with which to define the qualifying exposure schedule. Prescription in terms of the research metric “REC”, even if this were perfectly established, would offer claimants no advantage, as no mechanism exists at present to enable decision makers to relate this to claimants’ employment histories. Only limited data are available on risks expressed in more practically verifiable terms, such as years spent underground; such data as do exist have not related closely to estimates of diesel exposure. Risks may apply to some parts of the mining industry and not to others, but this remains unclear.
27. A second related challenge for prescription concerns identifying the likely levels of exposure to diesel emissions in British mines. While higher risks of lung cancer have been found in studied mines overseas (in the US, Puerto Rico, Germany and Sweden) and across a range of extractive activities (involving metal ore, potash, low silica limestone and salt), it remains unclear how close exposures in these studies are to those encountered typically in British mines. Substantial variability of exposure could exist, depending for example on the extent of vehicle usage and ventilation in different mines.
28. In this respect, the findings of the sole British study on diesel and lung cancer in miners (Miller *et al.*, 1997; Johnston *et al.*, 1997) count against prescription. Although this study did not have sophisticated estimates of exposure to elemental carbon with which to assess mortality risks, it identified a reduced overall risk of lung cancer in British coal miners, and at most a very weak relationship with proxies of cumulative exposure. A single study of this kind does not disprove the hazard posed by diesel emissions in mines; but it does provide evidence against a doubling of risk of lung cancer, at least in the studied British coal mines of the period, one possible explanation being that exposures were simply lower than in reports from other settings. Higher risks could pertain in other kinds of British mine or in British coal mines outwith the IOM’s investigation and the Council considered this possibility, but found no evidence for or against the proposition.
29. On balance the Council has concluded that it cannot define a practicable level of exposure to diesel emissions in mines and mining operations above which the risk of lung cancer could be said to be doubled and which could be used as a basis for developing a prescription schedule. For this reason it does not recommend prescription at present. However, the Council remains open to the possibility of prescribing should further evidence come to light. A watch will be maintained for new research in this area and further evidence on the topic would be welcomed, especially information on relevant patterns of exposure in the UK.
30. It should be stressed that a disease can still be occupationally-caused and an important focus for preventive activity at lower levels of RR than the threshold for prescription. The latter is used to allow attribution to work on the balance of probabilities in individual claimants, in line with the legislative requirements of the

IIDB Scheme. This Note should not be construed as indicating that the Council disagrees with IARC's classification of diesel engine exhaust as a human carcinogen.

This information note contains technical terms which are explained in an accompanying glossary.

References

- Attfield MD, Schleiff PL, Lubin JH, Blair A, Stewart PA, Vermeulen R, Coble JB, Silverman DT. The diesel exhaust in miner study: a cohort mortality study with emphasis on lung cancer. *J Natl Cancer Inst* 2012; 104: 869-83.
- Benbrahim-Tallaa L, Bann RA, Grosse Y, Lauby-Secretan B, El Ghissassi F, Bouvard V, Guha N, Loomis D, Straif K, International Agency for Research on Cancer Working Group. Carcinogenicity of diesel-engine and gasoline-engine exhausts and some nitroarenes. *Lancet Oncol* 2012; 13(7): 663-4.
- Bergdahl IA, Jonsson H, Eriksson K, Damber L, Javholm B. Lung cancer and exposure to quartz and diesel exhaust in Swedish iron ore miners with concurrent exposure to radon. *Occup Environ Med* 2010; 67: 513-8.
- Boffetta P, Stellman SD, Garfinkel L. Diesel exhaust exposure and mortality among males in the American Cancer Society prospective study. *Am J Ind Med* 1988; 14: 403-15.
- Guo J, Kauppinen T, Kyyronen P, Londoym ML, Keikkila P, Pukkala E. Occupational exposure to diesel and gasoline engine exhausts and risk of lung cancer among Finnish workers. *Am J Ind Med* 2004; 45: 483-90.
- HEI. Diesel Emissions and Lung Cancer: An Evaluation of Recent Epidemiological Evidence for Quantitative Risk Assessment, 2015. Available on the web at <http://pubs.healtheffects.org/view.php?id=446> (accessed November 2015).
- IARC. Diesel and gasoline engine exhausts and some nitroarenes. IARC monographs on the evaluation of carcinogenic risks to humans. Volume 105, 2013. IARC, Lyon, France.
- Johnston AM, Buchanan D, Robertson A, Miller BG. Investigation of the possible association between exposure to diesel exhaust particulates in British coalminers and lung cancer. Institute of Occupational Medicine Historical Research Report TM/97/04, 1997. Institute of Occupational Medicine, Edinburgh.
- Miller BG, Buchanan D, Hurley JF, Robertson A, Hutchison PA, Kidd MW, Pilkington A, Soutar CA. The effects of exposure to diesel fumes, low-level radiation, and respirable dust and quartz, on cancer mortality in coalminers. Institute of Occupational Medicine Historical Research Report TM/97/04, 1997. Institute of Occupational Medicine, Edinburgh.
- Mohner M, Kersten N, Gellissen J. Diesel motor exhaust and lung cancer mortality: reanalysis of a cohort study in potash miners. *Eur J Epidemiol* 2013; 28: 169-68.
- Neumayer-Gromen A, Razum O, Kersten N, Seidler A, Zeeb H. Diesel motor emissions and lung cancer mortality – results of the second follow-up of a cohort study in potash miners. *Int J Cancer* 2009; 124: 1900-6.
- Richiardi L, Mirabelli D, Calisti R, Ottino A, Ferrando A, Boffetta P, Merletti F. Occupational exposure to diesel exhausts and risk for lung cancer in a population-based case-control study in Italy. *Ann Oncol* 2006; 17: 1842-7.
- Silverman DT, Samanic CM, Lubin JH, Blair AE, Stewart PA, Vermeulen R, Coble JB, Rothman N, Schleiff PL, Travis WD, Ziegler RG, Wacholder S, Attfield MD. The diesel

exhaust in miners study: a nested case-control study of lung cancer and diesel exhaust. *J Natl Cancer Inst* 2012; 104: 855-68.

Sritharan J, Hardt J, Kone A, Harris A, Saini J, Demers P. Cancer risks among Canadian mining workers in a population-based cohort. *Occup Environ Med* 2014; 71(Suppl 1): A101.

Taeger D, Pesch B, Kendzia B, Behrens T, Jockel KH, Dahmann D, *et al.* Lung cancer among coal miners, ore miners and quarrymen: smoking-adjusted risk estimates from the synergy pooled analysis of case-control studies. *Scand J Work Environ Health* 2015; 41: 467-77.

Vermeulen R, Silverman DT, Garshich E, Vlaanderen J, Portengen L, Steenland K. Exposure-response estimates for diesel engine exhaust and lung cancer mortality based on data from three occupational cohorts. *Environ Health Perspect* 2014; 122: 172-7.

Glossary

Types of study

Cohort study: A study which follows up a population of individuals (usually defined by a workplace) over time and compared the rate of disease or mortality among those within the cohort or with an external comparison population. The outcome is expressed as a Rate Ratio or **Relative Risk**, **Standardised Incidence Ratio**, **Standardised Mortality Ratio**, or **Hazard Ratio** depending on the type of analysis and the disease outcome being studied.

Case-control study: A study which compares people who have a given disease (cases) with people who do not (non-cases, also known as controls) in terms of exposure to one or more risk factors of interest. Have cases been exposed more than non-cases? The outcome is expressed as an **Odds Ratio**, a form of **Relative Risk**.

Measures of association

Statistical significance and P values: Statistical significance refers to the probability that a result as large as that observed, or more extreme still, could have arisen simply by chance. The smaller the probability, the less likely it is that the findings arise by chance alone and the more likely they are to be 'true'. A 'statistically significant' result is one for which the chance alone probability is suitably small, as judged by reference to a pre-defined cut-point. (Conventionally, this is often less than 5% ($P < 0.05$)).

Relative Risk (RR): A measure of the strength of association between exposure and disease. RR is the ratio of the risk of disease in one group to that in another. Often the first group is exposed and the second unexposed or less exposed. *A value greater than 1.0 indicates a positive association between exposure and disease.* (This may be causal, or have other explanations, such as bias, chance or **confounding**.)

Odds Ratio (OR): A measure of the strength of association between exposure and disease. It is the odds of exposure in those with disease relative to the odds of exposure in those without disease, expressed as a ratio. For rare exposures, odds and risks are numerically very similar, so the OR can be thought of as a **Relative Risk**. *A value greater than 1.0 indicates a positive association between exposure and disease.* (This may be causal, or have other explanations, such as bias, chance or **confounding**.)

Standardised Mortality Ratio (SMR): A measure of the strength of association between exposure and mortality; a form of **Relative Risk (RR)** in which the outcome is death. The

SMR is the ratio of the number of deaths (due to a given disease arising from exposure to a specific risk factor) that occurs within the study population to the number of deaths that would be expected if the study population had the same rate of mortality as the general population (the standard).

By convention, SMRs (and standardised incidence rates (SIR) as described below) are usually multiplied by 100. Thus, an SMR (or SIR) of 200 corresponds to a RR of 2.0. For ease of understanding in this report, SMRs (or SIRs) are quoted as if RRs, and are not multiplied by 100. Thus, *a value greater than 1.0 indicates a positive association between exposure and disease.* (This may be causal, or have other explanations, such as bias, chance or **confounding**.)

Standardised incidence ratio (SIR): An SIR is the ratio of the observed number of cases of disease (e.g. cancer) to the expected number of cases, multiplied by 100. The ratio is usually adjusted to take account of differences in the population evaluated with the comparison or “normal population”, due to age, gender, calendar year, and sometimes geographical region or socioeconomic status.

Incidence Rate Ratio (IRR): A form of **Relative Risk**. The ratio of the **incidence rate** of a new event in an exposed population relative to an unexposed one.

Hazard Ratio: A form of **Relative Risk** used in survival analysis (a branch of statistics that deals with analysis of the elapsed time until events occur); the ratio of the hazard rate in the exposed to the unexposed (where a hazard rate represents the event rate at a given time, assuming survival until that time or beyond).

Other epidemiological terms

Incidence rate: The rate of occurrence of a new event of interest (e.g. cancer) in a given population over a given time period. (The rate is often expressed in terms of cases per year of ‘person-time’, and so incorporates the numbers at risk of the event, the time for which they are at risk and the numbers that go on to develop that event.)

Confidence Interval (CI): The **Relative Risk** reported in a study is only an *estimate* of the true value of relative risk in the underlying population; a different sample may give a somewhat different estimate. The CI defines a plausible range in which the true population value lies, given the extent of statistical uncertainty in the data. The commonly chosen 95% CIs give a range in which there is a 95% chance that the true value will be found (in the

absence of bias and confounding). *Small studies generate much uncertainty and a wide range, whereas very large studies provide a narrower band of compatible values.*

Confounding: Arises when the association between exposure and disease is explained in whole or part by a third factor (confounder), itself a cause of the disease, that occurs to a different extent in the groups being compared.

For example, smoking is a cause of lung cancer and tends to be more common in blue-collar jobs. An apparent association between work in the job and lung cancer could arise because of differences in smoking habit, rather than a noxious work agent.

Studies often try to mitigate the effects of ('control for') confounding in various ways such as: restriction (e.g. only studying smokers); matching (analyzing groups with similar smoking habits); stratification (considering the findings separately for smokers and non-smokers); and mathematical modelling (statistical adjustment).

Lagged analysis: This is a method of analysis in which it is assumed that exposure that occurs at a certain interval of time immediately before the occurrence of disease is not relevant to causation and should be excluded in the assessment of the relationship between exposure and disease.

*For example, in calculating the **incidence rates** of cancer in exposed and unexposed populations, a 10 year lagged analysis would discard in its calculations any exposures which occurred in the most recent ten years. Thus, for each person-year of follow-up, and each cancer case, exposure would only be assessed up until ten years beforehand.*

Job exposure matrix: This is a tool used to assess exposure to potential health hazards in epidemiological studies in which jobs are assigned their typical exposures and individuals are assumed, by virtue of their job title, to have incurred these exposures.

Appendix

Table 1 – Studies of diesel engine exhaust and lung cancer in miners

Reference, study period	Study type	Exposure assessment	Relative Risks (95% Confidence Interval) (Number of cases)	Additional information
Boffetta <i>et al.</i> , 1988 1982-1984	Sub-cohort of 2,034 miners from a study of >1,200,000 Americans and Puerto Ricans aged >30 (0.8% lost to follow-up)	Questionnaire to ascertain current job, last job if retired and job held longest. Occupation as a miner self-reported. Study limited by lack of information on exposure to diesel exhaust (21% of the cohort had missing data).	RR, miner vs. not miner unexposed to diesel exhaust: 2.67 (1.63 to 4.37, n = 15)	Analysis age- and smoking-adjusted. 3% of the cohort were of unknown smoking status and were excluded from related analyses. Subjects without diesel exhaust exposure tended to be older, and more often had missing data and a higher mortality rate. Only 14% of miners were classified as having definite exposure to diesel. Miners could have been exposed to other carcinogens, such as silica and radon.
Miller <i>et al.</i> , 1997; Johnston <i>et al.</i> , 1997 1959-1992	Cohort study of 18,166 UK coal miners from the Pneumoconiosis Field Research study with smoking data (<4% could not be traced)	Estimates of exposure to diesel emissions were based on 1) time spent travelling on diesel-drawn vehicles (reconstructed from time records and pit geology); 2) data on NO _x concentrations, available for some of the mines.	SMR for lung cancer (local rates): 0.86 (0.80 to 0.93, n = 632) No significant increase in risk was found by level of diesel exposure (both for unlagged analysis and analysis lagged by 15 years)	Exposure to respirable dust and quartz, radon and thoron daughters was available from previous analyses. Modelling adjusted for age, smoking habits at entry to the cohort, different calendar periods of cohort entry and (for some analyses) regional differences in background cause-specific mortality.
Guo <i>et al.</i> , 2004 1971-1995	All economically active Finnish men born during 1906-1945 who participated in the national population census of 1970 (follow up almost complete)	Occupation held for the longest period in 1970: classified by expert review as having been exposed to diesel exhaust (using NO ₂ in air as an indicator) but not gasoline exhaust (Finnish Job Exposure Matrix).	SIR for mine and quarry work involving metal ore: 3.26 (2.28 to 4.51, n=36) SIR for mine and quarry work involving non-metal ore: 1.85 (1.59 to 2.14, n=181) SIR for other and unspecified mine and quarry work: 1.73 (1.35 to 2.19, n=70)	Figures were unadjusted for smoking, and possible exposure to silica and radon.

Reference, study period	Study type	Exposure assessment	Relative Risks (95% Confidence Interval) (Number of cases)	Additional information
Richiardi <i>et al.</i> , 2006 1991-1992	595 incident cases of lung cancer and 845 population controls matched for age and sex in Turin, Italy (response 81% among cases; 85% among controls)	For certain pre-defined jobs with assumed high exposure, a diesel-specific job-specific question set was interviewer-administered	OR for miners: 0.53 (0.14 to 2.04, n=5)	Adjusted for age, sex, education level, smoking and having worked in occupations entailing exposure to known lung carcinogens.
Neumeyer-Gromen <i>et al.</i> , 2009 1970-2001	Cohort of 5,862 German potash miners who worked for at least a year underground (completeness of follow-up not stated)	Estimates of diesel exposure were obtained in 1992, and expressed as total carbon in respirable dust. Because technology had not changed, these levels were assumed to be representative of previous exposure.	Overall SMR: 0.73 (0.57 to 0.93, n= 61) RR for ≥ 4.90 mg/m ³ -years of carbon: 1.28 (0.61 to 2.71, n=61) RR for working underground ≥ 10 years: 1.50 (0.66 to 3.43, n=37) RR for ≥ 4.90 mg/m ³ -years of carbon, adjusted for time since hire and calendar year: 2.53 (1.13 to 5.69, n=61) RR for working underground > 10 years, adjusted for time since hire and calendar year: 3.30 (1.30 to 8.37, n=37)	Diesel exhaust was introduced into the mines in 1969. Tobacco smoking records were available for 80% of the cohort. Internal analysis adjusted for smoking, which led to higher risk estimates. Exposure to radon, silica dust, asbestos and heavy metals were considered insignificant.
Mohner <i>et al.</i> , 2013 1970-2001	Re-analysis of Neumeyer-Gromen <i>et al.</i> , 2009, controlling for potential confounders such as smoking and previous occupational history (completeness of follow-up not stated)	The job-exposure matrix from previous analysis was converted to REC, to allow comparison with results of other recent studies.	Adjusted RR for REC: 1 st tertile (<983 $\mu\text{g}/\text{m}^3$ -years) 1.00 2 nd tertile (983-1,500 $\mu\text{g}/\text{m}^3$ -years) 1.77 (0.85 to 3.69) 3 rd tertile (>1,550 $\mu\text{g}/\text{m}^3$ -years) 1.04 (0.47 to 2.27)	

Reference, study period	Study type	Exposure assessment	Relative Risks (95% Confidence Interval) (Number of cases)	Additional information
Bergdahl <i>et al.</i> , 2010 1958-2000	Cohort study of 8,321 iron ore miners with low exposure to radon, employed in 1923-1998 (completeness of follow-up not stated)	Historical exposures to radon, crystalline silica and diesel exhaust were assessed via a job exposure matrix using company measurement data.	SIR overall: 1.48 (1.22 to 1.78, n=112) RR for Kiruna mine: 0-10 ppm-years 1.09 (0.70 to 1.171, n= 31) 10-15 ppm-years 0.69 (0.27 to 1.72, n=5) >15 ppm-years 0.87 (0.42 to 1.83, n= 9) RR for Malmberget mine: 0-10 ppm-years of NOx, 2.41 (1.53 to 3.79, n=33) 10-15 ppm-years, 2.45 (1.29 to 4.64, n=12) >15 ppm-years, 3.36 (1.92 to 5.88, n=20)	The study group included both surface and underground miners. Both mines produced mainly magnetite. The Kiruna mine also produced small amounts of apatite, while the Malmberget mine extracted small amounts of haematite. The RRs present for diesel exhaust were unadjusted for radon and quartz (silica).
Attfield <i>et al.</i> , 2012 1960-1997	Cohort of 12,315 blue-collar workers who were employed in one of eight non-metal mines in the USA for at least 1 year after diesel equipment had been introduced (completeness of follow-up not stated)	Exposure to diesel exhaust was assessed blind to mortality data based on REC for all surface and underground jobs by year and facility using measurements taken during 1998-2001.	SMR overall: 1.26 (1.09 to 1.44, n=203) SMR for underground work: 1.21 (1.01 to 1.45, n=122) SMR for surface-only work: 1.33 (1.06 to 1.66, n=81) HR (internal analysis by quartile cumulative exposure $\mu\text{g}/\text{m}^3\text{-y}$ with 15 year lag): 1.0 (referent, n=30) 1.50 (0.86 to 2.62, n=31) 2.17 (1.21 to 3.88, n=30) 2.21 (1.19 to 4.09, n=31)	The mines were chosen to minimise exposure to silica, radon and asbestos and compromised one low silica limestone, three potash, one salt (halite) and three trona (sodium carbonate) operations.

Reference, study period	Study type	Exposure assessment	Relative Risks (95% Confidence Interval) (Number of cases)	Additional information
Silverman <i>et al.</i> , 2012 1960-1997	Case-control study nested within the cohort studied by Attfield <i>et al.</i> , 2012: 198 cases of lung cancer and 562 controls	As for Attfield <i>et al.</i> , 2012	OR in underground miners (quartiles of cumulative exposure with 15-year lag): 1.0 (referent, n=29) 2.46 (1.01 to 6.01, n=29) 2.41 (1.00 to 5.82, n=29) 5.10 (1.88 to 13.87, n=29)	Histories of tobacco smoking, occupation and previous respiratory diseases obtained by interview. Controls were randomly sampled from all members of the cohort who were alive before the day the case died and were matched on birth year, sex, ethnicity and mine. Increased risks with cumulative exposure were found both in smokers and non-smokers.
Sritharan <i>et al.</i> , 2014 (Abstract only, study period not given)	Cohort of 1.1 million male workers aged 25-74 (including >14,000 miners) created through linkage of the 1991 Census to the Canadian mortality, cancer registration databases and annual tax summary files (completeness of follow-up not stated)	Not stated but assumed to be based on job title.	No excess of lung cancer was found.	

RR = Relative Risk; SMR = Standardised Mortality Ratio; SIR = Standardised Incidence Ratio; OR = Odds Ratio; HR = Hazard Ratio. The meaning of these terms is explained in the glossary

Table 2– Pooled analysis of case control studies of diesel engine exhaust and lung cancer

Report data	Description	Exposure assessment	Relative Risks (95% Confidence Interval) (Number of cases)	Additional information
Taeger <i>et al.</i> , 2015	Pooled analysis 15,609 cases of lung cancer and 18,531 controls from 14 case-control studies (Synergy study)	A subject was coded as a coal or ore miner if he had ever worked as a miner in coal or ore mining, or as quarryman respectively. All other participants constituted the reference group.	Smoking adjusted analyses: RR for ever worked as a miner or quarryman: 1.55 (1.34 to 1.79, n=436) RR for ever worked as a coal miner: 1.44 (1.18 to 1.67, n=297) RR for ever worked as an ore miner: 2.34 (1.36 to 4.03, n=53) Analyses by duration of employment and time since last employment showed higher RRs for all above categories, but no strong evidence of a monotonic increasing risk.	Analyses were adjusted for smoking and employment in other at-risk occupations. 80% of controls were from general population. 80% of information on occupation and smoking was from face-to-face interviews.