BDE209 was associated with a significant increase of 2.48 nmol/L in total T4 in men ($p=0.011$), and with a close to significant increase in the free/total testosterone ratio of 6% in men ($p=0.053$). BDE47 and BDE153 were not associated with hormone levels.

Conclusions The clinical significance of high exposure to BDE209 in working adults is yet to be established, but endocrine effects were observed in this population. E-recycling workers are highly exposed to PBDEs among other substances, which may make them more vulnerable to hormonal disruption.

Mini-Symposium 4: Advances in Neurodegenerative Disease Epidemiology

O6E.1 SELF-REPORT OCCUPATIONAL EXPOSURES AND MND IN NEW ZEALAND

¹Grace Chen*, ¹Andrea 't Mannetje, ¹Jeroen Douwes, ²Leonard van den Berg, ¹Dave McLean, ³Neil Pearce, ⁴Hans Kromhout, ⁵Wendyl D'Souza, ⁶Melanie McConnell. ¹Centre For Public Health Research, Massey University, Wellington, New Zealand; ²Brain Centre Rudolf Magnus, Department of Neurology, University Medical Centre, Utrecht, The Netherlands; ³Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, UK; ⁴Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands; ⁵Department of Medicine, University of Melbourne, Melbourne, Australia; ⁶School of Biological Sciences, Victoria University, New Zealand

10.1136/OEM-2019-EPI.158

Background We have reported previously the results on a New Zealand population based case-control study evaluating occupations as risk factors for MND. The aim of this study was to investigate the associations between 11 different occupational exposure groups and the risk of MND by using self-reported job-related exposures.

Methods We recruited 321 cases through the New Zealand Motor Neurone Disease Association and hospital discharges records, and 605 population controls from the Electoral Roll between 2013 and 2016. A standardized questionnaire was used to obtain information on personal and demographic details, lifestyle factors and a full occupational history with detailed workplaces exposures. Unconditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals for MND. Analyses were adjusted for age, gender, ethnicity, socioeconomic status, education and smoking.

Results Significantly elevated risks for MND were observed for self-reported job related exposures to Fibres (OR=1.39, 95% CI 1.00–1.93); Fumigants (OR=2.44, 95% CI 1.35–4.23); Animal and Animal Products (OR=1.41, 95% CI 1.03–1.92); Other Chemicals (OR=1.53, 95% CI 1.14–2.05) and Fungicides/Insecticides/Herbicides/Timber Preservatives (OR=1.44, 95% CI 1.05–1.99)

Conclusions Our study shows various occupational related exposures with increased odds of MND. While study results need to be interpreted cautiously given the lack of direct exposure measures, these results, in particular exposure to Fumigants, Fungicides/Insecticides/Herbicides/Timber Preservatives which were consistent with our previous results on agriculture occupations and MND risk. Future studies will have a particular focus on exposures specific for certain job tasks and dose-response relationships.

O6E.2 EXPOSURE ASSESSMENT FOR A STUDY OF COGNITIVE IMPAIRMENT IN FORMER PROFESSIONAL FOOTBALLERS IN ENGLAND

¹Damien Mcelvenny*, ¹Ioannis Basinas, ¹Richard Graveling, ^{1,2}John Cherrie, ³Valeentina Gallo, ⁴Simon Kemp, ⁵Neil Pearce. ¹Institute of Occupational Medicine, Edinburgh, UK; ²Heriot-Watt University, Edinburgh, UK; ³Queen Mary, University of London, London, UK; ⁴Rugby Football Union, London, UK; ⁵London School of Hygiene and Tropical Medicine, London, UK

10.1136/OEM-2019-EPI.159

Evidence is accumulating on the possible increased risks of neurodegenerative disease in former (professional) sports persons. This study will assess the associations between a history of repetitive low-level head trauma and general and neurological health in retired professional footballers aged 50+ in England. The main exposure measures are concussions and cumulative lifetime repeated sub-concussive head impacts (RSHIs), either from heading footballs or other forces applied to the head. Information on factors associated with concussions and RSHIs will be collected via a structured questionnaire during face-to-face interviews.

Our approach will include:

- Literature search to identify potentially important proxy measures of RSHI during training and matches;
- Developing a model of cumulative RSHIs, based on the more strongly predictive variables, which may include playing position, the frequency of heading, the number of games played and training sessions attended, decade of play and the type of ball used.
- The model will be developed from analyses of head contacts from video footage of matches and training, at the individual level and in general, and from statistics on playing career. We will also consult a panel of former professional footballers on the exposure assessment.

The exposure data will be crucial to assess whether those with higher exposure within the study cohort are at increased risk compared to those with lower exposure.

O6E.3 CAN THE MULTISTAGE MODEL BE APPLIED TO AMYOTROPHIC LATERAL SCLEROSIS (ALS)?

Neil Pearce. London School of Hygiene and Tropical Medicine, London, UK

10.1136/OEM-2019-EPI.160

Background There are several intriguing features of amyotrophic lateral sclerosis (ALS). Some people with genetic susceptibility never develop ALS; ALS develops in late life and progresses rapidly; the same mutation can predispose to ALS or other diseases; ALS starts in one region and spreads; degeneration is specific to a subgroup of neurons; and ALS shows complex inheritance. Cancer shares many of these characteristics, and these have been incorporated into the Armitage-Doll multistage model. We therefore used this model to investigate the hypothesis that ALS is a multistage process.

Methods Incidence data by age and sex were generated from five ALS population registers, in Ireland, the Netherlands, Italy, Scotland and England; age and sex adjusted incidences were calculated for each register.

Findings 6274 cases were identified from 73 million people. There was a linear relationship between log incidence and log age in all five registers: Ireland $R^2=0.99$, Netherlands $R^2=0.99$, Italy $R^2=0.95$, Scotland $R^2=0.97$, England $R^2=0.95$, overall $R^2=0.99$. All five registers gave very similar estimates of the linear slope ranging from 4.5 to 5.1, with overlapping confidence intervals. Combining all five registers gave an overall slope of 4.8 (95% CI 4.5, 5.0) with similar estimates for males and females. In persons with known genetic mutations which predispose to ALS, the risk of ALS was higher, but the log-incidence/log-age slope was lower, as predicted by the multistage model.

Interpretation A linear relationship between the log incidence and log age of onset of ALS is consistent with a multistage model of disease. The slope estimate is about 5, suggesting that ALS is a 6-step process; the slope is 3–4 in persons with known genetic causes. These findings have implications for the search for causes of ALS, including occupational causes and gene-environment interactions.

O6E.4 METABOLOME AND EXPOSOME PROFILING: NEW OPPORTUNITIES TO STUDY RISK FACTORS FOR PARKINSON'S DISEASE

^{1,2}Susan Peters, ^{1,3}Douglas Walker, ⁴Gary Miller, ^{1,5}Marc Chadeau-Hyam, ⁵Paolo Vineis, ⁶Valentina Gallo, ^{1,7}Roel Vermeulen*. ¹Institute for Risk Assessment Sciences, Utrecht University, Utrecht, Netherlands; ²Neurology Department, University Medical Centre Utrecht, Utrecht, Netherlands; ³Icahn School of Medicine, Mount Sinai, USA; ⁴Emory University, Atlanta, USA; ⁵School of Public Health, Imperial College, London, UK; ⁶Queen Mary University of London, London, UK; ⁷Julius Center, University Medical Centre Utrecht, Utrecht, Netherlands

10.1136/OEM-2019-EPI.161

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer disease and is imposing an increasing social and economic burden in ageing populations. Although the role of environmental factors has been recognised, few established risk factors have been consistently identified. Evidence that exposure to pesticides, herbicides and metals increase PD risk is suggestive, but further research is needed to identify specific compounds that may play a causal role.

Large established prospective population studies offer an important opportunity for investigating risk factors in relatively rare diseases such as PD. Within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, 734 incident PD cases have been ascertained, for whom pre-diagnostic blood has been stored. A nested case-control study will be conducted, where one control per case will be selected by incidence density sampling matched by age at recruitment, sex and study centre.

Untargeted metabolomics can simultaneously characterize thousands of endogenous and exogenous compounds within a biological sample: the metabolome. Metabolome wide association studies (MWAS) have identified significant differences in the metabolomic profile of older adults with and without PD. We will employ an innovative approach combining liquid and gas phase chromatography with ultra-high-resolution mass spectrometry (LC/GC-UHRMS), to identify exogenous chemical exposures (e.g. pollutants, pesticides and medications), the exposome, in addition to the metabolome.

Disease specific variability in blood metabolite compositions may signify the presence of mechanistic aberrations contributing to PD pathogenesis. The combination of metabolome and exposome profiling provides a measure of the continuum from exposure to disease. Allowing previously unavailable richness and depth for characterizing the metabolome and exposome upon which novel discoveries in PD can be made.

The EPIC cohort allows us to perform a study to study the metabolome and exposome well before disease onset, to eliminate possible effects of levodopa medication or disease-related processes.

O6E.5 OCCUPATION AND RISK OF AMYOTROPHIC LATERALSCLEROSIS (ALS) IN DENMARK

^{2,3}Aisha Dickerson, ¹Johnni Hansen*, ⁵Marianthi-Anna Kiumourzoglou, ³Aron Specht, ⁴Ole Gredal, ^{2,3}Marc Weisskopf. ¹Danish Cancer Society Research Center, Copenhagen, Denmark; ²Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, USA; ³Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, USA; ⁴Danish Rehabilitation Center, Copenhagen, Denmark; ⁵Department of Environmental Health Services, Columbia University Mailman School of Public Health, New York, USA

10.1136/OEM-2019-EPI.162

Introduction Amyotrophic lateral sclerosis (ALS) is a rare and complex neurodegenerative disease, which is highly fatal. It is known that 5%–10% of ALS cases are hereditary, but apart from this the causes for sporadic of ALS are unknown. Some evidence, however, suggests that manifestation and progression may be associated with certain occupational exposures, e.g. exposure to formaldehyde, lead and military service. The aim of this study is to survey the occupational risk of ALS in Denmark based on nationwide registries.

Methods We identified 1826 ALS cases who were 25 years old or less in 1964 and diagnosed from 1982 to 2013 from the Danish National Patient Registry, which cover all hospitals in Denmark. We matched 100 ALS free population controls to each case based on birth year and sex. Information on demographic data were obtained from the national Population Register and linked by the unique personal identifier, assigned to all residents, to the Danish Pension Fund (DPF) to determine individual employment history from 1964. All employees in Denmark are compulsory members of DPF. Conditional logistic regression models were used for estimation of odds ratios OR and their 95% confidence intervals, adjusted for socioeconomic status, marital status and residential location.

Results We observed increased OR of ALS among men who worked in e.g. agriculture, hunting, forestry or fishing (OR=1.2; 1.0–1.5). There was also a positive association for men employed in construction (OR=1.2; 1.1–1.4). In women, no significant increases were observed, but a protective association was seen with employment in the cleaning industry (OR=0.7; 0.5–0.9).

Conclusions Our study shows various occupations with exposure to toxicants, such as diesel exhaust and lead, and strenuous physical activity associated with increased odds of ALS in men. Future studies should have a particular focus on gathering detailed information on physical exertion and exposure to specific chemicals.