Welcome to the British Regional Heart Study (BRHS) Annual Newsletter. We have had another busy period, with 33 published papers and 8 conference presentations during 2016-2017.

**UPDATE ON ACTIVITIES AND INITIATIVES**

**DATA COLLECTION:** The 2017 annual data collection is currently in progress, with a Postal Questionnaire sent out to participants and GP Record Reviews in progress. The response to data collection in 2016 continued to be high, with 65% of surviving participants responding to the postal survey and 97% of our colleagues in General Practices. We are indebted both to the cohort members and our colleagues in General Practices across England, Wales and Scotland for taking the time to complete these forms.

**OVERVIEW OF PAPERS PUBLISHED IN 2016-2017**
Reports from the BRHS group in the last year have addressed a range of issues relevant to the health of older people, with a particular emphasis on cardiovascular disease and its determinants. Several reports have examined scope for using novel risk markers to predict cardiovascular disease, stroke and heart failure. Frailty among older people has been an important theme, with reports on the prospective associations between frailty and the development of physical disability and risks of mortality and the associations between frailty and sensory impairments. Patterns of physical activity and sedentary behaviour in older men and their associations with novel cardiovascular risk factors, sarcopenia, sarcopenic obesity and subclinical vascular disease have been examined. There has been considerable interest in the associations between sleep patterns and cardiovascular disease, reflected here in a report on the associations between sleep duration, napping and heart failure risk. A series of reports have examined the influence of environmental temperature (particularly the effects of cold weather) on physical activity patterns in older people and its associations with cardiovascular risk. As in previous years, BRHS has participated in important collaborative genetic studies; recent reports have been disentangling the causal links between adiposity, renal disease, plasma urate and cardiovascular disease risk.

**WORK IN PROGRESS**

**Patterns of physical activity from mid to later life**
Current evidence suggests that physical activity declines with age, particularly between the fifth and ninth decades of life. The transition from middle age to later life coincides with a number of major life events (e.g. retirement) that may influence physical activity patterns. However, to date
very little is known about the long-term patterns of physical activity during this period and the consequences of these patterns on later health outcomes. Understanding these patterns may help the development of interventions aiming to promote maintenance of an active lifestyle into old age. Preliminary results have highlighted diverse patterns of physical activity over 20-years of follow up. Several factors were associated with maintenance of a physically active lifestyle, such as having a non-manual occupation, having children and absence of doctor-diagnosed health conditions. Future studies will seek to understand how these long-term patterns of physical activity are associated with CVD events and mortality.

**Socioeconomic factors and incidence of type 2 diabetes in older age**

Current evidence linking socioeconomic factors to incident Type 2 Diabetes Mellitus (T2DM) in older populations is conflicting. In the British Regional Heart Study, we investigated the prospective association of individual socioeconomic position and neighbourhood-level socioeconomic deprivation with incident T2DM in older British men. We also examined possible factors underlying these associations. Our investigations were based on follow-up of the cohort from age 60-79 years (in 1998-2000) for 14 years. We explored the role of individual socioeconomic position (occupational social class) and neighbourhood deprivation based on Index of Multiple Deprivation (IMD), a composite score of neighbourhood-level factors (income, employment, education, disability, crime, housing and living environment). We found that the risk of incidence of diabetes increased from higher to lower social class groups and from IMD quintile 1 (least deprived) to quintile 5 (most deprived). The association of social class with diabetes risk was largely attenuated on adjustment for body mass index (BMI) and further attenuated on adjustment for triglycerides. The greater risk of incident diabetes in those from deprived neighbourhoods was also attenuated on adjustment for BMI and for other lifestyle factors (smoking, physical activity and diet). Our findings show that manual social class and neighbourhood-level socioeconomic deprivation was associated with an increased risk of T2DM in older British men. For social class this was mostly explained by BMI and triglycerides. For neighbourhood-level socioeconomic deprivation it was largely explained by BMI and lifestyle factors. Our results support the need for public health initiatives specifically targeting obesity as a means towards reducing socioeconomic inequalities in type 2 diabetes in later life.

**Diet quality, sarcopenia and frailty**

We are currently investigating whether dietary quality is related to sarcopenia and/or frailty. We are using both *a priori* approaches (using predefined dietary scores based on dietary recommendations or guidelines) and *a posteriori* approaches, deriving dietary patterns from our data using principal component analysis. Our dietary data is collected in the form of a food frequency questionnaire, from which we derived the Healthy Diet Indicator (HDI) and the Elderly Dietary Index (EDI), both pre-defined scores. We identified three *a posteriori* patterns; (i) a prudent dietary pattern high in poultry, fish, vegetables, legumes, pasta and rice, and eggs, (ii) a high fat/low fibre pattern and (iii) a high sugar pattern. Men with a healthier diet, as indicated by the HDI, showed a lower risk of frailty and we also saw a trend for men with a higher score for the high sugar pattern to show a lower risk of frailty. When we looked at the five individual components of frailty, dietary patterns were most consistently associated with low physical
activity; a healthier diet indicated by the HDI or EDI was associated with a lower risk of physical inactivity, as was a higher score for the high fat / low fibre dietary pattern and the high sugar pattern. We have found no evidence of associations between diet quality and sarcopenia or sarcopenic obesity.

**Physical activity, sedentary behaviour and cardiac biomarkers**

As part of our work investigating how patterns of physical activity (PA) and sedentary behaviour (SB) are related to cardiovascular risk factors, we have investigated associations with markers of cardiac injury, specifically N-terminal pro-brain natriuretic peptide (NT-proBNP) and high sensitivity Troponin T (hsTnT). We found that relationships between physical activity and NT-proBNP or hsTnT are non-linear; biomarker levels are lower with higher total physical activity, steps, moderate/vigorous physical activity and light physical activity, but only at low to moderate levels of physical activity. These relationships were independent of sedentary behaviour. Biomarker levels increased linearly with increasing sedentary behaviour, but not independently of moderate/vigorous physical activity. Our data suggest that it is physical activity rather than sedentary behaviour which is driving the relationships with cardiac biomarkers. However, given the cross-sectional nature of our data we cannot exclude the possibility of reverse causality.

**Identifying those at high risk of living in cold homes**

We are investigating the effect of cold housing and mortality. This is important research as an estimated 5500 people die every year in England and Wales from living in a cold home. Our preliminary findings suggest that increasing financial difficulties and lower social class are not the only factors which increase older people’s difficulties to keep warm during winter. Factors such as social isolation, poor respiratory health and low physical function are also associated with living in cold homes. These findings could inform UK policies aimed to tackle the adverse effect of multiple risk factors associated with living in cold homes.

**Creatinine versus cystatin C for the assessment of chronic kidney disease in older adults.**

Chronic kidney disease (CKD) diagnosis relies on calculation of the estimated glomerular filtration rate (eGFR) commonly based on serum creatinine and its use in the older population may lead to inaccurate estimations of GFR. Cystatin C is an alternative GFR marker less influenced by exogenous factors. The CKD Epidemiology Collaboration (CKD-EPI) has developed an equation for estimating GFR using this marker (CKD-EPI_{Cys}). Whether this is a better indicator of CVD mortality in older adults than the CKD-EPI creatinine based equation (CKD-EPI_{Cr}) is still unclear. We have investigated the association between CKD classification, using CKD-EPI_{Cr} and CKD-EPI_{Cys}, and CVD mortality in older adults to assess whether there is any difference between the two equations. The hazard ratio for all CVD mortality in those with CKD stages 4 and 5 versus those with CKD stages 1 and 2 was 3.62 (95% CI, 2.08-6.3) and 2.83 (95% CI, 1.62-4.95) using CKD-EPI_{Cr} and CKD-EPI_{Cys} respectively. For all-cause mortality the hazard ratio was 2.57 (95% CI, 1.87, 3.54) and 2.09 (95% CI, 1.51, 2.88) using CKD-EPI_{Cr} and CKD-EPI_{Cys} respectively. Assessment of CKD using CKD-EPI_{Cys} does not improve prediction of all cause and CVD mortality in older British men compared to the CKD-EPI creatinine based equation.
Serum Magnesium and incident heart failure
We have examined the association between serum magnesium and incident heart failure (HF) in older men and investigated potential pathways including cardiac function, inflammation and lung function. Low serum magnesium (lowest quintile; <0.75 mmol/l) was associated with many adverse CVD risk factors including diabetes, heavy drinking, atrial fibrillation, poor lung function, inflammation, endothelial dysfunction and cardiac dysfunction. Serum magnesium was inversely related to risk of incident HF even after adjustment for conventional CVD risk factors, atrial fibrillation, markers of inflammation (IL-6) and endothelial dysfunction (vWF) \( p \text{(trend) } =0.03 \). Further adjustment for FEV1 and cardiac dysfunction (cardiac troponin T) attenuated the association but risk remained significantly reduced in those in the top quintile (≥0.87 mmol/l) compared to those in the lowest quintile. The potential beneficial effect of high serum magnesium was partially explained by its favourable association with CVD risk factors.

Serum uric acid, antihypertensive treatment and risk of incident heart failure
The role of serum uric acid (SUA) as a prognostic marker for incident heart failure (HF) in hypertensive subjects is uncertain. We have prospectively examined the relationship between SUA and incident HF in those on and not on antihypertensive treatment who were followed up for a mean period of 15 years. The men were divided into three groups of SUA concentrations/levels (<350, 350-410 and >410 mmol/l). Raised SUA was associated with significantly increased risk of HF in men on antihypertensive treatment (N=949) but not in those without (N=2491) \( p=0.003 \) for interaction). In men on antihypertensive treatment those with hyperuricemia (>410 mmol/l) had the most adverse biological risk profile for HF including the highest rates of atrial fibrillation and renal dysfunction and the highest mean level of BMI, c-reactive protein and cardiac function (cardiac troponin T). Treated hypertensive men with SUA levels > 410 mmol/l showed an increase in risk of HF of more than twofold compared to those on treatment with levels <350 mmol/l even after adjustment for lifestyle characteristics and biological risk factors. SUA improved prediction of HF beyond routine conventional risk factors \( p=0.02 \) for improvement in c-statistics.

EXTERNAL COLLABORATIONS
We continue to collaborate with several external collaborative initiatives, including the Emerging Risk Factor Collaboration (ERFC) and the University College London-Edinburgh-Bristol (UCLEB) Consortium. The research work that has been generated from these initiatives is included in the publication list.
PRESENTATIONS AT CONFERENCES

Oral presentations

Society for Social Medicine, York, UK. September 2016

• Associations between poor oral health and incident frailty and disability in a population-based sample of older British men. Ramsay SE et al.
• Self-reported frailty components predict incident disability, falls and all-cause mortality in later life: results from a prospective study of older British men. Wannamethee SG et al.
• The influence of life-course socioeconomic factors on oral health in older age: findings from a longitudinal study of older British men. Papachristou E et al.

International Association of Dental Research, San Francisco, USA. March 2017.

• Associations between poor oral health and frailty: results from a population-based cohort of older British men. Ramsay SE et al.

Poster presentations:

Society for Social Medicine, York, UK. September 2016

• Cross-sectional associations of objectively measured physical activity and sedentary time with sarcopenia and sarcopenic obesity in older men. Aggio D et al.
• Associations of outdoor temperature and cardiovascular disease risk factors in the elderly: evidence from two large Northern European studies. Sartini C et al.


• Associations of outdoor temperature and cardiovascular disease risk factors in the elderly: evidence from two large Northern European studies. Sartini C et al.


• Prospective associations of individual and neighbourhood-level socioeconomic factors with incidence of type 2 diabetes in older British men. Roberts D et al.

PUBLICATIONS:


**ACKNOWLEDGEMENTS**

We are extremely grateful to all the men participating in the BRHS, who continue to respond to our requests for help almost 40 years after initially agreeing to take part in the study! We also wish to express our thanks to the BRHS General Practices for their continuing help and support. The continuing support provided by the British Heart Foundation (including both Programme and Project Grant funding) is gratefully acknowledged. We would also like to thank the National Institute of Health Research and Dunhill Medical Trust for their current support and to the Medical Research Council, Department of Health and Diabetes UK for their support in previous years.

With best wishes on behalf of the BRHS team,

Professor Peter Whincup

Professor Goya Wannamethee

Directors of the BRHS Research Group