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 antepartum 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 $\geq$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 ($\geq$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).

The risk of stillbirth increased monotonically with increasing FPG, suggesting no biological justification for one GDM diagnostic threshold over another.

Conclusion Women with raised FPG experience higher risk of late stillbirth. If diagnosed with GDM and managed accordingly, this appears to be largely mitigated. Inconsistent diagnostic practices however leave many women with borderline hyperglycaemia exposed to higher risks of stillbirth.

OP81 A MULTI-OMICS APPROACH TO INVESTIGATE THE INFLAMMATORY RESPONSE OF LIFE COURSE SOCIOECONOMIC POSITION: FINDINGS FROM EPIC-ITALY

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Background Lower socioeconomic position (SEP) has consistently been associated with poorer health. Chronic inflammation has been proposed as having a prominent role in the construction of social inequalities in health. Disentangling the effects of social disadvantage along the life course on inflammation is key in elucidating biological mechanisms underlying socioeconomic disparities. In this study we investigate how life course socioeconomic conditions influence omics measures of inflammation at different molecular level traits from a subset of 173 Italian participants of the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort.

Methods We used genome-wide methylation and transcriptional profiles obtained from blood samples from 178 Italian participants of the EPIC cohort. Starting from 824 genes involved in human inflammatory responses and corresponding to 11 502 CpG sites, we first identified 61 potential *cis* acting CpG loci whose degree of methylation was associated with gene expression (eMS) at a Bonferonni correction, out of which 78.7% were inversely associated with gene expression in *cis*. We further investigate the relationships between indicators of SEP at 3 life stages through father's occupation, education and highest household occupation and the 61 cis eMS, involved in inflammation and functionnally relevant, separately and combined through an inflammatory methylome score. We finally investigated life course effects of early-life SEP experiences by sequentially controlling for time-ordered SEP.

Results Our results consistently show that participants with a less advantaged SEP in young adulthood or in adulthood exhibit, later in life, a lower inflammatory methylome score (β=-0.0075, P-value=0.0067, β=-0.0076, P-value=0.0073 for educational level and highest household occupational position respectively), hence suggesting an overall increased level of expression for the corresponding inflammatory-related genes. Adjusting for either behavioural factors (smoking status, alcohol consumption and physical activity) and bmi, or all of them together only marginally affected our results: effect size estimates showed consistent signs, and associations reach statistical significance (P<0.05) for both participant's education and highest household occupational position. Adopting a life course approach weakened these associations suggesting a common pathways between young and later in life SEP. Sensitivity analyses indicated that our findings were not affected by the way the inflammatory methylome score was calculated.

Conclusion Our results support the hypothesis that social inequalities impacts, independently from behavioural factors, adult physiology through inflammation and can be observed at the DNA methylation level. Understanding biological mechanisms by which social environment influences the inflammatory system has important implications in treatment and especially in prevention, by potentially identifying modifiable factors in the environment that affect physiological health.

OP82 DOES A RAPID REVIEW VERSION OF A LARGE EPIDEMIOLOGICAL SYSTEMATIC REVIEW FAIL TO IDENTIFY MANY ELIGIBLE STUDIES, AND WHAT IMPLICATIONS DOES THIS HAVE FOR THE RESULTS OF THE REVIEW?

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Background Systematic reviews (SR) are the gold standard evidence synthesis method. Rapid reviews (RR) have been proposed as an alternative method that may provide evidence in a more timely fashion to inform clinical decision making and policy making. However, RR may fail to identify all relevant evidence, which may bias the review conclusions. An analysis was conducted to compare SR and RR versions of a large epidemiological review in terms of completeness and efficiency of evidence retrieval and any differences in overall review findings.

Methods A SR on the political determinants of health was conducted with searches in November 2017 on 10 scholarly bibliographic databases using a combination of MeSH terms and key words, accompanied by a search on Google Scholar (GS) and backward citation chasing. Internationally comparative studies assessing the relationship between any of four political themes (democracy, globalisation, political tradition, and welfare state) and any population health outcome, excluding healthcare expenditure, were eligible for inclusion. A RR version of this review was conducted with the same search dates. The RR comprised a GS search for health plus each of 'politics', 'political' and the four political themes plus backward and forward citation chasing. The SR and RR were compared on completeness (% of total included studies identified), efficiency (% of reviewed records that were included) and results profile (% of included studies with positive vs non-positive results). Analysis was descriptive in terms of n(%) and used chi-square and McNemar test as appropriate in SPSS v.25.

Results 114 studies were eligible for inclusion, of which SR identified 101 (89%, due to absence of forward citation chasing) and RR 64 (56%, McNemar test p<0.001). SR reviewed 35,262 records (0.3% were included) and RR reviewed 92 records (70% were included). For the welfare state theme, 54 (77%) studies had positive results in SR vs 31(78%) in RR (chi-square=0.002, p=0.966), for political tradition theme 3 (60%)vs 2(50%, chi-square=0.090, p=0.764), for democracy theme 14(78%) vs 14(82%, chi-square=0.114, p=0.735), and for globalisation theme 3(17%) vs 5(38%, chi-square=1.873, p=0.171).