Welcome to the British Regional Heart Study (BRHS) Annual Newsletter. We have had another busy period, with 33 published papers and 11 conference presentations during 2015-2016.

**UPDATE ON ACTIVITIES AND INITIATIVES**

**DATA COLLECTION  Postal Questionnaire 2016** We are currently sending out a postal questionnaire to all surviving study participants, to provide an update on their health and health determinants. **Record Review 2016:** The annual review of participants’ GP records is also in progress; we thank our colleagues in General Practices across England, Wales and Scotland for taking the time to complete these forms, which provide an important update on the health of our cohort members.

**News from the team**

Professor Wannamethee and colleagues have received funding from the Dunhill Medical Trust to examine the association between Advanced glycation end products (AGEs) and frailty, body composition and incident mobility limitation and identify optimal dietary patterns associated with AGEs to reduce frailty and disability in the elderly.

**OVERVIEW OF PAPERS PUBLISHED IN 2015-2016**

Recent reports published by the BRHS group have again addressed a range of themes related to cardiovascular disease risk in older populations. The patterns of physical activity and sedentary behaviour in older men (assessed using accelerometry) and their associations with body fatness and cardiometabolic risk (including non-invasive markers) have been the subject of several recent reports. The associations between several potential metabolic predictors of heart disease and diabetes (copeptin, troponin, plasma sodium) have been examined. Body composition, particularly body fatness, continues to be an important theme; the influence of body fatness at different stages of the life course on cardiovascular disease and diabetes has been documented, while another report has drawn attention to the association between body fatness in later life and impaired cognitive function. The links between frailty, an important public health problem in later life and cardiovascular risk have been documented. In addition, associations between cardiovascular disease and other important health challenges in later life, including poor oral health and hearing impairment, have been documented. As in previous years, BRHS has participated in important genetic studies; in the current year these have been disentangling the causal links between cigarette smoking and body weight and between height and cardiovascular disease risk.

**WORK IN PROGRESS**

**Associations between hearing impairment and other health conditions including disability.** Hearing impairment is a common health problem in later life. However, relatively little population-based research has investigated the associations between hearing impairment and other health conditions including disability. In the BRHS questionnaire in 2003 (when men were aged 63-85
years), 27% reported hearing impairment (the use of a hearing aid and/or not being able to follow a TV programme at a volume others find acceptable). We investigated the association between reporting hearing in 2003 and the risk of developing difficulties walking, undertaking activities of daily living (ADL) (including getting dressed, showering, etc.) and performing instrumental activities of daily living (IADL) (including shopping, telephoning, etc.) over 2 years independent of age, social class, lifestyle factors and comorbidities. The results showed that those who could hear and used a hearing aid, and those who could not hear despite using a hearing aid had increased risks of IADL difficulties. This suggests that hearing impairment may increase the risks of developing difficulties undertaking IADL, which are important for maintaining functional independence in later life.

**Simple self-reported questions on frailty components can identify older people at high-risk of incident disability, falls and mortality**

Frailty is an important public health challenge for ageing populations. It is a state of age-related decline in physiological systems resulting in increased vulnerability to external stressors, and is associated with adverse outcomes including disability, falls, and mortality. Assessments of frailty components including grip strength, weight loss, physical activity and gait speed are complex or require objective measurements which are challenging in routine primary care practice. We, therefore, developed a simple assessment tool based on self-reported frailty components that could be used to identify people at-risk of disability, falls, and mortality. Using data from the most recent physical examination of the British Regional Heart Study (BRHS) participants at age 71-92 years in 2010-12, we have compared the ability of self-reported and objective frailty measures in predicting disability, falls and mortality over a three year period. Our results showed that information on self-reported slow walking speed, low physical activity and exhaustion were predictive of the development of disability over the three year period. Moreover, self-reported slow walking speed, low physical activity and weight decrease were predictive of falls. These measures were also significant predictors of all-cause mortality. The ability of these simple self-reported measures to predict these adverse outcomes was greater than that of the established frailty phenotype, which requires objective assessments. These findings offer a simple way to identify older people at high-risk for adverse outcomes associated with frailty and have important potential implications for the formulation of interventions and healthcare policies.

**Poor oral health in older people and its associations with frailty and disability**

At the most recent follow-up examination of the British Regional Heart Study at 71-92 years (2010-12), new measures of oral health were made in the cohort. These included assessments of tooth loss and periodontal (gum) disease as well as questions on dryness of mouth and impact of dental health on quality of life. Poor oral health is an important, yet under-researched, aspect of the health of older people. Oral health assessments in the BRHS have provided new opportunities to quantify the burdens of oral health problems in older people and to investigate their associations with other age-related conditions. In the BRHS 20% of participants (aged 71-92 years) had complete tooth loss, 43% had <21 teeth (the minimum number recognised for optimal function), 43% had periodontal disease, and 31% reported symptoms of dry mouth. These findings highlight the scale of oral health problems which have a significant impact on the nutritional intake and quality of life of older people.

Poor oral health is associated with frailty in older age. However, few studies have investigated this association with detailed measures of oral health and existing studies are mostly cross-sectional. In the BRHS, we investigated the prospective associations between oral health measures at 71-92 years and incident frailty and disability over a three-year follow-up period. We used data on 1,222 participants who were assessed through a questionnaire and a dental examination at 71-92 years,
and followed-up with a postal questionnaire in 2014. The results of this investigation showed that participants with complete tooth loss, dry mouth symptoms, and those with increasing number of oral health problems had significantly increased risks of becoming frail over the three-year follow-up. Poor self-rated oral-health, having less than 21 teeth, dry mouth symptoms and the presence of three or four oral health problems were also associated with incident disability. Overall, these findings suggested that several subjectively and objectively assessed oral health measures predict incident frailty and disability. Poor oral health appears to be an early marker of frailty and disability among the older population.

**Life-course socioeconomic factors and oral health in older age**

Socioeconomic disadvantage during childhood and adulthood is an established risk factor for oral health problems in middle-age. Recent attempts to identify life-course models that explain the relationship between socioeconomic position and oral health have been limited by cross-sectional study designs, limited measures of oral health, or lack of data covering the entire life-course. Moreover, whether life-course socioeconomic factors influence poor oral health in older age is not fully established. In the British Regional Heart Study we have investigated the influence of socioeconomic factors in childhood, middle-age and later life on poor oral health in older age (71-92 years). In particular, we investigated the influence of different life-course models (sensitive period, accumulation of risk, social mobility) on a range of oral health outcomes (tooth loss, periodontal disease and self-rated oral health). We used information on 1,903 men with available data on socioeconomic factors in childhood, middle-age (40-59 years) and later life (60-79 years); information on oral health was collected at 71-92 years during the re-examination at 2010-12. The results suggest that socioeconomic disadvantage in middle-age is associated with tooth loss at 71-92 years, while cumulative socioeconomic disadvantage across the life-course was associated with poor self-rated oral health at 71-92 years. No significant associations were observed between life-course socioeconomic factors and measures of periodontal (gum) disease. Overall, our findings suggested that the way in which socioeconomic influences affect oral health differ depending on the specific oral health outcome being studied.

**Physical activity and sedentary behaviour in relation to non-invasive vascular measures and ankle brachial index**

We continue to investigate how patterns of physical activity (PA) and sedentary behaviour (SB) are associated with cardiovascular risk factors and with non-invasive vascular measures as markers of CVD risk, and with ankle-brachial index (ABI) as a marker of peripheral arterial disease. Physical activity has been measured using accelerometry which allows us to examine the importance of different intensities of activity, moderate to vigorous activity, light activity and sedentary behaviour. We found that a higher total amount of physical activity and a higher number of daily steps were associated with potentially beneficial differences in carotid intima thickness (CIMT), distensibility coefficient (DC), carotid femoral pulse wave velocity (cfPWV), augmentation index (Alx) and ankle brachial pressure (ABI). More time in SB was associated with potentially adverse differences in non-invasive vascular measures and ABI. We found no evidence that bouts of PA lasting 10 minutes or more were differently related to outcomes from PA bouts lasting less than 10 minutes. The independence of PA and SB differed between vascular measures. More intensive PA showed a stronger association with ABI which persisted after adjustment for light PA or SB. Light PA was associated with cfPWV and CIMT. Older men may gain health benefits from light activity and also from bouts of moderate to vigorous activity lasting less than 10 minutes – forms of PA which receive little or no emphasis in current UK physical activity guidelines.
The influence of neighbourhood socioeconomic deprivation on poor oral health in older age

Socioeconomic inequalities in oral health are well-established. However, evidence on the influence of neighbourhood or area-level socioeconomic factors on poor oral health in older populations is limited. Therefore, in the British Regional Heart Study we aimed to examine the extent to which area-level deprivation is associated with poor oral health in older age (71-92 years), and whether this association is independent of individual-level socioeconomic position. Area or neighbourhood-level deprivation was based on the index of multiple deprivation (IMD) available at aggregate level for small geographical units referred to as ‘lower super output areas’ (LSOA) with an average of 1,500 people. The findings suggest that the risk of poor oral health (particularly periodontal [gum] disease, and poor self-rated oral health) was higher in older men in more deprived neighbourhoods. This increased risk was independent of individual social class, smoking, depression, social interactions and a history of diabetes. We also sought to identify the association of perceived neighbourhood quality indices with worse oral health in older age. Low scores of perceived neighbourhood safety as well as of a cumulative score of perceived neighbourhood quality (including local area services, safety, greenery and neighbourhood environment) were associated with a range of oral health outcomes (tooth loss, periodontal disease, poor self-rated oral health, and dry mouth symptoms). Our findings suggest that neighbourhood deprivation as well as neighbourhood quality factors are likely to play an important role in reducing inequalities in oral health in older populations.

sRAGE and associations with vascular disease

The soluble receptor for advanced glycation end products (sRAGE) has been implicated in diabetic vascular complications. We have examined the association between sRAGE and cardiac markers [NT-proBNP and cardiac troponin T (cTnT)] and subclinical vascular markers in older men with and without diabetes. Subclinical vascular measurements included carotid intima media thickness (cIMT), arterial stiffness [pulse wave velocity (PWV)] and arterial wave reflections [central augmentation pressure (AUG) and augmentation index (Alx)]. sRAGE was significantly and positively associated with NT-proBNP (but not cTnT) and AUG and Alx in both groups of men after adjustment for CVD risk factors including BMI, metabolic risk markers, renal function and inflammation. However, no association was seen between sRAGE and cIMT or arterial stiffness in either group. Higher plasma sRAGE was associated with increased Nt-proBNP and markers of arterial wave reflections in both men with and without diabetes.

Conjugated linoleic acid and incident heart failure

Evidence largely from animal studies suggests that conjugated linoleic acid (CLA) may have cardiovascular health benefits. We have examined the association between serum CLA and incident coronary heart disease (CHD) and heart failure (HF) in older men. A high throughput serum nuclear magnetic resonance (NMR) metabolomics platform was used to measure CLA concentration in serum expressed as a percentage of total fatty acids (CLA%). CLA% was strongly positively associated with blood lipids and inversely associated with inflammation and NT-proBNP (a marker of ventricular stress). No association was seen between CLA% and incident CHD. High CLA% was associated with significantly reduced risk of HF after adjustment for HF risk factors and inflammation but was attenuated after further adjustment by NT-proBNP. The data suggests that a diet rich in CLA may be protective against the development of HF in older men.
Explaining excess winter mortality from CVD

CVD mortality in the UK exhibits a marked seasonal variation and is markedly higher in winter. The influence of low temperature and of cold spells on CVD risk have been examined. The findings revealed that during a cold spell the risks of developing a cardiovascular event (e.g. stroke) were double those on non-cold days. There was a suggestion that cold temperatures increased the levels of a wide range of cardiovascular risk factors (e.g. blood pressure, lipids, and inflammatory biomarkers). This supports the possible mediating roles of these risk factors in increasing mortality at low temperatures, and suggests that variations in these factors could contribute to explaining the higher risks of CVD in winter.

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 are shown in the publication list.

PRESENTATIONS AT CONFERENCES

Oral presentations

The International Congress on Obesity Seoul, Korea, November 2015
- Invited speaker- Sarcopenia, sarcopenic obesity and cardiovascular disease. Wannamethee SG.

Society for Academic Primary Care (S.A.P.C.), Cambridge, January 2016
- Sensory impairments and incident disability in older British community-dwelling men: a 2-year follow-up study. Liljas AEM et al
- The relationships between adipose tissue deposition and sarcopenia with cognitive functioning in a population-based sample of older British men. Papachristou E. et al

Society for Social Medicine, Dublin, September 2015
- Body composition measures and cognitive functioning in older age: results from a cross-sectional study in older British me. Papachristou E. et al
- Objectively measured physical activity and sedentary behaviour in older adults: diurnal patterns and their determinants. Sartini C. et al.
- Cardiovascular risk factors over the adult life course: associations with carotid intima media thickness and carotid-femoral pulse wave velocity in older men in the British Regional Heart Study. Whincup PH. et al.

Poster presentations:

Wellcome Trust, Longitudinal Studies - Maximising their Value for Ageing Research, Cambridge, July 2015
- Sensory impairments and incident disability in older British community-dwelling men: a 2-year follow-up study. Liljas AEM et al

- Sensory impairments and incident disability in older British community-dwelling men: a 2-year follow-up study. Liljas AEM et al
Society for Social Medicine, Dublin, September 2015
- Hazards of cold spells for incidence of cardiovascular disease in older British men Sartini C. et al.

European Society Cardiology Congress, London, September 2015
- Cardiovascular risk factors over the adult life course: associations with carotid intima media thickness and carotid-femoral pulse wave velocity in older men in the British Regional Heart Study. Kapetanakis V, 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 Medical Research Council, National Institute of Health Research and Dunhill Medical Trust for their current support and to the 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