

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).