

results provide first time evidence that self-reported walking speed, an indicator of functional reserve, is associated with positive pregnancy related biomarker profiles and require independent confirmation. Given the lower physical activity and functional profile of Pakistani women, there remains high potential for behaviour change interventions in this population group. To realise this ambition further research must focus on understanding specific cultural and socio-economic barriers to implementation.

P38 SOCIAL ISOLATION IN RELATION TO VASCULAR DISEASE INCIDENCE AND MORTALITY AMONG 325,000 UK WOMEN; A PROSPECTIVE COHORT STUDY

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10.1136/jech-2018-SSMabstracts.164

Background Research suggests that social isolation may increase the risk of developing or dying from vascular disease, but the evidence is inconsistent and may be affected by confounding and reverse causation, whereby poor health leads to being more socially isolated. We examined the association between social isolation and vascular disease incidence and mortality in the Million Women Study after accounting for confounding and reverse causation biases.

Methods Among 3 25 770 women (mean age 68 years) without vascular disease or cancer, frequency of contact with family or friends, groups, and number in household was reported and used to calculate a three-item social isolation score. Cox regression was used to estimate the relative risks (RR) and 95% confidence intervals (CI) of coronary heart disease (CHD) and stroke incidence and mortality in relation to social isolation. To reduce reverse causation bias, women who reported fair/poor self-rated health were excluded. Analyses were adjusted for demographic (age, region), socioeconomic (education, area deprivation), behavioural (smoking, alcohol consumption, physical activity and body mass index), disability, and health-related (hypertension, diabetes) risk factors. We assessed the proportion of the association that could be explained by each risk factor by calculating the percentage reduction in the likelihood ratio X^2 test statistic after each adjustment.

Results During 6 years of follow-up, there were 10 853 incident CHD events, 557 CHD deaths, 6269 incident stroke events and 585 stroke deaths. Compared to the least isolated women, the most isolated women (12% of participants) were not at an increased risk of incident CHD ($RR=1.07$, 95% CI 1.01 to 1.14, $p=0.06$) but were at increased risk of CHD mortality ($RR=1.80$, 1.40–2.31, $p<0.0001$); they were also at an increased risk of stroke incidence ($RR=1.28$, 1.18–1.38, $p<0.0001$) and mortality ($RR=1.70$, 1.33–2.16, $p<0.001$). With the exception of stroke mortality, adjustment for confounders, particularly for the behavioural factors, led to large reductions in the X^2 test statistic (e.g. 92% for CHD incidence; 64% for CHD mortality; 67% for stroke incidence; and 41% for stroke mortality).

Conclusion We found no association between social isolation and CHD incidence, but social isolation was associated with increases in CHD mortality and stroke incidence and mortality. Given the attenuation in these associations after adjustment

for health and lifestyle factors, residual confounding cannot however be ruled out.

P39 INTERVENTION DIFFERENTIAL EFFECTS AND THRESHOLD SELECTION: AN EVALUATION OF METHODS ILLUSTRATED IN WEIGHT-MANAGEMENT STUDIES

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10.1136/jech-2018-SSMabstracts.165

Background Intervention differential effects (IDE) occur when *change* in a health outcome following an intervention depends upon the *baseline* value of that outcome. Oldham's method and multilevel modelling are methods used to detect IDEs. However, the conditions under which these methods are robust are not well documented. One condition that has not been explored is detection of IDEs in studies which recruit according to baseline health status (i.e. above a threshold). We hypothesised that recruiting/selecting above a threshold affects the reliability of existing methods to detect IDEs because of regression to the mean. We hypothesised that comparing these 'truncated' samples with a control group restores the robustness of these methods. Using weight-loss interventions as an example, we show how to overcome the challenges of regression to the mean in studies with threshold selection criteria.

Methods We simulated two datasets comprising repeated measures of body mass index (BMI) data for 1000 males aged 25–34 ('population' datasets). One dataset was simulated to have an IDE, and the other ('null') dataset was simulated without. Half the population in each dataset were simulated to receive a weight-loss intervention. To emulate real-world weight-loss interventions, we truncated each population dataset to select intervention and control group samples with BMI scores above ≥ 30 kg/m². Oldham's method and multilevel modelling were used on the 'population' intervention groups and corresponding 'truncated' samples for each simulation. We repeated each analysis to contrast the intervention and control group datasets (using Fisher's z-transformation and student's t-test for Oldham's method, and the likelihood ratio test for multilevel modelling). Simulations were repeated 10 000 times to generate Type I error rates and 95% credible intervals. Simulations were performed in R and MLwiN.

Results Under the null of no IDE, Oldham's method and the multilevel model yielded Type I error rates $>90\%$, confirming that selecting above a threshold leads to bias due to regression to the mean. Type I error rates returned to 5% for the multilevel model when a control group was introduced and the likelihood ratio test employed, while Type I error rates improved but remained elevated when Fisher's z-transformation and student's t-test were used to contrast groups.

Conclusion Our study shows that multilevel models can robustly detect IDEs in 'truncated' samples (selected above a threshold) if analyses involve a control group. For study designs that do not collect control group data (such as most evaluations of weight management programmes), the identification of IDEs currently remains intractable.