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Background Incidence of myocardial infarction (MI) in the UK general population has declined considerably in recent years. However it is unclear whether the decline in MI risk has occurred among people with diabetes. People with diabetes have an estimated two-fold excess risk of MI, compared to those without diabetes. A differential trend in MI incidence among diabetic patients could correspond to a rise or fall in this excess risk, which has implications for prognosis and management of diabetes. We compared recent trends in MI incidence among those with and without diabetes in a representative UK population sample, and estimated the excess risk of MI among diabetic patients in different calendar periods.
Methods The population sample comprised 2,927,137 patients (49% men) aged 30 years and over, with no prior MI, from 434 general practices belonging to The Health Improvement Network (THIN) UK-wide primary care database in 1995–2008. Incidence of MI in 1995–1998 was compared with that 10 years later in 2005–2008. Rate ratios comparing incidence over these intervals were estimated from multi-level Poisson regression (patients nested in practices), with an indicator for time interval as a covariate, adjusting for age and gender, with practice as a random effect. An interaction between time interval and an indicator for diabetes was used to assess whether the rate ratios comparing intervals differed among those with and without diabetes, and equivalently whether the excess relative risk among diabetic patients has changed over time.
Results In 1995–1998 age-standardised incidence rates for MI (per 1000 person years) among those without and with diabetes were 3.22 (95% CI 3.10–3.34) and 9.56 (8.42–10.7) respectively. In 2005–2008, corresponding incidence rates were 1.47 (1.44–1.50) and 4.43 (4.23–4.65). Among people without diabetes, the rate ratio comparing incidence in 2005–2008 with 1995–1998 was 0.46 (0.44–0.48). Among people with diabetes, the corresponding rate ratio was 0.31 (0.28–0.35), indicating a greater decline in MI incidence over the period ($p<0.001$ for interaction between interval and diabetes). Correspondingly, the rate ratio comparing incidence among those with diabetes to those without diabetes was attenuated from 2.70 (2.42–3.02) in 1995–1998 to 1.90 (1.80–2.00) in 2005–2008. Gender-specific analyses revealed the attenuation of the relative risks to be significant among both women and men.
Conclusion The excess risk of MI among diabetic patients appears to be falling over time. However, despite their improved prognosis, people with diabetes remain at a considerable excess risk of MI, emphasizing the need for continued concerted efforts to manage diabetes.

OP59 DO DEMANDS AND WORRIES FROM CLOSE SOCIAL RELATIONS INCREASE THE RISK OF SUBSEQUENT INCIDENT IHD HOSPITALIZATION? A 7 YEAR LONGITUDINAL STUDY OF MIDDLE-AGED DANISH MEN AND WOMEN

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Background The association between support from social relations and ischemic heart disease is well described, however the possible hazardous effects of negative aspects of social relations on cardiovascular health are less well known. The purpose of the present study was to analyze the possible influence of negative aspects of social relations (NASR) at baseline on the risk of development of ischemic heart disease (IHD) defined as incident hospitalized cases of acute myocardial infarction and chronic IHD during 7 year follow-up. NASR were defined as demands or worries from partner, children, family, and friends.
Methods Participants were included in a questionnaire-based study in 2000 and were a random sample (N=6767) of Danish men and women aged 40 or 50 years by October 1st 1999 from the Danish Longitudinal Study on Work, Unemployment and Health. Data for the present study are based on baseline questionnaire data in 2000 and register linked data from the period 2000–2007 on hospitalization for IHD (ICD10: I21–25). Cases of IHD (I21–25) four years prior to baseline were excluded from the analyses. In total 127 new cases of IHD were identified during follow-up.
Results Men who always or often experienced worries or demands from their partner had an increased risk of incident IHD compared to those who seldom/never experienced worries and demands HR(95%CI)=2.28(1.14–4.53) adjusted for age, socioeconomic status, cohabitation status, depressive symptoms, smoking and emotional support from all social relations . There was no association between demands/worries from partner and risk of development of IHD among women. Both men and women who experienced frequent worries and demands from their family (other than partner and children) were at increased risk of IHD HR=1.76(1.10–2.81) adjusted for above mentioned covariates and gender. Demands and worries from children and friends were not associated with significantly increased risk of IHD although estimates were in the same direction as for demands/worries from partner and family.
Conclusion For men, frequent demands and worries from a partner seem to be associated with increased risk of incident IHD hospitalization during 7 year follow-up. Demands/worries from family are risk factors for both women and men. Adjustment for the level of social support from all social relations did not change these conclusions. These findings confirm earlier findings of an association between NASR and self-reported angina pectoris. The weaker findings for women may partly be explained by the substantially smaller number of cases in this middle-aged cohort.

OP60 RISK OF FUTURE DEPRESSION IN PEOPLE WHO ARE OBESE BUT METABOLICALLY HEALTHY: THE ENGLISH LONGITUDINAL STUDY OF AGEING

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Background There is some evidence to suggest that obesity is a risk factor for the development of depression, although this is not a universal finding. This discordance might be ascribed to the existence of a 'healthy obese phenotype' – that is, obesity in the absence of the associated burden of cardio-metabolic risk factors. We examined whether the association of obesity with depressive symptoms is dependent on the individual's metabolic health.
Methods Participants were 3851 men and women (aged 63.0 ± 8.9 yrs, 45.1% men) from the English Longitudinal Study of Ageing, a prospective study of community dwelling older adults. Obesity was defined as body mass index ≥ 30 kg/m^2. Based on blood pressure, HDL-cholesterol, triglycerides, glycated haemoglobin, and C-reactive protein, participants were classified as 'metabolically healthy' (0 or 1 metabolic abnormality) or 'unhealthy' (≥ 2 metabolic abnormalities). Depressive symptoms were assessed at baseline and at 2 years follow up using the 8-item Centre of Epidemiological Studies Depression (CES-D) scale.
Results Obesity prevalence was 27.5%, but 34.3% of this group was categorized as metabolically healthy at baseline. Relative to non-obese healthy participants, after adjustment for baseline CES-D score and other covariates, the metabolically unhealthy obese participants had elevated risk of depressive symptoms at follow-up (odds ratio [OR] = 1.50, 95% CI, 1.05 – 2.15), although the metabolically healthy obese did not (OR=1.38, 95% CI, 0.88 – 2.17). We repeated the main analysis after excluding 451 participants with existing depressive symptoms (CES-D≥4) at baseline. There were 238 incident cases of depression at follow up, and in comparison

with healthy non-obese participants only the metabolically unhealthy obese participants had elevated odds of incident depression (OR=1.56, 95% CI, 1.09 – 2.22), but not their metabolically healthy obese counterparts (OR=1.45, 95% CI, 0.92 – 2.30) nor unhealthy non-obese participants (OR=1.38, 95% CI, 0.98 – 1.94). In further analysis we examined the associations between individual metabolic risk factors and depression. There was a dose-response association between the number of metabolic risk factors and risk of depression, although the risk only became significant in participants with more than one risk factor. Adverse triglycerides, impaired glycaemic control, and low grade inflammation were associated with depression at follow-up in models adjusted for age, sex and baseline CES-D score.

Conclusion The association between obesity and risk of depressive symptoms appears to be partly dependent on metabolic health, although further work is required to confirm these findings.

Population Based Studies: Intergenerational

OP61 IS MATERNAL IRON STATUS ASSOCIATED WITH OFFSPRING'S BLOOD PRESSURE AND ADIPOSITY? A MENDELIAN RANDOMIZATION STUDY

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Background Iron deficiency during pregnancy is a common problem. Experimental animal studies suggest that mothers deficient in iron during pregnancy are more likely to have offspring who become obese and have higher blood pressure. The use of random assortment of genes from parents to offspring can provide a method for assessing the causal impact of nutritional exposures, which is less likely to be influenced by confounding and reverse causality. The C282Y mutation in the *HFE* gene is robustly associated with iron stores, with those who carry the mutation having higher iron stores. Thus, this variant could be used as an instrumental variable to examine whether the association of maternal iron with offspring body mass index (BMI), waist circumference (WC) and blood pressure (BP) is causal.

Methods We conducted a Mendelian randomization study to examine the association between maternal iron status with offspring adiposity and BP in adulthood. Instrumental variable (IV) analysis, using maternal C282Y as a genetic instrument for mother's ferritin, was performed. IV analysis uses the proportion of the variation in maternal ferritin that is explained by C282Y to provide an unconfounded estimate of the relationship with offspring outcomes. The results were compared to the results of multivariable ordinary least squares (OLS) regression examining the same relationship. Male and female offspring of mothers from the UK Women Cohort Study (UKWCS) were approached, of whom 348 with mean age of 41 years completed the study. About half were offspring of C282Y carriers. Offspring's BP, height and weight were measured at their local medical practice. Participants were also asked to self-measure their WC at home.

Results Maternal C282Y was associated with maternal ferritin (mean difference per allele=84 g/l, 95% CI 31, 137, P=0.002). Using IV analyses, maternal ferritin was not associated with offspring's BP, BMI or WC. The first stage F statistic for the strength of the instrument was 10 (Kleibergen-Paap *rk* LM P-value=0.009). Maternal ferritin was associated with offspring diastolic BP, WC and BMI in univariable, but not in multivariable OLS analysis. There was no strong statistical evidence of a difference between the OLS and the IV models coefficients for any of the outcomes considered.

Conclusion We found no association between maternal iron status and offspring's BP and adiposity using both multivariable OLS and IV modeling with maternal C282Y mutation as the instrument. Further exploration of this relationship is needed in larger studies that have genetic variation assessed in both mother and offspring.

OP62 THE INFLUENCE OF PRENATAL MATERNAL AND PATERNAL ANXIETY AND DEPRESSION ON CARDIOVASCULAR BIOMARKERS IN THE CHILD AT AGE 10: FINDINGS FROM THE AVON LONGITUDINAL STUDY OF PARENTS AND CHILDREN (ALSPAC)

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Background The aim of the current study was to investigate whether exposure to prenatal maternal anxiety and depression influenced later offspring glucose, lipid and inflammatory markers via intrauterine mechanisms.

Methods Data from a prospective birth cohort based in the South West of England were used. Our analysis included 2839 mother-children duos and 2361 father-child duos for outcomes assessed at mean age 9.9 years (non-fasting cholesterol, triglycerides, low density and high density lipoprotein cholesterol (LDLc and HDLc), C-reactive protein (CRP) and interleukin 6 (IL–6) and 2011 and 1726 parent-child duos for outcomes at mean age 15.4 years (fasting glucose, insulin, lipids and CRP). We compared associations of maternal exposures with offspring outcomes to those of the same paternal exposures with offspring outcomes. The rationale for this comparison was that if maternal depression/anxiety influenced offspring outcomes via intrauterine mechanisms we would expect stronger maternal compared with paternal associations. We also examined whether any association of exposures during pregnancy reflected a postnatal effect, with persistence of depression/anxiety into the postnatal period.

Results Maternal anxiety at 18 and 32 weeks gestation, and maternal depression at 32 weeks gestation were associated with increased CRP in children at 9.9 years (mean difference (95% CI): 0.031 (0.005 to 0.057), 0.030 (0.004 to 0.056), and 0.021 (0.003 to 0.040) respectively), but not at 15.4 years. These associations remained when adjusting for potential confounders (maternal age, ethnicity, pre-pregnancy BMI, parity, social class, smoking and alcohol consumption). Paternal anxiety and depression (measured at 18 weeks gestation)were also associated with increased CRP in children at 9.9 years (mean difference (95% CI): 0.039 (0.003 to 0.076) and 0.026 (0–0.052) respectively), but not at 15.4 years. The magnitudes of the paternal associations were similar to those seen in mothers. Maternal and paternal postnatal depression/anxiety symptoms were also associated with offspring CRP at age 9.9 and appeared to explain much of the antenatal association.

There were no consistent associations between maternal or paternal anxiety or depression during the antenatal or postnatal periods and any of offspring glucose, insulin, IL-6 or lipids at either age.

Conclusion We have found evidence of a relationship between maternal and paternal anxiety and depression during pregnancy and CRP levels in childhood, which does not persist to adolescence. Our results suggest that these associations are unlikely to be explained by intrauterine mechanisms and may be explained by shared familial confounding or postnatal effects.

OP63 ASSOCIATIONS OF ALL-CAUSE AND CAUSE-SPECIFIC MORTALITY WITH BODY MASS INDEX IN A LARGE NORWEGIAN COHORT: USE OF OFFSPRING BODY MASS INDEX AS AN INSTRUMENTAL VARIABLE

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