

Plenary 1: Nutrition *in-utero*

Is nutrition *in utero* an antecedent of cardiovascular disease in later life?

RR Huxley¹, CG Owen², PH Whincup², DG Cook², J Rich-Edwards³, G Davey Smith⁴, R Collins⁵

¹The George Institute, University of Sydney

²Department of Community Health Sciences, St George's Hospital Medical School

³Department of Ambulatory Care and Prevention, Harvard Medical School

⁴Department of Social Medicine, University of Bristol

⁵Clinical Trial Service Unit & Epidemiological Studies Unit, University of Oxford

Background – The “fetal-origins” hypothesis of adult disease postulates that fetal undernutrition is associated with an increased susceptibility to the development of coronary heart disease (CHD) and allied disorders in later life. Individual published studies of the relation between size at birth and subsequent CHD risk factors have had limited statistical power to assess an association reliably, and explored the impact of confounding to differing degrees.

Review – A systematic review of the size and direction of the association between birthweight and subsequent coronary heart disease was conducted. Seventeen published studies of birthweight and subsequent coronary heart disease were identified including a total of 144,794 singletons. Relative risk estimates for the association between birthweight and coronary heart disease were obtained from sixteen of these studies. Additional data from two unpublished studies of 3801 individuals were also included. In total, the analyses included data from eighteen studies on 4210 non-fatal and 3308 fatal coronary heart disease events in 147,009 individuals. The mean weighted estimate for the association between birthweight and the combined outcome of non-fatal and fatal coronary heart disease was 0.84 (95% CI 0.81-0.88) per kg of birthweight. There was no strong evidence of heterogeneity between estimates in different studies ($p=0.09$) or of publication bias (Begg test $p=0.3$). Restricting the analysis to fatal coronary heart disease events had little effect on the overall mean weighted estimate (0.84, 95% CI 0.80-0.88). Fifteen studies were able to adjust for some measure of socioeconomic position, either in early or current life, but such adjustment did not materially influence the association: 0.85 (95% CI 0.81-0.90).

Conclusions – These findings are consistent with one kilogram higher birth weight being associated with 10-20% lower risk of subsequent coronary heart disease. Further studies are needed to establish whether the observed association reflects a stronger underlying association with a related exposure, or is due, at least in part, to residual confounding.