States. Studies of underground miners, who often were exposed to high concentrations of radon, have been used to estimate public health impacts of domestic radon exposure. The healthy worker survivor bias - a condition resulting when individuals in relatively good health tend to work longer and thus become more exposed than individuals in relatively poor health - may be influencing estimates of occupational radon impacts on lung cancer, but this bias has not been thoroughly explored.

Method We implemented G-estimation of a structural nested accelerated failure time model to adjust for time-varying confounding by employment history to partially control the healthy worker survivor bias in the Colorado Plateau uranium miners cohort.

Results 615 miners in our cohort died of lung cancer. Assuming no time-varying confounding, we estimate a time ratio (95% confidence intervals) per 1000 working level months of exposure of 1.55 (1.53, 1.58), and 1.95 (1.86, 2.04) when to control healthy worker survivor bias, a relative increase of 126%. Estimates of the radon-associated excess cases were 118 under standard methods and 179 when we controlled for the healthy worker survivor bias.

Conclusions There is evidence of a healthy worker survivor bias in standard analyses of the radon-lung cancer association in this cohort. The findings suggest need for further consideration of current estimates of the health impact of radon in occupational and environmental settings.

Conclusions Adverse mental health outcomes were found among individuals in the GuLF STUDY population but further work is necessary to clarify the factors leading to these outcomes.

Objectives During clinical observations of patients with heart diseases and stress related disorders, it has been observed increased pain sensitivity on specific locations on the skin of the sternum.

Method This sensitivity was measured as the pressure pain sensitivity (PPS) by Ull Metre instrument. Measured PPS values 60 or more indicate high PPS, values below 40 indicate low PPS.

Results There are presented results of PPS measurements in 371 men (av. age 43.6 + 10.4 years, 19–66 years); 345 of them were without diagnosis of disease. Average PPS values (whole group) were 36.6 + 9.5 (1. measurement) and 36.7 + 8.5 (2. measurement) (r = 0.89). Road drivers (177 men, PPS values 35.7 + 9.4, resp. 36.4 + 10.9) were not significantly different against other occupations (194 men, PPS values 36.5 + 9.5, resp. 37.8 + 11.4). Men with neuropsychological disorders were statistically significantly different against asymptomatic men (PPS values 50.8 + 14.8, resp. 67.3 + 11.4 vs. 38.8 + 13.3, resp. 35.5 + 5.9, p = 0.002, resp. less than 0.001) and also against men with different diagnosis (PPS values 50.8 + 14.8, resp. 67.3 + 11.4 vs. 38.8 + 13.3, resp. 43.4 + 19.7, p = 0.015, resp. 0.001). Men with other than neuropsychological symptoms doesn’t significantly in PPS values against asymptomatic men.

Conclusions Method of measurement of PPS could be helpful in medical fitness assessment to work in safety related occupations and is useful for health promotion intervention program. Supported by research project of Charles University in Prague PVO/UK P25/LF1/2.

Objectives The aim of our study is to validate and complement recently reported epigenetic biomarkers of exposure to tobacco smoke based on data from two cohorts and to characterise their prospective nature.

Method We used case-control data from studies nested in two prospective cohorts: the Italian component of the European Prospective Investigation into Cancer and Nutrition study (N = 620) and the Norwegian Women and Cancer study (N = 382) as a validation dataset. For each of the participant, genome wide methylation profiles were acquired from blood samples collected at enrolment using the Illumina HM450 DNA methylation array. We performed epigenome wide association studies within each dataset to assess the relation between methylation levels and smoking-related variables, controlling for technical variation (batch effects) and confounding factors (including white blood cell composition).
Oral presentation

**Results** We found 8 and 897 CpG sites differentially methylated in former and current smokers, while compared to never smokers, respectively. The 8 candidate markers of former smoking showed a gradual reversion of their methylation levels from those typical of current smokers to those of never smokers. Further analyses using cumulative (over varying time windows) smoking intensities, highlighted three classes of biomarkers: short and long term biomarkers (measuring the effect of smoking in the past 10, and in the past 10 to 30 years respectively), and lifelong biomarkers detected more than 30 years after quitting smoking.

**Conclusions** Genome-wide DNA methylation profiles show promising abilities to detect short-term to lifelong biomarkers of tobacco smoke exposure and, more generally, to potentially identity time-varying biomarkers of exposure.

**OBJECTIVES** To apply Marginal Structural Models (MSM) to address healthy workers survivor effect in a cohort study of active workers when time varying variables on health status and exposure are measured.

**Method** We used Cox MSMs and inverse probability weighting to assess the effect of PM$_{2.5}$ exposure on incident ischaemic heart disease (IHD) in an active cohort of 11 966 US aluminium workers. The outcome was assessed using medical claims data from 1998 to 2012. Quantitative exposure metrics of current exposure to PM$_{2.5}$ were dichotomized using different cutoffs and effects were assessed separately for smelters and fabrication. Risk score based on insurance claims was available as a time varying health status variable.

**Results** Defining binary PM$_{2.5}$ exposure by the 10th percentile cut-off, health status was affected by past exposure and predicted subsequent exposure in smelters, but not in fabrication. A Traditional cox model was appropriate for fabricators; the hazard ratio was 1.51 (95% CI: 1.12–2.06) and was attenuated when considering higher exposure cutoffs. In smelters, Cox MSM Hazard Ratios for IHD comparing the effect of exposure in a population had everyone always been exposed to everyone always unexposed, using the 10$^\text{th}$ percentile exposure cutoff was 1.83 (95% CI: 1.14–2.94). Higher exposure cutoffs also resulted in attenuated effects.

**Conclusions** Marginal Structural Models can be used in active employment occupational cohorts to assess time varying confounders. Results from the current study suggest that occupational exposure to PM$_{2.5}$ in the aluminium industry increases the risk of IHD in both smelters and fabrication.