analyses the lowest category of 25(OH)D concentration was defined as reference. Heterogeneity among studies was evaluated by using the Cochran Q test and quantified by using the I^2 statistical parameter. Stratified analyses were conducted to assess modification effects by selected factors. Publication bias was examined by using Funnel plot and Egger's regression asymmetry test. Random-effects meta-analyses were conducted using the *metafor* package in R.

Results Of 260 identified articles, 25 were included in the present review. Comparing the highest vs. the lowest category of prenatal 25(OH)D levels, the pooled beta coefficients were 0.95 (95% CI -0.03, 1.93; $p=0.05$) for cognition, and 0.88 (95% CI -0.18, 1.93; $p=0.10$) for psychomotor development. The pooled relative risk for ADHD was 0.72 (95% CI, 0.59, 0.89; $p=0.002$), and the pooled odds ratio for autism-related traits was 0.42 (95% CI, 0.25, 0.71; $p=0.001$). Stratified analyses showed stronger associations between 25(OH)D concentrations in early-mid pregnancy and cognition (beta coefficient 1.18, 95% CI -0.16, 2.51; $p=0.08$), psychomotor performance (beta coefficient 1.43, 95% CI -0.65, 3.52; $p=0.18$), and risk of autism-related traits (OR 0.28, 95% CI 0.19, 0.42; $p<0.01$). There was little evidence for protective effects of high prenatal 25(OH)D for language development and behavior difficulties.

Conclusion This meta-analysis provides supporting evidence that increased prenatal exposure to 25(OH)D levels is associated with improved cognitive development and reduced risk of ADHD and autism-related traits later in life. Associations represent a potentially high public health burden given the current prevalence of vitamin D deficiency and insufficiency among childbearing aging and pregnant women.

OP77

METHODS TO INCREASE RESPONSE RATES TO A POPULATION-BASED MATERNITY SURVEY: A COMPARISON OF TWO PILOT STUDIES

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Background Surveys are established methods for collecting population data that are unavailable from other sources; however, response rates to surveys are declining. This decline is exemplified in the National Maternity Surveys which are carried out in England at regular intervals by the National Perinatal Epidemiology Unit; the response rate declined from 63% in 2006 to 29% in 2016. A number of methods have been identified to increase survey returns yet response rates continue to fall. We evaluated the impact of five selected methods on the response rate to pilot surveys, conducted prior to the 2018 National Maternity Survey.

Methods The pilot National Maternity Surveys were cross-sectional population-based questionnaire surveys of women who were three months postpartum selected at random from birth registrations. Women received a postal questionnaire, which they could complete on paper, online or verbally over the telephone. An initial pilot survey was conducted (pilot 1, $n=1,000$) to which the response rate was lower than expected. Therefore, a further pilot survey was conducted (pilot 2, $n=2,000$) using additional selected methods with the specific aim of increasing the response rate. The additional selected methods used for all women in pilot 2 were: pre-

notification, a shorter questionnaire, more personable survey materials, an additional reminder, and inclusion of quick response (QR) codes to enable faster access to the online version of the survey. To assess the impact of the selected methods, response rates to pilot surveys 1 and 2 were compared.

Results The response rate increased significantly from 28.7% in pilot 1 to 33.1% in pilot 2 (+4.4%, 95%CI:0.88–7.83, $p=0.02$). Analysis of weekly returns according to time from initial and reminder mail-outs suggests that this increase was largely due to the additional reminder. Most respondents completed the paper questionnaire rather than taking part online or over the telephone in both pilot surveys. However, the overall response to the online questionnaire almost doubled from 1.8% in pilot 1 to 3.5% in pilot 2, corresponding to an absolute difference of 1.7% (95%CI:0.45–2.81, $p=0.01$), suggesting that QR codes might have facilitated online participation.

Conclusion Declining survey response rates may be ameliorated with the use of selected methods. Further studies should evaluate the effectiveness of each of these methods using randomised controlled trials and identify novel strategies for engaging populations in survey research.

Methodological Issues

OP78

A CAUSAL INFERENCE PERSPECTIVE ON COMPOSITIONAL DATA AND COLLIDER 'BIAS'

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Background Compositional data (CD) comprise the parts of some whole, for which all parts sum to that whole; the whole may vary across individual units of analysis or remain fixed. Such data are common in many contexts, where interest often lies in understanding the effect of a particular part in relation to a subsequent outcome. Many of the inherent challenges associated with analysing CD have been discussed previously, though not within a formal causal framework by utilising directed acyclic graphs (DAGs). We use DAGs to consider the specific issue of collider bias as it pertains to CD.

Methods We demonstrate how to depict CD using DAGs, and identify two distinct effect estimands in the generic case: (1) the 'unbiased' (total) effect, and (2) the 'collider biased' effect. We consider each effect in the context of three specific example scenarios involving CD with variable or fixed totals: (1) the relationship between the economically active population and area-level gross domestic product (GDP) (variable total); (2) the relationship between fat consumption and body weight (variable total); and (3) the relationship between time spent sedentary and body weight (fixed total). For each scenario, we consider the distinct interpretation of each effect, and the resulting implications for related analyses.

Results In scenario (1), the 'unbiased' effect represents the average change in GDP that results from adding economically active individuals to the area whilst doing nothing to the population of economically inactive individuals, whereas the 'collider biased' effect represents the average change that results from swapping economically inactive individuals for economically active ones. In scenario (2), the 'unbiased' effect

represents the average change in weight that results from adding fat to an individual's diet irrespective of other macronutrient consumption, whilst the 'collider biased' effect represents the average change that results in swapping 'other' macronutrient consumption for fat consumption. In scenario (3), only the 'collider biased' effect is estimable and causally meaningful; it represents the average change in weight that results from swapping time spent physically active for time spent sedentary.

Conclusion For CD with variable totals, both effects may be estimable and causally meaningful, depending upon the specific question of interest. Researchers should be clear about which effect is being sought and estimated, since they may be radically different quantities. For CD with fixed totals, only the 'collider biased' effect has any meaning. Careful attention must be paid to sensibly interpreting the relative effects that characterise this type of data.

OP79

GENETIC LIABILITY FOR ADHD AND PHYSICAL HEALTH OUTCOMES – A TWO-SAMPLE MENDELIAN RANDOMIZATION STUDY

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Background Attention-deficit/hyperactivity disorder (ADHD) is associated with a broad range of physical health problems, including cardiometabolic, neurological and immunological conditions. Determining whether ADHD plays a causal role in these associations is of great importance not only for early treatment and prevention but also because comorbid health problems further increase the serious social and economic impacts of ADHD on individuals and the society.

Methods We used a two-sample Mendelian randomization (MR) approach to examine the causal relationships between genetic liability for ADHD and previously implicated physical health conditions. Genetic variants associated with ADHD were obtained from the latest summary statistics for European ancestry from the combined PGC + iPSYCH meta-analysis of ADHD. Consistent effects obtained from IVW, weighted median and MR Egger methods were taken forward for sensitivity analysis. The direction of effect was investigated in a bidirectional MR analysis. Multivariable MR was applied to assess effects of genetic liability for ADHD when adjusted for genetic liability for childhood obesity and lifetime smoking heaviness.

Results We found evidence of a causal effect of genetic liability for ADHD on childhood obesity (OR:1.29 (95% CI:1.02,1.63)) and coronary artery disease (CAD) (OR:1.11 (95% CI:1.03,1.19)) with consistent results across different MR approaches. There was further evidence for a bidirectional relationship between genetic liability for ADHD and childhood obesity. The effect of genetic liability for ADHD on CAD was independent of smoking heaviness in a multivariable MR setting (OR:1.14 (95% CI:1.08,1.20)) but was attenuated when simultaneously entering genetic liability for childhood obesity (OR:1.06 (95% CI:0.95,1.17)). There was little evidence for a causal effect on other cardiometabolic, immunological, neurological disorders and lung cancer.

Conclusion Our findings strengthen the argument for early treatment and support for children with ADHD and their families and especially promoting physical activity and providing them with dietary advice to reduce the future risk for developing CAD.

OP80

RAISED GLUCOSE CONCENTRATION, DIAGNOSIS OF GESTATIONAL DIABETES, AND RISK OF LATE STILLBIRTH: A CAUSAL MEDIATION ANALYSIS IN A CASE-CONTROL STUDY FROM ENGLAND, UK

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Background Women with gestational diabetes mellitus (GDM) receive enhanced antenatal care due to assumed higher risks of adverse pregnancy outcomes. Existing observational studies however report surprisingly modest associations between GDM on outcomes such as late stillbirth (fetal death ≥ 28 weeks' gestation), provoking international debate about the value of proactively managing GDM. But existing studies have been performed in populations receiving enhanced care; which may be masking the true 'untreated' impact of the condition.

This study sought to estimate the distinct effects of raised glucose concentration and receipt of enhanced care on risk of late stillbirth in pregnant women without pre-existing (type 1 or type 2) diabetes.

Methods 291 case pregnancies ending in late stillbirth and 733 control pregnancies were recruited from 41 maternity units in England, UK during April 2014 to March 2016. 94 cases and 277 controls without pre-existing diabetes received a fasting plasma glucose (FPG) test. In England, GDM diagnosis is advised if $FPG \geq 5.6$ mmol/L, but other tests (such as 2-hour oral glucose tolerance tests) are generally preferred.

Causal mediation analysis was used to estimate the effects of raised FPG (≥ 5.6 mmol/L) and subsequent GDM diagnosis (as an instrument for receipt of enhanced care) on risk of late stillbirth. Odds ratios (OR) were estimated by logistic regression, conditioning on confounders identified by directed acyclic graph. The shape of association between FPG (as a continuous variable) and stillbirth was explored by locally-weighted scatterplot smoothing.

Results On average, women with raised FPG experienced twice the risk of stillbirth as women with normal FPG (OR=1.97, 95% CI=0.61–6.32) but this varied with GDM diagnosis (and hence receipt of enhanced care). Women with raised FPG *not* diagnosed with GDM had four-times higher risks of stillbirth than women with normal FPG (OR=4.22, 95% CI=1.04–17.02) while women with raised FPG who *were* diagnosed had similar risks as women with normal FPG (OR=1.10 95% CI=0.31–3.91). Stillbirth risk in women with raised FPG was thus around four-times lower for those who received a GDM diagnosis (OR=0.26, 95% CI=0.07–0.93).