

Wednesday 9 September

Parallel session A

Life course CVD

001 IS ACCELERATED POSTNATAL GROWTH ASSOCIATED WITH BLOOD PRESSURE IN CHILDHOOD?

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Objective: To investigate whether variations in growth patterns in early-life are associated with blood pressure at age 6.5 years by modelling detailed, individual growth trajectories between birth and 5 years of age.

Design: Prospective cohort study nested in a large randomised trial.

Setting: Belarus.

Participants: 10 494 children from Belarus who were born in one of 31 hospitals that participated in a cluster randomised trial of breastfeeding promotion intervention and had multiple measures of height and weight from birth to age 6.5 years. We analysed all 13 childhood growth measurements to develop a best-fitting linear spline random-effects model with 2 knots (thus dividing follow-up into 3 time periods, each with its own trajectory). The spline models were used to generate 4 random effects coefficients: birthweight; “early infant weight velocity” (birth–3 mo); “late infant weight velocity” (3 mo–1 yr) and “childhood weight velocity” (1–5 yrs). Each coefficient denotes an individual’s deviance from average birthweight or velocity at each time period; together, the coefficients are a within-subject summary of each child’s growth curve from birth to 5 years. The coefficients were converted into age-standardised z-scores to render them directly comparable.

Main Outcome Measures: Systolic and diastolic blood pressure (mm Hg) measured at age 6.5 years. Sex-specific OLS was used to investigate associations of each coefficient with blood pressure, controlled for hospital and baseline confounders.

Results: Birth-weight and weight velocity at all 3 time-periods were positively associated with blood pressure in boys. The change in systolic blood pressure per z-score increase in growth was 0.27 (95% CI 0.07 to 0.47) for birthweight; 0.47 (0.26 to 0.68) for “early infant weight velocity”; 0.70 (0.50 to 0.90) for “late infant weight velocity” and 0.96 (0.76 to 1.16) for “childhood weight velocity”. Associations were similar for girls (all p-values for interactions >0.1).

Conclusion: Children’s growth trajectory between birth and 5 years was positively associated with blood pressure at age 6.5 years. Associations increased in magnitude with age. Further analysis will investigate whether early or late infant growth have any additional influence on blood pressure levels in childhood, over and above weight at 6.5 years.

002 ELEVATED BLOOD PRESSURE IN EARLY ADULTHOOD AS A PREDICTOR OF LATER CORONARY HEART DISEASE MORTALITY: UP TO 83 YEARS FOLLOW-UP IN THE HARVARD ALUMNI HEALTH STUDY

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Objectives: Few studies have examined the association between blood pressure in early adulthood and later coronary heart disease

(CHD). In those that have, whether the impact of early adult blood pressure is mediated via blood pressure in middle age or, if it exerts an independent effect, has yet to be tested. We examined these issues using extended follow-up of the Harvard Alumni Study.

Design: Cohort study of male University students who had a physical examination at college entry between 1914 and 1952 (mean age 18.4 years) when data on CHD risk factors including blood pressure were measured directly. Study participants were traced, mailed a health questionnaire in 1962/1966 (mean age 45.3 years) which included enquiries regarding self-reported physician-diagnosed hypertension, and were followed for subsequent mortality experience – which is >99% complete – until the end of 1998. Blood pressure at college entry was categorised according to Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure criteria: normotensive (<120/<80 mm Hg), pre-hypertension (120–139/80–89 mm Hg), stage 1 hypertension (140–159/90–99 mm Hg) and stage 2 hypertension (≥160/≥100 mm Hg).

Setting: USA.

Participants: 15 488 men enrolled in Harvard University in the given years, who completed the subsequent health questionnaire, and whose vital status could be ascertained.

Main Outcome Measure: CHD death.

Results: Over a maximum of 83.5 years of follow-up (median 52.6 years), there were 1531 deaths from CHD. Following adjustment for age and other CHD risk factors (body mass index, cigarette smoking status and physical activity) at college entry, in comparison to men who were normotensive there was an elevated risk of CHD mortality in those categorised as pre-hypertensive (hazards ratio 1.21, 95% CI 1.07 to 1.36), stage 1 hypertensive (hazards ratio 1.46, 95% CI 1.25 to 1.70), and stage 2 hypertensive (hazards ratio 1.89, 95% CI 1.46 to 2.45) (test for trend: $p<0.001$). After additional adjustment for self-reported hypertension in middle-age, CHD risk in relation to college blood pressure was somewhat attenuated but remained elevated: pre-hypertensive (1.17; 1.03 to 1.32), stage 1 hypertensive (1.33; 1.14 to 1.56), stage 2 hypertension (1.63; 1.26 to 2.12) ($p<0.001$ test for trend).

Conclusion: In this cohort, higher measured blood pressure in early adulthood was associated with an elevated risk of CHD mortality several decades later, and these effects appear to be independent of self-reported hypertension in middle-age. These results may suggest that blood pressure lowering strategies should begin earlier in the life course than is currently the case.

003 WORKING CHARACTERISTICS AND CARDIOVASCULAR DISEASE: ARE ASSOCIATIONS CONFOUNDED BY EARLY LIFE RISK FACTORS?

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Objectives: Work characteristics, such as night work, long hours and psychosocial work stress, have been found to be associated with cardiovascular disease (CVD) but the pathways from work to increased CVD risk are unclear. Since numerous early life indicators of CVD risk have been identified, including prenatal, socio-economic, environmental, physical, cognitive and behavioural factors, it is possible that associations seen for work arise through pre-existing CVD risk prior to entering the labour market. To determine whether cross-sectional relationships seen for working characteristics and risk factors for CVD in mid-adult life are confounded by early life risk factors for CVD, the following questions are addressed: (i) are work characteristics associated with CVD risk factors independently of each other? (ii) do work

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characteristics interact so that combinations of factors carry cumulative risk for CVD? (iii) are associations explained by early life predictors of CVD risk.

Design: Birth cohort.

Setting: England, Scotland and Wales.

Participants: 7916 men and women in the 1958 British birth cohort who were in paid employment at 45 y.

Main Outcome Measures: Body mass index (BMI), waist circumference (WC), blood pressure (BP), triglycerides, total and high density lipoprotein (HDL) cholesterol, glycosylated haemoglobin (HbA1c), and inflammatory factors: fibrinogen, C-reactive protein (CRP).

Results: Night work was associated with adverse levels of most outcomes examined (except BP and total cholesterol). Working ≥ 48 h/week was associated with BMI and WC only; low job control with HDL, HbA1c, and inflammatory factors; low demands, rather than high demands, with systolic BP, triglycerides, HDL and inflammatory factors. Several work factor/CVD associations were weakened when mutually adjusted for each other and an interaction between night work and low demands was commonly found. Adjustment for childhood factors up to 16 y explained a substantial proportion of the associations. To illustrate, for BMI, adjustment for a range of childhood factors reduced the associations for night work/low demands (0.78 kg/m², 95% CI 0.35 to 1.21) and working ≥ 48 h/week (0.31 kg/m², -0.01 to 0.62) by 50% and 22%, respectively. However, BMI at 16 y accounted for 45% of the association between working ≥ 48 h/week and BMI at 45 y (adjustment for some childhood factors strengthened the association between work hours and BMI).

Conclusions: Initial findings suggest that childhood factors up to the age of 16 y explain a large proportion of the cross-sectional associations seen for work characteristics and risk factors for CVD in mid-adulthood suggesting that associations arise in part from social and health disadvantage originating earlier in life.

004 LIFECOURSE PREDICTORS OF ADULT FIBRINOGEN CONCENTRATIONS: THE NEWCASTLE THOUSAND FAMILIES BIRTH COHORT

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Objectives: To investigate the relative influences of early life and later determinants of plasma fibrinogen concentrations at age 49–51 years.

Design: Follow-up study of the Newcastle Thousand Families birth cohort established in 1947.

Participants: 173 men and 221 women who attended a clinical examination between October 1996 and December 1998 and also gave blood samples.

Main Outcome Measure: Concentration of plasma fibrinogen. This was analysed, using linear regression, in relation to a range of variables at different stages of life, including family history of cardiovascular disease, birth weight (standardised for gestational age and sex), duration breast fed, housing conditions at birth, history of childhood illness, cigarette smoking history, alcohol consumption, percent body fat, physical activity levels, and socio-economic status both at birth and in adulthood.

Results: Poorer housing conditions at birth ($p=0.001$), longer duration breast fed ($p=0.025$) and higher adult alcohol consumption ($p=0.002$) were all significant independent predictors of lower plasma fibrinogen concentration at age 49–51 years. In contrast, increasing body fat percentage ($p<0.001$) and being a current smoker ($p<0.001$) were both independently predictive of a

significantly higher fibrinogen concentration. No association was observed between plasma fibrinogen concentration and standardised birth weight or with time since stopping smoking the former smokers. Three significant interactions on adult fibrinogen levels were observed. (1) The effect of being a current smoker, relative to never smokers, was highest among those from the poorest quality houses at birth. (2) The effect of percent body fat was lower among never smokers. (3) The effect of percent body fat was greater among those with the highest alcohol consumption at age 49–51. A full path diagram, exploring the relative contributions, including an exploration of indirect pathways, will be presented.

Conclusions: Concentration of plasma fibrinogen in adulthood is influenced by a range of factors from different stages of life. Although birth weight was not a predictor, there were significant associations with housing conditions in early life and duration breast fed. Regardless, the total variation explained by early life factors was less than half of that explained by adult risk factors. Therefore, modification of adult exposures, particularly body fat percentage and smoking, would be the most likely way to reduce the concentration of plasma fibrinogen in adulthood, which may also reduce the risk of cardiovascular disease.

Maternal health

005 SOCIAL AND BIOLOGICAL DETERMINANTS OF REPRODUCTIVE SUCCESS IN SWEDISH MALES AND FEMALES BORN 1915–1929

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Objective: To investigate whether early life characteristics predict subsequent reproductive success in a post-demographic transition population; to ascertain the pathways mediating any observed effects; and to examine whether any of the above effects are gender-specific.

Design: Multi-generational data from a representative, population-based birth cohort and using linkage to routinely collected data.

Setting: Uppsala, Sweden.

Participants: 13 666 individuals born in Uppsala university hospital between 1915 and 1929, who were traced and linked to all registered descendants up to 2002.

Characteristics Measured at Birth: Birthweight for gestational age, preterm birth, birth multiplicity, birth order, mother's age, mother's marital status and family socio-economic position.

Measures of Reproductive Success: Primary measures: number of children; number of grandchildren. Secondary measures of the pathways to reproductive success: survival to age 15, survival from age 15 to age 50; probability of marriage; number of children within marriage; number of grandchildren at a given number of children.

Results: Reproductive success was associated with both social and biological characteristics at birth, and the effects of these characteristics were mediated via both mortality and fertility. In both sexes, a higher birthweight for gestational age, a term birth and a younger mother were independently associated with a greater number of descendants. A married mother and higher family socio-economic position were also associated a greater number of descendants in males (but not females), while in females (but not males) higher birth order was associated with higher reproductive success. These differences between the genders were mediated by the differential effects upon the probability of marriage in men and women. Probability of marriage was also affected by a range of other characteristics at birth including a lower probability of marriage for individuals of low birthweight and males who were