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Title: Chronic Obstructive Pulmonary Disease (COPD) Mortality and Diesel Exhaust in Miners

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Partnerships: National Cancer Institute, Division of Cancer Epidemiology and Genetics

<u>Topic</u>: Injury and Disease Exposure and Risk Factors Priority Area: Surveillance and Epidemiology Methods

Problem Statement and Justification: We propose to study chronic obstructive pulmonary disease (COPD) mortality among underground and surface miners in the Diesel Exhaust in Miners Study (DEMS). We focus on COPD, rather than asthma, because the airway inflammation enhanced by diesel particles appears to play a role in a broader array of respiratory and allergic diseases. In the original DEMS study, the SMR for COPD was 0.86, suggesting a slightly protective effect of work in the mines. Results stratified by work location were even more counterintuitive; the SMR was higher for miners who worked only on the surface than for miners who worked underground, 0.95 versus 0.80, respectively. Rather than accepting these SMRs at face value, we believe that together with the biologic literature, they provide compelling evidence of bias. SMRs rely on the general population as the unexposed reference group – a group which is not comparable to miners in terms of underlying health status since it includes individuals unfit for work. Thus the SMR for chronic lung diseases likely obscures the true diesel hazard in mines, particularly for underground miners. In a recent published review of the literature, we concluded that the evidence suggests diesel exhaust increases the risk of COPD, but that quantitative exposure metrics are needed to specify the exposure-response relation.

Impact of the Research: We propose to examine diesel exhaust-related risk of COPD, using data from DEMS, a NIOSH and NCI study of 12,315 miners in 8 U.S. non-metal mines. We will examine quantitative estimates of long term exposure to diesel exhaust, measured as respirable elemental carbon (REC), in relation to COPD mortality in miners who worked at the surface or below ground. We will apply the parametric g-formula, implemented as intervention studies designed to assess risk of COPD under a series of exposure scenarios based on plausible exposure limits for diesel exposure in mines. This approach addresses the healthy worker survivor effect (HWSE), as characterized by a time-varying confounder (leaving work) that is also caused by prior exposure and therefore on the causal pathway from exposure to death. Because the REC estimates were based on an extensive retrospective exposure assessment conducted by NIOSH scientists, this study will fill the scientific research gap. Because our analytic strategy addresses HWSE bias, we will be able to estimate the unbiased risk of COPD under specified exposure limits of diesel, which can be used to guide standards for both surface and underground mining.

Objectives and Research Approach: We will estimate a quantitative exposure-response curve for diesel exhaust and COPD mortality based on the NIOSH exposure assessment, using an internal reference group of lower exposed miners, and adjusting for confounding by smoking. We will also address the HWSE bias that arises when miners with respiratory symptoms leave work or transfer from underground to surface jobs with lower exposure. We will produce two manuscripts that will clarify the long-term risk of COPD and provide the health basis for considering diesel standards in mines.