Abstracts

Friday 11 September

Modelling and Methods

OP95 DEVELOPMENT AND VALIDATION OF A PREDICTION MODEL TO ESTIMATE AN INDIVIDUAL RISK OF 10-YEAR MORTALITY IN A LONGITUDINAL COHORT OF OLDER ENGLISH ADULTS USING ADVANCED STATISTICAL LEARNING METHODS

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Background Although we embarked on the era of the global increase in the ageing population, the recent declines in life expectancy simultaneously experienced by many high-income countries highlight a need for an accurate prediction model for estimating individual, rather than average, risk for mortality in older adults, based on readily accessible information about individuals’ lives, health and environment. Using advanced computer intensive statistical learning methods, we derived, evaluated and validated a prediction model of the 10-year risk for all-cause mortality in older adults from the general population.

Methods The model was developed using a prospective population-based cohort of English adults aged ≥50 years old from English Longitudinal Study of Ageing study. Having included a large pool of predictors, we employed cox proportional hazards model with regularisation by the least absolute shrinkage and selection operator (Cox-Lasso) to identity the most robust predictors of mortality and quantify their relative contribution to all-cause mortality in the next 10 years. The model was internally validated using Harrell’s optimism-correction procedure followed by external validation in the Health and Retirement Study, which is a nationally representative, longitudinal survey of adults aged ≥50 years old in the United States. The model’s prediction accuracy was evaluated with calibration, discrimination, sensitivity and specificity.

Results For model development, the sample comprised 9154 individuals; of these, 1240 (13.4%) died during the 10-year follow-up with an average length of survival of 70.2 months (SD=35.4). For external validation, the sample included 2573 individuals; of these, 491 (19.1%) died during the 10-year follow-up with an average length of survival of 77.7 months (SD=36.5). The prediction model selected 13 (15.5%) of n=84 prognostic factors, which included increasing age, male gender, low accumulated wealth, comorbid health conditions (i.e., previous diagnoses of cancer, chronic lung disease or stroke), functional difficulties (i.e., difficulty walking 100 yards, or doing work around house and garden) and worsening memory. External validation demonstrated good discrimination (c-index=0.69), calibration (calibration slope β=0.80), specificity (73.2%) and sensitivity (72.4%).

Discussion Our model is likely to provide accurate estimates of individual 10-year risk of mortality using information that is often available in patients’ reports. It is calibrated for individuals aged 50–75 years living in the UK but generalises reasonably well to other populations with similar underlying characteristics. The developed prediction model could be used to communicate risk to individuals and their families (if appropriate), guide strategies for risk reduction and design future studies targeting high risk subpopulations.

OP96 THE CAUSAL EFFECT OF BMI ON NEURODEVELOPMENT: A WITHIN FAMILY MENDELIAN RANDOMIZATION STUDY USING MOBA

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Background Childhood obesity is linked to poorer emotional health and neurodevelopmental problems but it is unclear if these associations are causal. Observational study designs are

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OP93 ABSTRACTS OF THE PREDICTION MODAL COHORT STUDY: A LARGE-SCALE PROSPECTIVE STUDY OF ALZHEIMER'S DISEASE USING THE UK BIOMED 2 FUNDING

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vulnerable to reverse causation and confounding. Mendelian randomization (MR) studies with even large numbers of unrelated individuals can suffer from familial biases, and dynastic effects (‘genetic nurture’) can be especially pronounced for socially patterned phenotypes like obesity. We introduce a ‘within-family’ MR (WFMR) design that uses genotyped mother-father-offspring trios to overcome these biases.

**Methods** In 5237 8-year-old children from the Norwegian Mother, Father and Child Cohort Study (MoBa), we estimated the effects of body mass index (BMI) on symptoms of depression, attention-deficit hyperactivity disorder (ADHD), anxiety, and autism spectrum disorder (ASD). Child height, weight, and outcomes were based on mother-reported information from questionnaires. We used polygenic risk scores (PRS) as instrumental variables for BMI, with and without adjustment for parents’ own PRS. PRS were calculated in PRCise, and all other analysis completed in STATAv15. PRS were calculated using genetic variants from the largest and most recent genome-wide association study (GWAS) for BMI.

**Results** Initial MR estimates implied a one-unit higher BMI increased depression symptoms by 0.12 (95%CI 0.05,0.20) and ADHD symptoms by 0.11(0.03,0.18) standard-deviations, and reduced symptoms of anxiety by -0.11(-0.19,-0.03) and symptoms of ASD by -0.05(-0.13,0.03). For ASD, associations did not differ substantially between symptoms related to social communication (-0.03(-0.12,0.05) and to repetitive behaviour (-0.04(-0.12, 0.03). Accounting for parental genotypes in WFMR made little difference to estimates, with no strong evidence of indirect effects of parental genotypes on offspring phenotype. Next steps will be to examine relationships using gene variants associated with BMI during childhood specifically, and to investigate the influence of depressive, ADHD, anxiety and ASD symptoms on childhood BMI.

**Conclusion** Influence of childhood BMI on emotional and neurodevelopmental health is not explained by family-level genetic biases, suggesting childhood BMI may affect these symptoms. Negative associations of BMI with anxiety are consistent with results from the UK Biobank, where genetic propensity for BMI was negatively associated with risk of self-reporting as a ‘nervous’ person. Intervening on childhood BMI may influence these outcomes.

**OP98** USING DELPHI METHODS TO INCREASE SEASONAL INFLUENZA VACCINATION IN HEALTHCARE WORKERS ACROSS LONDON


Background Seasonal influenza vaccination (SIV) uptake in healthcare workers (HCWs) across London has more than doubled since 2014/15 from 25% to 64% in 2018/19, but uptake is still less than the national average of 70%. Given the lack of certainty in the literature around interventions that work to improve uptake, particularly within the NHS and across a range of Trust types, the aim here is to determine which interventions have been effective (and ineffective) in increasing uptake in SIV in HCWs across the 36 acute, community, mental health and specialist trusts in London.

**Methods** The Delphi technique is a structured process that uses a series of questionnaires or ‘rounds’ to gather information until a group consensus is reached. An advantage of the methodology is that it can be used to collate expertise across enforcement. The aim of this study was to evaluate the effects of this program.

**Methods** This is a quasi-experimental control group study using a repeated cross-sectional design (baseline 2015, follow-ups 2016 and 2017). The setting was arenas hosting SPFL games in Stockholm (intervention area) and Gothenburg (comparison area). Professional actors (i.e. pseudopatrons) were trained to act a standardized scene of obvious intoxication while attempting to enter arenas and purchase alcohol at licensed premises inside arenas. To control for possible external factors, we also conducted alcohol purchase attempts at licensed premises outside arenas, where denial rates should remain stable. Spectators at arenas were randomly invited to provide BrAC-assessments using breathalyzers.

**Results** A total of 10178 BrAC-assessments were collected, 201 attempts to enter arenas, and 495 attempts to purchase alcohol at premises inside arenas. In the intervention area, denial rates toward obviously intoxicated spectators increased between the assessment points from 12.9% (95%CI 6.6–22.2) to 32.8% (22.5–44.6) at entrances and from 31.8% 25.4–39.0) to 56.8% (49.6–63.7) at premises inside arenas. Mean BrAC-level decreased between baseline and two-year follow-up from 0.063% (0.061–0.065) to 0.057% (0.054–0.059) and the proportion of spectators with high intoxication levels from 9.7% (8.7–10.7) to 5.9% (5.1–6.9). A similar pattern was observed in the comparison area, however, while the denial rate remained stable at premises outside arenas in the intervention area, it increased in the comparison area.

**Conclusion** Interpretation of results is complex due to improvements in the comparison area. However, unlike in the intervention area, denial rates increased at premises outside the arena in the comparison area, indicating that external factors have affected the arena in the comparison area. Results then suggest that the intervention was successful in increasing staff intervention toward obviously intoxicated spectators, thereby decreasing the overall intoxication levels. A limitation is the repeated cross-sectional design which limits conclusions on causality. The intervention has the potential to be implemented at other sporting events.