rich air particles, as reported in steel production process, constitutes an important source of metal exposure, in particular to iron.

Methods We measured 8-OHdG in mitochondrial DNA (mtDNA), by real-time PCR, in blood leukocytes from 113 healthy male foundry workers (mean age = 42.2 years, SD = 11.2) with high levels of exposure to metal-rich particles. Exposure to iron and others metals, was assessed in urine collected the same day of blood sampling, at the end of the standard working week. Multivariable regression models adjusted for age, body mass index (BMI), and smoking were designed to evaluate the relationship between urinary markers of exposure and 8-OHdG in mtDNA. To assure normal distribution, 8-OHdG in mtDNA data were $\log_e$ transformed, and the regression slopes were exponentiated to obtain the geometric mean ratio (GMR) for increments in one SD of exposure.

Results After a week of exposure, elevated levels of urinary iron, (mean Fe = 10.9 g/g creat, SD = 7.9) were found among enrolled workers. Individual exposure level resulted positively associated with 8-OHdG formation in mtDNA in peripheral blood leukocytes (GMR = 1.22 p = 0.03). The observed association was confirmed also after adjustment for potential confounders: age, BMI, and smoking (GMR = 1.22; p = 0.04).

Conclusions Our observation of exposure-related high levels of 8-OHdG suggests that iron exposure may induce mtDNA damage, a potential response to oxidative stress caused by iron-induced production of ROS. The potential toxicity of high-level of iron exposure due to 8-OHdG generation and its ability to induce G-T base modification deserves further investigation.

397 A TWO-YEAR FOLLOW-UP STUDY OF SALIVARY CORTISOL CONCENTRATION AND THE RISK OF DEPRESSION

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Objectives Demanding psychosocial working conditions are a suspected cause of depression. High cortisol concentration, a biomarker of an activated stress response, has been found in depressed patients. Increased physiological stress has been suggested as a mechanism linking psychosocial working conditions and depression. The aim of this study was to determine if a high level of salivary cortisol is a risk factor of depression.

Methods In 2007, we enrolled 4,467 public employees. Morning and evening salivary cortisol concentration were measured for each participant. Participants reporting high levels of depressive, burnout, or stress symptoms, assessed by questionnaires were assigned to a psychiatric interview. In this interview 98 participants were diagnosed with depression and subsequently excluded. Two years later in 2009, 2,920 participants who had provided at least one valid saliva cortisol measurement at baseline participated at follow up. The psychiatric interviews were

repeated and 62 cases of newly onset depression were diagnosed. Odds ratios of depression were estimated for every 1.0 nmol/l increase in morning, evening, and daily mean cortisol concentration, as well as for the difference between morning and evening cortisol concentration.

Results The risk of depression decreased by increasing daily mean cortisol concentration and by increasing difference between morning and evening concentrations, while morning and evening cortisol concentrations were not significantly associated with depression. The adjusted odds ratios for 1.0 nmol/l increase in morning, evening, and mean daily cortisol concentration were 0.69 (95% CI: 0.45–1.05), 0.87 (0.59–1.27), and 0.54 (0.32–0.90), respectively. The adjusted odds ratio for 1.0 nmol/l increase in difference between morning and evening concentration were 0.64 (0.46–0.90).

Conclusions This study did not support the hypothesis that high salivary cortisol concentration is a risk factor of depression, but indicate that low mean salivary cortisol concentration and a small difference between morning and evening cortisol concentration may be risk factors of depression.

398 OCCUPATIONAL NOISE EXPOSURE AND THE CORTISOL AWAKENING RESPONSE: THE IMPACT OF EXPOSURE LEVEL AND HEARING PROTECTION

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Objectives Environmental and occupational noise exposure have in some studies been related to increased risk of cardiovascular disease, hypothetically by activation of the hypothalamic-pituitary-adrenal (HPA) axis. The objective of this study was to investigate the relation between occupational noise exposure and the cortisol awakening response (CAR) as a measure of HPA activity.

Methods This cross-sectional study included 398 industrial workers and as a reference 63 financial workers. Noise exposure levels were recorded every 5 seconds at the dominant shoulder by personal dosimeters for 24 hours and we calculated the L_{Aeq} value for work hours. For 310 workers who kept a diary on the use of hearing protection devices (HPD), we subtracted 10 dB from every noise recording obtained during HPD use and estimated the L_{Aeq} value at the ear. The next day salivary cortisol level was measured at awakening and after 10–60 min and the CAR was defined as the difference between the two.

Results The mean measured noise exposure level was 79.7 dB (A) [range: 55.0–94.2] and the mean estimated level at the ear 77.6 dB(A) [range: 55.0–94.2]. In a linear regression model that adjusted for sex, age, calendar month, income, body mass index, sampling time and duration since occupational noise exposure, we observed no statistically significant exposure response relation between noise exposure level and CAR. This was neither the case in analyses of the effect of noise level estimated at the ear nor in internal analyses restricted to the industrial workers.

Conclusions Neither measured nor estimated occupational noise exposure level was associated with the cortisol awakening response the following day. Thus, we found no indication that

the glucocorticoid part of the HPA axis, measured through CAR, is involved in the causal pathway between occupational and environmental noise exposure and cardiovascular disease.

399 EXPOSURE TO PHTHALATES, PERFLUORINATED COMPOUNDS AND ORGANOCHLORINES AND PREGNANCY OUTCOMES IN WOMEN FROM GREENLAND, POLAND AND UKRAINE

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Objectives Evidence for effects of environmental contaminants on pregnancy outcomes remains inconclusive. We investigated the associations between multiple, correlated exposures and related pregnancy outcomes using Bayesian, multivariate dimension reduction, and shrinkage regression approaches to account for multiple testing and interrelatedness of exposures and outcomes.

Methods We evaluated a cohort of 1322 singletons, born to 547 mothers from Greenland, 197 from Warsaw, Poland, and 588 from Kharkiv, Ukraine, who were recruited in 2002–2004 during routine antenatal care visits. Three secondary metabolites of both diethylhexyl and diisononyl phthalates (DEHP, DINP), eight perfluorinated compounds (PFCs; including PFOS and PFOA), and organochlorines (*p,p*-DDE and PCB-153) were measured and detected in 72–100% of maternal serum samples. Outcomes were preterm birth (<37 weeks), birth weight, and small for gestational age (SGA; <10th percentile age- and gender-specific birth weight). We analysed exposures (clustered, high dimension predictors) and continuous and dichotomous outcomes with partial least squares (PLS) regression, and sparse PLS-discriminant analysis (sPLS-DA), respectively. We compared results with elastic net penalised regression, and Bayesian stochastic search variable selection with spike-and-slab priors of (nonlinear) generalised additive models.

Results While applied methods had various degrees of sparseness, we observed generally consistent associations between DEHP metabolites, several PFCs and both organochlorines, and decreased birth weight and increased risk of SGA. There was no clear evidence of associations between contaminants and preterm birth.

Conclusions Findings suggest that several environmental contaminants are independently associated with impaired fetal growth. Methods which account for correlations between variables and multiple testing may better discriminate robust exposure-response associations than conventional univariate linear and logistic regression models.

400 CIRCULATING SOLUBLE CD27 AND CD30 IN WORKERS EXPOSED TO 2, 3, 7, 8-TETRACHLORODIBENZO-P-DIOXIN (TCDD)

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Objectives Previous studies suggest that 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin (TCDD) exposure may be associated with non-Hodgkin lymphoma (NHL) but findings remain inconclusive. There is a need for mechanistic studies to evaluate the biologic plausibility of this association. In this cross-sectional study we investigated changes in plasma levels of two soluble markers of B cell activation, sCD27 and sCD30 and IL1RA, which have been found to be predictive of lymphoma, among workers from a Dutch historical cohort occupationally exposed to chlorophenoxy herbicides and contaminants including TCDD.

Methods Eighty-five workers who had been exposed to either high (n = 47) or low (n = 38) TCDD levels more than 30 years before serum collection were included in the current investigation. Plasma level of the sCD27, sCD30, and IL1RA was measured by ELISA. Current plasma levels of TCDD (TCDD_{Current}) were determined by high-resolution gas chromatography/isotope dilution high resolution mass spectrometry. TCDD blood levels at the time of last exposure (TCDD_{max}) were estimated using a one-compartment first order kinetic model.

Results Dose-response analyses showed no significant association between blood levels of sCD27, sCD30 and IL1RA and current and estimated past maximum TCDD levels although there was an indication of decreased levels of all markers with increasing TCDD level. Analyses excluding subjects with chronic diseases resulted in a significant decrease in IL1RA with increasing levels of TCDD.

Conclusions No significant dose-response relationship was observed between the measured markers and TCDD level in our study. However, there was a suggestion that sCD27, sCD30 and IL1-RA tended to decrease with increasing TCDD levels. This later observation is consistent with the earlier observation on decreasing cytokine levels with increasing exposures.

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401 COST-BENEFIT ANALYSIS OF INTERVENTIONS USING A PROBABILISTIC APPROACH: A CASE FOCUSING ON QUARTZ EXPOSURE IN THE DUTCH CONSTRUCTION INDUSTRY

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Objectives Ill-health due to exposure in the workplace results in high costs for employers, employees and society. Interventions can be costly and economic evaluations receive more and more attention in the decision making processes regarding investments, including for occupational health. To perform an economic evaluation information regarding the impact of interventions on exposure and subsequently, health and work performance is needed. Additionally, information regarding costs is needed. Meijster *et al.* (2011) presented an approach to evaluate the costs and benefits for different stakeholders. We further developed this approach into a probabilistic model to include variability for input parameters and obtain uncertainty estimates for output parameters. This approach is applied to a hypothetical case study focusing on reducing quartz exposure in the Dutch construction industry.

Methods The original cost-benefit approach was further developed into a probabilistic approach including Monte Carlo simulations using Excel spreadsheets. This enables the user to calculate total costs, total benefits, net costs and cost-effectiveness which can be easily applied for different intervention (s).