Methods One hundred and thirty-six cancer patients surveyed for an occupational disease of the bladder were investigated for the course of the disease. EDTA blood samples were drawn. Patients were genotyped for the following polymorphisms: N-acetyltransferase 2 (NAT2, substrate: aromatic amines), glutathione S-transferase M1 (GSTM1, substrate: reactive metabolites of PAH), glutathione S-transferase T1 (GSTT1, substrate: small molecules with 1 or 2 carbon atoms), UDP-glucuronyltransferase 1A2 rs11892031 (UGT1A2, substrate: aromatic amines), rs9642880 (close to c-Myc gene) and rs710521 (close to TP63). Frequencies of recurrences were analysed by means of chi-square test, relapse-free times were analysed by unadjusted Cox regression. The combined effect of the polymorphisms was analysed by means of the weighted polygenic risk score (PRS).
Results In 38% of the patients a recurrence was reported (median 1.54 years). All investigated polymorphisms except for rs710521 showed a tendency to more frequent recurrences and shorter recurrence-free times, in particular NAT2 (slow vs fast: hazard ratio HR 1.75, 95% CI: 0.98 to 3.12, p=0.0582), GSTM1 (positive versus negative: HR 1.77, 95% CI: 0.70 to 4.48, p=0.2222) and GSTM1 (negative vs positive, HR 1.37, 95% CI: 0.76 to 2, 45, p=0.2972). The PRS was significantly associated with shorter recurrence-free times (PRS >median vs PRS ≤median score: 18 vs 26 months, HR=1.93, 95% CI: 1.06 to 3.53; p=0.0327), the risk of recurrence was also higher (47% vs 31%, OR=1.94, 95% CI: 0.93 to 4.06, p=0.0757).
Conclusion Polymorphic xenobiotic metabolising enzymes may modulate the prognosis of occupational bladder cancer.

1712 CASE STUDY IN DATA ACCESS AND REANALYSIS: DIESEL ENGINE EXHAUST AND LUNG CANCER MORTALITY IN THE DIESEL EXHAUST IN MINERS STUDY (DEMS) COHORT USING ALTERNATIVE EXPOSURE ESTIMATES AND RADON ADJUSTMENT

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Introduction The Diesel Exhaust in Miners Study (DEMS), conducted by National Institute of Occupational Safety and Health (NIOSH) and National Cancer Institute (NCI), included 12 315 workers with 200 observed lung cancers from 8 U.S. non-metal mines (3 trona, 3 potash, 1 salt and 1 limestone). Retrospective cohort and case-control analyses by NIOSH and NCI scientists yielded a positive association between diesel exhaust exposure (DEE), represented by a respirable elemental carbon (REC) metric estimated retrospectively from carbon monoxide measurements, and lung cancer mortality. This finding was a major factor in the International Agency for Research on Cancer (IARC) classification of DEE as a human carcinogen.
Methods Our team was given access to the DEMS data and conducted analyses to first replicate the original analyses and then conduct extended re-analyses. Our re-analyses focused on

a. use of an alternative exposure metric developed using historical data on diesel equipment, engine horse power and ventilation rates without dependence on use of carbon monoxide as a surrogate for REC,
b. inclusion of radon as a covariate in statistical models, and
c. subgroup heterogeneity.

Results We found associations with cumulative REC and average REC intensity using the alternative REC estimates were generally attenuated compared with those found using the original DEMS REC estimate. Most findings were statistically nonsignificant, especially after control for radon exposure, which substantially weakened associations with the original and alternative REC estimates. No significant findings were detected among all miners who worked exclusively underground. However, associations were anomalously strong among limestone miners; no association with REC or radon was found among workers at the other seven mines.
Conclusions The large differences in results based on alternative exposure estimates, control for radon, and stratification by worker location or mine type highlight areas of uncertainty and the limited robustness of the DEMS data. These limitations must be considered in any extrapolation of the DEMS findings to other populations, and especially in using them for quantitative risk assessment. Moreover, the recently complete Advanced Collaborative Emissions Study (ACES) study sponsored by the Health Effects Institute and conducted at the Lovelace Respiratory Research Institute, Albuquerque, NM, indicated that chronic inhalation exposure of rats to low dilutions of exhaust from new technology diesel engines did not produce lung cancer. The results of both the DEMS and ACES findings will be reviewed to provide perspective for evaluating the cancer hazards of diesel-powered equipment, past, present and future.

1712a EVALUATING EXPOSURE TO DIESEL ENGINE EXHAUST

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Introduction Exposure to diesel engine exhaust continues to be a concern for employers who utilise either traditional (TDE) or new technology diesel (NTDE) exhaust-powered equipment. Such exposure may occur at elevated concentrations over a short period of time (acute) or at much lower concentrations on a daily basis over their working lifetime (chronic). Individuals in each of these exposure scenarios may present with different symptomology or health effects. In either case, accurately assessing an individuals exposure to diesel exhaust should be done in the context of appropriate toxicological endpoint of relevance (e.g., irritation, carcinogenicity, etc.).
Methods A review of the toxicological and industrial hygiene literature was conducted to identify historical trends in exposure sampling methodology and analytical surrogate chosen. Additional studies were reviewed which highlighted the important compositional distinctions between TDE and NTDE and also the reported symptomology which presented following acute exposures.
Results Historically, a number of analytical surrogates for diesel exhaust have been utilised to assess exposure including both particulate phase and gaseous compounds. While at the present time, sampling for elemental carbon or respirable elemental carbon (REC) is currently the most utilised surrogate, recent literature indicates that the elemental carbon fractions of TDE and NTDE may substantially differ. Furthermore, a number of studies noted that acute exposure to diesel exhaust may elicit transient irritant or neurophysiological effects