assignment, work area) that could be used to develop individual exposure estimates; and 4) availability of historical industrial hygiene data on diesel exposure and the feasibility of using these data, as well as It current exposure data, to estimate past exposure. The feasibility effort was conducted in two phases from 1992 to 1994. Non-metal mines were selected that had documented low levels (<0.1 WL) of radon. In Phase I, a telephone survey of the 41 U.S. underground non-metal mining operations that actively employed 50 or more employees was made to identify mines that had used diesel equipment for at least 10 years prior to 1980. Based on the telephone survey, 24 mines were chosen for site visits (Appendix A). Information from the site visits was used to rank the 24 mines for suitability for the main study (Appendix B). Phase II of the feasibility study was a comprehensive industrial hygiene survey of current and past exposure to diesel exhaust at one mine. This demonstrated that it was possible to link job history information collected from personnel records with environmental exposures measured both during 1976-1978 and currently.

4. STUDY OBJECTIVES AND OUTLINE

4.A Justification

Few mortality studies using quantitative measures of diesel exhaust directly to assess exposure-response exist. Those that do have defects and are incomplete. For this reason, NIOSH and NCI propose to undertake a comprehensive study to investigate lung cancer mortality and diesel exhaust exposure. The findings from the feasibility study indicate that a cohort and a nested case-control study of lung cancer among non-metal miners who have been exposed to diesel exhaust is feasible. Non-metal miners are an optimal study group to evaluate the relation between diesel exhaust exposure and lung cancer risk for several reasons. First, the feasibility study indicated that diesel exposure among the underground mining population is 5 to 40 times greater than that observed in other diesel-exposed populations. The high exposure levels will facilitate detection of exposure-response if such truly exists. Two surrogates of diesel exhaust exposure are nitrogen dioxide (NO_2) and elemental carbon. Woskie et al.[68] measured NO_2 levels at railroad yards and found arithmetic mean exposures of 111 ppb (SD = 104) for the highest exposure group (mechanic shop workers). During our feasibility study, we measured personal NO_2 exposures at one potash mine and found an arithmetic mean of 527 ppb (SD = 211) for the underground production workers.[c] Those heavily exposed workers (the belt crew) had average NO_2 exposures of 780 ppb (SD = 313). Submicrometer elemental carbon levels averaged 5.1 micrograms per cubic meter ($\mu g/m^3$) (SD = 3.4) for road (long distance) drivers in the trucking industry.[69] By comparison, underground production workers during our feasibility study were exposed to an average concentration of 237 $\mu g/m^3$ of elemental carbon (SD = 171), while underground foreman and maintenance workers had mean exposures of 160 and 50 $\mu g/m^3$ respectively. Second, this is the first cohort with adequate information to quantify historical exposures to diesel exhaust. The historical exposure assessment is particularly strengthened by the availability of industrial hygiene (IH) data from surveys carried out at non-metal mines in 1976 (Section 8.C.6.a). Third, the follow-up period for the cohort ranges up to 45 years, which should be sufficient to detect an elevation in lung cancer mortality. Fourth, information on cigarette smoking and other potential confounders will be obtained and controlled for in the analysis.

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[c] All underground workers apart from foremen and maintenance workers.

4.B Primary objectives

The principal objectives of the study are as follows:

i) To evaluate mortality, particularly from lung cancer, with regard to diesel exhaust exposure among non-metal miners, standardizing for age, smoking, and other potential confounders.

ii) To determine whether lung cancer mortality increases in relation to level of exposure to diesel exhaust after controlling for age, smoking, and other potential confounders.

iii) To evaluate the association between measured levels of diesel exhaust components in the air and: a) nitro-PAH derived metabolites in the urine, and b) DNA adducts in exfoliated epithelial bronchial and urothelial cells and peripheral white blood cells, using samples from miners who are currently occupationally exposed to diesel exhaust and from those who are not exposed.

4.C Study overview

The study will consist of a cohort mortality study, a nested case-control study based on lung cancer cases identified in the cohort study, and a biomarker study. Large mines (> 50 employees) known to have low levels of potential confounders (e.g., silica and radon) and moderate to high levels of diesel exhaust underground were selected as potential mines for study. Previous investigation has shown these mines to have suitable and comprehensive personnel records. Ten of these mines are expected to provide records for over 8,000 miners for input to a cohort mortality study (184,000 or more person-years).[d] An exposure assessment will be undertaken at each operating mine, and quantitative as well as cruder surrogate measures of worker exposures developed.

4.D Study power

The cohort study was designed to be large enough to provide sufficient cases for a case-control study of adequate power. For this reason, the following statement and discussion of power concentrates on the case-control study. However, it should be noted that the cohort study has greater than 90% power to detect a trend in RR from 1 for nonexposed to 1.4 for low/moderate exposure to 2.0 for high exposure, based on a 5% alpha level, and assuming 50% nonexposed, 25% low/moderate exposed, and 25% high exposed.[e] The power curve for the case-control study is shown in Figure 4.1. This shows that at a 4:1 matching ratio, an alpha level of 5%, an OR of 1.4 and 2.0 for the low/moderate and high exposure groups, respectively, and exposure distribution as noted above, the case-control study would have close to 80% power. Use of matching ratios less than 4:1 would provide unacceptably low power (especially for 2:1 or less). If the trend is 1 to 1.6 to 2.5 (an overall doubling in risk) with increasing exposure level, the power increases to over 95%. Finally, the power to detect an overall OR of 1.5 (i.e., OR = 1.3 and 1.7 for low/moderate and high exposure) is better than 50%.

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[d] Record collection will be organized such that mines of greatest utility to the study (i.e., with the highest exposures and best IH and personnel records) will be visited first. Record collection will be terminated as soon as we determine that the study will provide sufficient cases for the case-control study (see section 4.D). It is expected that only ten mines will have to be visited, and even fewer may be needed.

[e] The distribution of workers across the exposure groups was evaluated using the feasibility study information. Table A.1 in Appendix A shows part of this information (the percentage of workers underground, i.e., exposed to diesel exhaust, at each mine). This amounted to about 40% of the total, with 10% more coming from diesel exposed workers on the surface.