

**Poor Oral Health and Age-Related Health
Outcomes: Epidemiological Cohort
Studies of Older People in the United
Kingdom and United States of America**

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Abstract

Oral health problems have been found to be associated with disability, poor physical function, and mortality. However, cross-sectional and prospective associations are not well-established in older people, especially for self-reported oral health problems. Diet and inflammation are potential mediators in the association between poor oral health and risk of disability. However, evidence is limited. Additionally, gaps exist in the associations of poor oral health with different inflammatory markers. Inconsistent findings have also been reported for the associations between oral health and diet in older people. This thesis uses data from two population-based studies of older people, the British Regional Heart study (BRHS) and the US Health, Aging and Body Composition (HABC) Study. Data have been used to investigate cross-sectional associations of oral health problems with disability, physical function, inflammatory, haemostatic, and cardiac biomarkers, diet quality and dietary intake, and prospective associations of oral health with risk of disability, all-cause, cardiovascular disease (CVD), and respiratory mortality in older people. Oral health problems included objective (tooth loss, periodontal disease), and subjective (dry mouth, self-rated oral health) assessments and accumulation of oral health problems. Causal mediation was performed to test mediation through diet and inflammation. The main findings are that oral health problems were cross-sectionally associated with disability and poor physical function. Poor oral health (tooth loss, periodontal disease, dry mouth, cumulative oral health problems) was also associated prospectively with greater risk of developing disability, and all-cause, CVD and respiratory mortality. Some oral health problems were associated with increased inflammation, poor diet quality and poor nutritional intake. However, inflammation and diet did not appear to mediate the association of poor oral health with risk of developing disability. Finally, poor oral health is potentially an important risk factor for the onset of disability and all-cause and cause specific mortality in older people.

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Abbreviations

ADL: Activities of daily living

AFT: Accelerated failure time

BMI: Body mass index

BRHS: British Regional Heart Study

CHD: Coronary heart disease

CI: Confidence interval

CIF: Cumulative incidence function

COPD: Chronic obstructive pulmonary disease

CPITN: Community periodontal index of treatment needs

CRP: C-reactive protein

CVD: Cardiovascular disease

DII: Dietary Inflammatory Index

EDI: Elderly Dietary Index

ESI: Extent and Severity Index

FEV₁: Forced expiratory volume

FFQ: Food Frequency Questionnaire

FVC: Forced vital capacity

GP: General practitioner

HABC: Health, Aging, and Body Composition

HDL-c: High-density lipoprotein cholesterol

HEI: Healthy Eating Index

HR: Hazard ratio

HsTnT: High sensitivity Troponin T

IADL: Instrumental activities of daily living

ICD: International Classification of Diseases

IL-6: Interleukin-6

Khb: Karlson-Holm-Breen

LDCW: Long distance corridor walk

MET: Metabolic equivalent of task

NCDs : Non-communicable diseases

NDE : Natural direct effect

NHANES: National Health and Nutrition Examination Survey

NHS: National Health Service

NIE: Natural indirect effect

NRES: National Research Ethics Service

NT-proBNP: N-terminal pro-brain natriuretic peptide

OIDP: Oral impact on daily performance

OR: Odds ratio

PH: Proportional hazard

SHR: Subdistribution hazard ratio

TE: Total effect

TNF- α : Tumour Necrosis Factor -alpha

t-PA: tissue plasminogen activator

TR: Time ratio

UNC-15: University of North Carolina-15

vWF: von Willebrand factor

WHO: World Health Organization

XI: Xerostomia Index

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Chapter 1. Introduction

1.1. Introduction and Rationale for Thesis

1.1.1. *Oral health in older populations*

The ageing population has been increasing steadily worldwide (United Nations Department of Economic and Social Affairs, 2019). In the UK, it is projected that between 2014 and 2039 the population aged 60-74 years will increase from 9.7 to 12 million (Government Office for Science, 2016). Furthermore, the population over 75 years will rise from 5.2 to 9.9 million (Government Office for Science, 2016). The US Department of Health and Human Services reported that the population aged 65+ years increased by 34% between 2007 and 2017, with the population of people aged 85+ set to rise by 134% by 2040 (Administration for Community Living, 2018). Older people are particularly in greater risk of non-communicable diseases (NCDs) and disability, with expected increases in prevalence of both due to the rise of ageing populations (Divo *et al.*, 2014; World Health Organization, 2017). Above all, prevention of NCDs and disability can contribute significantly to achieving healthy ageing (Divo *et al.*, 2014; World Health Organization, 2017).

Aside from NCDs and disability, poor oral health is another prevalent condition in older people and has been recognised as a global public health problem (Peres *et al.*, 2019). Poor oral health consists of several oral health problems, including tooth loss, periodontal disease, dry mouth, and self-rated oral health. Dental problems can influence quality of life and general well-being of community dwelling older people (Eke *et al.*, 2016). Oral health problems are also implicated as risk factors in the development of disability, poor physical function, and increased mortality in older age (Friedman and Lamster, 2016; Alpert, 2017). Additionally, poor oral health can impact diet quality, contributing to malnutrition and a compromised diet, as well as increased inflammation (Scannapieco and Cantos, 2016; Gaewkhiew *et al.*, 2017; Marsman *et al.*, 2018). Both diet and inflammation are important components of healthy ageing, therefore highlighting the impact of dental problems on general health.

Oral health problems are preventable, and more focus should be given to prevention/intervention community programmes tailored to community-dwelling older people. In particular, recent recommendations included promotion of diet intervention campaigns for improvement of oral health in older populations (Public Health England, 2018). In addition, the World Health Organization (WHO), as part of its global strategy on healthy ageing, highlighted that affordable access to quality oral health care, should be part of strategies aiming to improve the health of older populations, making oral health essential for maintaining good general health (World Health Organization, 2017). As a result, more focus should be given to multidimensional prevention programs in community settings which aim to enhance access to dental treatments and support while being incorporated into community interventions aiming to improve other health conditions, such as chronic diseases (Public Health England, 2018; FDI World Dental Federation, 2020).

Although research has highlighted a range of associations between poor oral health and age-related health outcomes, such as disability, poor physical function, poor diet quality, increased inflammation, and risk of mortality, there are still many gaps that need to be addressed by epidemiological studies. Particularly, several studies which examined associations between poor oral health and the aforementioned health outcomes, have been conducted in middle-aged populations, and thus these associations remain unclear in older populations of community-dwelling individuals. Furthermore, there has been heterogeneity in the definition of poor oral health between studies, with most studies examining specific oral conditions and diseases (i.e. tooth loss, periodontal disease) and overlooking other dental problems including self-reported oral health measures, and consequently ignoring the multidimensionality of poor oral health. As a result, the associations between a range of oral health problems and these age-related health outcomes merit further investigation in older populations. Establishing these associations, is very important as even slight improvements in oral health of older people can significantly contribute to reduction of the burden of chronic conditions and poor overall health status in older people (Friedman and Lamster, 2016; Alpert, 2017).

1.1.2. Oral health problems, disability, and physical function

Disability represents the decrease in physical independence and the ability to perform everyday activities and is self-reported (Fong, 2019), whereas physical function is a measure of muscle strength, is assessed objectively through physical examination and can be a precursor of disability (Rantanen *et al.*, 1999). Both conditions are common conditions in older people (Rae *et al.*, 2010), with rates of disability projected to continue rising in older populations (Wittenberg *et al.*; Pieper *et al.*, 2000). Most importantly increases in the prevalence of disability and poor physical function are a direct consequence of increases in the population of older people (Okoro *et al.*, 2018). In older age, it has been suggested that individuals with dental problems are more likely to experience difficulties with their ability to perform activities of daily living, moving around and have decreased physical function (Tsakos *et al.*, 2015; Saintrain *et al.*, 2018). Therefore, in older adults, oral health problems may co-exist with disability and poor physical function. This can exacerbate already existing dental problems, through the inability to perform adequate dental hygiene or access dental services. However, dental problems can also be determinants of the onset of disability in later life, through pathways that remain unclear. Although both cross-sectional and prospective studies have investigated associations between dental problems and disability and physical function, several gaps remain. Particularly, most studies have not examined the associations of self-reported oral health problems, including dry mouth or poor self-rated oral health, and have focused primarily on periodontal disease and tooth loss (Glick *et al.*, 2016). Especially for studies on oral health and physical function, studies have suggested associations between tooth loss and poor physical function in older people. Furthermore, disability has been measured through different assessment tools, with few studies assessing disability through activities of daily living (ADL), instrumental activities of daily living (IADL), and mobility limitations (walk a quarter of a mile or going up a flight of stairs). Thus, more evidence is needed for the associations between dental problems and disability.

It is therefore important to assess both oral health and disability through various measures, which reflect the complexity of oral health and its impact on different functions of daily life. Finally, it is also essential to establish poor oral health as a

predictor of onset of disability, in order to protect physical independence of older people, which is a crucial component of healthy ageing.

1.1.3. Oral health problems with diet and inflammation

1.1.3.1. Inflammation

Ageing is characterised by an increase in levels of systemic inflammation (Singh and Newman, 2011; Franceschi and Campisi, 2014). Levels of inflammation tend to rise with increasing age and substantially impact general health of older people (Higgins and Higgins, 2003; deFilippi *et al.*, 2010; Singh and Newman, 2011; Wannamethee *et al.*, 2012). There is a range of important inflammatory markers during ageing, such as C-reactive protein (CRP), Interleukin-6 (IL-6), fibrin d-dimer, tissue plasminogen activator (t-PA), von Willebrand factor (vWF), Troponin T, and N-terminal pro-brain natriuretic peptide (NT-proBNP). These markers are associated with different biological processes and several chronic diseases as well as disability and eventually life expectancy.

One common characteristic of dental problems is oral inflammation, with oral bacteria from the mouth travelling to other parts of the body and therefore contributing to inflammation in other organs (Scannapieco and Cantos, 2016; Alpert, 2017), linking oral health to chronic diseases in older populations. In particular, dental problems such as tooth loss and periodontal disease have been found to be associated with increased levels of inflammatory, haemostatic, and cardiac biomarkers; however, most studies have been carried out in adult and middle-aged populations. As a result it is unclear whether similar associations exist in older populations. Another important gap is the paucity of data about the associations of self-reported oral health measures with increased inflammation in older age. Moreover, most studies have focused on markers including CRP and IL-6, with few studies examining the associations of poor oral health with haemostatic and cardiac biomarkers in older individuals. This is particularly important, because increased inflammation has been implicated in the causal pathway of the association between poor oral health and risk of developing disability in older people as poor oral health is associated with oral inflammation, oral inflammation with systemic inflammation, and

systemic inflammation could be a predictor of onset of disability (Alpert, 2017; Friedman and Shorey, 2019). Nevertheless, there is paucity of data on whether inflammation is indeed part of the causal pathway, as currently there are no studies identified using causal mediation analysis to examine its mediating effect.

1.1.3.2. Diet

Diet is implicated as a risk factor for the majority of chronic diseases and conditions, whereas improvement of diet has been incorporated in many intervention programmes to improve health. Furthermore, older adults with dental problems (i.e. tooth loss, periodontal disease) are more likely to have poor diet quality, with studies suggesting that diet patterns and intake of specific nutrients are closely connected to poor oral health (Moynihan, 2005; Savoca *et al.*, 2010; Watson *et al.*, 2019); however inconsistent findings have been reported with studies using different tools to measure diet quality. Furthermore, the relationships between self-reported oral health problems and diet quality are not well-established in older people. Dry mouth and poor self-rated oral health are indicators of the burden of chronic oral diseases and can therefore impact diet (Turner and Ship, 2007; Torres *et al.*, 2020). Previous research has also highlighted bi-directional relationships existing for dental problems and diet (Moynihan, 2005; Iwasaki *et al.*, 2012a). However, few studies have examined bi-directional associations of oral health problems and diet in the same population of older people. It is possible that through improvement of oral health, diet quality can be positively influenced and vice versa and thus resulting in gains for the prevention of chronic diseases in later life in older populations.

Diet may also play a mediating role in the association of oral health problems with risk of developing disability. Diet changes which are caused by dental problems, including low intakes of antioxidants or protein intake, could influence muscle strength and physical function (Cesari *et al.*, 2004; Hruby *et al.*, 2018) and therefore contribute to the development of disability. However, there is limited evidence from longitudinal studies on the role of diet quality scores as mediators in the association between poor oral health and risk of developing disability.

Establishing causal pathways, through diet and inflammation, can guide future intervention programmes for the improvement for oral health which could also potentially reduce risk of disability in older populations.

1.1.4. Oral health problems and mortality

Life expectancy in older populations has been improving during the past decades (World Health Organization, 2011). Chronic diseases such as cardiovascular disease and diseases of the respiratory system are among the most common causes of death in ageing populations (Sonnenschein and Brody, 2005; Eurostat, 2021). Oral health problems have been found to be predictors of shortened longevity, particularly all-cause, CVD, and respiratory mortality (Fukai *et al.*, 2007; Holm-Pedersen *et al.*, 2008; Schwahn *et al.*, 2013; Chen *et al.*, 2015; Manabe *et al.*, 2019; Qian *et al.*, 2020). However, most studies have examined associations between tooth loss, periodontal disease and risk of all-cause and cause specific mortality, with inconsistent findings being reported. Additionally, gaps exist for the associations of self-reported oral health problems as well as accumulation of oral health problems with all-cause, CVD, and respiratory mortality in populations of community-dwelling older people. As mentioned before, poor oral health is a multidimensional health problem, and in order to correctly predict its impact on survival it is essential to examine all different dental problems which affect older individuals. Additionally, previous studies have been carried out in middle-aged populations, and specific populations such as those living in nursing homes, therefore complicating the generalisability of reported results to the whole population of community-dwelling older people. Hence, further investigation of these associations is needed in order to establish which oral health problems are predictors of reduced survival in older people. Findings can be used to highlight the role that oral health plays in general health, and support the calls to include prevention of dental problems in policy targeting the reduction of the risk of NCDs and the enhancement of healthy ageing.

Therefore, this thesis will address several important questions about the associations of oral health problems with specific age-related health outcomes, including disability, physical function, diet, inflammation, and risk of disability and mortality, as well as the causal pathways through diet and inflammation. These questions have important public health implications in highlighting the need for improvement of

dental treatments and access to oral care, as well as optimal diet habits of older people and hence reduction of the risk of disability and mortality in older age.

1.2. Thesis Objectives

The overarching aim of this thesis is to investigate the associations of oral health problems with age-related health outcomes in older people in two population-based studies in the UK and USA. Therefore, the main objectives of this thesis are:

1. Examine the cross-sectional associations of objective and subjective oral health problems with disability and physical function in older people.
2. Examine the cross-sectional associations of objective and subjective oral health problems with inflammatory, haemostatic, and cardiac biomarkers in older people.
3. Investigate the associations of objective and subjective oral health problems with diet quality and dietary intake in older people.
4. First, investigate the prospective associations of objective and subjective oral health problems with risk of developing disability in older people. Then, determine the mediating effects of diet quality and inflammation on the prospective associations of oral health problems with risk of developing disability in older people.
5. Examine the association of objective and subjective oral health problems with risk of all-cause, CVD, and respiratory mortality in older people.

1.3. Overview of Methodology

To answer the objectives of this thesis, data from two population-based cohort studies of older people living in the UK and USA will be used. The British Regional Heart Study (BRHS) is an ongoing prospective cohort study which started at 1978-80 comprising white British men aged 40-59 years living across 24 British towns (Shaper *et al.*, 1981). Participants have been followed-up since baseline through physical examinations and postal questionnaires. In this thesis, data from the 20-

year (1998-2000), and 30-year (2010-2012) re-examinations, as well as data from postal questionnaires sent to participants in 2014 will be used. Furthermore, mortality data will be provided by the National Health Service Central Register and reports from general practitioners, while follow-up was carried out until June 2019.

The Health, Aging, and Body Composition (HABC) Study is a prospective cohort study which started in 1997-1998 and recruited 3075 white and African-American men and women aged 70-80 years living in Pittsburgh and Memphis, USA (Weyant *et al.*, 2004). Study participants were followed up until 2016, when the study ended. Data were collected through physical examinations, interviewed-administered questionnaires, home visits and phone calls (Health Aging and Body Composition Study, 2020). In this thesis, data from Year 1 (baseline), Year 2 (1998-1999) and Year 5 (2001-2002) will be used. Mortality data were collected through adjudication protocols reviewed by a HABC Study team of gerontologists and follow-up was conducted until September 2014. A more detailed description of the BRHS and HABC Study can be found in Chapter 3.

Data from the BRHS and HABC Study were derived from existing datasets, and therefore no data collection was necessary. Both studies had the necessary ethical approval. For the BRHS, ethical approval was provided by the National Research Ethics Service Committee, London. Written informed consent was obtained from individuals for their participation in the study, according to the Declaration of Helsinki. In the HABC Study, ethical approval was provided by University of Pittsburgh, University of Tennessee – Memphis, University of California San Francisco, and National Institutes of Health (NIH). Additionally, all participants provided written informed consent. Furthermore, to access datasets from both studies, approval was obtained from BRHS and HABC Study-National Institute of Aging data access committees. Ethical approval, through the project proposal (Ref: 4995/2018), was provided by Newcastle University. All data were anonymised and stored on secure networks at Newcastle University. Finally, while using data for this thesis information governance guidelines were followed. Both studies are suitable for examining the objectives of this thesis, since they comprise large populations of older people, have detailed and comparable oral health data (both objectively and subjectively assessed), have similarly measured data on disability, physical function, diet,

inflammation, and mortality. Both studies have carried out regular follow-ups which allowed the examination of risk of disability and mortality. Analyses of this thesis have been performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC), and STATA version 15.1 (Stata Corp LLC, College Station, Texas).

1.4. Structure of Thesis

This thesis comprises of the following Chapters. Chapter 2 provides background of epidemiological studies on the associations of oral health with inflammation, diet quality and dietary intake, mortality, disability, and physical function in older populations. Chapter 3 discusses the methodology and analytical plan for the analysis of data from the two following datasets: the British Regional Heart Study (BRHS) and the Health, Aging, and Body Composition Study (HABC Study). Chapter 4 is the first of five results Chapters and examines the cross-sectional associations of oral health problems with disability and physical function in older people, using data from the 30-year examination in the BRHS, and Year 2 in the HABC Study. Chapter 5 examines the cross-sectional associations of oral health problems with inflammatory, haemostatic, and cardiac biomarkers in older people, using data from the 30-year examination in the BRHS, and Year 2 in the HABC Study. Chapter 6 investigates associations between oral health problems and diet quality and intakes of specific nutrients in older age. For the cross-sectional analyses, data from the 30-year examination in the BRHS, and Year 2 in the HABC Study were used. In the BRHS for the association between change in diet quality over two time points (1998-2000, 2010-2012) and prevalence of oral health problems later (2010-2012) data from the 20- (1998-2000), and 30- year (2010-2012) re-examinations were used. Chapter 7 examines the associations of oral health problems with risk of developing disability in older age, using baseline oral health data from the 30-year re-examination in the BRHS, and Year 2 in the HABC Study and follow-up data on disability until 2014 in the BRHS and 2001-2002 (Year 5) in the HABC Study. Additionally, this Chapter will investigate the mediating roles of diet and inflammation using causal mediation analysis. For this analysis, data on confounders were measured at the 20-year re-examination in the BRHS and Year 1 in the HABC Study; oral health, diet and inflammation in the 30-year (BRHS) and Year 2 (HABC

Study); and follow-up was performed until 2014 (BRHS) and Year 5 (HABC Study). Chapter 8 examines the associations between oral health problems and all-cause, CVD, and respiratory mortality in older people, using baseline data on oral health and covariates from the 30-year re-examination (2010-2012) and mortality follow-up until June 2019 in the BRHS, and baseline data from Year 2 (1998-1999) and mortality follow-up until September 2014 in the HABC Study. Each results Chapter consists of introduction, methods, results, and discussion sections. Chapter 9 is the concluding Chapter which includes a summary of the key findings, comparison with previous studies, strengths and limitations, and implications for public health and future epidemiological studies.

1.5. Dissemination of thesis

Based on this thesis objectives, a list of three papers have been published in peer-reviewed journals (Appendix A, page 320). Additionally, a list of oral and poster presentations based on the materials of this thesis are presented in Appendix B (oral, page 321) and Appendix C (poster, page 322).

Chapter 2. Literature Review

2.1. Introduction

This Chapter discusses the epidemiology of oral health problems and reviews existing literature on the associations of oral health problems with disability, physical function, inflammation, diet, all-cause, CVD, and respiratory mortality in older people. Section 2.2. provides details about the search strategy and inclusion criteria. Section 2.3 describes the importance, epidemiology, definition, and assessment of oral health problems. Section 2.4 outlines the literature on oral health problems and disability and physical function, while section 2.7 describes the potential causal pathways underpinning the association between oral health problems and incidence of disability; section 2.5 describes the literature on oral health problems and inflammatory, haemostatic, and cardiac biomarkers; section 2.6 the literature on oral health problems and diet; and section 2.8 outlines the literature on oral health problems and all-cause, CVD and respiratory mortality. Finally, section 2.9 provides a summary of the main findings of the literature review.

2.2. Search strategy and inclusion criteria of studies included in literature review

Several searches were carried out to identify relevant observational cross-sectional and longitudinal studies investigating various oral health measures-both objectively and subjectively assessed, and the associations with disability, physical function, inflammatory haemostatic and cardiac biomarkers, dietary intake and diet quality, as well as risk of developing disability and mediating effects of diet and inflammation, and finally risk of all-cause, cardiovascular and respiratory mortality. For this purpose, keywords were entered into PubMed as title searches. Literature search started in March 2018 and was frequently updated and concluded in the beginning of 2021. There were no restrictions for date of publication. However, in most cases studies conducted in predominantly older populations were chosen. Only when studies in older populations were lacking, studies in middle-aged or both middle-aged and older adults were included. Different terms were used for poor oral health,

and searches were also performed for each oral health measure. Similar strategy was performed for the associations with each outcome i.e. separate searches for poor oral health and each measure of disability. Similar strategy was chosen throughout the literature search. Relevant publications were also found from reference lists from identified studies.

List of keywords: oral health, poor oral health, dental health, tooth loss, edentulism, periodontal disease, self-rated oral health, dry mouth, xerostomia, hyposalivation, difficulty eating, cumulative oral health problems, accumulation of oral health/dental problems, disability, functional disability, mobility limitations, ADL, IADL, physical function, handgrip strength, walking speed, gait speed, chair-stand test, inflammation, C-reactive protein/CRP, Interleukin-6/IL-6, fibrin d-dimer, von Willebrand/vWF, tissue plasminogen activator/t-PA, cardiac troponin T, NT-proBNP, diet quality or EDI or HEI, dietary/nutritional intake and intake of specific nutrients, compromised diet, malnutrition, antioxidants, diet, causal mediation, mediating role/effect, longitudinal, all-cause mortality, mortality, cardiovascular/CVD mortality, respiratory mortality, mortality-pneumonia, longevity, survival, competing risks, accelerated failure time model, older people/adults, ageing/aging population.

2.3. Overview of Poor Oral Health in Older Age

The mouth is an important organ of the digestive system which plays a key role in several functions in humans. It is responsible for chewing, swallowing, processing of food, but also for social activities such as smiling, and conversing (Lamster *et al.*, 2016). As a result of ageing many functions of the mouth tend to be negatively affected, leading to the development or worsening of oral (mouth) health problems (Lamster *et al.*, 2016). In older people, oral health problems are identified as oral conditions (no disease pathology present) and/or oral diseases. Oral diseases, such as periodontal disease, dental caries and oral conditions including tooth loss or dry mouth are the most common oral health problems in older age and can be indicators of poor general health status and can influence quality of life (Friedman and Lamster, 2016; Lamster *et al.*, 2016). Different ways of measurement exist for oral health problems, mainly divided between objective and subjective measures. Objective

measures/problems are assessed by trained professionals and include tooth loss and periodontal disease, whereas subjective measures/problems are based on self-reporting of individuals and includes self-rated oral health, dry mouth, and difficulty eating. Establishing the associations between these oral health problems and age-related health outcomes can clarify how different aspects of oral health are related to general health in older people.

2.3.1. Importance of oral health problems later in life

Although oral health has substantially improved the past years, it is still considered one the most important health problems in older people (Peres *et al.*, 2019). At least one third of the older population will experience one oral disease in their lifetime. The majority of oral diseases are preventable; however their prevalence continues to be high and keeps increasing in disadvantaged populations and low-income countries (Kassebaum *et al.*, 2017; Peres *et al.*, 2019). In the USA, periodontal disease has been described as a public health problem (Eke *et al.*, 2016). Additionally, worldwide dental caries is one of the most prevalent dental diseases which can start as early as childhood and continue to adulthood and older populations (Peres *et al.*, 2019; Tulek *et al.*, 2021). As part of recognising the importance of oral health in general health, the US president included oral health screening in the disease prevention and health promotion activities, which are part of the Older Americans Act (114th Congress, 2015-2016; Eke *et al.*, 2016). Nevertheless, globally poor oral health is a neglected public health problem, contrary to the accumulating evidence of its negative influence on well-being (Benzian *et al.*, 2011). Oral health is an integral part of general health, as it influences several functions of everyday life (Peres *et al.*, 2019). Particularly, it can have an impact on physical, psychosocial, and mental elements of well-being of older people. Additionally, oral health problems can contribute to increased costs for health services (Listl *et al.*, 2015). In the EU, 90€ billion were spent for oral diseases, which was in third place after diabetes, and cardiovascular disease (CVD) (Peres *et al.*, 2019). Nowadays, older individuals tend to keep their natural teeth for much longer compared to the past, and can therefore suffer from oral diseases for longer (Luo *et al.*, 2015). As a result, the need for dental services is greater among older people; however the increased costs and complexity of these

services can be a barrier for older people getting treatment for dental problems (Freed *et al.*, 2019; Peres *et al.*, 2019). This contributes to the accumulation of untreated oral health conditions in older individuals; something extremely important because it has been suggested that oral conditions are associated with several chronic conditions such as diabetes, CVD, disability, poor diet and nutritional deficiencies and mortality (Humphrey *et al.*, 2008; Tada and Miura, 2014; Han *et al.*, 2015; Liljestrang *et al.*, 2015; Friedman and Lamster, 2016; Kassebaum *et al.*, 2017; Koka and Gupta, 2018; Toniazzi *et al.*, 2018). Particularly, given the potential impact of poor oral health on disability and physical independence, it is evident why more attention needs to be given to oral diseases, especially how they affect older peoples' ability to perform everyday activities, which are a basic component of quality of life and overall well-being.

2.3.2. Epidemiology of oral health problems

Tooth loss (number of teeth)

Partial tooth loss is described as the incremental loss of natural teeth throughout one's life, with complete tooth loss (edentulism) being the undesirable endpoint (Thomson, 2014). Number of teeth can be assessed both objectively (trained professional) and subjectively (self-reported). Objective and subjective measures of tooth loss are highly correlated and have been validated in large studies of middle-aged populations, with few large validation studies in older people (Matsui *et al.*, 2016; Chatzopoulos *et al.*, 2018; Sekundo *et al.*, 2019). Moreover, in older populations it is essential to maintain a functional dentition, which according to the WHO's global goals for oral health is defined as having at least 21 natural teeth (Hobdell *et al.*, 2003).

Tooth loss is one of the most prevalent oral health problems, which usually is the result of other chronic oral diseases such as periodontal disease and untreated caries (Thomson, 2014; Peres *et al.*, 2019). Dental caries is a chronic dental condition, which can be the result of an imbalance between the minerals of the tooth and dental plaque (biofilm surrounding the tooth) (Tulek *et al.*, 2021). One of the main causes of caries lesions is the acid which is produced by bacteria which in turn

are produced by fermentable carbohydrates, i.e. free sugars (Peres *et al.*, 2019; Tulek *et al.*, 2021). Such sugars are included in frequently consumed nutritional products such as syrups, honey, fruit juices, and fruit juices concentrates (World Health Organization, 2015). Once acids are produced, important minerals are lost from hard tissues, including calcium and phosphate (Peres *et al.*, 2019). If the condition progresses to the creation of cavities then this can lead to pain, and discomfort and ultimately loss of teeth (Peres *et al.*, 2019). However, with appropriate oral hygiene and nutritional choices the effect of dental caries can be decreased or even fully controlled (Tulek *et al.*, 2021).

In the past, a common cause of edentulism was dental procedures, such as complete removal of dentition, while today such practices have been abandoned and therefore making partial tooth loss more common in older people (Thomson, 2014). In a UK survey (2015) in adults in England and Wales, it was reported that the prevalence of complete tooth loss was 30% in older people aged 75 to 85, and increased to 47% for individuals over 85 years (Public Health England, 2015). Absence of a functional dentition can have a substantial impact on the individual's oral health status, by influencing speaking, smiling / showing teeth without being embarrassed, conversing and/or cleaning practices (van de Rijt *et al.*, 2019). Additionally, having less than 21 teeth is related to low chewing ability, causes eating difficulties and can reflect past dental services (Marcenes *et al.*, 2013; Okamoto *et al.*, 2015; Okamoto *et al.*, 2019). It has also been suggested that tooth loss may indicate accumulation of health stressors throughout life and may therefore represent the burden of chronic diseases in older people (Friedman and Lamster, 2016). However, loss of teeth could also have a positive impact on older individuals if it provides relief from pain or symptoms of other oral diseases such as periodontal disease (Friedman and Lamster, 2016). Nevertheless, tooth loss has been found to be associated with several adverse health conditions including obesity, poor diet quality, diabetes, CVD, disability, frailty, respiratory diseases, dementia, and mortality (Castrejón-Pérez *et al.*, 2016; Felton, 2016; Friedman and Lamster, 2016; Kassebaum *et al.*, 2017; Toniazzi *et al.*, 2018).

Periodontal disease

Periodontal disease is a chronic inflammatory oral condition and can influence the area surrounding the teeth of individuals (Peres *et al.*, 2019). In periodontal disease oral microorganisms (bacteria) which exist in the oral cavity can create biofilms and contribute to the formation of dental plaque and oral inflammation (Pihlstrom *et al.*, 2005). Dental plaque contributes to the destruction of the periodontium and causes damage of surrounding tissue (Pihlstrom *et al.*, 2005). This can subsequently lead to loss of supporting connective tissue and alveolar bone resulting in the first signs of periodontal disease (Pihlstrom *et al.*, 2005). If periodontal disease is left untreated and therefore progresses to a more severe disease it can cause loosening of teeth and subsequent loss of infected teeth (Pihlstrom *et al.*, 2005).

Periodontal disease can be assessed through gingival bleeding, loss of attachment, and periodontal pocket depth. Periodontal disease can be objectively or subjectively assessed, with the majority of studies using objective measures. Subjective periodontal disease measurements may not be generalisable to all case definitions or severity of periodontal disease and response from participants can be affected by literacy, awareness and oral care habits (Eke *et al.*, 2013). Therefore, objective (clinical) assessment is a better way to assess periodontal disease in large and diverse populations. The WHO suggested the Community Periodontal Index of Treatment Needs (CPITN) which can assess and identify periodontal disease treatment needs in the population (Carlos *et al.*, 1986). CPITN assess, in a clinical setting, the presence of gingival bleeding, hardened dental plaque and periodontal pocket depth (Cutress *et al.*, 1987). This measurement is conducted in six parts of the mouth, and therefore does not provide a detailed description of the periodontal status of the full mouth (Carlos *et al.*, 1986). To address this limitation, Carlos *et al.* (1986) proposed a measurement tool which limits loss of information and could be used across different epidemiological studies with comparable measurements (Carlos *et al.*, 1986). This is the Extent and Severity Index (ESI) (Carlos *et al.*, 1986). This index uses assessments of loss of attachment and periodontal pocket depth and provides information and guidelines on establishing presence of periodontal pathology (extent) and severity of periodontal disease (Carlos *et al.*, 1986). It is a tool that is informative of disease trends across different populations rather than a diagnostic tool of periodontal disease (Carlos *et al.*, 1986).

In the UK, periodontal disease is among the most prevalent oral health problems (Public Health England, 2015). It was found that 60% of people aged 65-84 suffered from periodontal disease, while prevalence fell to 47% for those over 85 (Public Health England, 2015). This decrease is probably caused by the increase in edentulism in this population. In the US, in 2009-2010, the prevalence of periodontal disease was 70.1% for over 65 years old (Eke *et al.*, 2012). Overall, it is challenging to estimate the prevalence of periodontal disease because of different measurement methods used in studies (Thomson, 2014). Furthermore, past periodontal disease rates can be underestimated in older populations because periodontal disease is followed by tooth loss, with the remaining teeth being the healthier ones and therefore not fully identifying the life-course burden of this disease in older people (Thomson, 2014). The development of periodontal disease can be influenced by factors such as smoking, alcohol, vitamin deficiencies, as well as chronic diseases including diabetes, osteoporosis and immune dysfunction (Pihlstrom *et al.*, 2005). Particularly, similar to dental caries, consumption of free sugars included in sugar sweetened beverages, such as soft drinks can be a major cause of periodontal disease (Peres *et al.*, 2019; Çetinkaya and Romaniuk, 2020). Higher consumption of soft drinks, can lead to higher concentration of free sugars in the mouth, leading to increased demineralisation, and consequently contributing to increased rates of periodontal disease (Çetinkaya and Romaniuk, 2020). Moreover, presence of periodontal disease in older people has been found to be associated with CVD, impaired kidney function, frailty, and mortality (Humphrey *et al.*, 2008; Chen *et al.*, 2015; Castrejón-Pérez *et al.*, 2016).

Dry mouth (xerostomia)

Dry mouth is dryness of mouth perceived by an individual (Wiener *et al.*, 2010). Dry mouth should be distinguished from hyposalivation, which is reduced production of saliva (Wiener *et al.*, 2010). Hyposalivation is measured by assessing the volume of saliva produced and has been used in previous epidemiological studies (Syrjälä *et al.*, 2013; Iwasaki *et al.*, 2016a; Iwasaki *et al.*, 2018b). However, it is possible that an individual who experiences oral dryness can have normal production of saliva (Wiener *et al.*, 2010). Moreover, assessment of hyposalivation does not provide

information about short-term dry mouth symptoms which are caused by specific medications, with the time of day that the individual takes the specific medication influencing perception of dry mouth (Wiener *et al.*, 2010). Contrary to the straightforward assessment of hyposalivation, dry mouth is defined by a number of symptoms which indicate presence and severity of dryness of mouth (Thomson *et al.*, 1999). Single-item questions have been used in several epidemiological studies to assess dry mouth (Ide *et al.*, 2008). Nevertheless, it is hard to measure the full extent of dry mouth symptoms via a single-item questionnaire. To address these issues, the Xerostomia Index (XI) was developed (Thomson *et al.*, 1999). The XI can assess the individual's perception of dryness, the consequences of dry mouth, and symptoms of burning mouth which has been found to be associated with xerostomia previously (Thomson *et al.*, 1999; Liu *et al.*, 2018).

Prevalence of dry mouth increases with age and is a condition which is becoming increasingly common in older people (Liu *et al.*, 2012). A number of studies have investigated the prevalence of dry mouth, which varies from 12-39% in populations of older people (Thomson, 2015). Making global estimations about the prevalence of dry mouth is difficult due to the differences in the definition and measurement of dry mouth across studies (Thomson, 2015). Nevertheless, it can be estimated that around 20% of older individuals experience dry mouth (Orellana *et al.*, 2006; Thomson, 2014). Dry mouth can be caused by several conditions and is closely linked to systemic health, chronic diseases and medications (Turner and Ship, 2007). A number of prescribed medications for common diseases, including diabetes, can disrupt the salivary gland function and cause sensation of dry mouth in older patients. Furthermore, chronic autoimmune disorders, and head and neck radiation therapy for cancer are associated with a decrease in production of saliva (Shiboski *et al.*, 2007; Turner and Ship, 2007). Sensation of dry mouth can have a substantial impact on oral health, including periodontal disease, oral infections, chewing and swallowing difficulties (Han *et al.*, 2015).

Self-rated oral health

One of the main limitations of objective measures of oral health is the extensive nature of assessments which may be too demanding for older people as they can be affected by their overall well-being. As a result, there is a need of self-reported (subjective) tools which can accurately describe overall oral health status of older individuals. One such measure is self-rated oral health which is the perception of oral health status by the individual, similar to self-rated general health. Self-rated oral health is assessed via a single-item question asking the individual to rate their overall oral health as excellent, good, fair, poor.

Prevalence of poor self-rated oral health can be influenced by the prevalence and severity of other oral health problems. In previous studies prevalence of poor self-rated oral health ranged from 6.6 to 37% (Locker, 1997; Jones *et al.*, 2001; Wu *et al.*, 2011). However, these studies consisted of heterogeneous older populations, and it is hard to estimate the overall prevalence of poor self-rated oral health in older people.

Ratings of oral health (fair or poor) can be influenced by tooth loss, and periodontal disease (Locker, 1997; Wu *et al.*, 2011). Nevertheless it is difficult to distinguish which oral conditions influence perception of oral health. Furthermore, self-rated oral health can be an indicator of dental care and use of dental services, as those who report fair or poor oral health tend to brush their teeth less frequently and rarely visit the dentist (Locker, 1997). Moreover, an individual's self-perception can be substantially different from their dentist's or family's perception of their oral health, and therefore self-rated oral health can add valuable information (Undén and Elofsson, 2001; Torres *et al.*, 2020). Self-rating of oral health can also be predictive of general well-being (Brennan and Singh, 2011; Brennan *et al.*, 2018). Particularly, one study reported that as individuals were getting closer to their end of life they were more likely to report fair or poor self-rated oral health (Chen *et al.*, 2013). They also observed that as perception of general health worsened so did the perception of oral health (Chen *et al.*, 2013).

2.3.3. Conceptual framework for the influence of oral health on age-related health outcomes

As mentioned in sub-section 2.2.2, oral health problems are associated with several health outcomes in older people (Alpert, 2017). In ageing populations, disability and poor physical function are very critical to functional independence and can predict disease progression and eventually mortality (Pongiglione *et al.*, 2016; Quiñones *et al.*, 2016; Sheridan *et al.*, 2019). Older individuals with poor oral health, are more likely to experience some type of disability (i.e. difficulty in executing activities such as cooking, dressing, going to the bathroom by themselves) or decreases in physical function (i.e. slow walking speed or weak handgrip strength) (Jette *et al.*, 1993; Hämäläinen *et al.*, 2004; Yu *et al.*, 2011; Moriya *et al.*, 2012; Kamdem *et al.*, 2017; Shin, 2019; Yin *et al.*, 2020), but also tend to have shortened longevity than older individuals with better oral health (Holm-Pedersen *et al.*, 2008; Aida *et al.*, 2011; Linden *et al.*, 2012; Chen *et al.*, 2015). Therefore it can be conceptualised that individuals with poor oral health have poorer overall health status and that as the population is getting older, oral health problems and disability become more prevalent with both conditions co-existing and potentially influencing one another.

However, it is possible that oral health is not just a component of ageing, but it can also influence the onset of disability through its impact on diet and inflammation. Oral health problems, including tooth loss, periodontal disease, and dry mouth can affect chewing and swallowing and therefore can alter food choices, increase food avoidance and lead to poor diet quality (Moynihan, 2007). Having a compromised diet is a well-known risk factor of decreased muscle strength and disability (Cesari *et al.*, 2004; Hruby *et al.*, 2018; Parsons *et al.*, 2019). Additionally, oral health problems can be chronic conditions, characterised by presence of oral bacteria and oral inflammation (Pihlstrom *et al.*, 2005; Alpert, 2017). These bacteria can travel to other parts of the body and contribute to increases of inflammatory biomarkers (systemic, haemostatic, or cardiac) and onset/severity of chronic conditions, such as disability (Alpert, 2017). For example, those with tooth loss or periodontal disease tend to have high levels of systemic inflammatory (CRP, IL-6) markers, with few studies also suggesting presence of high levels of other biomarkers, including haemostatic (fibrin d-dimer, t-PA, vWF), and cardiac (Troponin T, NT-proBNP) in oral diseases. Nevertheless, there is still limited understanding of how oral health is related to

inflammatory markers and how this relation then impacts physical function, especially in older populations. Both diet and inflammation may reflect the health status of an individual and can significantly influence but also be influenced by poor oral health. Although these factors have been implicated in the pathway linking poor oral health to onset of disability in older age, they have not been established as mediators of this association yet.

Additionally, cross-sectional associations between poor oral health and disability, physical function, inflammation, and diet, as well as prospective associations of poor oral health with risk of developing disability and mortality are influenced by other factors which both affect poor oral health and age-related health outcomes, i.e. confounders. It has been established, that factors including age, socioeconomic status (measured either through social class or education), gender, race, smoking, alcohol, physical activity, history of chronic diseases/medical conditions, and body mass index/obesity can act as confounding variables in these associations (Friedman and Lamster, 2016; Dörfer *et al.*, 2017; Peres *et al.*, 2019). A diagram presenting the proposed conceptual framework can be found at the end of Chapter 2 (Figure 2.1, page 53).

In the next sections, existing evidence on the relationships of oral health problems with disability, physical function, diet, inflammation, and mortality will be discussed. Additionally, literature about the potential mediating role of diet and inflammation in the association between poor oral health and onset of disability will be described.

2.4. Oral Health Problems and Disability and Physical Function in Older Life

2.4.1. Epidemiology of disability and physical function

Disability

Disability is a common condition among older people. The most common self-reported indicators of disability are mobility limitations, activities of daily living (ADL) and instrumental activities of daily living (IADL). Mobility limitations are defined by difficulties in moving around the house, including walking short or long distances as well as going up the stairs. Mobility limitations are closely linked to physical function, and particularly slow walking speed (Chen and Wilmoth, 2004). It has been

suggested that mobility limitations can predict problems with ADL or IADL activities, since being able to move around is an important factor in both ADL and IADL (Chen and Wilmoth, 2004). In older people, ADL and IADL activities are used frequently to represent the ability to be independent in daily life. ADL activities are identified as activities concerning self-care, such as bathing, dressing and undressing or cooking by yourself (Katz, 1983). IADL activities indicate someone's ability to live independently in the community, and include activities such as driving a car, paying bills or taking medications by yourself (Katz, 1983). Both ADL and IADL activities are used in studies as indicators of independence, while mobility limitations can be an easier indirect measurement of physical function. One common way of assessing both ADL and IADL in epidemiological studies is the Katz scale (Katz, 1983).

In the UK, as a consequence of the increase of the population of older people, difficulties in performing at least one ADL are estimated to increase by 67% between 2015 and 2040 and by 116% between 2015-2070, reaching 7.6 million (Wittenberg *et al.*; Pieper *et al.*, 2000). According to the NHS, the most prevalent ADL difficulties are dressing or undressing yourself, going up and down the stairs or having a bath by yourself (Age UK, 2019). In the USA, the prevalence of mobility disability in ≥ 65 years was the highest (26.9%), and rates of any type of disability were higher in older people (Okoro *et al.*, 2018). Additionally, 5.5% reported difficulties with dressing or bathing (self-care), and 9.8% experienced problems with IADL activities (independent living) (Okoro *et al.*, 2018).

Decrease in independence can be a consequence of cognitive, balance or sensory impairments and can therefore represent physical function status and overall health (Age UK, 2019). Additionally, high prevalence of disability can influence overall health in older people. Particularly, disability has been found to be associated with chronic diseases, including CVD, diabetes, arthritis, and increased mortality (Pongiglione *et al.*, 2016; Quiñones *et al.*, 2016; Fong, 2019). Moreover, older individuals with any type of disability need health care and tend to use health care services more than older people without disabilities, resulting in high health care costs (Okoro *et al.*, 2018).

Physical function

Physical function is an indicator of muscle strength and function and could be a precursor of disability (Perera *et al.*, 2016). Physical function can be assessed through handgrip strength, walking speed, and the ability and speed to stand and sit on a chair. Handgrip strength and walking speed reflect overall muscle function and can be indicators of mobility limitations (Sallinen *et al.*, 2010). It is difficult to estimate global prevalence of poor physical function because there is not a universal definition of poor physical function. Moreover, specific cut-off points indicating impaired physical function have been used previously, but findings are restricted to specific populations and usually the generalisability to the whole community-dwelling older population can be challenging.

Physical function impairments are influenced significantly by muscle strength (Sallinen *et al.*, 2010). Decrease in muscle strength can be due to loss of muscle mass or muscle quality (Goodpaster *et al.*, 2006). However, it has been suggested that older individuals who maintain good levels of muscle mass, can have significant losses in muscle strength, a finding which highlights the importance of muscle quality in older people (Goodpaster *et al.*, 2006). Moreover, it has also been found that handgrip strength can predict deterioration of walking speed (Fragala *et al.*, 2016). Handgrip strength and walking speed are also basic components of sarcopenia and frailty, two common conditions in older people (Cruz-Jentoft *et al.*, 2010; Papachristou *et al.*, 2017). Similar to disability, physical function is crucial to everyday life and the ability to be independent, and can influence several age-related health conditions, with studies suggesting associations with CVD, cognitive decline, and mortality in older people (Studenski *et al.*, 2011; Veronese *et al.*, 2018; Chou *et al.*, 2019; Smith *et al.*, 2019).

2.4.2. Associations of oral health problems with disability and physical function

2.4.2.1. Cross-sectional studies between oral health problems and disability

Several studies have investigated the cross-sectional associations between oral health problems and disability in older people (Jette *et al.*, 1993; Takata *et al.*, 2008; Yu *et al.*, 2011; Peltzer *et al.*, 2014; Wang *et al.*, 2014; Saintrain *et al.*, 2018). All

identified studies were large population-based studies from different countries around the world with the majority of them consisting of predominantly older people which in most cases were randomly selected. Additionally, all studies performed similar statistical analysis, i.e. descriptive statistics and regression analysis while adjusting for confounders. However, studies have used different tools to measure disability and few studies have examined whether poor oral health is associated with measures of disability including mobility limitations, ADL, or IADL difficulties. Particularly, only two studies examined the associations between poor oral health and ADL and IADL difficulties (Yu *et al.*, 2011; Saintrain *et al.*, 2018). Out of these studies, only one reported associations between tooth loss and greater odds of having ADL difficulties (Saintrain *et al.*, 2018). Likewise, tooth loss was found to be associated with greater odds of IADL difficulties in only one study of a population of people aged ≥ 60 years (Yu *et al.*, 2011); pointing to the presence of inconsistent results.

Furthermore, the two studies examining the associations of poor oral health with mobility limitations used different definitions of mobility limitations (Jette *et al.*, 1993; Wang *et al.*, 2014). Jette *et al.* assessed mobility limitations by asking participants about their ability to walk, bed transfer, and get outside- observing that those with mobility disability were more likely to experience tooth loss (Jette *et al.*, 1993). In the other study, mobility was assessed through questions included in the National Health Interview Survey in Taiwan, where participants had to report their ability to perform 8 specific movements (Wang *et al.*, 2014). None of the studies defined mobility limitations as the ability of the individual to walk or climb stairs, which is a surrogate measure of walking speed and muscle strength (Visser *et al.*, 2005; Parsons *et al.*, 2019). Nevertheless, in both studies associations were established between having less than 20 teeth and mobility disability (Jette *et al.*, 1993; Wang *et al.*, 2014).

Previous studies have focused on the associations of one oral health problem, predominantly tooth loss or chewing problems with disability, with only one study assessing oral health through both objective and subjective oral health problems (Jette *et al.*, 1993; Takata *et al.*, 2008; Yu *et al.*, 2011; Peltzer *et al.*, 2014; Wang *et al.*, 2014; Saintrain *et al.*, 2018). Moreover, there was only one study investigating the association between periodontal disease and disability in older people. Particularly, those with severe periodontal disease were at greater odds of IADL

difficulties but not ADL in a population aged 60 years or older (Yu *et al.*, 2011). Additionally, no associations were present for moderate periodontal disease, highlighting the potential effect of disease severity in the association (Yu *et al.*, 2011).

There is not a strong evidence base on the associations of self-rated oral health and dry mouth with disability in older people. There is only one study examining the associations of subjective oral health problems with disability in older age. Saintrain *et al.* examined the relationships of dry mouth with ADL difficulties, but did not observe any significant associations in people 60 years or older (Saintrain *et al.*, 2018). Similarly, research gaps also exist for the association between accumulation of oral health problems and disability in older age.

In summary, few of the identified studies utilised a small sample size, used different measurement tools for oral health (objective or subjective assessment), disability and physical function. Moreover, some studies examined associations in older people of the same age and did not use a wide age range. Additionally, the question of representativeness exists for some of the identified studies, because participants residing in one city or area were included and therefore it is unclear whether reported associations are representative of the whole older population under investigation. Finally, due to the cross-sectional design, studies cannot ascertain direction of associations. However, there is a large and robust evidence base on the associations of tooth loss and disability in older people, with paucity of data existing for associations of periodontal disease, dry mouth, self-rated oral health, and accumulation of oral health problems with disability.

2.4.2.2. Cross-sectional studies between oral health problems and physical function

Studies have shown that tooth loss is associated with poor physical function cross-sectionally (Hämäläinen *et al.*, 2004; Moriya *et al.*, 2012; Tsakos *et al.*, 2015; Kamdem *et al.*, 2017; Shin, 2019). Such findings have been provided by population-based studies in older populations, including both men and women which in most cases were randomly selected, and have used similar assessments of physical function, either handgrip strength or walking speed. Furthermore, the majority of

studies conducted similar statistical analysis, i.e. logistic regression while adjusting for confounders. Four studies examined the association between tooth loss and handgrip strength, and suggested that tooth loss was associated with weak handgrip strength (Hämäläinen *et al.*, 2004; Moriya *et al.*, 2012; Kamdem *et al.*, 2017; Shin, 2019). However, differences existed in the way that tooth loss was assessed. Moriya *et al.* examined the association of tooth loss with weak handgrip strength indirectly by testing the association between chewing ability and handgrip strength in older individuals aged ≥ 65 years (Moriya *et al.*, 2012). They suggested that dentition status (with or without occluding pairs of teeth) influences handgrip strength through its influence on chewing ability and not directly (Moriya *et al.*, 2012). The other three studies used number of teeth which was objectively assessed during an oral examination (Hämäläinen *et al.*, 2004; Kamdem *et al.*, 2017; Shin, 2019).

Contrary to tooth loss, the association between periodontal disease and handgrip strength is not well established. Only one study of older Finnish individuals aged 80 years examined this association, but did not observe any differences in the odds of having weak handgrip strength between those with and without periodontal disease (Hämäläinen *et al.*, 2004).

Furthermore, the relationship between poor oral health and slow walking speed was investigated by two studies (Tsakos *et al.*, 2015; Kamdem *et al.*, 2017). Tsakos *et al.* studied the association between tooth loss and walking speed in older British individuals and reported that at the study's baseline individuals with complete tooth loss had significantly slower walking speed compared to participants who retained their natural teeth (Tsakos *et al.*, 2015). Additionally, Kamdem *et al.* examined the relationship of missing teeth with slow walking speed through chewing ability, and reported that chewing ability was associated cross-sectionally with slow walking speed in community-dwelling individuals aged ≥ 65 years living in Lausanne (Kamdem *et al.*, 2017). They suggested that impaired chewing ability, which is caused by tooth loss, can lead to balance and posture difficulties and consequently decline in physical strength and function (Kamdem *et al.*, 2017). As a result, there is only one study examining the direct cross-sectional relationship of number of teeth with slow walking speed in older people. Additionally, no studies were identified examining the association of periodontal disease with slow walking speed.

Some of the studies identified in the literature search had a small sample size (<500 participants), and did not use a nationally representative sample (Hämäläinen *et al.*, 2004; Moriya *et al.*, 2012). Furthermore, oral health variables, such as tooth loss were not assessed objectively in identified studies, different cut-offs were used to dichotomize physical function variables, while one study examined associations in participants of the same age and not a wide age range. Finally, due to the cross-sectional design studies cannot ascertain direction of associations.

None of the studies identified investigated the association of subjective oral health problems or accumulation of oral health problems with handgrip strength or walking speed in older people. Also, no studies were identified on the association between poor oral health and slow chair-stand speed in older age.

In summary limited evidence exists on the associations between objective oral health problems with different measures of physical function, whereas the association of subjective oral health problems with poor physical function remains unclear.

2.4.2.3. Prospective studies between oral health problems and incident disability

To date, studies have suggested that oral health problems are associated with onset of disability later in life (Holm-Pedersen *et al.*, 2008; Aida *et al.*, 2012; Komiyama *et al.*, 2016; Komiyama *et al.*, 2020; Yin *et al.*, 2020). These studies had a prospective cohort design, were performed in large predominantly older populations, performed similar statistical analyses and adjusted for several confounders. However, the majority of these studies have been conducted in older Japanese populations, and onset of disability has not been assessed through mobility limitations, ADL or IADL difficulties but through other validated measures of disability (Aida *et al.*, 2012; Komiyama *et al.*, 2016; Sato *et al.*, 2016; Komiyama *et al.*, 2020). In particular, in three studies conducted in older Japanese populations, incidence of disability was defined as the newly-qualified older people for insurance benefit due to their disability status (Aida *et al.*, 2012). Disability was assessed by trained interviewers by asking a set of questions and has been used for a long period by Japanese local governments (Aida *et al.*, 2012). These studies showed that partial and complete tooth loss were associated with increased risk of developing functional disability in

older Japanese community-dwelling people, establishing lack of a functional dentition (in this case less than 20 teeth) as an independent risk factor of onset of disability (Aida *et al.*, 2012; Komiyama *et al.*, 2016; Komiyama *et al.*, 2020). In addition, another study which was conducted in an older Danish population, assessed disability through the Avlund Mob-H scale, which included questions on walking indoors, transferring, getting outdoors, walking outside in nice weather, and climbing stairs (Holm-Pedersen *et al.*, 2008). They showed that tooth loss was associated with incident disability in the 10-years follow-up analysis, but not in the 15- and 20-years of follow-up analyses (Holm-Pedersen *et al.*, 2008). Only two studies assessed onset of disability through ADL (Katz scale) and IADL (Lawton scale) (Zhang *et al.*, 2018; Yin *et al.*, 2020). Zhang *et al.* identified onset of disability as the decline in ADL or IADL, and did not report any associations between tooth loss and declines in ADL and IADL, in an older US population (Zhang *et al.*, 2018). Contrary to this, Yin *et al.* examined the association between tooth loss and onset of ADL (Katz) and IADL (Lawton) difficulties in an older British population, and found that having less than 20 teeth was associated with incident ADL and IADL disability after 2 years of follow up (Yin *et al.*, 2020).

Mobility limitations is an important aspect of independence in older age and can be linked to prior poor physical function (Visser *et al.*, 2005). However, none of these studies investigated the association of tooth loss with onset of mobility limitations, assessed through the ability to walk a quarter of mile or climb a flight of stairs. Additionally, differences existed in the measurement of tooth loss and definition of functional dentition. Particularly, some studies used self-reported tooth loss (Aida *et al.*, 2012; Sato *et al.*, 2016; Zhang *et al.*, 2018; Yin *et al.*, 2020), whereas others assessed number of teeth during oral examination (Holm-Pedersen *et al.*, 2008; Komiyama *et al.*, 2016; Komiyama *et al.*, 2020). Generally, clinical assessment of tooth loss is preferred because self-reported tooth loss may introduce bias. Moreover in most populations functional dentition was defined as having at least 20 teeth (Holm-Pedersen *et al.*, 2008; Aida *et al.*, 2012; Komiyama *et al.*, 2016; Komiyama *et al.*, 2020; Yin *et al.*, 2020), whereas in Zhang *et al.* as having lost only 2 teeth (Zhang *et al.*, 2018); with both definitions being different from the one proposed by the WHO (at least 21 teeth) (Hobdell *et al.*, 2003). Additionally, some of these studies had a short follow-up period, and it is possible that healthier individuals

participated in data collection which may have led to underestimation of reported associations. Furthermore, since all studies were prospective, there is always the risk of loss to follow-up. Therefore, associations between tooth loss and onset of mobility limitations, ADL or IADL still remain unclear.

Furthermore, only one of the existing studies examined the associations between a subjectively assessed oral health problem and onset of disability. Particularly, this study focused on self-rated oral health, and showed that poor self-rated oral health at baseline was associated with decline in ADL but not IADL over time in an older US population (Zhang *et al.*, 2018).

In summary, mixed results exist for the associations between tooth loss and onset of ADL and IADL difficulties. Additionally, there is a lack of evidence on the association between tooth loss and onset of mobility limitations. Furthermore, there is substantial paucity of data about the associations of other oral health problems, including periodontal disease, dry mouth, self-rated oral health, and accumulation of oral health problems with risk of developing disability (mobility limitations, ADL, IADL) in older people.

2.5. Oral Health Problems and Inflammatory, Haemostatic, and Cardiac Biomarkers

2.5.1. Epidemiology of inflammatory, haemostatic, and cardiac biomarkers

Inflammation in older populations can be described by various markers of inflammation (Singh and Newman, 2011). In this thesis specific markers were used, including systemic, haemostatic, and cardiac biomarkers. In the next sub-sections, the epidemiology of these biomarkers will be described.

2.5.1.1. Systemic inflammatory markers

C-reactive protein (CRP)

CRP is a plasma protein which was discovered in 1930 by Tillet and Francis in patients suffering from pneumonia (Tillett and Francis, 1930; Bray *et al.*, 2016). CRP

responds to acute infection and inflammation or tissue injury and plays an integral role in the immune response of the body (Bray *et al.*, 2016). Levels of CRP can be affected by other inflammatory markers, such as Interleukin-6 (IL-6) (Singh and Newman, 2011). Increases in levels of CRP can be caused by ageing and several diseases including CVD, arthritis, or conditions such as disability (Kuo *et al.*, 2006; Sproston and Ashworth, 2018). Additionally there are biological and lifestyle factors which can influence CRP levels including gender, smoking, blood pressure, lipids, and BMI (Hage and Szalai, 2007; Sproston and Ashworth, 2018).

Interleukin-6 (IL-6)

IL-6 is a cytokine which is produced by few different type of cells, including cells of the immune system, vascular endothelial cells, adipocytes, and cells of the skeletal muscle (Singh and Newman, 2011). IL-6 levels are extremely sensitive to ageing, and even healthy older individuals can have increased levels of IL-6, without presence of infection (Singh and Newman, 2011). Interestingly, IL-6 can contribute to both elevation and decrease of inflammation (Maggio *et al.*, 2006). Chronically high levels of IL-6 are the main contributors of increased levels of CRP in older people (Roubenoff *et al.*, 1998; Singh and Newman, 2011). Production of IL-6 is influenced by several factors, including physical activity, BMI, and diet (Maggio *et al.*, 2006). It has been established that a combination of low caloric diet and physical activity can significantly reduce levels of IL-6 (Maggio *et al.*, 2006). Furthermore, previous research has indicated that high levels of IL-6 can contribute to insulin resistance, frailty, disability and decreased muscle strength, cancer, and CVD (Kritchevsky *et al.*, 2005; Maggio *et al.*, 2006).

2.5.1.2. Haemostatic markers

Fibrin d-dimer

Fibrin d-dimer consists of fibrin polymers and is an indicator of fibrinolysis and thrombosis (Riley *et al.*, 2016). High levels of fibrin d-dimer can reflect increased thrombosis (Riley *et al.*, 2016). As a diagnostic tool, levels of fibrin d-dimer are being utilised to diagnose deep venous thrombosis and pulmonary embolism (Tita-Nwa *et*

al., 2010). As most inflammatory markers, levels of fibrin d-dimer increase with age (Tita-Nwa *et al.*, 2010). However, fibrin d-dimer levels can be increased without the presence of thrombosis in older people (Tita-Nwa *et al.*, 2010). Therefore, it has been hypothesised that these abnormally increased fibrin d-dimer levels in older people, may be a consequence of increased fibrinolysis and a proinflammatory state which are attributed to ageing (Tita-Nwa *et al.*, 2010). Elevation in fibrin d-dimer has been found to be associated with race, total cholesterol, blood lipids, and BMI (Pieper *et al.*, 2000; Tita-Nwa *et al.*, 2010), as well as disability, stroke, and mortality (Pieper *et al.*, 2000; Wannamethee *et al.*, 2012; Wannamethee *et al.*, 2014) in older people.

von Willebrand Factor (vWF)

vWF is a plasma glycoprotein which plays an important role in vascular injury, and is a marker of endothelial dysfunction which is crucial to coagulation (Lip and Blann, 1997; Kawecki *et al.*, 2017). Levels of vWF are influenced by age and elevated vWF can lead to arterial and venous thrombosis (Kawecki *et al.*, 2017; Wannamethee *et al.*, 2017). Moreover, high levels of vWF are associated with greater risk of myocardial infarction and coronary events especially in patients with previous cardiovascular events (Vischer, 2006). vWF is highly correlated with fibrin d-dimer and is associated with stroke, atrial fibrillation, and mortality in community dwelling older adults (Wannamethee *et al.*, 2012; Wannamethee *et al.*, 2017; Zhong *et al.*, 2018).

Tissue plasminogen activator (t-PA)

t-PA is a protease which activates fibrinolysis and influences platelet function (Zhuang *et al.*, 2015). In other words, it assists in the activation of coagulation, which leads to thrombosis, which is extremely important during a vascular injury (Zhuang *et al.*, 2015). High levels of t-PA can be influenced by age and tend to differ between individuals with previous cardiovascular disease and healthy individuals (Wiman *et al.*, 2000; Wannamethee *et al.*, 2012). Elevated t-PA indicates increased thrombosis, and therefore t-PA has been used as a diagnostic tool for small and large vessel

disease, myocardial infarction and stroke (Zhuang *et al.*, 2015). Factors including gender, BMI, physical activity, and smoking are predictive of high levels of haemostatic factors, such as t-PA (Geiser *et al.*, 2017; Parsons *et al.*, 2017). Furthermore, increased levels of t-PA have been shown to be predictive of type 2 diabetes, and frailty (Eliasson *et al.*, 2003; Reiner *et al.*, 2009).

2.5.1.3. Cardiac biomarkers

Cardiac Troponin T

Cardiac Troponin T is part of the troponin complex and is generally found in cardiac and skeletal muscles (Xu *et al.*, 2013). Cardiac Troponin T is produced as a response to myocardial injury (Fan *et al.*, 2018). Elevated Troponin T is a diagnostic tool for myocardial infarction, heart failure and coronary heart disease in adults (Saunders *et al.*, 2011; Fan *et al.*, 2018). Levels of cardiac Troponin T are associated with age, with higher levels being reported in older people (Higgins and Higgins, 2003). In a healthy population, levels of Troponin T are generally non detectable due to their low concentration (Saunders *et al.*, 2011). It has been suggested that gender, diabetes, hypertension, smoking, total blood cholesterol, triglycerides, and levels of systemic inflammation (CRP) are associated with higher levels of Troponin T (Saunders *et al.*, 2011). Additionally, elevated Troponin T is associated with greater incidence of heart failure, hospitalisation due to heart failure, and mortality (Saunders *et al.*, 2011; Welsh *et al.*, 2019).

N-Terminal pro brain natriuretic peptide (NT-proBNP)

NT-proBNP is part of a prohormone called proBNP (Poortvliet *et al.*, 2015). NT-proBNP is released as a response to the ventricular wall being under stress, hypoxia, and in atrial fibrillation after increasingly regular atrial myocyte contractions (Poortvliet *et al.*, 2015). Alongside cardiac Troponin T, NT-proBNP is used as a diagnostic tool for heart failure (Poortvliet *et al.*, 2015). Elevated levels of NT-proBNP are highly correlated with levels of Troponin T (Eggers *et al.*, 2009). Moreover, NT-proBNP levels are correlated with fibrin d-dimer and vWF levels, showing that increased coagulation can contribute to increased cardiac stress (Wannamethee *et*

al., 2017). History of heart disease influences levels of NT-proBNP, with those with cardiac disease history having higher levels of NT-proBNP than healthy older individuals (Wannamethee *et al.*, 2017). Elevated NT-proBNP is associated with older age, gender, smoking, hypertension, diabetes, BMI, physical activity, total blood cholesterol, and history of myocardial infarction or stroke or vascular disease in older people (Wijsman *et al.*, 2014; Parsons *et al.*, 2018). Furthermore, increased levels of NT-proBNP are associated with greater risk of cognitive decline, heart failure, and CVD mortality in older individuals (Wijsman *et al.*, 2014; Poortvliet *et al.*, 2015).

2.5.2. Cross-sectional associations between oral health problems and inflammatory, haemostatic, and cardiac biomarkers in older people

2.5.2.1. Oral health problems and the association with levels of systemic inflammatory markers (CRP, IL-6)

Studies have reported associations between tooth loss, periodontal disease and high levels of CRP and IL-6 in populations consisting of both middle-aged and older individuals (Noack *et al.*, 2001; Amar *et al.*, 2003; Lowe *et al.*, 2003; Joshipura *et al.*, 2004; You *et al.*, 2009). Particularly, Lowe *et al.* found that self-reported tooth loss was associated with increased levels of CRP and IL-6 (Lowe *et al.*, 2003). However, gender differences existed, with associations with CRP being observed only in men, whereas associations with IL-6 were reported only in women (Lowe *et al.*, 2003). Furthermore, You *et al.* observed that as tooth loss was increasing so did levels of CRP (You *et al.*, 2009). However, Joshipura *et al.* did not report any associations between self-reported tooth loss and increased levels of CRP after adjusting for confounders in individuals aged 40-75 years old (Joshipura *et al.*, 2004). These inconsistent findings provide limited evidence about the associations of tooth loss with systemic inflammatory markers, especially in older people.

Furthermore, six studies investigated whether levels of CRP differed between those with and without periodontal disease; five of them were conducted in populations consisting of both middle-aged and older individuals, and only one in an older community-dwelling population (Loos *et al.*, 2000; Noack *et al.*, 2001; Amar *et al.*,

2003; Joshipura *et al.*, 2004; Montebugnoli *et al.*, 2004; Bretz *et al.*, 2005). Three of these studies (both middle-aged and older people) indicated that those with severe/advanced periodontal disease had higher CRP levels compared to those with no periodontal disease (Noack *et al.*, 2001; Amar *et al.*, 2003; Joshipura *et al.*, 2004). However, one study did not report any associations between periodontal disease and high levels of CRP in a population including middle-aged and older individuals (Montebugnoli *et al.*, 2004). Furthermore, the only study which examined the association of periodontal disease with increased levels of IL-6, did not report any significant associations in a population of middle-aged people (Loos *et al.*, 2000). Likewise, the only study carried out in older people living in the USA, was not able to establish any associations between periodontal disease and high levels of CRP and IL-6 after adjusting for age, gender, race, smoking, diabetes and BMI (Bretz *et al.*, 2005).

The majority of these studies assessed tooth loss and periodontal disease through a clinical examination, examined associations in large population-based samples, performed regression analyses and adjusted for several confounders. However, there are some limitations. Only one study was conducted in a predominantly older population, and the rest of studies consisted of both middle-aged and older people. Although, four of the identified studies had randomly selected participants, most of them included participants with specific outcomes, i.e. periodontal disease, coronary heart disease. Furthermore, some of these studies included only men, and three studies utilised self-reported measures of periodontal disease and tooth loss. Finally, all identified studies were cross-sectional, and therefore it is hard to establish causality.

Currently, the associations of subjective oral health problems with elevated CRP and IL-6 are unknown and to my knowledge have not been investigated in older people. Dry mouth, self-rated oral health, and accumulation of oral health problems are linked to oral and chronic diseases and can therefore be associated with high levels of inflammation.

2.5.2.2. Oral health problems and the association with levels of haemostatic biomarkers (fibrin d-dimer, vWF, t-PA)

Fewer studies have investigated the relationships of poor oral health with elevated haemostatic markers in populations including both middle-aged and older individuals, and have produced inconsistent findings.

Particularly, a study in a population of individuals aged 40-75 years old, did not find any associations between self-reported tooth loss and increased levels of t-PA, and vWF after adjusting for confounders (Joshipura *et al.*, 2004). Furthermore, Montebugnoli *et al.* examined the associations between periodontal disease and haemostatic (fibrin d-dimer, vWF) biomarkers in individuals aged 40-65 years (Montebugnoli *et al.*, 2004). They reported associations for periodontal disease and increased levels of vWF, but did not observe any associations with elevated fibrin d-dimer (Montebugnoli *et al.*, 2004). Similar findings for the association between periodontal disease and vWF were reported by a study conducted in another mixed population of both middle-aged and older individuals (Joshipura *et al.*, 2004). When the same study examined the associations between periodontal disease and elevated t-PA, no associations were observed (Joshipura *et al.*, 2004).

Both identified studies were large population-based studies which conducted similar statistical analyses and adjusted for several confounders. However they included both middle-aged and older men. One study recruited health professionals (Joshipura *et al.*, 2004), while the other included randomly selected men with CHD diagnosis (Montebugnoli *et al.*, 2004), something that complicates generalisability of findings. Additionally, tooth loss and periodontal disease were self-reported and due to the cross-sectional design, it is hard to make assumptions about direction of the associations.

Similar to CRP and IL-6, previous research has focused on objective oral health problems, tooth loss and periodontal disease, with no studies identified on dry mouth, self-rated oral health or accumulation of oral health problems and their associations with haemostatic markers.

2.5.2.3. Oral health problems and the association with levels of cardiac biomarkers (Troponin T, NT-proBNP)

Only one study identified examined the association between poor oral health and elevated cardiac biomarkers in community-dwelling adults with no previous history of a CVD event (Leira and Blanco, 2018). Leira et al. examined the association between periodontal disease and NT-proBNP levels in adults (≥ 18 years) (Leira and Blanco, 2018). They found that periodontal disease was associated with increased levels of NT-proBNP. They also observed that severity of periodontal disease was correlated with levels of NT-proBNP (Leira and Blanco, 2018). Furthermore, another study observed that individuals with stable coronary heart disease who suffered from tooth loss were more likely to have high levels of NT-proBNP when compared to those with functional dentition (Vedin *et al.*, 2017). However, it is unclear whether these results can be generalised to older community-dwelling individuals. Additionally, to my knowledge there were no studies examining associations between poor oral health and high levels of Troponin T in community-dwelling adults or older people. As a result, associations between oral health problems (both objective and subjective) and high levels of cardiac biomarkers remain unknown in older populations. Poor oral health has been found to be associated with the development of CVD, and it is highly probable that it can also be linked to CVD-related biomarkers (Alpert, 2017).

However, these two studies were heterogeneous with differences in study design and sample size. Leira and Blanco, recruited adult (≥ 18 years) patients with periodontal disease and without from a previous case-control study, and had a small sample size (Leira and Blanco, 2018). However, periodontal disease was assessed through a detailed clinical examination, and multivariable regression analyses was conducted adjusted for confounders. Moreover, Vedin et al. used data from a large sample of participants from a clinical study from 39 countries, which recruited individuals ≥ 60 years old with stable CHD (Vedin *et al.*, 2017), and assessed tooth loss through questionnaires. Nevertheless, multivariable regression analyses was performed which was adjusted for several confounders.

In summary, inconsistent results have been provided by studies examining associations of tooth loss and periodontal disease with high levels of inflammatory,

and haemostatic biomarkers, whereas limited evidence exists for the association with cardiac biomarkers in community-dwelling older people. Moreover, the associations between dry mouth, self-rated oral health, accumulation of oral health problems and elevated inflammatory, haemostatic, and cardiac biomarkers in older people are unknown. Subjective oral health problems reflect different aspects of oral health and can be used to examine how self-perception of poor oral health influences health-related biomarkers in older people.

2.5.2.4. Pathway connecting oral health problems with inflammatory markers

Periodontal disease is characterised by bacterial infection (Kinane *et al.*, 2017). Dental plaque which is created by oral pathogens leads to the creation of lesions in the oral cavity which then contribute to increased inflammation and immune response (Kinane *et al.*, 2017). Furthermore, bacteria from the oral cavity can enter the blood circulation and travel to other parts of the body where they can contribute to inflammation, including thrombosis and creation of atherosclerotic plaques (Alpert, 2017). Moreover, it is possible that mouth lesions may be a result of chronic diseases including diabetes, cardiovascular disease or respiratory disease (Alpert, 2017). It has been suggested that tooth loss can be a result of both chronic periodontal disease and comorbidities, with both conditions being associated with chronic inflammation (Friedman and Lamster, 2016). In other words, chronic periodontal disease can cause oral inflammation and subsequently contribute to infection and inflammation in other organs, but oral inflammation can also be a result of chronic diseases which are already linked to increased levels of inflammation. A frequently neglected oral health problem, dry mouth could be associated with increased inflammation through its relationship with several chronic diseases, since it is a side effect of many commonly-prescribed medications in older people (Alpert, 2017). Moreover, dry mouth can exacerbate existing oral health problems and therefore contribute to oral and systemic inflammation (Han *et al.*, 2015). Likewise, poor self-rated oral health and accumulation of oral health problems reflect oral health status and burden of oral diseases and hence can be associated with disease-related biomarkers.

2.6. Oral Health Problems and Diet Quality and Dietary Intake

2.6.1. Epidemiology of nutrition in ageing populations

Ageing is associated with several changes in nutritional intake and food behaviour (Clegg and Williams, 2018; Robinson, 2018). Diet quality represents the variety, quality, and quantity of foods consumed, with poor diet quality being characterised by decreased consumption of fruits and vegetables, grains, legumes, and increased intakes of meat, fat (saturated, trans-fat), sugar, salt and alcohol (Robinson, 2018). Diet quality could be affected by various factors, such as social class, education, previous health behaviours as well as medical history and medications (Clegg and Williams, 2018; Robinson, 2018). Previous studies have reported that the most common changes in diet quality are increases in consumption of lower density foods, including foods high in energy and fat, as well as following a diet with low variety (Robinson, 2018). Adequate protein intake has been highlighted by previous research as an integral part in maintaining muscle strength and muscle mass in older people (Clegg and Williams, 2018). Moreover, meat is a common source of protein and vitamins (B,A, iron), but according to the type of meat and cooking practices it can also be a source of harmful fat (Rohrmann and Linseisen, 2016). In particular, processed meat is an important source of saturated and trans-fat with its consumption remaining high in older people (Savoca *et al.*, 2009). Food Frequency Questionnaires (FFQ) are commonly used to assess dietary intake, with tools including the Elderly Dietary Index (EDI) and the Healthy Eating Index (HEI) measuring diet quality (Bowman *et al.*, 1998; Kourlaba *et al.*, 2009).

The estimation of the prevalence of poor diet quality is significantly influenced by the assessment methods and definition of poor diet quality. In a study consisting of 4 European countries, it was observed that poor diet quality scores varied significantly between countries, with different components influencing poor diet quality in each country (Irz *et al.*, 2014). Nevertheless, in all countries, a small proportion of individuals reported good diet quality (Irz *et al.*, 2014). Furthermore, in older British adults, it has been found that only 50% met the current recommendations on protein intake (0.75 g/kg/day) (Morris *et al.*, 2020). In a recent epidemiological analysis in the USA, it was found that older people consumed more processed meat than those aged 35-64 years (Zeng *et al.*, 2019). Moreover, it has been estimated that only 21

to 37% of men and 29 to 45% of women aged 65 adhered to the current fruits and vegetables recommendations (Nicklett and Kadell, 2013).

Diet quality, can be affected by several psychosocial (depression, isolation) and physiological factors (decreased lean mass, sarcopenia, frailty) factors associated with ageing (Clegg and Williams, 2018). Additionally, these factors can contribute to a decrease in appetite, which can directly impact food selection and intake (Clegg and Williams, 2018). Inability to perform everyday activities such as cooking can also influence food preparation and subsequently diet variety (Clegg and Williams, 2018). Furthermore, a diet poor in important micro- and macronutrients can lead to losses in mineral bone density and muscle strength and increase the risk of falls and disability (Cesari *et al.*, 2004; Clegg and Williams, 2018). Moreover, low intake of vitamins and antioxidants has been found to be associated with chronic diseases, including CVD, and impaired cognitive function (Collaboration, 2002; Clegg and Williams, 2018; Ford and Almeida, 2019).

2.6.2. Cross-sectional associations between oral health problems and diet quality and dietary intake in older people

A number of cross-sectional studies have reported associations between oral health problems and poor diet quality (Ervin and Dye, 2009; Savoca *et al.*, 2009; Zhu and Hollis, 2014; Watson *et al.*, 2019). However, findings are inconsistent. Savoca *et al.* examined the association between tooth loss and diet quality, which was measured by the Healthy Eating Index (HEI) in a population of older individuals in the USA (Savoca *et al.*, 2009). They reported that older people with ≥ 11 natural teeth had a better diet quality (higher HEI scores) when compared to older individuals with 0-10 natural teeth (Savoca *et al.*, 2009). Similar findings were reported by Zhu *et al.* (Zhu and Hollis, 2014). Nevertheless, a third study examining this association in older people in the USA, did not report any associations between number of teeth and diet quality (assessed by HEI) (Ervin and Dye, 2009). However in this study, dental implants were also included in the tooth count (Ervin and Dye, 2009). Another study using the Diet Variety score, suggested a weak association between tooth loss and diet quality in older adults (Marshall *et al.*, 2002). Finally, in a Japanese study of older adults, no associations were observed between tooth loss and food diversity

(another indicator of diet quality) in men, whereas in women those with <20 teeth had significantly lower scores of food diversity (Iwasaki *et al.*, 2015). However, in these 4 studies, 3 different index scores were used to assess diet quality, which may account for these inconsistent results.

Inconsistent results have also been reported for the association between tooth loss and consumption of fat and total energy in older people. Watson *et al.* did not report any differences in total intake of energy and total and saturated fat intakes between those with natural teeth and those without natural teeth but wearing dentures (Watson *et al.*, 2019). Similar null findings were reported by Ervin *et al.* (Ervin and Dye, 2009). However, two other studies reported that those with 0-10 teeth consumed more calories from fats when compared to those with at least 11 teeth (Marcenes *et al.*, 2003; Savoca *et al.*, 2009). On the contrary, Sheiham *et al.* observed that among older adults who retained their teeth, those who experienced tooth loss consumed less saturated fats compared to those who had a functional dentition (Sheiham and Steele, 2001). Furthermore another study established that those with less than 20 teeth, with or without replaced teeth consumed less calories compared to those with a complete dentition (21-28 teeth) (Ervin and Dye, 2012).

In addition, individuals with tooth loss were found to be at greater odds of consuming fewer foods rich in protein, fibre, calcium, iron, and vitamins B, E and C, particularly less fruits and vegetables, and eat more foods with high content of sugar (Marcenes *et al.*, 2003; Yoshida *et al.*, 2011). Furthermore, several studies have reported strong associations between complete and partial tooth loss with low consumption of fruits and vegetables (Tsakos *et al.*, 2010).

Moreover, the associations between periodontal disease and diet quality/intake are not well-established in older people. Previous studies have shown that adults with periodontal disease consumed foods rich in B12, folic acid, and poor in vitamin C, with low-fat content, and were also more likely to avoid foods (Quandt *et al.*, 2010; Hamasaki *et al.*, 2017); however more studies are needed to replicate these findings. Furthermore, nutritional intake can also affect onset and progression of periodontal disease, with studies suggesting that having good diet quality, and following a diet rich in antioxidants and vitamins can lead to improvement of periodontal disease in older people (Jauhiainen *et al.*, 2016; Iwasaki *et al.*, 2018a; O'Connor *et al.*, 2019).

Additionally, intake of saturated fats may also play a role in periodontal disease with higher intakes of saturated fat being associated with greater odds of having periodontal disease in an older Japanese population (Iwasaki *et al.*, 2011a).

The associations between subjective oral health problems and diet outcomes in older community-dwelling people remain unclear as well. One study examined the association between dry mouth and diet quality (HEI score) in older people living in the USA, and showed that those experiencing dry mouth had higher intakes of sweetened drinks, consumed the daily recommended portions of fruits and vegetables, had lower intakes of whole grains, and were more likely to avoid certain foods (Quandt *et al.*, 2010; Quandt *et al.*, 2011). Additionally, a study in a Japanese older population, found that older individuals with low production of saliva had lower intakes of vitamins D, and E, vegetables and fish when compared to those with normal saliva production (Iwasaki *et al.*, 2016a). Moreover, older adults with fair or poor self-rated oral health were more likely to avoid foods and consume less fruits and vegetables when compared to those with good or excellent self-rated oral health in two populations of older people (Quandt *et al.*, 2010; Amarasena *et al.*, 2018). Nevertheless, none of the existing studies identified have examined the association of accumulation of oral health problems with diet quality and dietary intake in older people. With the number of oral problems increasing with age, it is crucial to identify potential associations between the burden of oral health and diet quality.

The majority of identified studies had a large nationally representative randomly selected sample of older adults (men and women) with various age ranges, assessed tooth loss through clinical examination, utilised standard nutritional methodologies and validated diet scores, conducted regression analyses and adjusted for several confounders. In addition to examining associations in community-dwelling older people, two studies investigated associations in institutionalised older people (Sheiham and Steele, 2001; Marcenes *et al.*, 2003). Only two studies had a small sample size (Yoshida *et al.*, 2011; Iwasaki *et al.*, 2015), and two studies used self-reported tooth loss (Tsakos *et al.*, 2010; Watson *et al.*, 2019). Additionally, one study was only representative of low-income older adults in the UK (Tsakos *et al.*, 2010), three studies were representative only of the rural population of older people of a specific region in the USA (Savoca *et al.*, 2009; Quandt *et al.*, 2010; Quandt *et al.*, 2011), and one study examined the associations

in a nationally representative sample of adults in Japan (Hamasaki *et al.*, 2017). Some studies had a narrow age range, and therefore results may not be generalisable to other age groups. Moreover, the majority of studies were cross-sectional, and because diet intake was self-reported there is always the risk of measurement error, i.e. underreporting of energy intake. Nevertheless, some studies examined prospective associations between diet and poor oral health and vice versa, thus establishing bi-directional associations between poor oral health and diet in older people.

In summary, evidence suggests that bi-directional associations exist between oral health and diet, such as that oral health problems influence food choices and subsequent diet quality whereas poor diet quality and low intakes of fruits and vegetables influence progression and severity of oral diseases including tooth loss and periodontal disease (Moynihan, 2005; Iwasaki *et al.*, 2011a; Iwasaki *et al.*, 2011b; Iwasaki *et al.*, 2012a; Iwasaki *et al.*, 2012b; Iwasaki *et al.*, 2018a). However, more studies are needed to clarify the associations between oral health problems and diet in community-dwelling older people, particularly the relationships with specific nutrients.

2.6.2.1. Pathway connecting oral health problems with poor diet intake and dietary intake

Oral health problems, including tooth loss, periodontal disease and dry mouth can influence chewing and swallowing ability in older people (Bortoluzzi *et al.*, 2012). Tooth loss can lead to loss of bone tissue and muscles necessary for chewing, contributing subsequently to chewing difficulties among older adults (Moynihan and Bradbury, 2001; Bortoluzzi *et al.*, 2012). As a result individuals experiencing these problems tend to change their food intake and generally avoid specific foods, particularly those which are hard to chew such as raw fruits and vegetables, and fresh foods including seeds (tomatoes, grapes, whole grain bread) (Moynihan and Bradbury, 2001; Bradbury *et al.*, 2008). Furthermore, teeth are necessary for the preparation of food for digestion and particularly to create small pieces of food which can then be swallowed (Okamoto *et al.*, 2015). For the preparation of food bolus, saliva plays a very important role, and presence of dry mouth or low production of

saliva can negatively influence preparation of food and therefore swallowing (Gupta *et al.*, 2006). This can lead to food avoidance and choice of foods which are easy to chew and swallow. Additionally, people experiencing dry mouth, may reduce consumption of dry foods, including whole grain bread, and consume more liquid products such as fruit juice or canned fruits (Quandt *et al.*, 2011). Finally, it should be mentioned that poor oral health and poor diet quality have common risk factors, particularly adverse health behaviours. Those who smoke, consume increased amount of alcohol, are inactive, obese, and generally have worse health are more likely to have poor oral health and poor diet quality, highlighting a common background of health behaviours (Takata *et al.*, 2004; Hanioka *et al.*, 2007; Makhija *et al.*, 2007; Peltzer *et al.*, 2014; Ufholz and Harlow, 2017).

2.7. Pathways Connecting Oral Health Problems with Onset of Disability in Older People

Previous research has suggested that a compromised diet and high levels of inflammatory markers, such as CRP and IL-6 may mediate the association between oral health and incident disability in older people (Aida *et al.*, 2012; Komiyama *et al.*, 2016; Zhang *et al.*, 2018). Poor diet quality and high levels of inflammation may synergistically influence impaired physical performance and development of disability. As highlighted by a previous review, diet patterns characterised by high consumption of meat or Western-like diets were associated with increased levels of CRP and IL-6 in older people (Barbaresko *et al.*, 2013), suggesting a bi-directional relationship between diet and inflammation. However, to date no studies have performed causal mediation analysis to examine whether these two factors are indeed mediators in the association between poor oral health and onset of disability in older people. The only study identified which performed causal mediation analysis, investigated the mediating role of eating difficulties in the associations between tooth loss and incident ADL and IADL disability in older British people (Yin *et al.*, 2020). It was reported that the association between severe tooth loss (<20 teeth) and onset of ADL disability was mediated (10.35 %) by eating difficulties (Yin *et al.*, 2020). However, eating difficulties did not mediate the associations between tooth loss and

onset of IADL disability (Yin *et al.*, 2020). Eating difficulties are linked to diet and can be an indirect marker of poor diet quality.

The mediation through inflammation hypothesis is based on the potential link between oral health problems and increased oral and systemic inflammation. It has been suggested that individuals experiencing oral health problems are more likely to have increased levels of biomarkers such as CRP, and IL-6 (Noack *et al.*, 2001; Amar *et al.*, 2003; Lowe *et al.*, 2003; Joshipura *et al.*, 2004). Increased systemic inflammation (CRP, IL-6) can lead to loss of muscle mass and muscle strength, therefore contributing to decrease in ability to perform everyday activities or ability to move around (Wannamethee *et al.*, 2014). Coagulation markers such as fibrin d-dimer may act through a different mechanistic pathway, by influencing the production of cytokines which participate in endothelial and vascular functions (Wannamethee *et al.*, 2014). Oral health problems, including tooth loss, periodontal disease, and dry mouth can lead to increases in these inflammatory markers which in turn can influence muscle strength and contribute to onset of disability in older people. However, currently, there is limited understanding of which inflammatory markers are associated with poor oral health in older age and how these factors are implicated in the pathway connecting oral health and onset of disability.

A similar pathway exists for the mediating role of poor diet quality. Individuals with oral health problems are in greater risk of food avoidance, poor diet variety and nutritional deficiencies and this can impact various aspects of health (Moynihan, 2005). Fruits, vegetables, some legumes and wholegrain products, contain micronutrients which have antioxidant properties (Parsons *et al.*, 2019). High plasma concentrations of α -tocopherol, vitamin C and β -carotene, which reflect levels of antioxidants, were associated with better muscular skeletal strength, physical function and performance (Cesari *et al.*, 2004). Also, presence of free radicals and increased oxidation is associated with physical decline in older people (Cesari *et al.*, 2004). Additionally, oxidative stress can lead to increased levels of inflammation, and therefore contribute to the onset of disability through the inflammation pathway (Cesari *et al.*, 2004). However, in everyday life, nutrients can act both synergistically and antagonistically and beneficial effects from specific nutrients may be reduced by consumption of other nutrients (Barbaresko *et al.*, 2013). Therefore the mediating effect of overall diet quality may be of higher value than specific nutrients.

Nevertheless, due to mixed results on the associations of oral health problems with diet quality, before examining any mediating roles, it is important to clarify which oral health problems are associated with poor diet quality or diet components in older people.

2.8. Oral Health Problems and Mortality

2.8.1. Associations of oral health problems with all-cause mortality in older people

Several studies have established associations between tooth loss and greater risk of all-cause mortality in older populations (Fukai *et al.*, 2007; Holm-Pedersen *et al.*, 2008; Ansai *et al.*, 2010; Hayasaka *et al.*, 2013; Schwahn *et al.*, 2013; Hirotsu *et al.*, 2015; Hu *et al.*, 2015; Renvert *et al.*, 2015). However, these studies have provided inconsistent results. Overall, previous studies have suggested that as the number of missing teeth increased so did the risk of all-cause mortality in older Asian populations (Ansai *et al.*, 2010; Hayasaka *et al.*, 2013; Hirotsu *et al.*, 2015; Hu *et al.*, 2015; Hiratsuka *et al.*, 2019). Likewise, Fukai *et al.* examined the association between tooth loss and all-cause mortality in different age groups of older Japanese people (60-69, 70-79, ≥ 80 years) (Fukai *et al.*, 2007). In the ≥ 80 group those with ≥ 10 remaining teeth had 54% cumulative survival rate, while those with less than 10 teeth had 25% cumulative survival rate after 15 years of follow-up (Fukai *et al.*, 2007). The remaining studies have been conducted in older Western populations (Ajwani *et al.*, 2003a; Hämäläinen *et al.*, 2003; Holm-Pedersen *et al.*, 2008; Schwahn *et al.*, 2013; Renvert *et al.*, 2015). A study in an older Swedish population, suggested that complete tooth loss was associated with higher risk of all-cause mortality after 21 years of follow-up, however no associations were observed for partial tooth loss (Holm-Pedersen *et al.*, 2008). Another study, which measured tooth loss as the number of teeth that were lost and replaced, suggested that among those with tooth loss having at least 9 unreplaced teeth was associated with increased risk of all-cause mortality after 10 years of follow-up (Schwahn *et al.*, 2013). However, a number of studies failed to observe associations between tooth loss and risk of all-cause mortality (Ajwani *et al.*, 2003a; Hämäläinen *et al.*, 2003; Ando *et al.*, 2014; Renvert *et al.*, 2015).

Furthermore, associations between periodontal disease and risk of all-cause mortality remain unclear (Ajwani *et al.*, 2003a; Ajwani *et al.*, 2003b; Linden *et al.*, 2012; Chen *et al.*, 2015; Renvert *et al.*, 2015). Two studies in older community-dwelling people indicated that periodontal disease was associated with greater risk of all-cause mortality (Linden *et al.*, 2012; Chen *et al.*, 2015). However, two other studies, one in older Finnish individuals aged 70-85 years and one in older Swedish people (60-96 years), did not report any associations between periodontal disease and all-cause mortality after different periods of follow-up (Ajwani *et al.*, 2003a; Renvert *et al.*, 2015).

In all identified studies participants were randomly selected and the majority of them were large population-based studies of older people. Additionally, in most cases both men and women participated and were followed for a long period of time, tooth loss and periodontal disease were assessed through a clinical examination, survival analyses were conducted and adjusted for several confounders. However, the majority of studies took place in specific cities or regions and therefore may not be representative of the whole population of older people of each country, some studies had a narrow age range at baseline and short follow-up period. Moreover, in three studies participants were middle-aged at baseline (Fukai *et al.*, 2007; Schwahn *et al.*, 2013; Ando *et al.*, 2014) and in two studies only men were recruited (Linden *et al.*, 2012; Ando *et al.*, 2014). Finally, due to the prospective design it is possible that there was attrition bias and that healthier individuals participated in data collection.

Associations between subjective oral health problems and all-cause mortality are also not well-established. There were no studies identified for the association between dry mouth (self-perceived) and risk of all-cause mortality, but only for a surrogate measure of dry mouth-hyposalivation (low production of saliva). In an older Japanese population (70 years) the association between hyposalivation and risk of all-cause mortality was examined after 10 years of follow-up (Iwasaki *et al.*, 2018b). It was suggested that hyposalivation was associated with increased risk of all-cause mortality in older men (Iwasaki *et al.*, 2018b). However, hyposalivation does not entirely reflect perception of dry mouth, and therefore the association of dry mouth with risk of all-cause mortality in older people is not known. Furthermore, the only study examining the association between poor self-rated oral health and risk of all-cause mortality was conducted in a population of community-dwelling people ≥ 45

years in Australia, and it suggested that fair/poor self-rated oral health was associated with greater risk of all-cause mortality after adjustment for confounders (Joshy *et al.*, 2016). Nevertheless, this finding does not provide evidence of whether this association exists in older people. Finally, a study examining the associations between accumulation of oral conditions in individuals living in nursing homes found that as the number of oral symptoms increased so did the risk of all-cause mortality (Lindroos *et al.*, 2019). However, individuals living in nursing homes have worse oral and general health status and as a result findings of this study may not be generalisable in older community-dwelling people.

In summary, inconsistent results have been reported for the associations between objective (tooth loss, periodontal disease) oral health problems and risk of all-cause mortality, whereas associations of subjective oral health problems remain still unknown in community-dwelling older people.

2.8.2. Associations of oral health problems with CVD mortality in older people

CVD mortality is one of the most common causes of death in older people, even though rates have been in decline (Bhatnagar *et al.*, 2016). Studies have suggested associations between poor oral health and CVD mortality in older people (Ajwani *et al.*, 2003a; Schwahn *et al.*, 2013; Ando *et al.*, 2014; Chen *et al.*, 2015). However, inconsistent findings have been reported for the association of objective oral health problems (tooth loss, periodontal disease) and risk of CVD mortality, whereas relationships for subjective oral health problems remain unclear.

For tooth loss, three studies examined the associations with risk of CVD mortality. Aida *et al.* reported that those who had ≤ 19 teeth and difficulty eating had greater risk of CVD mortality when compared to older individuals with ≥ 20 teeth after 4.28 years of follow-up (Aida *et al.*, 2011). These findings were supported by another study which found that among individuals with tooth loss, those with at least 9 unreplaced teeth had greater risk of CVD mortality (Schwahn *et al.*, 2013).

Nevertheless, Ando *et al.* did not observe any associations between tooth loss and risk of CVD mortality in another population of older Japanese individuals aged 65-79 years after 5.6 years of follow-up (Ando *et al.*, 2014).

Furthermore, only two studies have examined the association of periodontal disease with CVD mortality and have provided inconsistent results. In an older Taiwanese population mortality rates from cardiovascular disease were higher in those with periodontal disease compared to those without (Chen *et al.*, 2015). Additionally when survival analysis was performed, periodontal disease was associated with greater risk of CVD mortality after 3 years of follow-up in the fully adjusted model (Chen *et al.*, 2015). However, no associations were observed between periodontal disease and risk of CVD mortality in a German population of older community-dwelling people (Schwahn *et al.*, 2013).

Only one study identified examined the association between a subjective oral health problem (dry mouth) and risk of CVD mortality, with no studies on self-rated oral health or accumulation of oral health problems in older people identified. In particular, in an older Japanese population dry mouth (mouth feels sticky) was not associated with greater risk of CVD mortality in adults aged 40-79 years (Ide *et al.*, 2008). However, since this study included both middle-aged and older people it is possible that these findings may differ in older people.

The majority of identified studies were large nationally representative population-based cohort studies and all of them performed survival analyses and adjusted for confounders. Only one study assessed tooth loss through questionnaires (Aida *et al.*, 2011), two studies had short follow-up periods (Aida *et al.*, 2011; Chen *et al.*, 2015), three studies included middle-aged individuals at baseline, and one study recruited only men. Due to the prospective design it is possible that there was attrition bias and that healthier individuals participated in data collection.

Finally, none of the studies identified have performed competing risks analysis for the associations between poor oral health and CVD mortality. Competing risks analysis for CVD mortality takes account of the competing risk of non-CVD deaths, and in the presence of competing risks leads to more reliable estimations of hazard ratios (Austin *et al.*, 2016). In particular, with CVD mortality being among the most prevalent causes of death in older populations, it is crucial to provide robust effect estimates for the associations between exposures and risk of CVD mortality.

In conclusion, inconsistent results have been reported for associations of tooth loss and periodontal disease with risk of CVD mortality, whereas associations of dry

mouth, self-rated oral health, and accumulation of oral health problems remain unknown.

2.8.3. Associations of oral health problems with respiratory mortality in older people

Respiratory (any respiratory disease, flu, infectious diseases) mortality rates remain still high in older people and tend to increase with age (Saliccioli *et al.*, 2018). Some studies have established associations between poor oral health and risk of respiratory mortality (Ide *et al.*, 2008; Aida *et al.*, 2011; Suma *et al.*, 2018; Manabe *et al.*, 2019; Qian *et al.*, 2020). The majority of studies have focused on the associations between tooth loss, periodontal disease and risk of respiratory mortality.

In particular, two studies in older Japanese populations showed that having less than 20 teeth, which represented a functional dentition, was associated with greater risk of total respiratory mortality (includes all respiratory causes of death) and mortality due to pneumonia (Aida *et al.*, 2011; Manabe *et al.*, 2019). Similar results were reported by another study in Japanese dentists, aged 26-98 years (Suma *et al.*, 2018). Moreover, when the study sample was restricted to those aged ≥ 50 years associations did not change substantially (Suma *et al.*, 2018). However, a study conducted in an older Chinese population (≥ 75 years) which performed a competing risks analysis to examine whether other non-respiratory causes of death influenced risk of respiratory mortality did not report any differences in the risk of respiratory mortality between those with tooth loss and those with a functional dentition (Qian *et al.*, 2020).

Two studies have examined the associations between periodontal disease and risk of respiratory mortality. However, there were differences in the measurement of respiratory mortality, with one assessing the risk of total respiratory mortality, whereas the other one used mortality due to pneumonia as the outcome (Awano *et al.*, 2008; Qian *et al.*, 2020). Although pneumonia is one of the most common respiratory infections, the influence of other respiratory diseases, or infections on the risk of respiratory mortality should not be ignored. Awano *et al.* reported that having ≥ 10 teeth with periodontal disease was associated with higher risk of mortality due

to pneumonia in an older Japanese population (Awano *et al.*, 2008). Similar findings were observed in another study in an older Chinese population aged ≥ 75 years, where severe periodontal disease was associated with greater risk of total respiratory mortality, even after taking account of the competing risk of other non-respiratory deaths (Qian *et al.*, 2020).

Currently, only one study examined the association between dry mouth (mouth feels sticky) and risk of death from pneumonia in Japanese adults aged 30-79 years, and showed that those who replied yes had a two-fold greater risk of mortality due to pneumonia (Ide *et al.*, 2008). However, this study included both middle-aged and older individuals and therefore it is unclear whether these findings can be generalised to older populations. Additionally, no studies identified have investigated the association between self-rated oral health or accumulation of oral health problems with the risk of respiratory mortality in older people.

The majority of identified studies were large population-based cohort studies of older people with both men and women, while two studies included middle-aged individuals at baseline. All studies had a prospective study design, conducted survival analyses and adjusted for several confounders. Objective measures of oral health were self-reported in the majority of studies, and only one study performed clinical oral examination. Additionally, one study recruited dentists, and may not be representative of older community-dwelling older people (Suma *et al.*, 2018), and in another study participants who were referred for periodontal treatment were included in the study (Qian *et al.*, 2020). Due to the prospective design it is possible that there was attrition bias and that healthier individuals participated in data collection.

In summary, inconsistent findings exist for the associations of tooth loss and risk of total respiratory mortality, whereas there is significant paucity of data about the associations of periodontal disease, subjective oral health problems and accumulation of oral health problems with risk of total respiratory mortality.

2.9. Summary

Oral health problems, including tooth loss, periodontal disease and dry mouth are highly prevalent among older people. Worldwide, poor oral health is becoming more

common in adults. In the USA, periodontal disease was declared a public health problem, highlighting the importance of oral health problems (Eke *et al.*, 2016). Previous research has shown that older individuals with tooth loss are more likely to experience disability (ADL, IADL) and poor physical function (handgrip strength, walking speed). However, associations between tooth loss and mobility limitations and chair-stand speed still remain unclear. Furthermore, research gaps exist on the cross-sectional associations of other oral health problems, including periodontal disease, dry mouth, poor self-rated oral health, and accumulation of oral health problems with measures of disability (mobility limitations, ADL, IADL) and physical function (handgrip strength, walking speed, chair-stand speed). Disability and physical function can be identified by different measures and clarifying associations with different oral health problems will help highlight the influence of poor oral health in different aspects of everyday life in older people. Additionally, similar gaps are identified for the prospective associations of poor oral health with risk of developing disability in older people, where only associations between tooth loss and risk of disability have been reported. Moreover, previous research has recognised that increased inflammation and poor diet quality may act as potential mediators in the association between poor oral health and risk of developing disability in older people. However, this hypothesis has not been investigated through causal mediation analysis in longitudinal studies of older people, and therefore it is unclear whether high levels of inflammation and poor diet quality do indeed mediate this association in older age. Moreover, gaps also remain around associations between poor oral health and inflammation and diet in older age.

In particular, studies have reported cross-sectional associations between tooth loss, periodontal disease, and systemic inflammatory markers (CRP, IL-6) in middle-aged populations; however these associations remain unknown in older people, especially for subjective oral health problems. Additionally, inconsistent findings have been reported for the relationships between objective oral health problems and levels of haemostatic markers in older people, with evidence on subjective oral problems missing. Moreover, the associations of both objective and subjective oral health problems with cardiac biomarkers remain unknown. Cross-sectional associations have also been demonstrated between poor oral health and diet quality and dietary intake. However, findings between studies were inconsistent and diet quality was

measured differently across studies. Inconsistent findings have also been reported for the associations between tooth loss and specific nutrient intakes in older people. Again, few studies examined associations for subjective oral health problems. Establishing associations between poor oral health and increased inflammation and poor diet will assist in examining the causal pathways underpinning the relationships of oral health with risk of developing disability.

Studies have also shown associations between objective oral health problems and all-cause, CVD, and respiratory mortality in older people; however these findings are inconsistent. Additionally, there is a paucity of data for the associations of subjective oral health problems as well as accumulation of oral health problems with risk of all-cause, CVD, and respiratory mortality in community-dwelling older people, with the few existing studies being conducted in middle-aged populations, those living in nursing homes, or measuring oral health problems in different ways.

In summary, key gaps identified in this literature review were: a) limited evidence on the cross-sectional associations between subjective oral health problems and disability, physical function, inflammatory markers, diet quality and dietary intake, all-cause and cause specific mortality in older adults; b) few studies examining associations of oral health problems in older adults with incident mobility limitations, ADL and IADL using similar definitions; c) few studies investigating the associations of oral health problems with haemostatic and cardiac biomarkers; d) lack of studies using causal mediation analysis to investigate the mediating effects of diet quality and inflammation on the association of poor oral health with incident disability in older people.

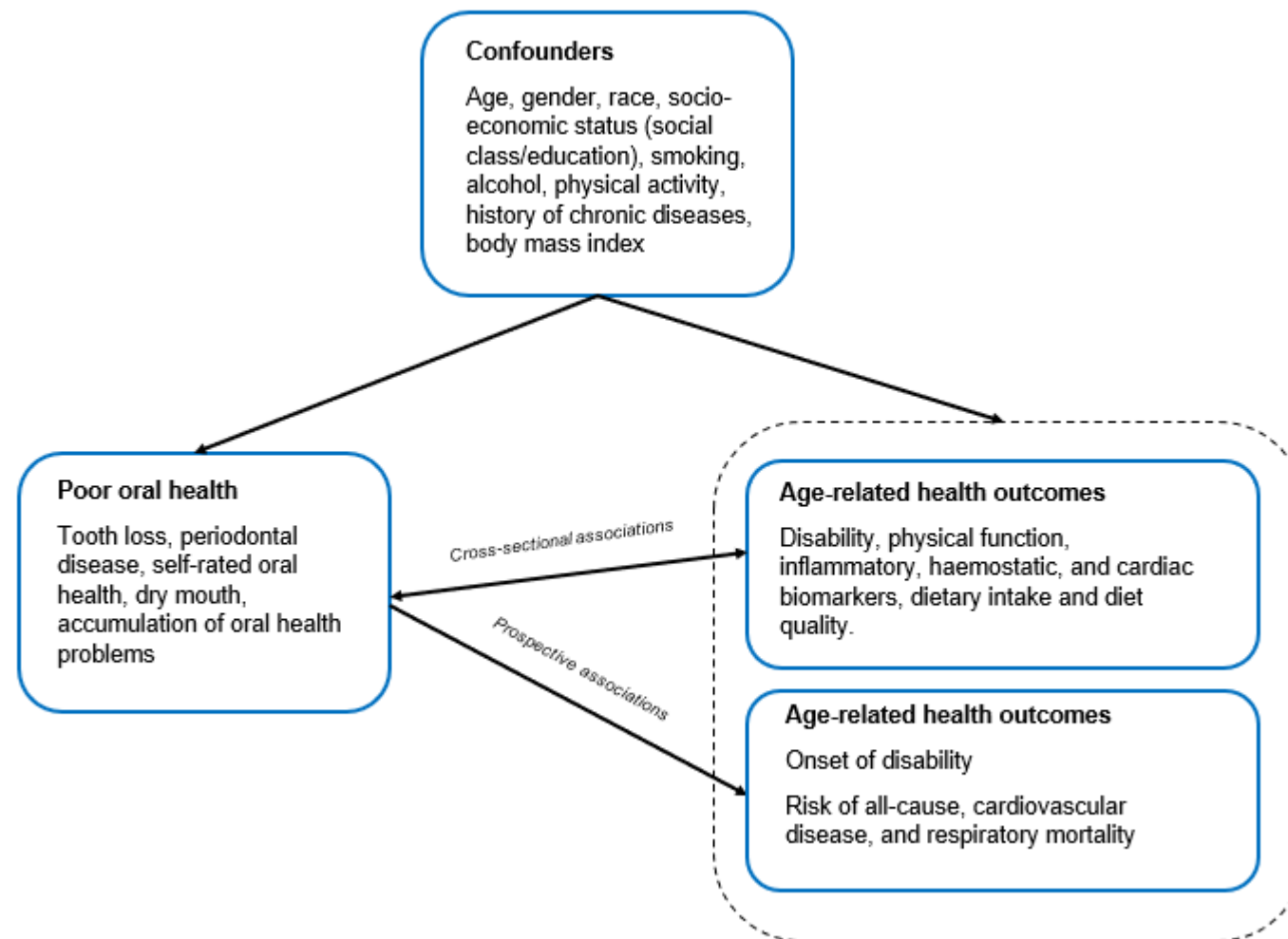


Figure 2.1. Conceptual framework for associations of poor oral health with age-related health outcomes^a.

^a In this diagram the most frequently-used confounders are included

Chapter 3. Methodology

3.1. Introduction

This thesis comprises epidemiological analysis of data from two population-based studies of older people: the British Regional Heart Study (BRHS), and the Health, Aging and Body Composition (HABC) Study. The BRHS was initiated in 1978-1980 and 7735 men were recruited from 24 towns across the UK. The HABC Study was initiated in 1997-1998 and 3075 men and women were recruited living in Memphis, Tennessee and Pittsburgh, Pennsylvania, USA. Since baseline, in both studies, participants have been followed and asked about health behaviours, conditions, and mortality. Data collection was carried out through physical examinations and questionnaires. In the BRHS, re-examinations were conducted 20 and 30 years after baseline, where information on oral health, disability, physical function, inflammation, diet, lifestyle factors and medical history was collected. Likewise, in the HABC Study, re-examinations were carried out 1 year after baseline in 1998-1999 and in 2001-2002, where information on oral health, disability, physical function, inflammation, diet, lifestyle factors and medical history was also collected.

This Chapter includes an overview of the study design and methodology used in both cohorts (sections 3.2 and 3.5), a description of data used in the thesis (sections 3.3 and 3.6), the strengths and limitations of data used for analysis in the two studies (sections 3.4 and 3.7), details on attrition and missing data (section 3.8), and a brief description of statistical methods (section 3.9). Specific details of the statistical analysis performed to investigate the objectives of this thesis will be described in each of the relevant Chapters.

3.2. British Regional Heart Study

3.2.1. *Description of cohort*

The British Regional Heart Study (BRHS) (<https://www.ucl.ac.uk/epidemiology-health-care/research/primary-care-and-population-health/research/brhs/index.htm>) is a prospective cohort study of cardiovascular disease (CVD) in a socioeconomically

and geographically representative sample of British men aged 40-59 years who were randomly recruited from a general practice across 24 British towns (Shaper *et al.*, 1981). At baseline (1978-1980) 7735 men were examined. Since then, study participants have been followed up with interviews including questions about lifestyle, morbidity, and mortality until the present. The BRHS aimed to explain the substantial regional variations in mortality from cardiovascular disease in Great Britain, by assessing the role of environmental, socioeconomic, and behavioural factors (Pocock *et al.*, 1980; Shaper *et al.*, 1981). Over time, as the cohort has aged, there has been an increasing focus on the aetiology and prevention of cardiovascular disease in older ages.

3.2.2. Selection Procedures

The towns chosen were representative of all major geographic regions in Great Britain (England, Scotland, and Wales) and were selected according to the following criteria (Shaper *et al.*, 1981):

1. All standard geographical regions should be represented.
2. Towns should be discrete entities with populations of 50000-100000 at the 1971 Census. In England one larger town was included (Ipswich). In Scotland, some towns below 50000 were considered to obtain a reasonable number of suitable towns.
3. The choice of towns within regions should reflect the variations in mortality from CVD and water hardness.
4. Towns were to be representative of the region in socioeconomic terms.
5. Towns with noticeable population movement or with unusual population structure were excluded.
6. The study included some towns that were apparent "outliers" when CVD mortality and water hardness were plotted against each other, for example Hartlepool, Exeter, and Harrogate.

7. When similar towns met the above criteria, random selection was made between the towns.

Figure 3.1 (page 88) presents a map of all 24 towns included in the BRHS. Table 3.1 (page 93) shows the list of towns of the BRHS and the standardised mortality ratios for all cardiovascular disease in men aged 35-64, number of men examined and the response rate.

Participants were selected from one general practice in each town to achieve a good initial response and subsequent feedback (Shaper *et al.*, 1981). General Practices were chosen according to their size (practice population >7500), representativeness of socioeconomic composition and characteristics of the town population and willingness of the General Practice to participate. According to the sex and age register of each General Practice, 450 men aged 40-59 years were randomly selected and then stratified into equally sized five-year age groups (40-44, 45-49, 50-54 and 55-59 years). Men with severe mental or physical disability were excluded (6-10% per practice). The remaining participants (~10000) were invited to participate via signed letters by the general practitioners encouraging them to attend the cardiovascular health check at a local venue, usually the practice premises. Out of these 10000 men, 7735 were included in the study, resulting in a response rate of 78%, with 18 of the 24 towns having a response rate of 75% or more (Table 3.1, page 93) (Shaper *et al.*, 1981). Therefore, the study's total sample size was equal to 7735 men, with approximately 300 men per town (Shaper *et al.*, 1981; Walker *et al.*, 2004).

3.2.3. Baseline examination

At baseline (1978-1980), all 7735 participants attended physical examinations which were conducted at each town. These examinations were performed by a team of trained nurses and were completed by 1980. Measurements included height, weight, blood pressure, electrocardiogram, and lung function. In addition, a blood sample was collected, and men also completed a nurse-administered questionnaire on lifestyle factors and health and medical history. Ethical approval was provided by the

National Research Ethics Service (NRES) Committee, London. All participants provided written informed consent, according to the Declaration of Helsinki.

3.2.4. Follow-up of participants from baseline

Since baseline, participants have been followed-up on lifestyle factors through postal questionnaires, on morbidity data from local GPs and on mortality by the NHS Central Register (Walker *et al.*, 2000; Walker *et al.*, 2004; Lennon *et al.*, 2015), as presented in Figure 3.2 (page 89). Re-examinations took place 20-years (1998-2000) and 30-years (2010-2012) from baseline.

3.2.4.1. Mortality

Information on mortality was collected through the established procedure of “flagging” participants for follow-up in the NHS Central Register in Southport for England and Wales, and in Edinburgh for Scotland (Walker *et al.*, 2004). Death certificates which are sent by the NHS Central Register comprise identification details, date and place of death and cause of death coded using the International Classification of Diseases ninth revision (ICD-9) and subsequently the tenth edition (ICD-10). GPs also verified fatal events which was part of a periodic review. Every two years a standard medical record review form was sent to each of the 24 practices requesting confirmation of each participant’s continuing registration, current address, and information on any new non-fatal (cardiovascular disease, cancer, diabetes) and fatal events which had occurred in the past two years.

Individuals who re-register with another practice are traced by using information from the local health authority. Currently, the study consists of over 850 general practices across the UK and follow-up has been achieved for 98% of surviving participants.

3.2.4.2. Follow-up questionnaires

Postal self-administered questionnaires included questions on medical history, health, lifestyle, and socioeconomic factors. These questionnaires have been sent in

regular intervals since baseline in 1978-1980 (see Figure 3.2). After baseline, the next questionnaire was sent in 1983-1985, and was followed by postal questionnaires in 1992 and 1996. At the 20-year re-examination, a questionnaire was filled out by participants and a separate Food Frequency Questionnaire (FFQ) was also sent (see sub-section 3.3.6). Then, questionnaires were also sent in 2003, 2005 and 2007. As part of the 30-year re-examination, a questionnaire including the FFQ was completed, and was followed by a postal questionnaire in 2014. Since 2014, questionnaires are being sent annually.

3.3. BRHS Data Used in This Thesis

In this thesis, BRHS data primarily from the 30-year re-examination (2010-2012) were used, when data on oral health was collected for the first time in the cohort. Data were used to examine the cross-sectional associations of oral health problems with disability, physical function, inflammation, and diet. Additionally, data were used to assess the prospective associations of poor oral health with risk of developing disability and risk of mortality, as well as the mediating effects of diet and inflammation on the associations between oral health and risk of developing disability.

Follow-up data on disability were collected until 2014 (questionnaire), and on mortality until June 2019. Moreover, this thesis used data (a) on socioeconomic status collected at baseline (1978-1980), and (b) on several covariates collected at the 20-year re-examination (1998-2000), including, lifestyle factors, medical history, physical factors (height, weight) and diet quality. Data collection and definition of oral health problems (exposure), outcome variables, and confounding variables are described below.

3.3.1. Measures of oral health

Oral health measures at the 2010-2012 re-examination consisted of objective and subjective oral health problems. Objective oral health problems included number of teeth (tooth loss), and periodontal disease. Number of teeth and periodontal disease

were assessed during an oral examination. Assessments were performed by a trained research nurse. Subjective oral health problems were measured through a postal questionnaire and comprised self-rated oral health, dry mouth, difficulty eating, and sensitivity to hot/cold/sweets. Details on sample size and missing data will be presented in section 3.8.

3.3.1.1. Objective oral health problems

Tooth loss included a count of natural teeth. Periodontal disease consisted of loss of attachment and pocket depth. Pocket depth assesses the distance between the gum tissue and its attachment to the tooth, whereas loss of attachment measures the distance between the point at which the gum is attached and the 'neck' of the tooth where the gum is attached in a healthy tooth (Ramsay *et al.*, 2015b). These measurements were performed in six index teeth (three in the upper arch and three in the lower arch), one per mouth sextant of the mouth (Ramsay *et al.*, 2015b). First molars were assessed in the four posterior sextants, and right central incisors in the two anterior sextants; where the first molar was missing, the following tooth was chosen in order of priority: second premolar, first premolar, second molar; if the central incisor was missing, the next mesial tooth available in that sextant was chosen (Ramsay *et al.*, 2015b). Loss of attachment was measured at 2 sites (mesiobuccal and distobuccal) on each index tooth and pocket depth was assessed in one site, the mesiobuccal. During the examination, a Community Periodontal Index of Treatment Needs (CPITN) probe was used, with a 0.5 mm ball-ended tip with markings at 0 to 3.5, >3.5 to 5.5 and >5.5 mm (Ramsay *et al.*, 2015b). Examiners (research nurses) underwent extensive training and calibration including a pilot prior to the study and a calibration check during the study (Ramsay *et al.*, 2015b). The range of agreement between the examiner and the trainer ranged from 89% to 95%. Due to the extensive nature of the physical examination, which the oral examination was part of, and the advanced age of the men (71-92 years), number of teeth and periodontal disease were the only objective oral health measures (Ramsay *et al.*, 2015b).

3.3.1.2. Subjective oral health problems

Self-rated oral health: The question “Would you say your dental health is excellent, good, fair, poor” was used to assess self-rated oral health.

Dry mouth: The Xerostomia Inventory (XI) was used to assess dry mouth (Thomson *et al.*, 1999). Xerostomia measures the perception of dry mouth (Thomson *et al.*, 1999). The XI consists of 11 items, and is a validated tool which aims to assess the wide range of dry mouth symptoms and their severity (Thomson *et al.*, 1999).

Participants were asked whether in the past 4 months they experienced the following symptoms: mouth feels dry, difficulty eating dry foods, getting up at night to drink, mouth feels dry when eating a meal, sip liquids to aid swallowing food, sucking sweets to relieve dry mouth, difficulties swallowing certain foods, skin of face feels dry, eyes feel dry, lips feel dry, inside of nose feels dry. Responses to each question were never, hardly ever, occasionally, fairly often or very often.

Difficulty eating: The question assessing difficulty eating was included in the Oral Impact on Daily Performances (OIDP) questionnaire (Tsakos *et al.*, 2001). Men were asked whether in the past 6 months any oral health problems caused difficulty eating.

Sensitivity to hot/cold/sweets: Participants were asked how often their teeth or gums were sensitive to hot or cold or sweets. Participants could respond never, hardly never, occasionally, fairly often, very often.

3.3.2. Measures of socio-demographic and lifestyle factors

Socioeconomic position: The longest-held occupation was the measure of socioeconomic position and was recorded at study entry through a nurse-administered questionnaire when participants aged 40-59 years. Individuals were classified, according to the Registrar General's Classification of Occupations (General, 1991), into six occupational social class categories: I (professional occupations e.g. barristers, physicians, engineers), II (intermediate occupations e.g. teachers, sales managers), III non-manual (skilled non-manual occupations e.g. clerks, shop assistants), III manual (skilled manual occupations e.g. bricklayers,

coalminers), IV (partly skilled occupations e.g. bus conductors, postmen) and V (unskilled occupations e.g. porters, general labourers). Then, social class was categorised in two groups: manual (III-V) and non-manual (I-III).

Smoking status: Smoking data from the 20-year (1998-2000) and 30-year (2010-2012) re-examinations were used. Smoking was created according to data from self-reported questionnaires from different time points. In 1992, smoking status was divided to the following four categories: never smokers, long-term ex-smokers (those who were non-smokers in 1992, and those who were ex-smokers at the baseline in 1978-1980), recent ex-smokers (non-smokers in 1992, and quit smoking between 1978-1980 and 1992), and current smokers. Participants who reported that they did not smoke at 1998-2000 had their answers compared to 1992, classifying them as ex-smokers or non-smokers. The same procedure for the classification of smoking was followed in 2010-2012. Then, in both time points, smoking was categorised as current smokers, ex-smokers, and non-smokers.

Alcohol consumption: In the 20-year re-examination (1998-2000) participants were asked about their alcohol consumption (daily/most days; weekends only; occasional; special occasions only; none) through a self-administered questionnaire. They also had to estimate the quantity of drinks during the days that they drank (None; 1-2 drinks; 3-6 drinks; >6 drinks). Then, according to these two questions, participants were categorised into five groups which represented their weekly alcohol intake: none (0 drinks/week); occasional (<1 unit/week); light (1-15 units/week, which included weekend 1-2 units, weekend 3-6 units and daily 1-2 units); moderate (16-42 units/week, which included daily 3-6 units and weekend >6 units); heavy (>42 units/week, which included >6 units daily) (Wannamethee and Shaper, 1997; Wannamethee *et al.*, 2005). In the 30-year re-examination (2010-2012) alcohol intake was based on one question from the self-administered questionnaire asking men about their current frequency of drinking (daily/most days; weekends only; occasional; special occasions only; none).

Physical activity: In the self-administered questionnaire at the 20-year (1998-2000) and 30-year (2000-2012), men were asked about the usual patterns of physical activity under the headings of regular walking or cycling, recreational activity, and sporting (vigorous) activity. Regular walking and cycling related to weekday journeys,

which included travel to and from work. Recreational activity comprised gardening, pleasure walking, and do-it-yourself jobs. Sporting activity consisted of running, golf, swimming, tennis, sailing, and digging. A physical activity score was calculated based on the frequency and type of physical activity (Wannamethee *et al.*, 2002). Scores were assigned for each type of activity and duration on the basis of the intensity and energy demands of the activities reported (Wannamethee and Shaper, 1992). Total score represents the amount of physical activity performed for each participant. According to this score, six groups were created: inactive (score 0-2), occasional (score 3-5; regular walking or recreational activity only), light (score 6-8; more frequent recreational activities or vigorous exercise less than once a week), moderate (score 9-12; cycling or very frequent recreational activities or sporting activity once a week), moderately-vigorous (score 13-20; sporting activity at least once a week or frequent cycling, plus frequent recreational activities or walking, or frequent sporting activity only), and vigorous (score ≥ 21 ; very frequent sporting exercise or frequent sporting exercise plus other recreational activities). This particular physical activity score has been validated at baseline (1978-1980), at the 20-year and 30-year re-examinations against heart rate and lung function (FEV₁) in participants without pre-existing coronary heart disease (CHD) (Wannamethee and Shaper, 1992; Wannamethee *et al.*, 2002). Additionally, physical activity measured at 30-year has been further validated against accelerometer data from the same time point (Jefferis *et al.*, 2016).

Anthropometric measurements: At both the 20-year and 30-year re-examinations weight and height were measured while participants were standing. Height was measured with a Harpenden stadiometer to the last complete 0.1 cm. At 20-year, weight was measured with a Soehnle digital electronic scale to the last complete 0.1 kg. At the 30-year re-examination, weight was measured by Tanita MA-418-BC body composition analyser (Tanita, Tokyo, Japan). To calculate Body Mass Index (BMI) data from weight and height measurements were used ($\text{weight}/\text{height}^2$). To classify participants into BMI groups the WHO cut-off points were used (normal $<25\text{kg}/\text{m}^2$, overweight ≥ 25 , obese $\geq 30\text{kg}/\text{m}^2$) (World Health Organization, 2000).

3.3.3. Physical measurements

At the physical examination in 2010-2012, blood pressure was measured in duplicate in the right arm with an Omron blood pressure recorder (Ramsay *et al.*, 2015a). During the measurement the participant was seated and the arm was supported (Whincup *et al.*, 1992). Blood pressure was adjusted for observer variation (Bruce *et al.*, 1988). The mean of the two blood pressure recordings was used in the analysis (Ramsay *et al.*, 2015a). According to the International Society for Hypertension Guidelines (2003), if systolic blood pressure was ≥ 160 mmHg or diastolic blood pressure ≥ 90 mmHg then participants were classified as having hypertension. Forced expiratory volume (FEV₁) and Forced Vital Capacity (FVC) were assessed while men were standing and without nose clips, with a Vitalograph Compact II instrument (Ramsay *et al.*, 2015a). This instrument was calibrated at least twice daily using a precision syringe (Ramsay *et al.*, 2015a). FEV₁ was recorded for the best test, defined in accordance with the American Thoracic Society recommendations (Ramsay *et al.*, 2015a). It has been shown that dividing by height is the best way to standardise lung function for stature (Cole, 1975; Ramsay *et al.*, 2015a). FEV₁ and FVC were height standardised to the average height, 1.71 m, in the study. Additionally, a FEV₁/FVC ratio was created representing lung function. Participants with a FEV₁/FVC ratio smaller than 0.70 were classified as having COPD, based on the Global Initiative for Chronic Obstructive Lung Disease.

3.3.4. Blood measurements

Fasting serum samples of blood lipids and inflammation markers were measured at the 30-year re-examination in 2010-2012. Blood lipids included total triglycerides and high-density lipoprotein cholesterol (HDL-C), which were assessed with enzymatic colorimetric assays using methods of Nauck *et al.* and Wahlefeld *et al.*, respectively (Wahlefeld and Bergmeyer, 1974; Nauck *et al.*, 1997; Ramsay *et al.*, 2015a).

A number of inflammatory, haemostatic, and cardiac biomarkers were also assessed. Plasma concentration of C-reactive protein (CRP) was assayed by ultra-sensitive nephelometry (Dade Behring, Milton Keynes, UK). Plasma concentration of Interleukin-6 (IL-6) was assayed using a high-sensitivity ELISA (R&D Systems,

Oxford, UK) (Zonoozi *et al.*, 2019). Concentrations of fibrin d-dimer and tissue plasminogen activator (tPA) (Asserachrom assays; Stago, Theale, UK), as well as von Willebrand Factor (vWF) antigen (Technozym assay; Pathway Diagnostics, Dorking, UK), were measured using high-sensitivity enzyme-linked immunosorbent assays (Parsons *et al.*, 2017). Plasma concentrations of high sensitivity Troponin T (hsTnT), and N-terminal pro brain natriuretic peptide (NTproBNP) were measured using the Elecsys 2010 electrochemiluminescence method (Roche Diagnostics, Burgess Hill, UK) (Zonoozi *et al.*, 2019).

3.3.5. Prevalent disease and medications

In 1998-2000 and 2010-2012 participants were asked through self-administered questionnaires if their doctor had told them that they had heart attack (coronary thrombosis or myocardial infarction), angina, stroke, diabetes, heart failure and cancer. Individuals answered with a 'yes' or 'no' response.

Medications causing xerostomia: In 2010-2012, information on medications prescribed to participants was collected. Medications which are known to cause dry mouth/xerostomia including bronchodilators (anticholinergics), medications for diabetic neuropathy, specific gastrointestinal drugs, Parkinson's disease drugs, antimuscarinic medications, tricyclic antidepressants, selective serotonin reuptake inhibitors (antidepressants), cancer medications, antihistamines, antipsychotics, use of baclofen, use of bupropion, use of clonidine (antihypertensive; migraine; Tourette's syndrome; sedation), 5HT1 antagonist drugs (CVD), opioids, use of tizanidine and diuretics were used to create this variable. Then it was classified according to number of medications used: 0, 1, and ≥ 2 .

3.3.6. Dietary intake

At the 20-year and 30-year re-examinations participants completed a postal Food Frequency Questionnaire (FFQ) (see Appendix E, page 329 for a copy). The aim of the creation of the FFQ was to be used in the World Health Organization's Monitoring Trends and Determinants in Cardiovascular Disease Survey (Who and

Monica Project Principal Investigators, 1988; Atkins *et al.*, 2015) and for the Scottish Heart Health Study (Bolton-Smith *et al.*, 1991). It has been validated against weighed food intakes in British populations (Yarnell *et al.*, 1983; Bolton-Smith and Milne, 1991; Atkins *et al.*, 2015). All participants reported their frequency of consuming 86 food items. To assess frequency of consumption men had to select one of the following responses 1, 2, 3, 4, 5, 6, or 7 days per week, monthly, or rarely/never. Food items were grouped as follows: (1) meat; (2) fish; (3) vegetables - fresh, tinned, dried, frozen; (4) fresh fruit; (5) cheese; (6) bread; (7) breakfast cereal; (8) biscuits, puddings, and sweets; (9) egg; (10) other foods; (11) drinks and juices (non-alcoholic); (12) fats. To calculate the total amount of macronutrient and micronutrient intakes a validated computer program was used (Atkins *et al.*, 2015). In particular, food frequency was multiplied by the standard portion sizes for each food and by the nutrient composition of the foods obtained from the UK food composition tables (Holland *et al.*, 1991). The following data were derived: total energy intake (kcal/day), total fat, saturated and polyunsaturated fat intakes (g/day), carbohydrates (g/day), protein (g/day) and fibre. Additionally, for micronutrients mean intakes of vitamins C, E, A, and K1 and iron (mg/day) were calculated.

Fat intake was expressed as percentages of energy intake (Willett *et al.*, 1997). Energy intakes were examined for extreme values (500-8000 kcal/day in men) (Goldberg *et al.*, 1991; Atkins *et al.*, 2015). Only 2 participants were outside these limits, and it was decided to include them in the analysis.

3.3.7. Disability

At the 30-year re-examination (2010-2012) and re-examination in 2014 postal self-administered questionnaires were used to assess disability. Disability was assessed through 3 different self-reported measures, including mobility limitations, activities of daily living (ADL) and instrumental activities of daily living (IADL). For mobility limitations participants were asked whether they experienced difficulty going up or down stairs and walking 400 yards. Participants had to respond as 'yes' or 'no'. Individuals experiencing any difficulty were classified as having mobility limitations. For ADL, participants were asked whether they had any difficulty or needed help getting in and out of bed, dressing and undressing yourself, bathing or showering,

feeding yourself, including cutting food, and getting to and using the toilet. For IADL, individuals were asked if they experienced any difficulty or needed help with shopping for personal items, preparing your own meals, using telephone by yourself, managing money, or using public transport. For both ADL and IADL items, responses included no difficulty, some difficulty, and unable to do or need help. Participants choosing some difficulty or unable to do/need help for any of the ADL or IADL items were marked as having ADL or IADL difficulties, respectively.

Participants who had not responded to any of the ADL or IADL questions (n=44) were excluded from the analysis.

3.3.8. Physical Function

In 2010-2012 physical function was measured during the physical examination. Physical function measures included handgrip strength, walking speed, and chair-stand speed. For the measurement of handgrip strength the Jamar Hydraulic Hand Dynamometer Model J00105; Sammons Preston Rolyan, Bolingbrook, IL was used (Lennon *et al.*, 2015). Handgrip strength was assessed 3 times for each hand, and then the highest measurement was used (Kotronia *et al.*, 2019). To measure walking speed participants were asked to walk on their own or with assistance (walking stick, walker) 3 meters at normal pace (Papachristou *et al.*, 2017). Then their speed was assessed as time (seconds). For chair-stand speed, participants sat on a chair and were asked to stand and sit 5 times at a normal pace. Then the time (seconds) to complete this task was used to measure the chair-stand speed.

Those who were unable to complete the physical function measurements (handgrip strength n=483; walking speed n=551; chair-stand speed n=537) were excluded from the analysis.

3.3.9. Mortality

All-cause mortality was defined as death from any cause. CVD mortality was defined as all fatal CVD events (ICD-9 codes 390-459). Respiratory mortality was defined as all fatal respiratory events (ICD-9 codes 461-5198). Deaths were ascertained from

the NHS Central Register (as described in sub-section 3.2.4). Follow-up data for all-cause, CVD, and respiratory mortality were available from 30-year re-examination (2010-2012) until June 2019.

3.4. Strengths and Limitations of the BRHS

3.4.1. Strengths of the BRHS

The BRHS is a suitable cohort for studying the objectives of this PhD thesis. The 30-year re-examination in 2010-2012 provides detailed oral health data (exposure), as well as extensive information about inflammation, diet, disability and physical function which will be the main outcomes. Additionally, the 20-year re-examination (1998-2000) provides extensive dietary data which will be used to assess changes in diet over a period of 10 years, as well as details on several lifestyle and behavioural factors. The BRHS also provides continuous follow-up over an extensive period of time, with regular measurements of disability, and mortality. As a result, I will be able to examine the prospective associations between oral health problems and incidence of disability and mortality in older men.

Moreover, the BRHS is geographically and socioeconomically representative of the middle-aged population of men across the UK (Walker *et al.*, 2004). Additionally, the BRHS has benefited from high response rates since baseline, especially for mortality (>98%) (Walker *et al.*, 2000; Lennon *et al.*, 2015). At the start of the study (1979-1980) the characteristics of non-respondents (those who declined or failed to reply to the invitation and one reminder) were examined. Those who did not participate in the study were younger, more likely to be unmarried, and more likely to be less skilled workers compared to men who participated in the study (Walker *et al.*, 1987). Furthermore, information on causes of deaths was obtained and mortality rates were compared between respondents and non-respondents, and it was found that in the first three years of the study non-respondents had higher mortality rates than respondents, but this trend declined over time to non-significant levels. Respondents and non-respondents had also similar CVD mortality rates, and therefore analysis for CVD mortality conducted in this thesis should not be influenced by non-respondents.

Details on attrition in the 30-year re-examination (2010-2012) and missing data for all exposure and outcome variables will be presented later in section 3.8.

3.4.2. Limitations of the BRHS

Data collection for the BRHS was performed in towns of low mobility and individuals living in inner cities of high mobility, and ethnic minorities were not included in the study population (Walker *et al.*, 2004). Therefore, the study is not representative of women and ethnic minorities. However, restricting data collection in low mobility places enabled the study to retain high response rates. Moreover, in this thesis data from the Health, Aging and Body Composition (HABC Study) study, which consisted of older white and African-American men and women, were used to examine the same associations as in the BRHS. Hence, despite the fact that these two studies cannot be directly compared, it will be useful to see whether similar associations are reported in both studies.

3.5. The Health, Aging and Body Composition (HABC) Study

3.5.1. Description of cohort

The Health, Aging and Body Composition (HABC) Study (<https://healthabc.nia.nih.gov/>) is a prospective cohort including 3075 African-American and white men and women aged 70-79 years at baseline in 1997-1998, from Pittsburgh, PA and Memphis, TN, USA (Health Aging Body Composition Study, 2004). At baseline, 41.7% were African-American, whereas 51.5% were white men and women (Santanasto *et al.*, 2016). Participants who had difficulty with activities of daily living or lower-extremity functions, such as difficulty walking one-quarter mile or climbing 10 steps without resting were excluded from the study at baseline (Health Aging Body Composition Study, 2004). Furthermore, those with recent treatment for cancer, participation in a lifestyle intervention trial, or intention to move out of the study location within 3 years of baseline were also excluded at baseline (Health Aging Body Composition Study, 2004). Since baseline, study participants have been followed up for several lifestyle factors, morbidity, and mortality until 2014. The

HABC Study aimed to investigate the association between changes in body composition and functional decline (Health Aging Body Composition Study, 2004).

3.5.2. Selection procedures

Participants were recruited from a random sample of Medicare beneficiaries and supplemented by community-based recruitment of black participants in designated ZIP code areas in and around Pittsburgh and Memphis (Health Aging Body Composition Study, 2004).

3.5.3. Baseline examinations

At baseline (1997-1998), all 3075 participants attended physical examinations. These examinations were performed by trained research staff and were completed by 1998. Measurements included height, weight, blood pressure, electrocardiogram, physical function, body composition, and lung function. In addition, a blood sample was collected, and participants completed an interviewer-administered questionnaire on lifestyle factors and health and medical history at the clinic visit site, core home visit or phone call. The study protocol and informed consent forms were approved by the Institutional Review Boards of the University of Pittsburgh, the University of Tennessee, the University of California, San Francisco, and National Institutes of Health (Health Aging Body Composition Study, 2004).

3.5.4. Follow-up of participants from baseline

Since baseline, participants have been followed-up on lifestyle factors through interviewer-administered questionnaires, on morbidity data from participant reports obtained at the clinic visit and mortality from hospital records, death certificates, obituaries, and next-of-kin interviews, as presented in Figure 3.3 (page 90). There were yearly clinic examinations for six years with phone calls every 6 months to update functional and health status. Additional examinations took place at follow-up years eight and ten (Health Aging and Body Composition Study, 2020). The study

also collected data and adjudicated major incident health events including cardiovascular events, cancers, fractures, dementia, diabetes, and other illnesses related to hospitalizations and medical expenditures (Health Aging and Body Composition Study, 2020). Adjudication helps establish the study's endpoints i.e. fatal events, particularly delineating primary and secondary (contributing) causes of death. More details about the process of adjudication will be discussed in sub-section 3.5.4. Follow-up was extended to 16 years.

3.5.4.1. Mortality

Information on mortality was collected through hospital records, death certificates, obituaries, and next-of-kin interviews were obtained for all deaths occurring on or before September 30, 2014 (Santanasto *et al.*, 2016). Causes of death were adjudicated according to review of medical records (including death certificates, hospital reports, event specific documentation), proxy information, face sheet or physician attestation with ICD codes and Discharge summary (if in-hospital death), and/or autopsy report by an independent HABC Study committee of geriatricians (Cesari *et al.*, 2012).

3.5.4.2. Follow-up questionnaires

Interviewer-administered questionnaires included questions on medical history, health, lifestyle, and socioeconomic factors. Questionnaires were completed at the clinic visit site, home visits and phone calls at regular intervals (yearly) since baseline in 1997-1998 (see Figure 3.3). In Year 2 (1998-2000) a separate FFQ was also administered (see sub-section 3.6.6). This was the only time point in the HABC Study that an FFQ was completed by all participants. An FFQ was also completed in Year 3 (2000-2001) but only for individuals participating in the Energy Expenditure Sub-study of the HABC Study.

3.6. HABC Study Data Used in This Thesis

In this thesis, HABC Study data have been used to examine the cross-sectional associations between oral health problems and disability, physical function, inflammation, and diet. Additionally, data were used to assess the prospective associations of poor oral health with incident disability and risk of mortality, as well as the mediating effects of diet and inflammation on the association between poor oral health and risk of developing disability. To study the cross-sectional associations, data from Year 2 (1998-1999) were used. Oral health data were collected at one time point at 1998-1999. Follow-up data on disability were collected until Year 5 (2001-2002) (questionnaire), and on mortality until September 2014. Moreover, data on covariates used in this thesis were collected at Year 1 (1997-1998) and Year 2 (1998-1999) including lifestyle factors, medical history, and physical factors (height, weight). Data on smoking, alcohol and physical activity were available only at baseline (1997-1998) and not in Year 2 (1998-1999). Data collection and definition of oral health problems (exposure), outcome variables, and covariates are described below.

3.6.1. Measures of oral health

Poor oral health was divided in objective and subjective oral health problems. Objective oral health problems included number of teeth (tooth loss), and periodontal disease. Number of teeth and periodontal disease were assessed during an oral examination. Subjective oral health problems were measured through an interviewer-administered questionnaire and comprised self-rated oral health, dry mouth, difficulty eating, and limitation of food due to gum problems. Details on sample size and missing data will be described in section 3.8.

3.6.1.1. Objective oral health measures

The oral examination was carried out separately and took place between year 1 and year 3. At the oral examination, participants were asked about their oral health status to determine eligibility for the complete periodontal exam. Information was collected

about the participant's demographics, medical history, dental history, frequency of dental care, and frequency of brushing and flossing (Weyant *et al.*, 2004). The dental history (oral health questionnaire) consisted of history of periodontal disease, tooth loss, tooth mobility, problems or pain with chewing/oral function, and the use of dentures (Weyant *et al.*, 2004). After the interview, and according to their eligibility participants received an oral examination. Those who were not eligible for the complete periodontal exam, included participants who were excluded due to medical contraindications (requirement of antibiotic prophylaxis before periodontal probing) and those who did not have any natural teeth (see Appendix H, pages 354-355). These individuals underwent a simple examination of the mouth (number of teeth, denture use) (Weyant *et al.*, 2004). The rest of participants, underwent the full periodontal examination (Weyant *et al.*, 2004).

To measure pocket depth and loss of attachment a UNC-15 periodontal probe was used at six sites per tooth (mesiobuccal, buccal, distobuccal, mesiolingual, lingual, and distolingual)-full mouth measurement (Weyant *et al.*, 2004). Two assessments were performed at each probing site. First, the distance from the free gingival margin to the cemento-enamel junction was assessed (Weyant *et al.*, 2004). Next the distance from the free gingival margin to the base of the pocket was assessed, which represents pocket depth (Weyant *et al.*, 2004). To calculate loss of attachment the first measure was subtracted from the second to derive loss of attachment when the free gingival margin was coronal to the cemento-enamel junction and by adding the two measures when the free gingival margin was apical to the cemento-enamel junction (Weyant *et al.*, 2004). Examinations were performed by a dental hygienist or a periodontist. Each examiner was assisted by a data recorder (Weyant *et al.*, 2004). A 90% agreement between examiners was agreed before the beginning of the study.

3.6.1.2. Subjective oral health measures

Subjective oral health problems were assessed through interviewer-administered questionnaire.

Self-rated oral health: Participants were asked to rate their overall oral health as excellent, good, fair, and poor.

Dry mouth: Participants were asked whether their mouth felt dry when they were eating. They could respond as yes, no or do not know.

Difficulty eating: Participants were asked how often, during the past 3 months, have they had trouble chewing food or eating because of problems with their teeth or gums. Responses were most of the time, some of the time, a little of the time, none of the time, do not know.

Limit of food due to gum problems: Participants were asked whether they limited kinds or amounts of food they eat because of problems with their teeth or dentures. Responses included: always, often, sometimes, seldom, never, do not know.

3.6.2. Measures of socio-demographic and lifestyle factors

Gender, race, and education: Information on gender, race and education was collected at baseline (1997-1998). Participants provided information about the highest grade or year that they completed. According to their responses' education was classified as less than high school, high school graduate, and postsecondary.

Smoking status: Information on smoking was collected at baseline. Participants were asked if they had smoked at least 100 cigarettes in their entire life and if they smoke cigarettes now. If they never smoked 100 cigarettes then they were classified as never smokers, if they smoked at least 100 cigarettes and smoked at baseline then they were classified as current smokers, and those who had smoked 100 cigarettes but did not smoke at baseline were classified as former smokers.

Alcohol consumption: At baseline participants were asked how many drinks they have had in a typical week during the past 12 months. According to the responses, individuals were classified as no consumption in past year, less than once per week (occasional drink but less than once per week), 1-7 times per day (1-3 or 4-7 drinks per week), and more than one per day (8-14, 15-21, 22-27 or ≥ 28 drinks per week).

Physical activity: At baseline, physical activity was assessed via an interviewer-administered instrument derived from the leisure-time physical activity questionnaire, which was supplemented with questions on lower-intensity activities commonly performed by older adults (Taylor *et al.*, 1978; Health Aging Body Composition

Study, 2004). Activities included household chores (outdoor chores, heavy chores, grocery shopping, and laundry), walking + stairs (exercise walking, other walking, stair climbing), exercise/recreation (aerobic dance, weight training, high and medium intensity activities), and work, volunteer, and caregiving. For each activity, participants were asked whether they had done the activity ≥ 10 times in the past 12 months (Health Aging Body Composition Study, 2004). If the answer was yes, they were asked whether the activity was performed in the past 7 days, and, if yes, the number of times they performed the specific activity and how long was each session (Health Aging Body Composition Study, 2004). For activities including moderate and vigorous exercise, the levels of intensity was also asked (Health Aging Body Composition Study, 2004). Each exercise category was allocated approximate metabolic equivalent unit (MET) values to calculate a weekly energy expenditure estimate in $\text{kcal} \cdot \text{kg}^{-1} \cdot \text{wk}^{-1}$ for each type of activity (Ainsworth *et al.*, 2000; Health Aging Body Composition Study, 2004). Then each estimate was summed up to derive a total physical activity (in kcal/kg/wk) variable.

Anthropometric measurements: At baseline (Year 1) and at Year 2 (1998-1999) weight and height were measured in light clothing without shoes. Height was measured with a Harpenden stadiometer. Weight was assessed by a standard balance beam scale and was recorded to the nearest 0.1 kg (Health Aging Body Composition Study, 2004). To calculate Body Mass Index (BMI) data from weight and height measurements were used (weight/height^2). To classify participants into BMI groups the WHO cut-off points were used (normal $<25\text{kg/m}^2$, overweight ≥ 25 , obese $\geq 30\text{ kg.m}^2$) (World Health Organization, 2000).

3.6.3. Physical measurements

At the physical examination in 1998-1999, blood pressure was assessed by mercury sphygmomanometer while participants were seated after 5 minutes of rest (Odden *et al.*, 2016). The average of two measurements was used (Odden *et al.*, 2016). According to the American College of Cardiology/American Heart Association, if systolic blood pressure was $\geq 180\text{mmHg}$ or diastolic blood pressure $\geq 80\text{ mmHg}$ then participants were classified as hypertensive. Additionally, at Year 2 respiratory rate was measured as inspirations per 30 seconds.

3.6.4. Blood measurements

Fasting samples of total cholesterol and inflammation markers were measured at Year 2 (1998-1999). Fasting levels of total blood cholesterol were assessed by VITROS; Johnson & Johnson, Rochester, NY (Kanaya *et al.*, 2002).

For the measurement of CRP and IL-6 participants had to fast overnight. CRP was measured in anticoagulated EDTA plasma by an automated chemiluminescent immunoassay system (IMMULITE, Diagnostic Products Corporation, Los Angeles) (Izano *et al.*, 2016). Serum IL-6 levels were assessed in duplicate EDTA plasma by a high sensitivity Quantikine colorimetric immunoassay kit from R&D Systems (Minneapolis, MN) (Izano *et al.*, 2016). Measurements were performed by the Wake Forest University laboratory.

3.6.5. Prevalent disease and medications

In 1997-1998 and 1998-1999 participants were asked through interviewer-administered questionnaires if their doctor had told them that they had heart attack, angina, chest pain, stroke, transient ischemic attack, diabetes, and heart failure. Individuals answered with a 'yes' or 'no' response.

Medications causing xerostomia: In 1998-1999, information on medications prescribed to participants was collected. Data on the following medications causing xerostomia were available: tricyclic antidepressants and selective serotonin reuptake inhibitors (antidepressants), antihypertensives, diuretics, indapamide (diuretic), medications for congestive heart failure, and bronchodilators. Then, the variable was classified according to number of medications, 0, 1 and ≥ 2 .

3.6.6. Dietary intake

In Year 2 (1998-1999) participants completed an interviewer-administered FFQ (see Appendix H, page 347). To estimate usual nutrient and food group intake an FFQ was developed and modified for the Health ABC study by Block Dietary Data

Systems (Berkeley, CA) and included 108 food items (Health Aging Body Composition Study, 2004). The FFQ was based on the National Health and Nutrition Examination Survey (NHANES) III study. In particular, the HABC Study FFQ was created according to 24-h dietary recall data from the NHANES III for older adults aged over 65 years and who were either non-Hispanic white or African-American living in the Northeast or South (Health Aging Body Composition Study, 2004; Hengeveld *et al.*, 2018). Interviewers were highly trained and used wood blocks, real food models, standard kitchen measures, and flash cards to assist participants in estimating the accurate portion size (Health Aging Body Composition Study, 2004; Hengeveld *et al.*, 2018). To assess frequency of consumption participants had to select one of the following responses: never, 1-11 times/year, once/month, 2-3 times/month, once/week, twice/week, 3-4 times/week, 5-6 times/week, and every day (see Appendix H, page 347). Block Dietary Diet Systems (Berkeley, California) estimated intakes of nutrients, energy, and food groups (Health Aging Body Composition Study, 2004). The recommended serving sizes according to the Food Guide Pyramid were also used for this estimation. Several macronutrients and micronutrients intakes were estimated. Macronutrients included total fat, saturated, trans-fatty and omega-3 fatty acids, total carbohydrate, protein, and fibre intake. Fat, carbohydrate, and protein intakes were also provided as percentages of calories. Micronutrients comprised vitamins A,B,C,D,E, and several minerals (magnesium, calcium, iron, selenium, manganese).

According to cut-offs provided by Harvard University's nutrient database, men with caloric intake below 800 kcal; women below 500; men above 4200 kcal; and women above 3500 kcal should be excluded (Seidemann *et al.*, 2018). However, only 77 (2.6%) participants reported extreme energy values and thus were not excluded from the analyses.

3.6.9. Mortality

All-cause mortality was defined as death from any cause. CVD mortality was defined as all fatal CVD events according to the adjudication protocol (review of medical records, proxy interview, autopsy report, death certificates) described in sub-section 3.5.4. Likewise, respiratory mortality was defined as all fatal respiratory events

according to the HABC Study adjudication protocol. Follow-up data for all-cause, CVD, and respiratory mortality were available from Year 2 (1998-1999) until September 2014.

3.6.7. Disability

At Year 2 (1998-1999) and Year 5 (2001-2002) interviewer-administered questionnaires were used to assess disability measures. Mobility limitations, and activities of daily living (ADL) were used to measure disability. For mobility limitations, participants were asked whether they experienced any difficulty or needed help walking 1 quarter of a mile or climbing 1 flight. Individuals experiencing any difficulty/needing help were classified as having mobility limitations. For ADL, participants were asked whether they had any difficulty or needed help getting in and out of bed, dressing yourself, or bathing. Participants experiencing difficulty/needing help with any activity were classified as having ADL difficulties.

3.6.8. Physical function

At 1998-1999 walking speed and handgrip strength were measured as part of the physical examination. Walking speed was assessed by the HABC Study Long Distance Corridor Walk (LDCW) (Simonsick *et al.*, 2001). Walking speed was measured during the LDCW sub-study and therefore was not measured for all participants. The HABC Study LDCW consists of a two-stage walking test at the participants pace and it was created to assess cardiorespiratory fitness longitudinally in an initially well-functioning cohort of 70 year olds (Simonsick *et al.*, 2001). During the first stage participants walk for 2 minutes as a warm-up exercise, in which distance is recorded and the first 20 meters is timed (Simonsick *et al.*, 2001). This stage is also useful for spotting the participants who are unable to walk a longer distance. At the second stage participants were asked to walk 400 meters, which is almost equal to the distance an average healthy older adult can cover in 6 minutes (Butland *et al.*, 1982; Harada *et al.*, 1999; Simonsick *et al.*, 2000; Simonsick *et al.*, 2001). Additionally, the 400m walking distance can approximate the distance (1/4 mile) which is commonly used as self-report measure of mobility limitations (Rosow

and Breslau, 1966; Simonsick *et al.*, 2001). Then, walking speed was measured as the time (seconds) taken to complete the LDCW (400m).

Handgrip strength was measured twice at each hand by an isometric Jamar Hydraulic Hand Dynamometer and the highest reading was used (Alley *et al.*, 2014; Kotronia *et al.*, 2019).

3.7. Strengths and Limitations of the HABC Study

3.7.1. Strengths of the HABC Study

The HABC Study is a suitable cohort for studying the objectives of this PhD thesis. At Year 2 (1998-1999) detailed data on oral health data (exposure), as well as extensive information about inflammation, diet, disability, and physical function were provided. Continuous follow-up over an extensive period of time was achieved, with regular measurements of disability, physical function, and mortality. Therefore, the prospective associations between oral health problems and risk of developing disability and risk of mortality in older men will be investigated. Furthermore, the HABC Study comprises data which are generally comparable to the measurements of the BRHS, and similar analyses can be performed.

In the HABC Study retention has been achieved for the majority of men and women, with 99% of participants accounted for (Health Aging and Body Composition Study, 2020). Since baseline where 3075 participants were recruited, close to 2100 individuals completed the first six of the yearly examinations and 1400 completed all eight contract-sponsored in-clinic examinations (Health Aging and Body Composition Study, 2020). The HABC Study provides detailed data on the reasons that participants did not attend clinic visits, including death, illness, change of address. Moreover, telephone interviews and home visits were conducted for individuals who could not attend the clinic and therefore eliminating attrition. During the first 5 years of the study, the main reason for being lost to follow-up was death (n=263, 77%). Details on attrition and missing data for all exposure and outcome variables will be presented later in section 3.8.

3.7.2. Limitations of the HABC Study

The HABC Study recruited individuals living in two areas of the USA, Pittsburgh, and Memphis. Additionally, at baseline only older people with good physical function were included, therefore the study population may not be representative of the whole population of community-dwelling older people in the USA (Yaffe *et al.*, 2003). Furthermore, cardiac and haemostatic markers of inflammation as well as IADL were not available in the HABC Study, whereas the chair-stand test was performed to a subset of the study population and therefore these variables were not utilised in the analyses for the HABC Study in this thesis.

3.8. Attrition and Missing Data

3.8.1. Attrition

3.8.1.1. British Regional Heart Study

At baseline in 1978-1980, almost 10000 men aged 40-59 years old were invited by their GPs to participate in the BRHS (Walker *et al.*, 2004). A small number of men (<10) from each of the 14 towns were not invited due to being mentally or physically unable to participate in the study. Out of those 10000 men, 7735 individuals (78% response rate) were finally recruited in the study (Walker *et al.*, 2004). At the 20-year re-examination in 1998-2000, a total of 5516 surviving participants were invited to participate. Out of those individuals, 1264 did not respond to the invitation resulting in 4252 (77% response rate) men participating in the 20-year re-examination by completing questionnaires and attending the physical examination (Walker *et al.*, 2000). At the 30-year re-examination in 2010-2012, 4421 participants had died, 87 were lost to follow-up due to change of address, NHS cancellations and withdrawal from the study, resulting in 3227 surviving participants. Out of those participants, 90 men were not invited to participate because of living too far, being too ill, were excluded by their GP, were lost or the invitation was returned to the sender (Lennon *et al.*, 2015). Therefore, 3137 surviving participants were invited to participate. Out of those 3137 participants, 990 men did not complete the postal questionnaires (68% response rate) and 1415 men did not attend the physical examination (55%

response rate). This resulted in a sample of 2147 participants completing the postal questionnaires and 1722 individuals attending the physical examination in 2010-2012. Out of the 1722 men who took part in the examination, 1634 attended the regional sites, and 88 participants were visited at their homes (Lennon *et al.*, 2015). Finally, in 2014, 2658 individuals were invited to participate in the postal survey, and 1655 of those surviving participants completed and returned a postal questionnaire. In that year a physical examination was not carried out. Attrition and response rates are presented in Figure 3.4 (page 91).

3.8.1.2. Health, Aging and Body Composition (HABC) Study

At baseline (Year 1) in 1997-1998, 3075 participants were recruited in the HABC Study. At Year 2 (1998-1999), the same participants were invited to participate in the study. Out of the 3075 participants, 77 did not participate (97.5% response rate). Out of those 77 individuals, 29 were deceased, 14 were unable to be contacted, 15 refused to give a reason for not participating, and the rest were either too ill, too busy, far from the clinic, lived in a nursing home or withdrew from the study. As a result, 2998 men and women were invited to participate. Out of those 2998 study subjects, 2732 visited the clinic site, 98 were visited at home, and 168 participated in a phone interview. All 2998 completed the interviewer-administered questionnaires (97.5% response rate) – however fewer questions were asked by interviewers at home visits and phone calls, and 2830 participants participated in the physical examinations (clinic and home visit) (94.4% response rate). Some physical examination measurements were performed only at the clinic site or were part of a sub-study and therefore sample size can vary for several variables. During Year 2, participants were also invited to participate in a dental and periodontal sub-study. Only participants who could go to the clinic site participated in the periodontal sub-study, and data were not collected at home visits. A total of 2768 participants were invited to participate in the sub-study, with 1975 participants having data on number of teeth (part of a general oral examination) (71.3% response rate). Additionally, out of the 1843 who were available to participate in the full periodontal examination, 38 refused participation, 441 were ineligible because of medical contraindications, and 193 were excluded because they did not have any natural remaining teeth, thus resulting in 1171 men and women (63.5% response rate) participating in the full

periodontal exam (Weyant *et al.*, 2004). At Year 5 in 2001-2002, out of the 2947 participants who were invited to participate, 2279 participants attended the clinic visit, 85 were visited at home, and 266 had a phone interview, resulting in a total of 2630 participants (89.2% response rate). Attrition and response rates are presented in Figure 3.5 (page 92).

3.8.2. Missing data

In the BRHS, details on missing data of exposures and outcomes are presented in Table 3.2 (page 94). Information on missing data in the HABC Study are presented in Table 3.3 (page 96). In the BRHS we observed that participants with missing data on oral health problems and main outcomes, were slightly older, were more likely to be in manual social class, consumed less alcohol, were less physically active and were more likely to report fair/poor general health. In the HABC Study, participants with missing data were more likely to be African-American, current and former smokers, spent fewer years in school, consumed less alcohol, and were more likely to report poor general health. These findings, in both studies, show that participants with adverse health behaviours and worse health were more likely to have missing data. However, in both studies, as described in Table 3.2 and Table 3.3. a small number of participants had missing data and therefore no missing data analysis, such as multiple imputation or inverse probability weighting was carried out.

3.9. Statistical Methods

Statistical analyses were performed in SAS v 9.4 software (SAS Institute, Inc, Cary, NC) and STATA 15.1 (Stata Corp LLC, College Station, Texas). The main statistical methods used in this thesis are described below. Details about handling and categorisation of exposures, outcomes and covariates are included in each of the relevant results Chapters.

3.9.1. Logistic regression analysis

Logistic regression is suitable to examine associations between a categorical outcome (binary or ordinal or nominal) and one or more categorical or continuous independent (exposure) variables (Peng *et al.*, 2002). The basic concept revolves around the logit, which is the natural logarithm of an odds ratio (Peng *et al.*, 2002). Contrary to linear regression, errors are not normally distributed and also do not stay constant across the range of data (Peng *et al.*, 2001). Furthermore, logistic regression does not require the exposure and outcome to be normally associated because it applies a logit-transformation to the outcome variable (Peng *et al.*, 2002). In other words, logistic regression predicts the logit of outcome (Y) from exposure (X). Essentially, the logit represents the odds of getting/having the exposure (Y). An odds ratio represents the probabilities (π) of Y happening to probabilities ($1 - \pi$) of Y not happening (Peng *et al.*, 2002). To calculate the odds ratio of an outcome the odds in the exposed group are divided by the odds in the unexposed group.

When the outcome is categorical but not binary, either ordinal or nominal, then logistic regression can be extended to accommodate these types of categorical outcomes. When the outcome is ordered (ordinal logistic regression) the ranks of the outcome Y are used (Harrell, 2015). The main assumption of this model is that the outcome is ordered. Similar to binary logistic regression, in polytomous logistic regression, odds ratios are provided for each level of the categorical outcome variable.

Logistic regression was used to examine cross-sectional associations of oral health problems with (a) disability and physical function (Chapter 4), (b) inflammatory, haemostatic, and cardiac biomarkers (Chapter 5), (c) diet quality and dietary intake (Chapter 6). Additionally, logistic regression was used to investigate the prospective associations of oral health problems with risk of disability (Chapter 7). Ordinal regression was used to examine one association between oral health problems and dietary intake (processed meat) as well as the relationship between change in diet quality and poor oral health later in life (Chapter 6).

3.9.2. Survival analysis

Survival analysis is used to investigate the probability of having an event when time to a binary event is the main outcome of interest (Sterne and Kirkwood, 2003). Time to event is defined as the time from a predetermined time point (baseline / entry to the study) until the outcome/event of interest has occurred. Time to event is also called survival time. In cases when individuals do not experience the outcome of interest, is lost to follow-up or dies from another cause than the one under investigation, they are censored.

3.9.2.1. Cox proportional hazards model

Cox proportional hazards models are used to examine the association between an exposure and the time to event outcome variable and has been used extensively in epidemiological studies. In order to perform Cox proportional hazards analysis, the proportional hazards (PH) assumption needs to be satisfied. In particular, hazard ratios are assumed to be constant over time. There are few tests which can be performed to check whether this assumption is violated, with the most common that of Schoenfeld residuals (Schoenfeld, 1982). To calculate the hazard ratio the following model is used:

$$h(t) = h_0(t) \times \exp(\beta_1 x_1 + \beta_2 x_2 + \dots + \beta_p x_p) \quad (1)$$

where $h(t)$ is the hazard at time t , h_0 is the baseline hazard, and x_1 to x_p are the p exposure variables.

Cox proportional hazards analysis has been carried out to examine the association of oral health problems with risk of all-cause mortality (Chapter 8).

3.9.2.2. Competing risks analysis

A competing risk is an event which takes place before the main outcome of interest. For example, when the outcome of interest is death from cardiovascular disease, non-cardiovascular deaths are a competing risk. Individuals who die from a non-cardiovascular cause are no longer at risk of dying from cardiovascular causes

(Austin *et al.*, 2016). In competing risks, the cumulative incidence function (CIF) is calculated, which allows for estimation of the incidence of the occurrence of an event while taking the competing risk into account (Austin *et al.*, 2016). In competing risks only one event can take place for each individual. Therefore, CIF estimates the probability of having an event before time t and before the occurrence of another event (Austin *et al.*, 2016). When Kaplan Meier curves are used in the presence of competing risks, hazard ratios can be overestimated, and therefore use of competing risks analysis can provide more reliable effect estimates (Austin *et al.*, 2016). When the aim of a study is to estimate the incidence of an outcome then the Fine-Gray subdistribution model should be performed (Fine and Gray, 1999; Austin *et al.*, 2016). The Fine-Gray model uses a modification of the Cox PH model to calculate the subdistribution hazard ratio (SHR) (Cox, 1972). The SHR has the following mathematical formula:

$$H_{sk}(t) = \lim_{\delta t \rightarrow 0} \left\{ \frac{P(t < T \leq t + \Delta t, D = k | T > t \cup T \leq t \cap D \neq k)}{\delta t} \right\}, (2)$$

which represents the instantaneous risk of failure at time t from a specific cause k given that this individual has not yet experienced this specific event/cause of death (Fine and Gray, 1999). The estimation of the SHR includes those who have not experienced the event yet as well as those who have previously experienced a competing event (Austin *et al.*, 2016).

Competing risks analysis has been performed for the association of oral health problems with risk of CVD mortality, in the presence of competing risks from non-CVD causes of death.

3.9.2.3. Accelerated Failure Time Models

In longitudinal studies of older people, the probability of the proportional hazards assumption being violated increases with increasing age (Gore *et al.*, 1984). In cases when the proportional hazards assumption is violated the Accelerated Failure Time (AFT) analysis can be carried out. In the AFT model, an acceleration factor is

included in the hazard (Coppini *et al.*, 2000). The acceleration factor accounts for increasing of the occurrence of the event of interest. The AFT model assumes that the logarithm of time to event has a linear relationship with the exposure, where the errors are independently and identically distributed and follow the survival distribution function (Coppini *et al.*, 2000). The only difference between an AFT model and a simple linear regression model is that the errors in the AFT model are not normally distributed. To perform AFT analysis, a survival distribution needs to be chosen for survival time. The Weibull survival distribution accounts for survival distributions that are not constant over time, particularly survival time increases, decreases or is constant and the distribution is equal to an exponential distribution (Verma *et al.*, 2018).

The survival and hazard functions in an AFT model are:

$$s_i(t) = \exp [-a(\exp\{bxi\} t)^b] \quad (3) \text{ and,}$$

$$h_i(t) = (\exp\{bxi\})^b abt^b - 1, \quad (4)$$

where $s_i(t)$ is the survival function and $h_i(t)$ is the hazard function, a and b are the parameters for the Weibull distribution, and $\exp\{bxi\}$ corresponds to the acceleration factor (ϕ). When the acceleration factor (ϕ) is higher than 1 then the hazard function increases while the survival function decreases. Likewise, when $\phi < 1$ then the hazard function decreases, while the survival function increases (Coppini *et al.*, 2000).

AFT analysis was conducted to examine the association between oral health problems and respiratory mortality.

3.9.3. Causal mediation analysis

Causal mediation analysis aims to examine the causal pathways and mechanisms which underlie complex associations between an exposure and outcome. Mediation analysis can identify the variables which mediate the association between an exposure and an outcome and check whether this association is due to these variables partially or totally. These variables are called mediators. Effects for the causal models are generally decomposed to total, direct, and indirect effects (Pearl,

2001). There are two methods which have been used in causal mediation analysis: the difference and product methods (VanderWeele, 2016). This thesis will focus on the difference method. The difference method uses two regression models, where the first model is a simple regression of the outcome on the exposure. The coefficient produced by this regression model represents the total effect of the exposure on the outcome. The second model is similar to the first, with the addition of the mediator. The difference between the coefficients of the first and second regression models represents the indirect effect (effect of the mediator on the association between exposure and outcome). The exposure coefficient provided by the second regression model (including mediator) represents the direct effect of the exposure on the outcome.

In order to appropriately interpret the causal effects strong assumptions about confounding need to be made (VanderWeele, 2016).

1. Control for confounding between exposure and outcome.
2. Control for confounding between mediator and outcome.
3. Control for confounding between exposure and mediator.
4. No confounder of mediator-outcome is affected by the exposure.

Some of the covariates included in assumptions 1-3 may influence exposure, mediator, and outcome. This does not create any problems and these confounders do not need to be distinguished. However, when mediation analysis is performed it is assumed that all potential confounders are included in the model. Assumptions 1 and 3 are important for the estimation of total effects, assumption 2 is needed for the estimation of direct and indirect effects (VanderWeele, 2016). Additionally, potential interactions between the exposure and mediator can result in biased effect estimates (i.e. biased to the null) and therefore should be tested and considered when interpreting causal effects (Breen *et al.*, 2013).

In linear models the sum of the direct and indirect effect is used to calculate the total effect, however this cannot be done in logit models because regression coefficients and error variance cannot be separately identified (Winship and Mare, 1983). In other words, only the ratio of these effects can be identified. To decompose non-linear models an alternative method was developed by Karlson, Holm and Breen (khab) (Breen *et al.*, 2013). The khab method can be applied in situations when the

outcome of mediation analysis is categorical and the decomposition methods of linear models cannot be applied (Breen *et al.*, 2013).

In this thesis, causal mediation analysis was carried out to investigate the mediating effects of diet and inflammation on the association of oral health markers with risk of developing mobility limitations.

3.9.4. Bonferroni corrections for multiple comparisons

In both studies multiple comparisons were performed for some of the thesis objectives. As the number of hypothesis testing increases so does the risk of type I error (false positive results). A common method to address this issue is the Bonferroni correction, where the p-values are corrected to avoid type I error (Armstrong, 2014). However, application of correction methods for multiple testing is still debated and sometimes it can create additional problems, including masking existing significant associations (Rothman, 1990). Therefore, in this thesis no Bonferroni corrections were applied.

3.9.5. Effect modification by gender and race in the HABC Study

Previous research has suggested potential gender and race differences in the associations between poor oral health and age-related health outcomes. To check whether gender and race modified the observed associations in the HABC Study, an interaction term between exposure and gender or race was entered (separately for gender and separately for race) in regression models to test for significant interaction. If the p-value was smaller than 0.05 then a significant interaction was present.



Figure 3.1. Map showing the 24 British towns of the British Regional Heart Study.

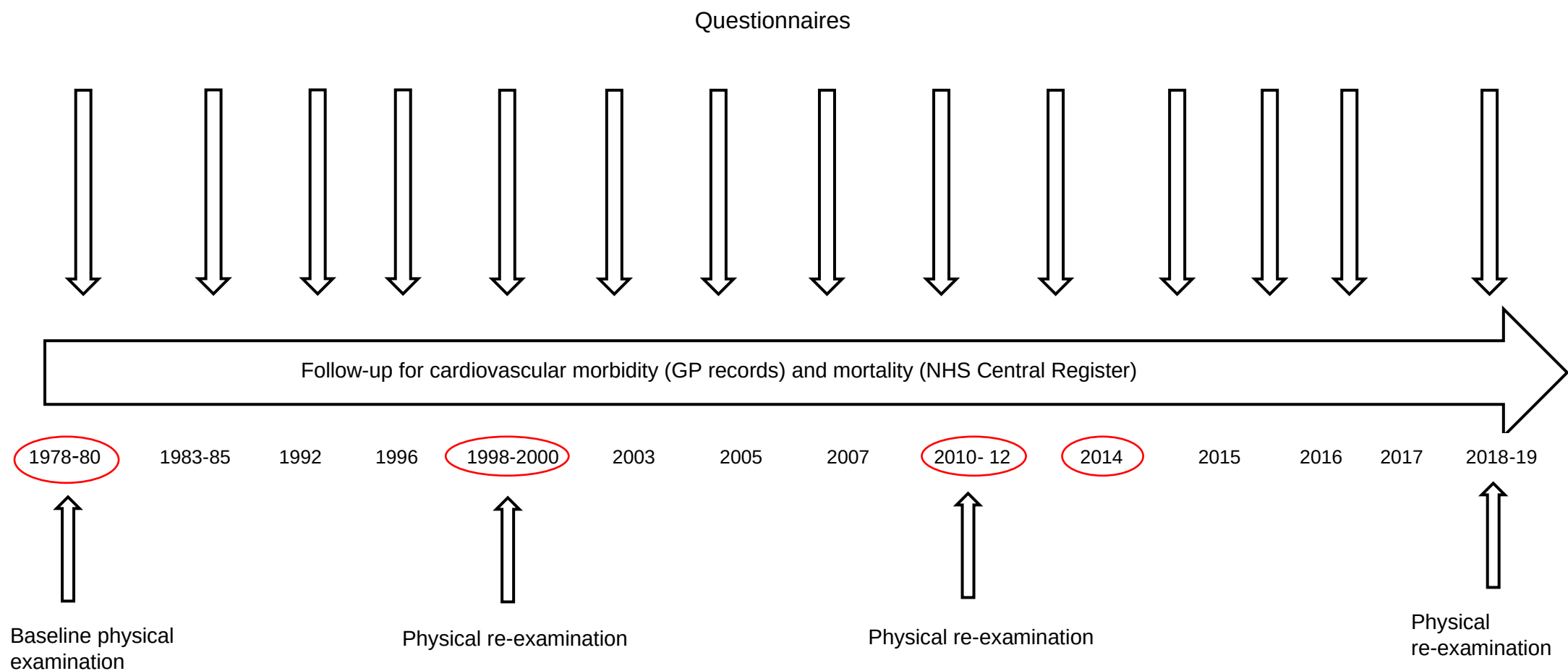


Figure 3.2. Timeline showing follow-up of the British Regional Heart Study cohort^a.

^athose circled in red represent data used in this study.

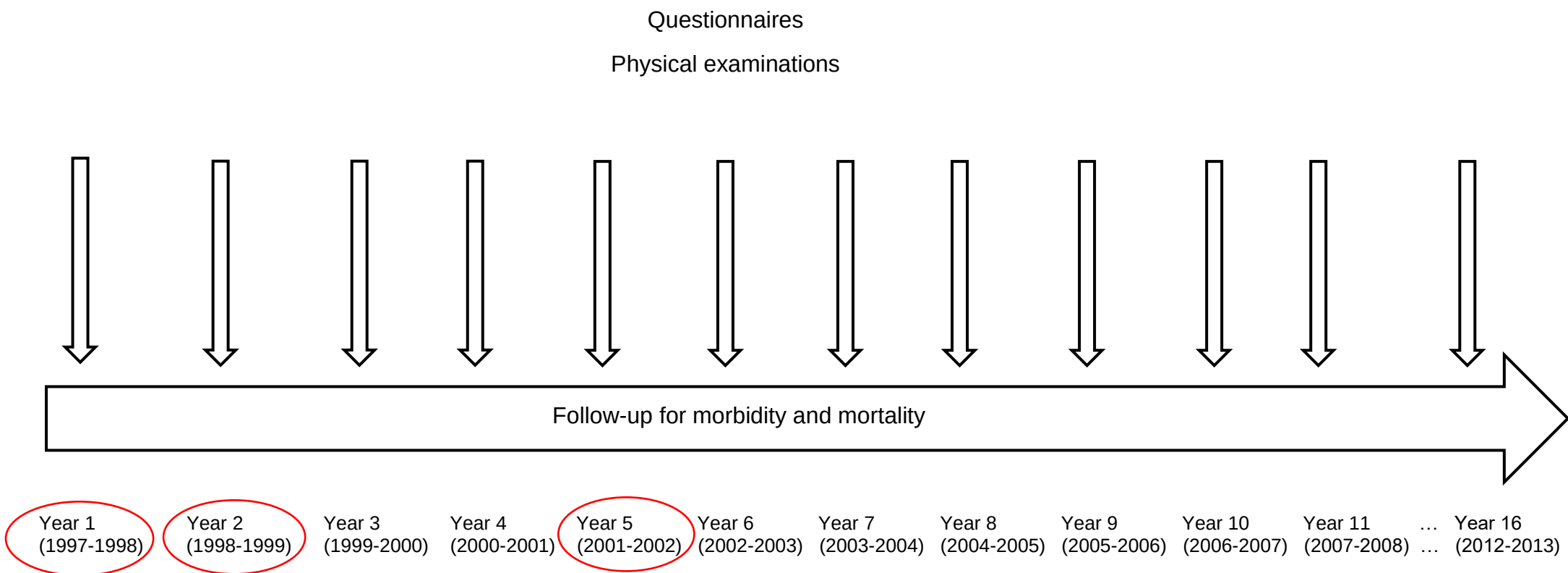


Figure 3.3. Timeline showing follow-up of the HABC Study cohort^{a,b}.

^athose circled in red represent data used in this study.

^bYears 12, 13 measurements only in a subset of participants; Years 14, 15 only telephone interviews (questionnaires).

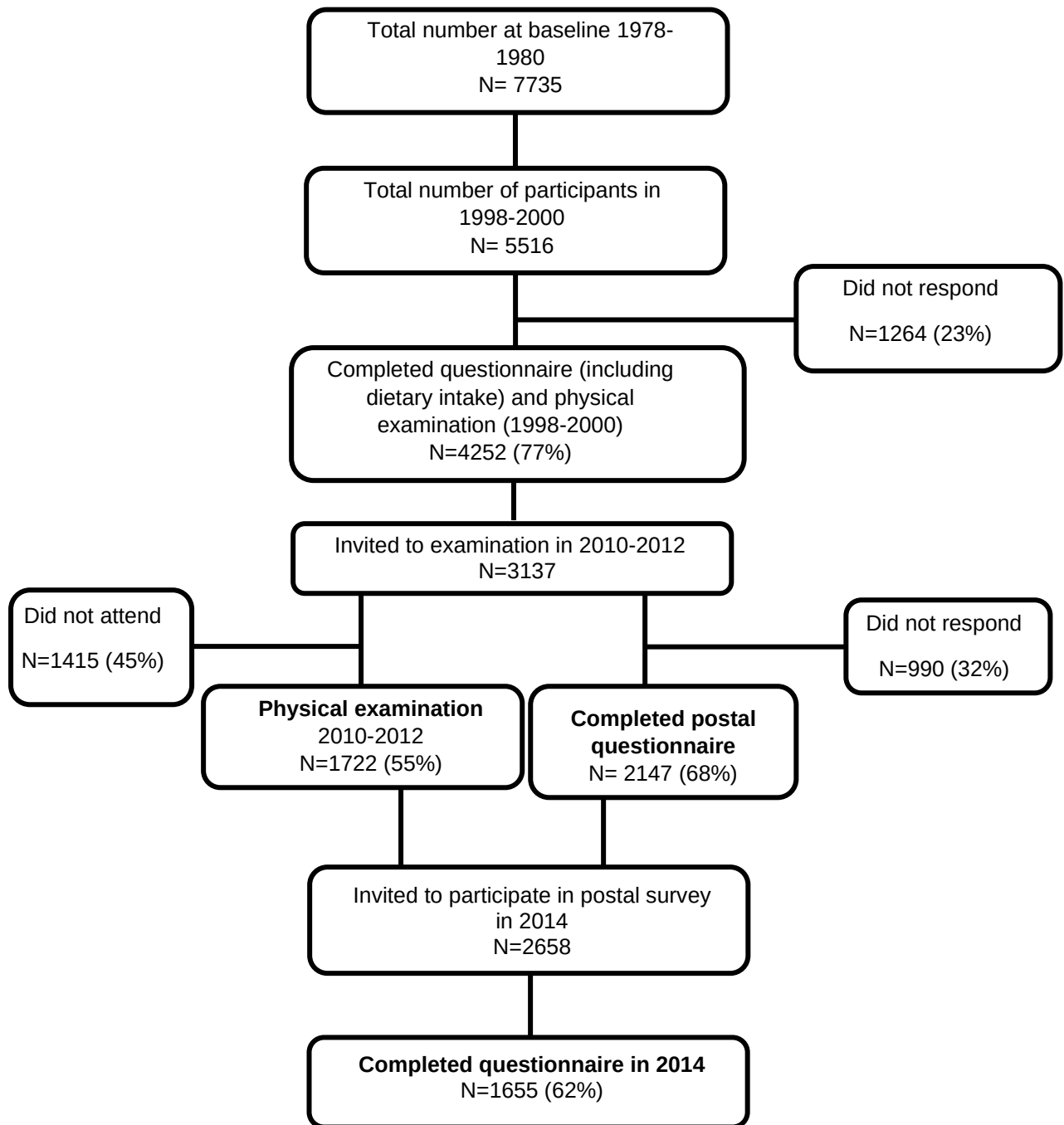


Figure 3.4. Attrition and response rates from baseline (1978-1980) until 2014 in the BRHS.

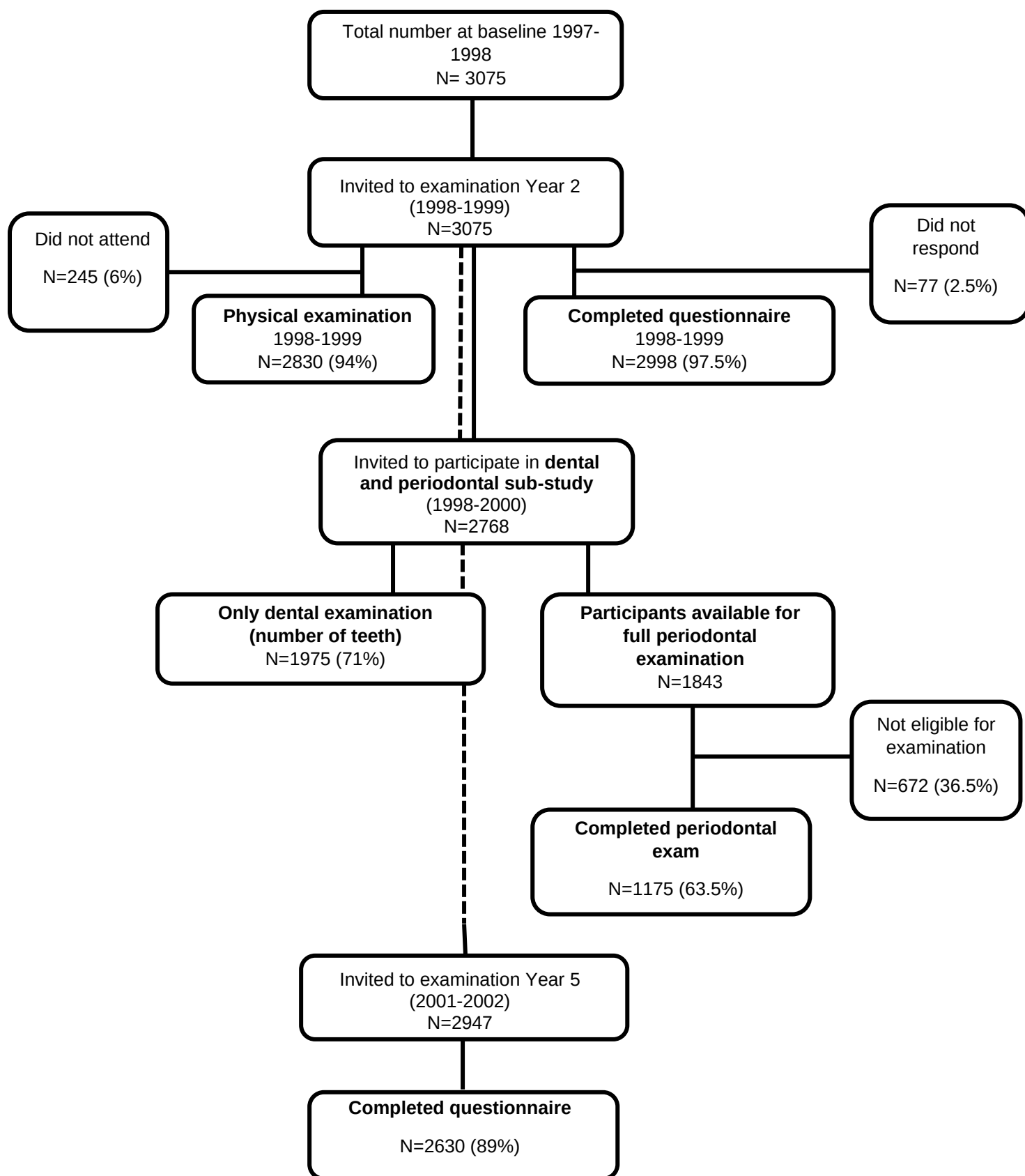


Figure 3.5. Attrition and response rates from baseline (1997-1998) until Year 5 (2001-2002) in the HABC Study.

Table 3.1 Towns included in the British Regional Heart Study.

Town	Standardised mortality ratios for cardiovascular disease in men aged 35-64 years in 1969- 1973	Men examined (n)	Response Rate (%)
Ayr	140	301	70
Bedford	80	303	73
Burnley	114	286	80
Carlisle	121	389	85
Darlington	109	382	82
Dewsbury	142	326	79
Dunfermline	118	350	80
Exeter	90	332	84
Falkirk	98	308	75
Gloucester	84	309	73
Grimsby	96	318	71
Guildford	78	335	82
Harrogate	82	280	77
Hartlepool	101	334	70
Ipswich	92	362	85
Lowestoft	85	324	83
Maidstone	99	319	72
Mansfield	95	321	80
Merthyr Tydfil	135	282	76
Newcastle-upon-Lyme	115	293	77
Scunthorpe	109	313	76
Shrewsbury	95	310	83
Southport	114	322	80
Wigan	134	337	77

Table 3.2. Missing data on exposure (oral health problems), and outcomes (disability, physical function, inflammation, and diet) in the BRHS.

Oral health problems	Those with missing data N (%)	Those with data N (%)
Objective (oral examination) n=1722		
Number of teeth	487 (3.6)	1660 (96.4)
Periodontal disease ^a (n=1322)	76 (5.7)	1246 (94.3)
Subjective (questionnaire) n=2147		
Self-rated oral health	108 (5)	2039 (95)
Dry mouth	113 (5.3)	2034 (94.7)
Difficulty eating	668 (31.1)	1479 (68.9)
Sensitivity to hot/cold/sweet	196 (9.1)	1951 (90.9)
Outcomes (Q30, 2010-2012)		
Disability (questionnaire, n=2147)		
Mobility limitations	42 (2.0)	2105 (98)
Activities of Daily Living (ADL)	44 (2.0)	2103 (98)
Instrumental Activities of Daily Living (IADL)	44 (2.0)	2103 (98)
Physical Function		
(Physical examination, n=1722)		
Handgrip strength	58 (3.4)	1664 (96.6)
Walking speed	109 (6.3)	1613 (93.7)
Chair-stand speed	112 (6.5)	1610 (93.5)
Inflammation		
(Physical examination, n=1722)		
CRP	121 (7.0)	1601 (93)
IL-6	104 (6.0)	1618 (94)
Fibrin d-dimer	112 (6.5)	1610 (93.5)
vWF	112 (6.5)	1610 (93.5)
t-PA	112 (6.5)	1610 (93.5)
High sensitivity Troponin T	119 (6.9)	1603 (93.1)
NTproBNP	119 (6.9)	1603 (93.1)
Diet (FFQ ^b , n=2147)		
Diet quality (EDI score)	240 (11.2)	1907 (88.8)
Total Intake of calories	185 (8.6)	1962 (91.4)
Percentage of energy from saturated fat	362 (16.9)	1785 (83.1)

^aAssessment was performed among those who attended the physical examination and had remaining teeth

^bFFQ: Food Frequency Questionnaire

Table 3.2 (*continued*). Missing data on exposure (oral health problems), and outcomes (disability, physical function, inflammation, and diet) in the BRHS.

Diet (n=2147)	Those with missing data	Those with data
	N (%)	N (%)
Fruits and vegetables	180 (8.4)	1967 (91.6)
Protein Intake	64 (3.0)	2083 (97)
Processed meat	0 (0.0)	2147 (100)
Vitamin C	58 (6.7)	2089 (97.3)
A-tocopherol (vit E)	418 (19.5)	1729 (80.5)
Outcomes (2014)		
Disability (questionnaire, n=1655)		
Mobility limitations	28 (1.7)	1627 (98.3)
Activities of Daily Living (ADL)	7 (0.4)	1648 (99.6)
Instrumental Activities of Daily Living (IADL)	7 (0.4)	1648 (99.6)
Outcome (1998-2000)		
Diet quality (EDI)^c (questionnaire, n=4252)	328 (7.7)	3924 (92.3)

^cEDI: Elderly Dietary Index

Table 3.3. Missing data on exposure (oral health problems), and outcomes (disability, physical function, inflammation, and diet) in the HABC Study.

Oral health problems	Those with missing data N (%)	Those with data N (%)
Objective (oral examination)		
Number of teeth (n=1975)	1 (0.05)	1974 (99.95)
Periodontal disease ^a (n=1171)	38 (3.2)	1133 (96.8)
Subjective (questionnaire, n=2998)		
Self-rated oral health	272 (9.1)	2726 (90.9)
Dry mouth	272 (9.1)	2726 (90.9)
Difficulty eating	270 (9)	2728 (91)
Limit of food due to gum/teeth problems	271 (9)	2727 (91)
Outcomes (Year 2, 1998-1999)		
Disability (questionnaire)		
Mobility limitations, n=2998	0 (0)	2998 (100)
Activities of Daily Living (ADL), n=2732 ^b	0 (0.0)	2732 (100)
Physical Function		
Handgrip strength (physical examination, n=2830)	473 (16.7)	2357 (83.3)
Walking speed (n=1880) ^c	5 (0.3)	1875 (99.7)
Inflammation		
(Physical examination, n=2830)		
CRP	56 (2)	2774 (98)
IL-6	94 (3.4)	2736 (96.7)
Diet (FFQ, n=2732)^d		
Diet quality (HEI score) ^e	31 (1.1)	2701 (98.9)
Total Intake of calories	0 (0.0)	2732 (100)
Percentage of energy from saturated/trans fat	19 (0.7)	2713 (99.3)
Percentage of energy from sweets and soda	0 (0.0)	2732 (100)
Fruits and vegetables	19 (0.7)	2713 (99.3)
Protein Intake	19 (0.7)	2713 (99.3)
Processed meat	19 (0.7)	2713 (99.3)
Vitamin D	19 (0.7)	2713 (99.3)

^aeligible for full periodontal exam

^bADL questions were only asked at the clinic visit

^cthose who completed the long-distance corridor walk, according to eligibility criteria

^dFFQ: Food Frequency Questionnaire

^eHEI: Healthy Eating Index

Table 3.3 (*continued*). Missing data on exposure (oral health problems), and outcomes (disability, physical function, inflammation, and diet) in the HABC Study.

Outcomes (Year 5, 2001-2002)		
Disability (questionnaire)		
Mobility limitations, n=2630	2 (0.1)	2628 (99.9)
Activities of Daily Living (ADL), n=2279 ^b	0 (0.0)	2279 (100)

^b ADL questions were only asked at the clinic visit

Chapter 4. Cross-Sectional Associations of Oral Health Problems with Disability and Physical Function in Older People in the UK and USA

4.1. Summary

Oral health problems, including tooth loss, periodontal disease, and dry mouth, are common health conditions in older people. Poor oral health is associated with poor quality of life. Additionally, dental problems are associated with disability and poor physical function in older people. Most importantly, poor oral health and disability can co-exist in older people. However, these associations are not well established, especially for subjective (self-reported) oral health problems as well as different measures of disability and physical function. In this Chapter, cross-sectional associations of objective and subjective oral health problems with disability and physical function in two population-based studies of older people were investigated. The British Regional Heart Study (BRHS) comprised 2147 older British men aged 71-92 years living in 24 towns across the UK. The Health, Aging, and Body Composition Study (HABC) Study consisted of 3075 older men and women aged 71-80 years, living in Pittsburgh and Memphis, USA. Oral health problems included objective (tooth loss, periodontal disease), and subjective (dry mouth, self-rated oral health, difficulty eating, sensitivity to hot/cold/sweets and limitation of food due to gum problems) measures. Measures of disability consisted of mobility limitations, Activities of Daily Living (ADL), and Instrumental Activities of Daily Living (IADL) (only in the BRHS). Physical function was measured through handgrip strength, walking speed and chair stand speed (only in the BRHS). Logistic regression was performed to assess the associations. Tooth loss, dry mouth, fair/poor self-rated oral health, and accumulation of oral health problems were associated with greater odds of mobility limitations, ADL and IADL difficulties. Periodontal disease was associated with weak handgrip strength (OR=1.59, 95% CI 1.14-2.20), whereas fair/poor self-rated oral health and dry mouth were associated with slow walking speed (OR=1.16, 95% CI 1.03-1.30; OR=1.75, 95% CI 1.22-2.50, respectively). Associations of fair/poor self-rated oral health and dry mouth with slow walking speed did not remain

significant after adjusting for self-rated general health. In summary, older individuals with poor oral health are more likely to experience disability and have decreased physical function.

4.2. Introduction

Ageing is characterised by an increased prevalence of oral health problems (Ramsay *et al.*, 2015b). It has been suggested that older individuals with poor oral health are more likely to experience disability and poor physical function (Yu *et al.*, 2011; Peltzer *et al.*, 2014; Wang *et al.*, 2014; Saintrain *et al.*, 2018). However, it is unclear whether various oral health problems are related with different measures of disability (mobility limitations, ADL, IADL) and physical function (handgrip strength, walking speed, chair-stand speed). Establishing these associations can help understand all the different ways through which oral health influences independence in older life.

Additionally, as described in Chapter 2 (sub-section 2.3.2) the majority of associations have been reported for objective oral health problems (tooth loss, periodontal disease) (Hämäläinen *et al.*, 2004; Yu *et al.*, 2011; Peltzer *et al.*, 2014; Tsakos *et al.*, 2015; Saintrain *et al.*, 2018). However, inconsistent results have been reported for these associations. Additionally, there is limited understanding of how or whether subjective (self-reported) measures of oral health (dry mouth, self-rated oral health) are associated with disability and physical function. These measures can be easier to assess and can also be used as proxy measures of oral health status. Additionally, subjective oral health problems are influenced by chronic oral conditions including tooth loss and periodontal disease and can indirectly represent the burden of chronic oral health problems (Chen *et al.*, 2013; Han *et al.*, 2015).

Establishing detailed associations for oral health problems with disability and physical function (see Figure 4.1, page 115) can indicate how oral health is linked with chronic conditions in older populations. This can provide essential evidence for future studies to focus on identifying the potential pathways which underlie these relationships in older people and consequently design targeted intervention programmes for the improvement of oral health in older people.

4.3. Aim and Objectives

This Chapter aims to investigate the associations of objective and subjective oral health problems with disability and physical function in older people. The objectives of this Chapter are:

- I. To examine the cross-sectional associations between objective and subjective oral health problems and disability (ADL, IADL, mobility limitations) in older people.
- II. To examine the cross-sectional associations between objective and subjective oral health problems and physical function (handgrip strength, walking speed, chair-stand speed) in older people.

4.4. Methods

Analyses in this Chapter are based on cross-sectional data from the BRHS and HABC Study. Details on both the BRHS and HABC Study, including selection of participants, data collection, and data verification can be found in Chapter 3 (Sections 3.2 and 3.5). This section (section 4.4) focuses on data used for the analyses presented in this Chapter.

4.4.1 Subjects and methods of data collection

In the BRHS, cross-sectional data from the 30-year re-examination in 2010-2012 were used, when participants were aged 71-92 years. In this wave, 2147 older men completed the self-administered questionnaire (68% response rate) and 1770 older men participated in the physical examination (55% response rate). Questionnaires and physical examination included information on oral health, lifestyle and behavioural factors, chronic diseases, disability, and physical function. More details are provided in Chapter 3 (section 3.2).

In the HABC Study, cross-sectional data from the Year 2 examination in 1998-1999 were utilised, when participants were aged 71-80 years. In this wave, 2998 older men and women completed questionnaires (97.5% response rate), 1975 underwent

a dental examination, and 2830 individuals participated in the physical examination. Questionnaires and examinations provided information on oral health, lifestyle and behavioural factors, chronic diseases, and inflammatory markers. Further details are described in Chapter 3 (section 3.5).

4.4.2. Oral health

4.4.2.1. Objective oral health problems

In both studies, number of natural teeth and periodontal disease (loss of attachment and pocket depth) were assessed by a trained professional. In both studies, number of teeth was categorised as: (1) 5-level category (0 teeth, 1-7 teeth, 8-14 teeth, 15-20 teeth, ≥ 21 teeth); (b) complete tooth loss (0 teeth vs. ≥ 1 teeth); (c) partial tooth loss (<21 teeth vs. ≥ 21 teeth) (Hobdell *et al.*, 2003). Having 21 teeth or more represents a functional dentition (i.e. the minimum number of teeth) needed for optimal chewing/eating ability (Hobdell *et al.*, 2003). Periodontal disease was grouped according to the Extent and Severity Index (Carlos *et al.*, 1986). Loss of attachment was categorised as follows: in the BRHS, $>20\%$ sites affected >5.5 mm vs. $\leq 20\%$ sites affected, and in the HABC Study, $>20\%$ sites affected ≥ 3 mm vs. $\leq 20\%$ sites affected. For pocket depth the following groups were created: in the BRHS, $>20\%$ sites affected >3.5 mm vs. $\leq 20\%$ sites affected, and in the HABC Study, $>20\%$ sites affected ≥ 3 mm vs. $\leq 20\%$ sites affected. More details are described in Chapter 3 (sub-section 3.3.1).

4.4.2.2. Subjective oral health problems

In both studies, subjective oral health problems were measured through questionnaires. Self-rated oral health was classified as excellent/good and fair/poor. In the BRHS, dry mouth was assessed using the Xerostomia Inventory (XI) (Thomson *et al.*, 1999). The 11 item-scale was combined to create a 3-level category: no dry mouth symptoms, 1-2, and ≥ 3 dry mouth symptoms. In the HABC Study, dry mouth was grouped as either experiencing dry mouth when eating or not. A cumulative measure was also created in both studies, to account for the burden of oral health problems. In the BRHS, it comprised ≥ 3 dry mouth symptoms, <21

natural teeth, any difficulty eating and sensitivity to hot/cold/sweets; in the HABC Study it was based on having dry mouth when eating, <21 natural teeth, difficulty eating, and limitation of food consumed because of gum problems. In both studies, difficulty eating was classified as yes vs. no. In the BRHS, a binary variable was created for sensitivity to hot/cold/sweets (yes vs. no/rare). In the HABC Study, the frequency of limitation of food because of problems with teeth or dentures was categorised as frequent limitation of food vs. rare/no limitation. More details for these oral health problems can be found in Chapter 3 (sub-sections 3.3.1 and 3.6.1).

4.4.3. Disability

In both studies, information on disability was collected through questionnaires. In the BRHS, mobility limitations was classified according to whether individuals had difficulty going up or down stairs or walking 400 yards. Difficulty with any of these activities was categorised as mobility limitation. Participants who faced difficulties or needed help with doing any of the following five activities: getting in and out of a chair, dressing and undressing yourself, bathing or showering, feeding yourself, including cutting food, or getting to and using the toilet, were classified as having problems with ADL (Kotronia *et al.*, 2019). IADL difficulties were categorised according to any difficulty or needing help with shopping for personal items, preparing your own meals, using telephone by yourself, managing money, or using public transport (Kotronia *et al.*, 2019). In the HABC Study, mobility limitations was grouped according to any difficulty walking 1 quarter of a mile or climbing 1 flight. ADL difficulties were classified according to experiencing any difficulty or needing help with dressing, getting in and out of bed, and/or bathing on your own. In the HABC Study, there was no information available on IADL. All disability measures were dichotomised (yes/disability vs. no).

4.4.4. Physical function

Physical function measures were assessed during physical examinations in both studies. In the BRHS, handgrip strength was assessed 3 times for each hand, and then the highest measurement was used (Lennon *et al.*, 2015; Kotronia *et al.*, 2019).

Walking speed was measured as the time required to walk 3 meters at normal pace (Papachristou *et al.*, 2017; Kotronia *et al.*, 2019). Chair stand speed was assessed as time taken (in seconds) for participants to sit and stand from a chair 5 times (Kotronia *et al.*, 2019). In the HABC Study, handgrip strength was assessed twice for each hand, and the highest reading was used (Alley *et al.*, 2014; Kotronia *et al.*, 2019). Walking speed was measured as the time (seconds) to walk 400m at a steady rate (LDCW) (Simonsick *et al.*, 2001; Kotronia *et al.*, 2019). Information on chair stand speed was available only for a subset of the HABC Study population. Therefore the association between oral health and chair stand speed was examined only in the BRHS. All physical function measures were first divided into quintiles. Quintiles have been used frequently in studies examining associations with physical function, because the use of quintiles reflects physical function as a continuum, but also enables researchers to report the best and worst levels of physical function (Peeters *et al.*, 2013).

Once quintiles were created, then they were dichotomized with the bottom quintile the outcome for handgrip strength (weakest) (*BRHS, overall range 0-59 kg, bottom quintile: 0-22 kg, reference group: 23-59 kg; HABC Study, overall range 4.59-79 kg, bottom quintile: 4.59-23.65 kg, reference group: 23.75-79 kg*), and the top quintiles as the outcome for walking speed (slowest) (*BRHS, overall range 1.75-19.13 s, reference group: 1.75-4.12 s, top quintile: 4.13-19.13 s; HABC Study, overall range 52.37-641.09 s, reference group: 52.37-361.47 s, top quintile: 361.56-641.09 s*) and chair-stand speed (*BRHS, overall range 2.10-49.06 s, reference group: (2.10-16.25 s, top quintile: 16.28-49.06 s)*).

4.4.5. Socio-demographic, lifestyle factors, and chronic diseases

In both studies, information on socioeconomic status, smoking, physical activity, history of cardiovascular disease (CVD), history of diabetes, and self-rated general health were measured through questionnaires as described in Chapter 3 (sub-sections 3.3.2 and 3.6.2). In the BRHS, socioeconomic status was based on occupational class, which was categorised as manual and non-manual. In both studies, smoking was classified in three categories: current smokers, former smoker (have been a smoker in the past), and never smoker. In the BRHS, physical activity was grouped into six groups according to intensity and frequency of exercise

(inactive; occasional; light; moderate; moderately vigorous and vigorous), whereas in the HABC Study physical activity was assessed as kcal/kg/wk spent on various activities and used as a continuous variable (see sub-section 3.6.2). In the HABC Study, education (years of education) was the indicator of socioeconomic status, and it was categorised as less than high school, high school graduate, and postsecondary education. Information on the number of prescribed medications causing xerostomia (dry mouth) was also used in the analysis. Self-rated general health was based on participants rating their general health as excellent, good, fair, and poor.

4.4.6 Statistical Analysis

For each study multivariate logistic regression was performed separately, to assess the associations between objective and subjective oral health problems and disability and physical function in older people. All physical function variables were divided into quintiles. For handgrip strength the bottom quintile (weakest grip strength) was the outcome of interest, whereas for walking speed and chair stand speed (only in the BRHS) the top quintiles (slowest speed) were the outcomes of interest in the logistic regression models. Odds ratios (OR) with 95% confidence intervals (CI) were provided. In the BRHS, regression analyses were adjusted for age (continuous), social class (binary), smoking (3-levels), physical activity (5-levels), history of CVD and diabetes. In the HABC Study, models were adjusted for age (continuous), gender (male/female), race (White, African-American), education (3 levels), smoking (3 levels), physical activity (continuous), history of CVD, and diabetes. Moreover, in both studies, models for dry mouth were adjusted for medications causing xerostomia.

4.4.6.1. Sensitivity Analysis

As part of sensitivity analysis, all analyses were adjusted further for self-rated general health, to test whether reported associations were due to general health status.

4.5. Results

Tables 4.1. and 4.2 presents the prevalence of population characteristics in the BRHS and HABC Study. In addition, Table 4.3 shows the prevalence of oral health problems in both studies. In the BRHS, the prevalence of having <21 teeth was 64%, 20% for complete tooth loss, 24% and 29% had >20% sites with loss of attachment and pocket depth, respectively. Additionally, 35% reported fair/poor self-rated oral health, 15% difficulty eating, 23% experienced sensitivity to hot/cold/sweets, 62% had at least 1 dry mouth symptom, and 36% at least 2 oral health problems. In the HABC Study, the prevalence of complete tooth loss was 11% and 52% for having <21 teeth, 64% reported >20% with loss of attachment while 55% had >20% sites with pocket depth. For subjective problems, 31% reported fair/poor self-rated oral health, 20% experienced difficulty eating, 14% limited their food because of gum problems, 4% had dry mouth when eating, and 22% reported having at least 2 oral health problems.

For population characteristics, in the BRHS, mean age was 78.4 years, 54% were in non-manual class, 38% were never smokers and 4% were current smokers. Additionally, 20% were inactive, 23% were diagnosed with CVD, and 16% with type 2 diabetes. In the HABC Study, mean age of the population was 74.7 years, 49% were male, and 40% African-American. For years of education, 24% reported less than high school and 44% postsecondary education. Furthermore, 44% were never smokers and 10% were current smokers, mean physical activity was 82.9 kcal/kg/week, 4% had history of CVD, and 5% reported history of type-2 diabetes.

4.5.1. Associations of oral health problems with disability

4.5.1.1. Associations of oral health problems with mobility limitations

Odds ratios (OR) and 95% CIs for the associations for oral health problems with mobility limitations, in the BRHS are presented in Table 4.4. Having 0, 1-7, and 8-14 teeth when compared to ≥ 21 teeth were associated with mobility limitations in the age adjusted models (n=1630), but did not remain after adjusting for age, social class, smoking, physical activity, history of CVD and diabetes (n=1465). No

associations were observed for periodontal disease with mobility limitations. Fair/poor self-rated oral health when compared to excellent/good self-rated oral health was associated with mobility limitations in both age (n=2014) and fully adjusted models (n=1800) (fully adjusted, OR= 1.44, 95% CI 1.12-1.85). Having ≥ 3 dry mouth symptoms was also associated with mobility limitations after adjusting for confounders (n=1802) (OR= OR=2.89, 95% CI 2.14-3.91). The association remained even after adjusting for medications causing xerostomia (n=1792). Cumulative oral health problems was associated with mobility limitations in the age (n=2091) and fully adjusted models (n=1874) (≥ 3 vs. 0 problems, fully adjusted, OR=2.83, 95% CI 1.71-4.67).

Table 4.5 shows the ORs and 95% CIs for the associations of oral health problems with mobility limitations in the HABC Study. Having 0, 1-7, and 8-14 teeth when compared to ≥ 21 teeth were associated with mobility limitations in the age adjusted models (n=1973), but after adjusting for age, gender, race, education, smoking, physical activity, and history of CVD and diabetes (n=1932), only the association for 8-14 teeth remained (OR=1.44, 95% CI 1.06-1.98). Periodontal disease (pocket depth, $>20\%$ sites affected vs. $\leq 20\%$ sites) was associated with mobility limitations in the age adjusted model (n=1136) (OR=1.44, 95% CI 1.09-1.91), but did not remain after full adjustment (n=1126). Fair/poor self-rated oral health was associated with mobility limitations after adjustment for confounders (n=2709) (OR=1.19, 95% CI 1.10-1.30). Dry mouth was also associated with mobility limitations in both age (n=2719) and fully adjusted models (n=2706) (fully adjusted, OR= 2.26, 95% CI 1.50-3.39). Further adjustment for medications causing xerostomia did not alter this association (n=2700). Finally, ≥ 3 oral health problems (vs. 0 problems) was associated with mobility limitations in the fully adjusted model (n=2716) (OR=2.19, 95% CI 1.56-3.07).

4.5.1.2. Associations of oral health problems with ADL difficulties

Odds ratios (OR) and 95% CIs for the associations of oral health problems with ADL difficulties in the BRHS are presented in Table 4.4. Having 8-14 teeth was associated with ADL difficulties in both age (n=1631) and fully adjusted models (n=1462) (fully adjusted, OR= 1.65, 95% CI 1.05-2.57). No associations were

observed between periodontal disease and ADL difficulties. Fair/poor self-rated oral health was associated with ADL difficulties only in the age adjusted model (n= 2015). Having ≥ 3 dry mouth symptoms was also associated with ADL difficulties after adjusting for confounders (n=1795) (OR=2.68, 95% CI 1.94-3.69). This associations remained after adjusting for medications causing xerostomia (n=1785). Having ≥ 3 oral health problems was associated with ADL difficulties in both age (n=2103) and fully adjusted models (n=1867) (fully adjusted, OR=4.19, 95% CI 2.36-7.43).

Odds ratios (OR) and 95% CIs for the associations of oral health problems with ADL difficulties in the HABC Study are presented in Table 4.5. Having 8-14 teeth (vs. ≥ 21 teeth) was associated with ADL difficulties in both age (n=1944) and fully adjusted models (n= 1932) (fully adjusted, OR=1.74, 95% CI 1.23-2.47). No associations were observed for periodontal disease and ADL difficulties. Fair/poor self-rated oral health was associated with ADL difficulties in the age (n=2718) and fully adjusted models (n=2705) (OR=1.27, 95%CI 1.15-1.41). Experiencing dry mouth when eating was also associated with ADL difficulties after adjusting for confounders (n=2706) (OR=2.23, 95% CI 1.46-3.41). No changes were observed after adjusting for medications causing xerostomia (n=2700). Cumulative oral health problems (≥ 3 vs. 0 problems) was associated with ADL difficulties in both age (n=2732) and fully adjusted models (n=2716) (fully adjusted, OR=2.63, 95% CI 1.81-3.81).

4.5.1.3. Associations of oral health problems with IADL difficulties (BRHS)

This analysis was only performed in the BRHS. Odds ratios (OR) and 95% CIs for the associations for oral health problems with IADL difficulties in the BRHS are presented in Table 4.6. Having 0, and 8-14 teeth when compared to ≥ 21 teeth were associated with IADL difficulties in the age adjusted models (n=1631), but only the association for complete tooth loss (0 teeth) remained after full adjustment (n=1462) (OR= 1.82, 95% CI 1.12-2.95). No associations were observed between periodontal disease and IADL difficulties. Fair/poor self-rated oral health was associated with IADL difficulties in both age (n=2015) and fully adjusted models (n=1793) (fully adjusted, OR=1.66, 95% CI 1.24-2.22). Having ≥ 3 dry mouth symptoms was associated with IADL difficulties after full adjustment (n=1795) (OR=3.11, 95% CI 2.30-4.21). Further adjustment for medications causing xerostomia did not change

this association (n=1785). Having ≥ 3 oral health problems was associated with IADL difficulties in both age (n=2103) and fully adjusted models (n=1867) (fully adjusted, OR=5.94, 95% CI 3.10-11.37).

4.5.2. Associations of oral health problems with physical function

4.5.2.1. Associations of oral health problems with weak handgrip strength

The associations between oral health problems and handgrip strength in the BRHS are presented in Table 4.7. Periodontal disease (pocket depth) was associated with the bottom quintile (weakest) of handgrip strength in both age (n=1204) and fully adjusted models (n=1084) (fully adjusted, OR= 1.59, 95% CI 1.14-2.20). No other associations were observed between oral health problems and weak handgrip strength.

The ORs and 95% CIs for the associations between oral health problems and handgrip strength in the HABC Study are presented in Table 4.8. Dry mouth was associated with the bottom quintile (weakest) of handgrip strength in both age (n=2348) and fully adjusted models (n=2340) (fully adjusted, OR=2.43, 95% CI 1.47-4.01). This association remained even after adjusting for medications causing xerostomia (n=2334). No other associations between oral health problems and weak handgrip strength were observed in the HABC Study.

4.5.2.2. Associations of oral health problems with slow walking speed

Odds ratios and 95% CIs for the associations between oral health problems and slow walking speed in the BRHS are presented in Table 4.7. Having 0 teeth when compared to ≥ 21 teeth was associated with the top quintile (slowest) of walking speed in the age adjusted model (n=1553) (OR=1.82, 95%CI 1.29-2.57), but did not remain after adjusting for confounders (n=1387). Fair/poor self-rated oral health was associated with the top quintile of walking speed only in the age adjusted model (n=1541) (OR=1.44, 95% CI 1.10-1.87). Having at least 3 dry mouth symptoms was associated with the top quintile of walking in the age adjusted model (n=1541), and remained after adjustment for confounders (n=1396) and medications causing

xerostomia (n=1390) (fully adjusted, OR=1.75, 95% CI 1.22-2.50). Cumulative oral health problems (≥ 3 vs. 0 problems) was associated with the top quintile of walking only in the age adjusted model (n=1613).

The ORs and 95% CIs for the associations between oral health problems and slow walking speed in the HABC Study are presented in Table 4.8. Complete tooth loss (0 vs. ≥ 21 teeth) was associated with the top quintile (slowest) of walking speed in the age adjusted model (n=1359) (OR=2.02, 95% CI 1.30-3.12), but did not remain after adjusting for confounders (n=1355). No associations between periodontal disease and slow walking speed were observed. Fair/poor self-rated oral health was associated with the top quintile of walking speed in both age (n=1872) and fully adjusted models (n=1865) (fully adjusted, OR=1.16, 95% CI 1.03-1.30). Cumulative oral health problems (2 vs. 0, and ≥ 3 vs. 0 oral health problems) was associated with top quintile of walking speed in the age adjusted model (n=1880), but did not remain in the fully adjusted models (n=1872).

4.5.2.3. Associations of oral health problems with slow chair-stand speed (BRHS)

This analysis was only performed in the BRHS. Odds ratios and 95% CIs for the associations between oral health problems and slow chair-stand speed in the BRHS are presented in Table 4.9. Having 0, and 8-14 teeth (vs. ≥ 21 teeth) were associated with the top quintile (slowest) of chair stand speed in the age adjusted models (n=1550), but did not remain in the fully adjusted models (n=1384). Having at ≥ 3 dry mouth symptoms was associated with the top quintile of chair stand speed only in the age adjusted model (n=1537). Having ≥ 3 oral health problems (vs. 0 problems) was associated with the top quintile of chair-stand speed again only in the age adjusted model (n=1610).

4.5.2.4. Sensitivity analysis- further adjustment for self-rated general health

In the BRHS, when regression models were further adjusted for self-rated general health the associations of tooth loss with ADL and IADL difficulties were no longer significant (Appendix J, Tables J1 and J2). Furthermore, the associations of self-

rated oral health with disability measures did not remain (Appendix J, Tables J1 and J2). For physical function, associations of dry mouth with slow walking speed also did not remain after further adjustment for self-rated general health (Appendix J, Table J4). In the HABC Study, the association of self-rated oral health with mobility limitations and slow walking speed did not remain after adjusting for self-rated general health (Appendix J, Table J3). The rest of the reported associations remained in both studies.

4.6. Discussion

4.6.1. Summary of main findings

This Chapter examined the cross-sectional associations between objective and subjective oral health problems and measures of disability and physical function in older people living in the UK and USA. The most prevalent oral health problems were tooth loss, periodontal disease, fair/poor self-rated oral health, and dry mouth. Tooth loss was associated with mobility limitations, ADL and IADL difficulties. Fair/poor self-rated oral health, dry mouth, and cumulative oral health problems were associated with mobility limitations, ADL and IADL difficulties. For physical function, associations between periodontal disease and weakest handgrip strength were observed. Moreover, fair/poor self-rated oral health was associated with slowest walking speed, whereas dry mouth was associated with weakest handgrip strength and slowest walking speed. Some of these associations did not remain after adjusting for self-rated general health.

4.6.2. Comparisons with previous studies

4.6.2.1. Associations of oral health problems and disability

In the BRHS, partial and complete tooth loss were associated with disability, but these associations were abolished after adjusting for self-rated general health. It is possible that the relationship between tooth loss and disability may be a result of poor general health status. Tooth loss may also be a consequence of the accumulation of life stressors and adverse health behaviours (Friedman and

Lamster, 2016). However, in the HABC Study, the reported associations between tooth loss and disability remained. These findings are in accordance with previous studies (Yu *et al.*, 2011; Wang *et al.*, 2014; Komiyama *et al.*, 2016; Saintrain *et al.*, 2018). Individuals with a higher number of remaining teeth, are more likely to have better oral care practices, including brushing their teeth and visiting the dentist often (Wang *et al.*, 2014). Furthermore, tooth loss has been associated with (a) low intake of nutrients and poor diet quality (Ritchie *et al.*, 2002; Hung *et al.*, 2005), as well as (b) increased rates of inflammatory markers associated with chronic diseases (C-reactive protein (CRP), Interleukin-6 (IL-6), fibrin d-dimer) (Lowe *et al.*, 2003; You *et al.*, 2009; Kotronia *et al.*, 2020). Therefore, it can be hypothesised that the association between tooth loss and disability may be partially or totally caused by compromised diet and high levels of systemic inflammation. Identifying the inflammatory and diet components linked to oral health is essential in establishing the causal pathway involved in this association, as well as indicating whether poor oral health could influence disability directly (Chapters 5-inflammation, Chapter 6-diet, Chapter 7-causal mediation analysis).

An association between dry mouth and greater odds of disability was also observed. Dry mouth is an oral health condition which is prevalent in older people and can be a consequence of medications which are commonly prescribed for chronic diseases such as diabetes (Thomson *et al.*, 1999; Thomson, 2014). However, reported associations remained even after adjustment for medications causing xerostomia. Dry mouth can lead to the development of ulceration and contribute to oral inflammation, and this can cause problems with swallowing and eating which can then impact nutritional intake and contribute to the risk of developing disability (Walls and Steele, 2004; Han *et al.*, 2015). Finally, accumulation of oral health problems was associated with disability in both studies. These associations show that the presence of more than one oral conditions, suggesting a poor oral health status, is independently linked to disability in older people, and attention should be given to the improvement of oral health of older people in order to improve other aspects of their health status.

4.6.2.2. Associations of oral health problems and poor physical function

In the BRHS, periodontal disease was associated with weak handgrip strength. A previous study did not report a cross-sectional association between periodontal disease and handgrip strength, but observed that periodontal disease at baseline was associated with decline in handgrip strength later in life (Hämäläinen *et al.*, 2004). Periodontal disease is a chronic inflammatory disease which can exacerbate oral inflammation and contribute to inflammation levels in other parts of the body (Kinane *et al.*, 2017). Additionally, periodontal disease has been found to be associated with high levels of systemic inflammatory markers including CRP, and IL-6 (Noack *et al.*, 2001; Amar *et al.*, 2003). Periodontal disease can lead to tooth loss, which is linked to chewing problems, decreased consumption of specific foods (e.g. protein), and this can contribute to decreased muscle strength and therefore poor physical function (Walls and Steele, 2004; Hruby *et al.*, 2018). No associations were reported for tooth loss and poor physical function, in contrast to previous studies (Brand *et al.*, 2015; Tsakos *et al.*, 2015).

Furthermore, fair/poor self-rated oral health and dry mouth were associated with slow walking speed, but these associations did not remain after adjusting for self-rated general health. This demonstrates that these associations are explained by overall health status in the older populations included in this study. In a previous study, examining the association between dry mouth and components of frailty in the BRHS, it was reported that dry mouth was associated with handgrip strength and walking speed (Ramsay *et al.*, 2018b). Individuals experiencing dry mouth may be those with poor health behaviours, including snacking, and worse health outcomes. Self-rated oral health and dry mouth can be indicators of the overall oral health status, which in turn may be influenced by the overall general health status of an individual (Ikebe *et al.*, 2007). Generally, it has been suggested that individuals with poor oral health are more likely to experience disability and decreased physical function and also have worse overall health (Wang *et al.*, 2014).

4.6.3. Strengths and limitations

4.6.3.1. Strengths of this study

In this study the associations between objective and subjective oral health problems with a range of measures of disability (mobility limitations, ADL, IADL) and physical function (handgrip strength, walking speed, chair-stand speed) were examined in two population-based studies of older people living in the UK and USA. In this Chapter associations between subjective oral health problems and disability and physical function were established, therefore providing much needed evidence for the relationship between subjective dental problems such as dry mouth and self-rated oral health and disability and physical function in older populations. Additionally, a composite variable of oral health problems depicting the burden of oral health was created, and associations with disability were reported. Objective and subjective oral health problems were not correlated and therefore using both groups of markers is of high importance, because objective measures may not be indicative of the perception of oral health status by individuals and vice versa (Kotronia *et al.*, 2019).

4.6.3.2. Possible bias and limitations

This study was cross-sectional. Therefore, a causal relationship or the direction of associations between poor oral and disability and physical function cannot be established. However, the findings are supported by results from a longitudinal study in the BRHS where oral health was associated with incidence of frailty (Ramsay *et al.*, 2018b). Nevertheless, prospective studies are required to determine whether oral health is linked to development of disability in older people.

Subjective oral health problems, such as dry mouth, were reported by participants. It has been shown that self-reported measures of oral health could be subject to response bias (Ikebe *et al.*, 2007). Nonetheless, these self-reported measures are important in measuring the impact that oral health problems have on individuals because they can negatively influence quality of life.

In terms of population characteristics, both cohorts may not be representative of the whole population of older people (Shaper *et al.*, 1981; Walker *et al.*, 2004). In the

HABC Study, at baseline, individuals with any functional disability were excluded from the study, and therefore participants may be healthier than the rest of the community-dwelling older population (Yaffe *et al.*, 2003). As a result, findings may not be generalisable to the general older population of the USA. Likewise, the BRHS comprises men, of predominantly white British ethnic origin, and as a result the findings may not be applicable to older women or individuals from other ethnic groups (Shaper *et al.*, 1981).

In both studies, individuals with missing data were more likely to smoke, be less physically active, slightly older and have a poorer health status. (Yaffe *et al.*, 2003). Therefore, selection bias may be present, and the reported associations for poor oral health with disability and physical function may be underestimating the true level of associations.

Moreover, regression models were adjusted for a number of confounders, but there is the possibility of unmeasured or uncontrolled confounding, and therefore the risk of residual confounding (Liang *et al.*, 2014).

4.7. Conclusions

Tooth loss, dry mouth, and cumulative oral health problems were associated with mobility limitations, ADL and IADL difficulties, independent of age, socioeconomic status, lifestyle factors, chronic diseases. Periodontal disease was associated with weak handgrip strength, whereas dry mouth and fair/poor self-rated oral health were associated with slow walking speed. The associations for dry mouth and self-rated oral health did not hold after adjustment for self-rated general health. However, the cross-sectional nature of this Chapter cannot establish whether poor oral health is associated with the risk of developing disability in older people. Furthermore, it is crucial to identify the diet and inflammation components which are related to poor oral health and then investigate whether these components are part of the causal pathway linking oral health with disability. The associations between oral health and markers of inflammation will be investigated in Chapter 5, whereas the associations between oral health and diet in Chapter 6. Chapter 7 will examine the prospective associations between oral health problems and risk of developing disability in older

people and the mediating effects of diet and inflammation. Validating these hypotheses will help in designing intervention programmes which could focus on the improvement of oral health, leading to the amelioration of chronic diseases.

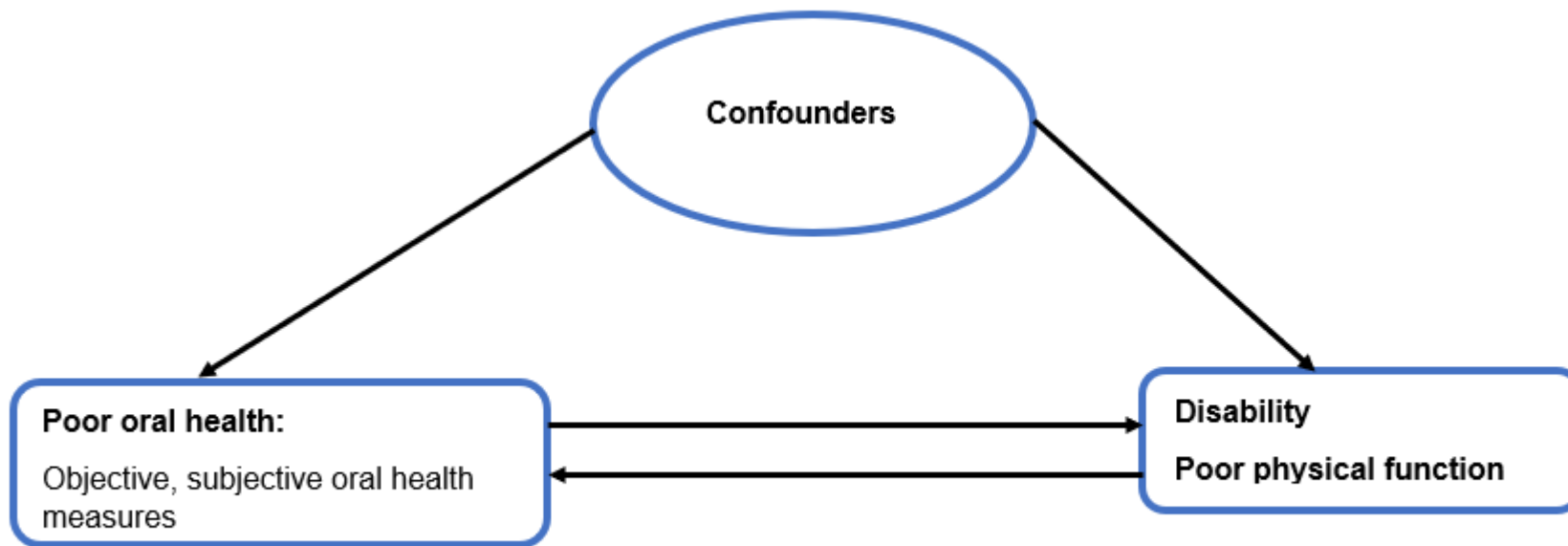


Figure 4.1. Bi-directional associations between poor oral and disability and poor physical function.

Table 4.1. Prevalence of population characteristics (socio-demographic, lifestyle factors, and chronic diseases) in the BRHS and the HABC Study.

BRHS (n=2147)			HABC Study (n=2998)		
Population Characteristics			Population Characteristics		
Age categories (n=2147)	N	(%)	Age categories (n=2998)	N	(%)
70-74	578	(27)	<70	1	(0.3)
75-79	795	(37)	70-74	1527	(51)
80-84	511	(24)	75-79	1273	(43)
85-89	213	(10)	80-84	197	(7)
≥90	50	(2)			
			Gender (n=2998)		
			Male	1491	(48)
			Female	1584	(52)
			Race (n=2998)		
			White	1794	(58)
			African-American	1281	(42)
Social class (n=2084)			Education (n=3067)		
Nonmanual	1081	(52)	Less than high school	775	(26)
Manual	1003	(48)	High school graduate	1000	(33)
			Postsecondary	1292	(42)
Smoking (n=2134)			Smoking (n=2998)		
Never smoker	768	(36)	Never smoker	1348	(44)
Current smoker	91	(4)	Current smoker	318	(10)
Former smoker	1275	(60)	Former smoker	1404	(46)
Alcohol			Alcohol		
Daily	757	(36)	More than 1 per day	227	(7)
Weekends only	389	(19)	1-7 times per week	655	(21)
Occasionally once or twice/month	307	(15)	Less than once per week	635	(21)
Special occasions	307	(15)			
None	292	(14)	No consumption in past year	1546	(51)
Physical activity (n=2002)					
Inactive	405	(20)			
Occasional	475	(24)			
Light	447	(22)			
Moderate	278	(14)			
Moderate-vigorous	232	(12)			
Vigorous	165	(8)			
History of CVD (n=2093)	500	(24)	History of CVD (n=2732)	104	(4)
History of diabetes (n=2090)	321	(16)	History of diabetes (n=2726)	140	(5)
Body Mass Index			Body Mass Index		
Normal	486	(28)	Normal	963	(34)
Overweight	875	(51)	Overweight	1192	(42)
Obese	343	(20)	Obese	673	(24)
Hypertension	473	(28)	Hypertension, n (%)	765	(25)
C-reactive protein (CRP)^a (mg/ml)			C-reactive protein (CRP) (ug/ml)		
High	535	(33)	High	924	(33)
Medium/low	1066	(67)	Medium/low	1856	(67)
Interleukin-6 (IL-6)^a (pg/ml)			Interleukin-6 (IL-6) (pg/ml)		
High	539	(33)	High	912	(33)
Medium/low	1079	(67)	Medium/low	1868	(67)

^a All inflammatory markers were divided into tertiles; 3rd/top tertile reflects high levels, 2nd tertile medium levels, 1st/bottom tertile low levels.

Table 4.1 (*continued*). Prevalence of population characteristics (socio-demographic, lifestyle factors, and chronic diseases) in the BRHS and the HABC Study.

BRHS (n=2147)		
Population Characteristics		
	N	(%)
Fibrin d-dimer^a (ng/ml)		
High	537	(33)
Medium/low	1073	(67)
Von Willebrand Factor^a (vWF) (IU/dL)		
High	537	(33)
Medium/low	1073	(67)
Tissue Plasminogen Activator^a (t-PA) (ng/ml)		
High	537	(33)
Medium/low	1073	(67)
High Sensitivity Troponin T^a (ng/l)		
High	534	(33)
Medium/low	1069	(67)
N-terminal pro brain natriuretic peptide^a (NTproBNP) (ng/l)		
High	534	(33)
Medium/low	1069	(67)

^a All inflammatory markers were divided into tertiles; 3rd/top tertile reflects high levels, 2nd tertile medium levels, 1st/bottom tertile low levels.

Table 4.2. Median and Interquartile Range (IQR) of population characteristics (lifestyle factors, and biological factors) in the BRHS and the HABC Study.

BRHS (n=2147)			HABC Study (n=2998)		
Population Characteristics			Population Characteristics		
	Median	(IQR)		Median	(IQR)
EDI score	25	(23-27)	Physical activity^{a,b} (kcal/kg/wk)	64.5	(38-106)
FEV1/FVC ratio	0.75	(0.70-0.80)	HEI score	71	(61-79)
Triglycerides (mmol/l)	1.14	(0.84-1.54)	Respiration rate (insp/30 sec)	9	(8-10)
HDL (mmol/l),	1.40	(1.16-1.68)	Total blood cholesterol (mg/dl)	204	(179-229)

EDI: Elderly Dietary Index; HEI: Healthy Eating Index

CRP: C-reactive protein; IL-6: Interleukin-6

^aTotal kcal/kg/wk from household chores, walking and stairs, exercise or recreation activities and work or volunteering or caregiving

^bPhysical activity median according to age groups: <70yrs=85, 70-74yrs=70, 75-79yrs=61.50, 80-84yrs=57 kcal/kg/wk

Table 4.3. Prevalence of oral health problems in British Regional Heart Study (BRHS) and the Health, Aging, and Body Composition (HABC) Study.

BRHS (n=2147)			HABC Study (n=2998)		
Oral health problems			Oral health problems		
Objective	N	(%)	Objective	N	(%)
<i>Tooth loss</i> (n=1660) ^a			<i>Tooth loss</i> (n=1974) ^a		
Complete tooth loss	338	(20)	Complete tooth loss	207	(11)
<21 teeth	1066	(64)	<21 teeth	1031	(52)
<i>Markers of periodontal disease</i>			<i>Markers of periodontal disease</i>		
>20% sites with loss of attachment >5.5mm (n=1246) ^a	303	(24)	>20% sites with loss of attachment ≥3mm (n=1133) ^a	721	(64)
>20% sites with pocket depth >3.5mm (n=1245) ^a	365	(29)	>20% sites with pocket depth ≥3mm (n=1136) ^a	627	(55)
Subjective			Subjective		
Fair/poor self-rated oral health (n=2039) ^a	719	(35)	Fair/poor self-rated oral health (n=2718) ^a	829	(31)
Difficulty eating (n=1544) ^a	231	(15)	Difficulty eating (n=2729) ^a	534	(20)
Sensitivity to hot/cold/sweets (n=1951) ^a	453	(23)	Limitation of food due to gum problems (n=2722) ^a	388	(14)
<i>Dry mouth symptoms</i> (n=2034) ^a					
0 dry mouth symptoms	762	(37)	Dry mouth when eating (n=2719) ^a	107	(4)
1-2 dry mouth symptoms	666	(33)			
≥3 dry mouth symptoms	606	(30)			
<i>Cumulative oral health problems</i> (n=2147) ^a			<i>Cumulative oral health problems</i> (n=2762) ^a		
≥2 oral health problems	766	(36)	≥2 oral health problems	617	(22)

^aSample size of participants with data

Table 4.4. Odds ratios (95%CI) for the associations of oral health problems with mobility limitations, and Activities of Daily Living (ADL) difficulties in British men aged 71-92 years in the BRHS.

Oral Health Problems	Mobility limitations (n=564; 27%)			ADL difficulties (n=412; 20%)		
	N (%) ^b	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	N (%) ^b	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss		<i>N=1630</i>	<i>N=1465</i>		<i>N=1631</i>	<i>N=1462</i>
≥21 teeth	106 (18%)	1.00	1.00	70 (12%)	1.00	1.00
15-20 teeth	68 (20%)	1.10 (0.78, 1.56)	0.93 (0.62, 1.38)	44 (13%)	1.07 (0.71, 1.60)	0.97 (0.62, 1.53)
8-14 teeth	79 (30%)	1.85 (1.31, 2.60)	1.48 (0.98, 2.22)	57 (22%)	1.90 (1.29, 2.81)	1.65 (1.05, 2.57)
1-7 teeth	38 (32%)	1.90 (1.22, 2.98)	1.23 (0.73, 2.07)	22 (18%)	1.39 (0.81, 2.36)	1.02 (0.56, 1.86)
0 teeth	103 (31%)	1.73 (1.26, 2.39)	1.14 (0.76, 1.69)	76 (23%)	1.80 (1.24, 2.60)	1.28 (0.82, 1.99)
Complete tooth loss						
≥1 teeth	291 (22%)	1.00	1.00	193 (15%)	1.00	1.00
0 teeth	103 (31%)	1.36 (1.04, 1.79)	1.01 (0.72, 1.42)	76 (23%)	1.45 (1.07, 1.98)	1.12 (0.78, 1.62)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=1225</i>	<i>N=1116</i>		<i>N=1224</i>	<i>N=1112</i>
≤20%	190 (21%)	1.00	1.00	103 (11%)	1.00	1.00
>20%	69 (23%)	1.11 (0.81, 1.52)	0.91 (0.63, 1.32)	38 (13%)	1.18 (0.82, 1.70)	1.14 (0.76, 1.71)
Self-rated oral health		<i>N=2014</i>	<i>N=1800</i>		<i>N=2015</i>	<i>N=1793</i>
Good or excellent	290 (22%)	1.00	1.00	217 (17%)	1.00	1.00
Fair or poor	241 (34%)	1.78 (1.45, 2.18)	1.44 (1.12, 1.85)	170 (24%)	1.53 (1.21, 1.92)	1.23 (0.94, 1.60)
Dry mouth symptoms		<i>N=2011</i>	<i>N=1802</i>		<i>N=2012</i>	<i>N=1795</i>
0	135 (18%)	1.00	1.00	92 (12%)	1.00	1.00
1-2	153 (23%)	1.40 (1.08, 1.82)	1.26 (0.92, 1.72)	108 (16%)	1.43 (1.06, 1.94)	1.24 (0.88, 1.75)
≥3	245 (41%)	3.05 (2.37, 3.92)	2.89 (2.14, 3.91)	188 (31%)	3.12 (2.35, 4.13)	2.68 (1.94, 3.69)
Cumulative oral health problems^c		<i>N=2091</i>	<i>N=1874</i>		<i>N=2103</i>	<i>N=1867</i>
0	43 (13%)	1.00	1.00	24 (7%)	1.00	1.00
1	232 (23%)	1.82 (1.27, 2.59)	1.27 (0.83, 1.93)	161 (16%)	2.20 (1.40, 3.45)	1.64 (0.98, 2.72)
2	191 (36%)	3.44 (2.38, 4.99)	2.25 (1.45, 3.48)	146 (27%)	4.36 (2.75, 6.91)	3.29 (1.96, 5.52)
≥3	98 (44%)	4.62 (3.04, 7.03)	2.83 (1.71, 4.67)	81 (36%)	6.36 (3.85, 10.51)	4.19 (2.36, 7.43)

^a adjusted for age, social class, smoking, physical activity, history of CVD and diabetes

^b number and percentage of participants for each oral health measure that has either mobility limitations or ADL difficulties

^c <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 4.5. Odds ratios (95%CI) for the associations of oral health problems with mobility limitations, and Activities of Daily Living (ADL) difficulties in American men and women aged 71-80 years in the HABC Study.

Oral Health Problems	Mobility limitations (n=882; 29%)			ADL difficulties (n=467; 17%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss		<i>N=1973</i>	<i>N=1932</i>		<i>N=1944</i>	<i>N=1932</i>
≥21 teeth	212 (23%)	1.00	1.00	138 (15%)	1.00	1.00
15-20 teeth	90 (25%)	1.16 (0.87, 1.54)	0.95 (0.70, 1.29)	61 (17%)	1.19 (0.85, 1.65)	1.15 (0.82, 1.62)
8-14 teeth	96 (34%)	1.78 (1.33, 2.37)	1.44 (1.06, 1.98)	68 (25%)	1.86 (1.34, 2.58)	1.74 (1.23, 2.47)
1-7 teeth	55 (30%)	1.49 (1.05, 2.11)	1.12 (0.77, 1.65)	33 (18%)	1.30 (0.86, 1.98)	1.24 (0.79, 1.93)
0 teeth	70 (34%)	1.72 (1.24, 2.38)	1.02 (0.70, 1.49)	30 (15%)	1.01 (0.66, 1.55)	0.91 (0.57, 1.44)
Complete tooth loss						
≥1 teeth	453 (26%)	1.00	1.00	300 (17%)	1.00	1.00
0 teeth	70 (34%)	1.46 (1.07, 1.98)	0.94 (0.66, 1.33)	30 (15%)	0.85 (0.57, 1.28)	0.74 (0.48, 1.15)
Periodontal disease (% of sites with pocket depth ≥3 mm)		<i>N=1136</i>	<i>N=1126</i>		<i>N=1132</i>	<i>N=1126</i>
≤20%	103 (20%)	1.00	1.00	83 (16%)	1.00	1.00
>20%	165 (26%)	1.44 (1.09, 1.91)	1.18 (0.87, 1.60)	96 (15%)	0.93 (0.68, 1.29)	0.97 (0.69, 1.36)
Self-rated oral health		<i>N=2718</i>	<i>N=2709</i>		<i>N=2718</i>	<i>N=2705</i>
Good or excellent	435 (23%)	1.00	1.00	278 (15%)	1.00	1.00
Fair or poor	300 (36%)	1.31 (1.21, 1.41)	1.19 (1.10, 1.30)	185 (22%)	1.30 (1.18, 1.43)	1.27 (1.15, 1.41)
Dry mouth		<i>N=2719</i>	<i>N=2706</i>		<i>N=2719</i>	<i>N=2706</i>
No	689 (26%)	1.00	1.00	428 (16%)	1.00	1.00
Yes	52 (49%)	2.66 (1.80, 3.92)	2.26 (1.50, 3.39)	35 (33%)	2.49 (1.64, 3.78)	2.23 (1.46, 3.41)
Cumulative oral health problems^b		<i>N=2761</i>	<i>N=2716</i>		<i>N=2732</i>	<i>N=2716</i>
0	173 (22%)	1.00	1.00	108 (14%)	1.00	1.00
1	355 (26%)	1.23 (1.00, 1.52)	0.98 (0.78, 1.22)	202 (15%)	1.08 (0.84, 1.39)	1.07 (0.82, 1.39)
2	120 (31%)	1.53 (1.16, 2.01)	1.14 (0.85, 1.53)	86 (22%)	1.70 (1.24, 2.33)	1.61 (1.16, 2.24)
≥3	107 (48%)	3.28 (2.40, 4.49)	2.19 (1.56, 3.07)	71 (32%)	2.88 (2.03, 4.08)	2.63 (1.81, 3.81)

^aadjusted for age, gender, race, education, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 4.6. Odds ratios (95%CI) for the associations of oral health problems with Instrumental Activities of Daily Living (IADL) difficulties in British men aged 71-92 years in the BRHS.

Oral Health Problems	IADL difficulties (n=367; 17%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss		<i>N=1631</i>	<i>N=1462</i>
≥21 teeth	56 (10%)	1.00	1.00
15-20 teeth	45 (14%)	1.40 (0.92, 2.14)	1.31 (1.12, 2.95)
8-14 teeth	44 (17%)	1.75 (1.13, 2.69)	1.54 (0.92, 2.58)
1-7 teeth	20 (17%)	1.54 (0.88, 2.70)	1.00 (0.51, 1.95)
0 teeth	74 (22%)	2.16 (1.46, 3.19)	1.82 (1.12, 2.95)
Complete tooth loss			
≥1 teeth	165 (13%)	1.00	1.00
0 teeth	74 (22%)	1.65 (1.20, 2.26)	1.51 (1.03, 2.22)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=1224</i>	<i>N=1112</i>
≤20%	124 (13%)	1.00	1.00
>20%	48 (16%)	1.11 (0.74, 1.65)	0.94 (0.59, 1.50)
Self-rated oral health		<i>N=2015</i>	<i>N=1793</i>
Good or excellent	182 (14%)	1.00	1.00
Fair or poor	171 (24%)	1.90 (1.50, 2.41)	1.66 (1.24, 2.22)
Dry mouth symptoms		<i>N=2012</i>	<i>N=1795</i>
0	77 (10%)	1.00	1.00
1-2	109 (17%)	1.80 (1.31, 2.48)	1.67 (1.15, 2.47)
≥3	164 (27%)	3.11 (2.30, 4.21)	2.90 (2.01, 4.18)
Cumulative oral health problems^b		<i>N=2103</i>	<i>N=1867</i>
0	20 (6%)	1.00	1.00
1	146 (14%)	2.02 (1.17, 3.48)	1.77 (0.98, 3.19)
2	128 (24%)	3.84 (2.23, 6.62)	3.01 (1.65, 5.49)
≥3	82 (36%)	7.67 (4.34, 13.57)	5.94 (3.10, 11.37)

^aadjusted for age, social class, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 4.7. Odds ratios (95%CI) for the associations of oral health problems with handgrip strength, and walking speed in British men aged 71-92 years in the BRHS.

Oral Health Problems	Bottom quintile of handgrip strength (n=347; 21%) (0-22 kg)			Top quintile of walking speed (n=337; 21%) (4.13-19.13 s)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss		<i>N=1606</i>	<i>N=1429</i>		<i>N=1553</i>	<i>N=1387</i>
≥21 teeth	111 (19%)	1.00	1.00	91 (16%)	1.00	1.00
15-20 teeth	59 (18%)	0.87 (0.61, 1.23)	0.89 (0.61, 1.29)	49 (15%)	0.89 (0.60, 1.30)	0.63 (0.41, 0.98)
8-14 teeth	58 (23%)	1.13 (0.78, 1.63)	1.11 (0.74, 1.66)	60 (25%)	1.51 (1.03, 2.20)	1.00 (0.64, 1.56)
1-7 teeth	26 (22%)	0.98 (0.60, 1.60)	1.00 (0.59, 1.72)	29 (26%)	1.44 (0.88, 2.36)	0.93 (0.53, 1.62)
0 teeth	79 (24%)	1.10 (0.78, 1.54)	1.20 (0.82, 1.76)	96 (31%)	1.82 (1.29, 2.57)	1.16 (0.77, 1.74)
Complete tooth loss						
≥1 teeth	254 (20%)	1.00	1.00	229 (18%)	1.00	1.00
0 teeth	79 (24%)	1.11 (0.83, 1.49)	1.21 (0.87, 1.68)	96 (31%)	1.64 (1.22, 2.19)	1.30 (0.92, 1.84)
Periodontal disease (% of sites with pocket depth >3.5 mm)		<i>N=1204</i>	<i>N=1084</i>		<i>N=1233</i>	<i>N=1111</i>
≤20%	153 (18%)	1.00	1.00	158 (18%)	1.00	1.00
>20%	86 (25%)	1.54 (1.13, 2.08)	1.59 (1.14, 2.20)	70 (20%)	1.12 (0.81, 1.53)	1.18 (0.82, 1.68)
Self-rated oral health		<i>N=1588</i>	<i>N=1425</i>		<i>N=1541</i>	<i>N=1387</i>
Good or excellent	224 (21%)	1.00	1.00	185 (18%)	1.00	1.00
Fair or poor	105 (19%)	0.83 (0.64, 1.08)	0.83 (0.62, 1.10)	128 (25%)	1.44 (1.10, 1.87)	1.00 (0.73, 1.35)
Dry mouth symptoms		<i>N=1587</i>	<i>N=1433</i>		<i>N=1541</i>	<i>N=1396</i>
0	107 (18%)	1.00	1.00	91 (15%)	1.00	1.00
1-2	118 (22%)	1.34 (1.00, 1.80)	1.25 (0.91, 1.72)	106 (21%)	1.51 (1.10, 2.08)	1.34 (0.93, 1.91)
≥3	102 (22%)	1.20 (0.88, 1.63)	1.15 (0.83, 1.61)	120 (28%)	1.98 (1.44, 2.72)	1.75 (1.22, 2.50)
Cumulative oral health problems^b		<i>N=1663</i>	<i>N=1483</i>		<i>N=1613</i>	<i>N=1443</i>
0	63 (19%)	1.00	1.00	51 (16%)	1.00	1.00
1	169 (22%)	1.09 (0.79, 1.52)	1.16 (0.81, 1.66)	146 (19%)	1.18 (0.83, 1.68)	0.84 (0.56, 1.26)
2	81 (21%)	0.98 (0.67, 1.42)	1.03 (0.68, 1.56)	85 (23%)	1.39 (0.94, 2.07)	0.92 (0.58, 1.44)
≥3	34 (20%)	0.93 (0.58, 1.49)	1.03 (0.61, 1.74)	55 (35%)	2.49 (1.57, 3.93)	1.52 (0.90, 2.57)

^aadjusted for age, social class, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 4.8. Odds ratios (95%CI) for the associations of oral health problems with handgrip strength, and walking speed in American men and women aged 71-80 years in the HABC Study.

Oral Health Problems	Bottom quintile of grip strength (n=469; 20%) (4.59-23.65 kg)			Top quintile of walking speed (n=375; 20%) (361.56-641.09 s)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth Loss		<i>N=1683</i>	<i>N=1676</i>		<i>N=1359</i>	<i>N=1355</i>
≥21 teeth	159 (20%)	1.00	1.00	49 (7%)	1.00	1.00
15-20 teeth	59 (19%)	0.94 (0.68, 1.32)	0.85 (0.59, 1.24)	20 (8%)	1.44 (0.99, 2.09)	1.08 (0.73, 1.62)
8-14 teeth	36 (16%)	0.75 (0.50, 1.11)	0.66 (0.42, 1.03)	19 (12%)	1.52 (0.99, 2.32)	1.08 (0.68, 1.71)
1-7 teeth	24 (15%)	0.76 (0.48, 1.22)	0.71 (0.42, 1.21)	11 (10%)	1.55 (0.94, 2.56)	1.08 (0.63, 1.85)
0 teeth	30 (18%)	0.90 (0.58, 1.38)	0.72 (0.43, 1.21)	15 (11%)	2.02 (1.30, 3.12)	1.15 (0.70, 1.89)
Complete tooth loss						
≥1 teeth	278 (18%)	1.00	1.00	99 (8%)	1.00	1.00
0 teeth	30 (18%)	0.98 (0.64, 1.49)	0.86 (0.53, 1.40)	15 (11%)	1.63 (1.08, 2.47)	1.06 (0.67, 1.68)
Periodontal disease (% of sites with loss of attachment ≥3 mm)		<i>N=1008</i>	<i>N=1004</i>		<i>N=817</i>	<i>N=814</i>
≤20%	55 (15%)	1.00	1.00	18 (6%)	1.00	1.00
>20%	114 (18%)	1.20 (0.84, 1.70)	1.46 (0.98, 2.17)	39 (8%)	0.98 (0.67, 1.45)	0.92 (0.61, 1.40)
Self-rated oral health		<i>N=2346</i>	<i>N=2338</i>		<i>N=1872</i>	<i>N=1865</i>
Good or excellent	317 (19%)	1.00	1.00	101 (7%)	1.00	1.00
Fair or poor	148 (21%)	1.07 (0.98, 1.17)	1.06 (0.96, 1.18)	74 (15%)	1.31 (1.18, 1.46)	1.16 (1.03, 1.30)
Dry mouth		<i>N= 2348</i>	<i>N= 2340</i>		<i>N=1870</i>	<i>N=1863</i>
No	430 (19%)	1.00	1.00	167 (9%)	1.00	1.00
Yes	33 (37%)	2.58 (1.65, 4.03)	2.43 (1.47, 4.01)	8 (14%)	1.78 (0.98, 3.25)	1.54 (0.82, 2.89)
Cumulative oral health problems^b		<i>N=2357</i>	<i>N=2348</i>		<i>N=1880</i>	<i>N=1872</i>
0	130 (19%)	1.00	1.00	35 (6%)	1.00	1.00
1	235 (20%)	1.06 (0.84, 1.35)	1.01 (0.77, 1.32)	91 (10%)	1.86 (1.40, 2.48)	1.40 (1.03, 1.91)
2	63 (19%)	1.00 (0.72, 1.40)	0.92 (0.63, 1.34)	28 (11%)	1.97 (1.35, 2.87)	1.31 (0.88, 1.97)
≥3	41 (22%)	1.23 (0.82, 1.83)	1.06 (0.67, 1.67)	22 (18%)	2.35 (1.47, 3.76)	1.40 (0.84, 2.33)

^aadjusted for age, gender, race, education, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 4.9. Odds ratios (95%CI) for the associations of oral health problems with chair-stand speed in British men aged 71-92 years in the BRHS.

Oral Health Problems	Top quintile of chair-stand speed (n=390; 24%) (16.28-49.06 s)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss		<i>N=1550</i>	<i>N=1384</i>
≥21 teeth	112 (20%)	1.00	1.00
15-20 teeth	62 (20%)	1.53 (1.11, 2.12)	1.19 (0.81, 1.75)
8-14 teeth	71 (29%)	1.48 (0.93, 2.36)	1.23 (0.73, 2.06)
1-7 teeth	34 (31%)	1.49 (1.05, 2.12)	1.22 (0.82, 1.83)
0 teeth	99 (32%)	0.94 (0.66, 1.34)	0.83 (0.56, 1.22)
Complete tooth loss			
≥1 teeth	279 (23%)	1.00	1.00
0 teeth	99 (32%)	1.36 (1.02, 1.80)	1.15 (0.83, 1.61)
Periodontal disease (% of sites with pocket depth >3.5 mm)		<i>N=1229</i>	<i>N=1108</i>
≤20%	194 (22%)	1.00	1.00
>20%	82 (23%)	1.06 (0.79, 1.44)	0.96 (0.69, 1.35)
Self-rated oral health		<i>N=1537</i>	<i>N=1384</i>
Good or excellent	226 (22%)	1.00	1.00
Fair or poor	141 (27%)	1.28 (0.99, 1.64)	1.01 (0.76, 1.35)
Dry mouth symptoms		<i>N=1537</i>	<i>N=1393</i>
0	123 (21%)	1.00	1.00
1-2	116 (23%)	1.14 (0.85, 1.53)	0.96 (0.70, 1.33)
≥3	131 (30%)	1.56 (1.17, 2.09)	1.33 (0.96, 1.84)
Cumulative oral health problems^b		<i>N=1610</i>	<i>N=1440</i>
0	53 (16%)	1.00	1.00
1	184 (24%)	1.56 (1.11, 2.20)	1.23 (0.84, 1.81)
2	101 (27%)	1.75 (1.20, 2.55)	1.38 (0.90, 2.10)
≥3	52 (33%)	2.24 (1.43, 3.52)	1.58 (0.95, 2.63)

^aadjusted for age, social class, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Chapter 5. Cross-Sectional Associations of Oral Health Problems with Inflammatory, Haemostatic, and Cardiac Biomarkers in Older People in the UK and USA

5.1. Summary

The prevalence of oral health problems continues to be high in community-dwelling older people. Oral health problems have been found to be associated with chronic diseases, such as cardiovascular diseases, particularly coronary heart disease, and may also be associated with biomarkers of inflammation related to chronic conditions. However, associations between oral health problems and inflammatory markers are not well established in populations of older people, especially with haemostatic and cardiac biomarkers. In this Chapter, cross-sectional associations of objective and subjective oral health problems with inflammatory (systemic) (C-reactive protein (CRP), interleukin-6 (IL-6)), haemostatic (fibrin d-dimer, von Willebrand factor (vWF) and tissue plasminogen activator (t-PA)), and cardiac (high sensitivity Troponin T (hsTnT, N-terminal pro brain natriuretic peptide (NTproBNP)) biomarkers in older people were examined. For this purpose, data from two population-based studies were used. The British Regional Heart Study (BRHS) comprised 2147 older British men aged 71-92 years living in 24 towns across the UK. The Health, Aging, and Body Composition (HABC) Study consisted of 3075 older men and women aged 71-80 years, living in Pittsburgh and Memphis, USA. Objective oral health problems included (tooth loss, and periodontal disease), and subjective (self-rated oral health, dry mouth, difficulty eating, sensitivity to hot/cold/sweets (BRHS), and limitation of food due to gum problems (HABC Study)). A composite variable for accumulation of oral health problems was also created. Logistic regression was used to assess the relationships. Poor oral health, particularly tooth loss was associated with increased levels of inflammatory, haemostatic, and cardiac biomarkers. Periodontal disease was only associated with high levels of hsTnT (odds ratio (OR)=1.49, 95% CI 1.08, 2.07). Accumulation of oral health problems was associated with increased levels of inflammatory markers (CRP, IL-6), and haemostatic markers (vWF). In summary, older individuals with

poor oral health are at greater odds of having high levels of inflammatory, haemostatic and cardiac biomarkers when compared to those with good oral health.

5.2. Introduction

Oral health problems, including tooth loss, periodontal disease and dry mouth, are identified as common health conditions in older people (Ramsay *et al.*, 2015b). Additionally, older people are more prone to increased levels of systemic inflammation (Singh and Newman, 2011). As mentioned in Chapter 2 (sub-section 2.4.2) previous research has reported associations between oral health problems and high levels of inflammation, with dental conditions co-existing with increased inflammation (see Figure 5.1, page 140). However, these associations are not well established in older populations. The majority of studies have been conducted in middle-aged populations and have focused on objective measures of oral health (periodontal disease, tooth loss). Thus, there is limited evidence on whether subjective (self-reported) oral health problems (dry mouth, self-rated oral health) are linked to increased levels of inflammation in older people. Furthermore, studies have focused on CRP and IL-6 and there is substantial lack of evidence on haemostatic and cardiac biomarkers. CRP and IL-6 represent systemic inflammation and can be linked to a number of geriatric syndromes. Haemostatic markers are related to atherosclerosis and cardiovascular disease, whereas cardiac biomarkers are associated with coronary heart disease. Therefore, each group of inflammatory markers represent a different disease pathology, and it is essential to establish the associations with poor oral health in older populations. Additionally, inflammatory markers, including CRP, IL-6 or fibrin d-dimer have been found to be associated with decreased muscle strength and physical performance in older people (Mary McGrae *et al.*, 2003; Singh and Newman, 2011). As a result it has been speculated that increased inflammation may play a mediating role in the association between oral health problems and development of disability in older people.

In summary, it is important to pinpoint the associations of different oral health problems with a range of markers of inflammation (see Figure 5.1, page 140) in order to better understand the way that oral health influences chronic diseases and health status in older people. Moreover, establishing these associations could help

disentangle the causal pathways that underpin the associations between poor oral health and risk of developing disability.

5.3. Aim and Objectives

This Chapter aims to examine the cross-sectional associations of objective and subjective oral health problems with inflammatory, haemostatic, and cardiac biomarkers in two studies of community-dwelling older people living in the UK and USA – the British Regional Heart Study (BRHS) (UK) and the Health, Aging and Body Composition (HABC Study) (USA). The objective of this Chapter is:

- I. To investigate the cross-sectional associations of objective and subjective oral health problems with inflammatory (CRP, IL-6), haemostatic (fibrin d-dimer, vWF, t-PA), and cardiac (hsTnT, NT-proBNP) biomarkers in older people.

5.4. Methods

An overview of both studies has been presented in Chapter 3 (sections 3.2 and 3.5). Relevant data for the analyses of this Chapter's objectives will be described below.

5.4.1. Subjects and methods of data collection

In the BRHS, cross-sectional data from the 30-year re-examination in 2010-2012 were used, when participants were aged 71-92 years. In this wave, 2147 older men completed the self-administered questionnaire (68% response rate) and 1770 older men participated in the physical examination (55% response rate). Information on markers of inflammation was selected at the physical examination. More details are provided in Chapter 3 (section 3.3).

In the HABC Study cross-sectional data from the Year 2 examination in 1998-1999 were utilised, when participants were aged 71-80 years. At this wave, 2998 older men and women completed questionnaires (97.5% response rate), 1975 underwent a dental examination, and 2830 individuals participated in the physical examination.

Information on inflammatory markers was provided at the physical examination. Further details are described in Chapter 3 (section 3.6).

5.4.2. Oral health

5.4.2.1. Objective oral health problems

Number of teeth and periodontal disease were assessed by trained professionals in both studies. Three categories were created for tooth loss: 5-level group (0, 1-7, 8-14, 15-20, ≥ 21 teeth), and two binary (<21 teeth vs. ≥ 21 teeth; 0 teeth vs. ≥ 1 teeth). Having ≥ 21 teeth indicated a functional dentition (Hobdell *et al.*, 2003). Periodontal disease was measured according to Extent and Severity Index (Carlos *et al.*, 1986) and included loss of attachment and pocket depth. Then it was grouped in two binary variables according to percentage of sites affected (>20% sites affected vs. $\leq 20\%$ sites). Further details can be found in Chapter 3 (sub-sections 3.3.1 and 3.6.1).

5.4.2.2. Subjective oral health problems

Data from questionnaires were used to assess dry mouth (0, 1-2, ≥ 3 dry mouth symptoms), self-rated oral health (excellent/good vs. fair/poor), difficulty eating (yes vs. no), sensitivity to hot/cold/sweets (yes vs. no/rare), limitation of food due to problems with teeth or dentures (yes vs. no/rare). Cumulative oral health problems included ≥ 3 dry mouth symptoms, <21 natural teeth, any difficulty eating and sensitivity to hot/cold/sweets in the BRHS; in the HABC Study it consisted of having dry mouth, <21 natural teeth, difficulty eating, and limitation of food because of gum problems. More details on these oral health measures can be found in Chapter 3 (sub-sections 3.3.1. and 3.6.1).

5.4.3. Inflammatory, haemostatic, and cardiac biomarkers

In both studies, inflammatory, haemostatic, and cardiac biomarkers were measured during the physical examination. In the BRHS, a fasting blood sample was collected and included plasma levels of CRP, IL-6, fibrin d-dimer, vWF, t-PA, hsTnT, and NT-proBNP. In the HABC Study, blood samples were collected only for CRP and IL-6. In both studies, inflammatory, haemostatic, and cardiac biomarkers were divided into tertiles. Inflammation was divided to tertiles to reflect low, medium, and high levels of inflammatory markers.

5.4.4. Socio-demographic, lifestyle factors, and chronic diseases

In both studies, information on socioeconomic status, smoking, history of cardiovascular disease (CVD), and history of diabetes were measured through questionnaires (Weyant *et al.*, 2004; Lennon *et al.*, 2015). BMI was measured at the physical examinations. More details are provided in Chapter 3 (sub-sections 3.3.2 and 3.6.2).

5.4.5. Statistical Analysis

For each study, separate logistic regression models were performed. These regression models were used to assess the relationships of objective and subjective oral health problems with inflammatory, haemostatic, and cardiac biomarkers. In logistic regression a binary variable was created for markers of inflammation where the top tertile was the outcome of interest (i.e. high level of biomarker). Odds ratios (OR) with their 95% CIs were provided. In the BRHS, regression models were adjusted for age, social class, smoking, history of CVD and diabetes, and BMI. In the HABC Study, regression models were adjusted for age, gender, race, education, smoking, history of CVD and diabetes, and BMI.

5.4.5.1. Sensitivity Analysis

Sensitivity analysis was conducted by adding CRP to the fully adjusted models to test whether associations between poor oral health and IL-6, haemostatic, and

cardiac biomarkers were attenuated after adjustment for CRP, as a marker of general inflammation. Results from the sensitivity analysis can be found in the Appendix (Appendix K).

5.5. Results

Prevalence of oral health problems and population characteristics have been presented in the Table 4.1 in Chapter 4.

In the BRHS, CRP values ranged from 0.05-239.84 mg/L, IL-6 from 0.15-30 pg/ml, fibrin d-dimer from 25-2000 ng/ml, vWF from 19.45-433.17 IU/dL, t-PA from 1.5-50 ng/ml, hsTnT from 1.5-407.1 ng/L, and NT-proBNP from 2.5-15899 ng/L. In the HABC Study, CRP values ranged from 0.10-141 ug/ml, and IL-6 from 0.30-32.87 pg/ml.

5.5.1. Associations of oral health problems with inflammatory biomarkers (CRP, IL-6)

Table 5.1 shows the odds ratios (OR) with 95% confidence intervals (CIs) for the association of objective and subjective oral health problems with top tertiles of CRP and IL-6 in the BRHS.

Complete tooth loss when compared to ≥ 21 teeth (functional dentition) was associated with high levels of CRP, in both age (n=1544) and fully adjusted models (n=1431) (OR= 1.90, 95% CI 1.41-2.56; OR= 1.52, 95% CI 1.09-2.13, respectively). Partial tooth loss (<21 vs. ≥ 21 teeth) was also associated with high levels of CRP after full adjustment (n=1431) (OR=1.31, 95% CI 1.02-1.68). For periodontal disease a borderline association was observed in the model adjusted for social class, smoking, history of CVD and diabetes, and BMI (n=1096) (OR=1.34, 95% CI 0.99-1.81). Fair/poor self-rated oral health and dry mouth were not associated with increased levels of CRP. Having ≥ 3 oral problems was associated with the top tertile of CRP in the age adjusted model (n=1601) (OR=1.54, 95% CI 1.03-2.31), but the association was attenuated and did not remain after adjustment for confounders (n=1484) (OR=1.37, 95% CI 0.89-2.12).

For IL-6, complete tooth loss when compared to ≥ 21 teeth was associated with top tertile of IL-6 in the age adjusted model (OR= 1.47, 95% CI 1.09-1.99), but this association did not remain in the fully adjusted model (n=1448) (OR= 1.22, 95% CI 0.87-1.71). Partial tooth loss was associated with high levels of IL-6 only in the age adjusted model (n=1560) (OR= 1.35, 95% CI 1.08-1.70). Periodontal disease was associated with the top tertile of IL-6 only in the age adjusted model (n=1181) (OR=1.39, 95% CI 1.04-1.85). Fair/poor self-rated oral health, dry mouth and cumulative oral health problems were not associated with increased levels of IL-6.

Odds ratios (OR) and 95% CIs for the association of objective and subjective oral health problems with top tertiles of CRP and IL-6 in the HABC Study are presented in Table 5.2. Having 0, 1-7, 8-14, and 15-20 teeth when compared to ≥ 21 teeth were associated with the top tertile of CRP in the age adjusted model (n=1936) (OR=1.89, 95% CI 1.37-2.60; OR=2.02, 95% CI 1.45-2.82; OR=1.67, 95% CI 1.25-2.22; OR= 1.65, 95% CI 1.27-2.15, respectively). After adjustment (n=1901), most of these associations remained, excluding 8-14 teeth (0 teeth, OR=1.57, 95% CI 1.10-2.25; 1-7 teeth, OR= 1.52, 95% CI 1.07-2.18; 15-20 teeth, OR= 1.39, 95% CI 1.05-1.84). Partial tooth loss (<21 vs. ≥ 21 teeth) was also associated with increased levels of CRP after adjustment for gender, race, education, smoking, history of CVD and diabetes, and BMI (n=1901) (OR=1.40, 95% CI 1.13-1.75). Periodontal disease was not associated with the top tertile of CRP. Fair/poor self-rated oral health was associated with high levels of CRP in the age adjusted model (n=2683) (OR=1.23, 95% CI 1.04-1.47), but this association did not remain in the fully adjusted model (n=2670). Dry mouth was not associated with high levels of CRP. Cumulative oral health problems was associated with the top tertile of CRP in both age (n=2720) and fully adjusted models (n=2681) (fully adjusted model, ≥ 3 vs. 0 problems: OR=1.42, 95% CI 1.01-1.00).

Having 0, 1-7, and 8-14 teeth when compared to ≥ 21 teeth were associated with increased levels of IL-6 in the age adjusted models (n=1936) (OR= 1.56, 95% CI 1.13-2.15; OR=1.74, 95% CI 1.25-2.43; OR=1.88, 95% CI 1.42-2.48, respectively). After adjusting for confounders (n=1901), only the relationship for 8-14 teeth remained (OR=1.45, 95% CI 1.07-1.96). Periodontal disease was not associated with high levels of IL-6. Fair/poor self-rated oral health was associated with elevated IL-6 only in the age adjusted model (n=2683) (OR=1.34, 95% CI 1.13-1.59).

Cumulative oral health problems was associated with the top tertile of IL-6 in both age (n=2720) and fully adjusted models (n=2681) (fully adjusted, ≥ 3 vs. 0 problems: OR=1.65, 95% CI 1.19-2.31).

5.5.2. Associations of oral health problems with haemostatic biomarkers (fibrin d-dimer, vWF, t-PA)

The HABC Study did not have data on haemostatic markers and therefore this analysis was only performed in the BRHS. Tables 5.3 and 5.4 present the results for the association of objective and subjective oral health problems with top tertiles of fibrin d-dimer, vWF, and t-PA in the BRHS. Having 0 and 1-7 teeth (vs. ≥ 21 teeth) were associated with increased levels of fibrin d-dimer in both age (n=1552) and fully adjusted models (n=1435) (fully adjusted, OR=1.64, 95% CI 1.16-2.30; OR=1.93, 95% CI 1.22-3.05, respectively). Likewise, complete tooth loss (0 vs. ≥ 1 teeth), and partial tooth loss (< 21 vs. ≥ 21 teeth) were associated with the top tertile of fibrin d-dimer in both models (fully adjusted, OR=1.38, 95% CI 1.03-1.85; OR= 1.37, 95% CI 1.05-1.77, respectively). Periodontal disease, fair/poor self-rated oral health, and dry mouth were not associated with elevated fibrin d-dimer. Having 2 oral health problems was associated with the top tertile of fibrin d-dimer only in the age adjusted model (n=1610) (OR= 1.48, 95% CI 1.06-2.07).

No associations were observed for complete and partial tooth loss and the top tertile of vWF. A borderline association was present between periodontal disease and high levels of vWF in the age adjusted model (n=1169) (OR= 1.32, 95% CI 0.99-1.75) but it was further attenuated after adjusting for confounders (n=1093) (OR= 1.17, 95% CI 0.87-1.58). Fair/poor self-rated oral health was associated with the top tertile of vWF only in the age adjusted model (n=1540) (OR= 1.31, 95% CI 1.05-1.64). No associations were observed for dry mouth. Lastly, having 2 oral health problems was associated with elevated vWF in both age (n=1610) and fully adjusted models (n=1489) (OR=1.51, 95% CI 1.09-2.08; OR=1.49, 95% CI 1.05-2.09, respectively). For ≥ 3 oral health problems a borderline association was observed in the age adjusted model (n=1610) (OR= 1.49, 95% CI 1.00-2.24) which did not change significantly after adjusting for confounders (n=1489) (OR=1.49, 95% CI 0.97-2.30).

Partial and complete tooth loss, and periodontal disease were not associated with the top tertile of t-PA. Fair/poor self-rated oral health was associated with high levels of t-PA in the age adjusted model (n=1540) (OR=1.31, 95% CI 1.05-1.63), but was attenuated to borderline significance after adjusting for social class, smoking, history of CVD and diabetes, and BMI (n=1433) (OR= 1.27, 95% CI 1.00-1.61). Dry mouth and cumulative oral health problems were not associated with the top tertile of t-PA.

5.5.3. Associations of oral health problems with cardiac biomarkers (hsTnT, NT-proBNP)

The HABC Study did not have data on cardiac biomarkers and as a result this analysis was only performed in the BRHS. ORs and 95% CIs for the associations between poor oral health and top tertiles of hsTnT and NT-proBNP can be found in Table 5.5. Having 0 teeth when compared to ≥ 21 teeth was associated with high levels of hsTnT, in the age adjusted model (n=1547) (OR= 1.42, 95% CI 1.03-1.96), but did not remain significant after adjusting for social class, smoking, history of CVD and diabetes, and BMI (n=1434). Partial tooth loss (<21 vs. ≥ 21 teeth) was associated with the top tertile of hsTnT in both age (n=1547) and fully adjusted models (n=1434) (fully adjusted, OR= 1.32, 95% CI 1.01-1.74). Periodontal disease was associated with high levels of hsTnT in both models (fully adjusted, OR=1.49, 95% CI 1.08-2.07). Fair/poor self-rated oral health, and dry mouth were not associated with the top tertile of hsTnT. A borderline association was observed for 2 oral health problems (vs. 0 problems) in the age adjusted model (n=1603) (OR=1.41, 95% CI 1.00-2.00) but was further attenuated after adjustment for confounders (n=1486) (OR=1.33, 95% CI 0.91-1.93).

Having 15-20 teeth (vs. ≥ 21 teeth) was associated with the top tertile of NT-proBNP in the fully adjusted model (n= 1434) (OR= 1.40, 95% CI 1.01-1.94). Periodontal disease was not associated with high levels of NT-proBNP. Having at least 2 dry mouth symptoms was associated with the top tertile of NT-proBNP in the age adjusted model (n=1529) (OR= 1.37, 95% CI 1.04-1.81) but did not remain after adjusting for confounders (n=1429). Fair/poor self-rated oral health and cumulative oral health problems were not associated with elevated NT-proBNP.

5.6. Discussion

5.6.1. Summary of main findings

This Chapter has examined the cross-sectional relationships of objective and subjective oral health problems with inflammatory, haemostatic, and cardiac biomarkers in older people in two population-based studies in the UK and USA. In the BRHS, tooth loss was associated with high levels of CRP, fibrin d-dimer, hsTnT, and NT-proBNP after adjusting for age and other confounding factors. Furthermore, cumulative oral health problems were associated with increased levels of vWF. In the HABC Study, tooth loss and cumulative oral health problems were associated with high levels of CRP and IL-6 after adjusting for confounders.

5.6.2. Comparison with previous studies

5.6.2.1. Poor oral health and inflammatory markers (CRP, IL-6)

Partial and complete tooth loss were associated with increased levels of CRP in both studies. This finding is in accordance with previous studies, which were conducted in middle-aged populations (Lowe *et al.*, 2003; You *et al.*, 2009). In the HABC Study, tooth loss and cumulative oral health problems were associated with increased levels of IL-6, independent of confounders. This finding for tooth loss also agrees with previous studies, where tooth loss, particularly complete tooth loss, was associated with high levels of IL-6 (Lowe *et al.*, 2003). Tooth loss could be related to inflammation due to its influence on dietary intake. Tooth loss can lead to chewing and swallowing difficulties, which are common in older people (Okamoto *et al.*, 2012; Okamoto *et al.*, 2015). A combination of tooth loss and impaired chewing ability, can significantly affect food choices of older people, leading to a less diverse diet characterised by food avoidance and low consumption of antioxidants and vitamins (Moynihan and Bradbury, 2001; Lowe *et al.*, 2003; Bradbury *et al.*, 2008). A diet with decreased consumption of fruits and vegetables can influence levels of inflammation including CRP, and IL-6 (Lowe *et al.*, 2003). Moreover, it is possible that individuals with tooth loss may be predisposed to systemic inflammation (Lowe *et al.*, 2003) and that tooth loss can be an indicator of accumulation of life stressors (Friedman and

Lamster, 2016). As a result these individuals are in higher risk of developing chronic diseases and consequently higher levels of inflammation (Friedman and Lamster, 2016). Furthermore, the observed association between cumulative oral health problems and elevated IL-6 shows that the existence of more than one oral health conditions is linked to increased inflammation in older people and highlights the importance of management of poor oral health.

In the BRHS, borderline associations were observed between periodontal disease and high levels of CRP and IL-6 after adjusting for smoking, chronic diseases, and BMI. Previous studies have shown stronger associations between periodontal disease and increased levels of CRP and IL-6 (Noack *et al.*, 2001; Amar *et al.*, 2003; Bretz *et al.*, 2005). However, some of these studies have been carried out in mixed populations of middle-aged and older people. Additionally, it is possible that this difference may be due to the fact that previous studies examined the association between severity of periodontal disease and inflammation, rather than the presence of periodontal disease (as done in this thesis) (Noack *et al.*, 2001; Amar *et al.*, 2003; Bretz *et al.*, 2005). Also individuals participating in our study may have had a better periodontal status and only the healthier teeth remained and therefore examined for loss of attachment and pocket depth (Kotronia *et al.*, 2020).

In the HABC Study, associations of fair/poor self-rated oral health and dry mouth with high levels of CRP and IL-6 were attenuated after adjustment for smoking, chronic diseases, and BMI. Smoking can influence oral dryness, and chronic diseases can cause xerostomia as a consequence of side effects of medications (Han *et al.*, 2015; Thomson, 2015).

5.6.2.2. Poor oral health and haemostatic biomarkers (fibrin d-dimer, vWF, t-PA)

Complete and partial tooth loss were associated with high levels of fibrin d-dimer, after adjusting for confounders. To date there were no studies identified examining tooth loss and the association with levels of fibrin d-dimer. According to previous studies, tooth loss can be a result of periodontal disease and root caries (Ravald and Johansson, 2012). Periodontal disease is a chronic inflammatory disease, which is characterised by a high number of bacteria (dental plaque) in the oral cavity (Ravald

and Johansson, 2012). Dental plaque can interact with the immune system of the individual and contribute to increased inflammation in other parts of the body (Kinane *et al.*, 2017). Interestingly, oral bacteria may also contribute to the formation of atherosclerotic plaques and thus lead to high levels of inflammation linked to cardiovascular disease (Alpert, 2017). It should be added that levels of fibrin d-dimer tend to increase in older populations, which can influence fibrinolysis and systemic inflammation (Wilson *et al.*, 2003). Additionally, fibrin d-dimer is associated with the development of chronic health conditions including stroke, functional disability, disability, and mortality (Pieper *et al.*, 2000; Wilson *et al.*, 2003; Wannamethee *et al.*, 2012). It is possible that dental problems can contribute to high inflammation levels and increased fibrinolysis, already elevated in older people due to ageing, and therefore further affect levels of fibrin d-dimer in older people (Kotronia *et al.*, 2020). This also highlights the potential mediating role of fibrin d-dimer in the association between poor oral health and development of disability in older populations.

Furthermore, fair/poor self-rated oral health was associated with high levels of t-PA and cumulative oral health problems with increased levels of vWF. Self-rated oral health is a simple tool which can assess oral health status of older people and indicate the impact of dental conditions on everyday life (Wu *et al.*, 2011). In one study, self-rated oral health declined as individuals reached the end of their life (Chen *et al.*, 2013). It is possible that this decrease may be a result of comorbidities and poor overall health (Chen *et al.*, 2013). Therefore poor self-rated oral health may co-exist with increased inflammation and can be an indirect indicator of deterioration of one's health status and of the presence of chronic diseases, such as cardiovascular disease. Similar to CRP and IL-6, the observed association for cumulative oral health problems highlights the potential impact of the accumulation of oral conditions on inflammation and therefore chronic diseases.

5.6.2.3. Poor oral health and cardiac biomarkers (*hsTnT*, *NT-proBNP*)

Partial tooth loss and periodontal disease were associated with high levels of *hsTnT* after adjusting for confounders. The associations for periodontal disease remained even after further adjusting for CRP (sensitivity analysis). Troponin T is a regulatory

protein which can detect myocardial injury and is used for the diagnosis of myocardial infarction (Thygesen *et al.*, 2007; Seliger *et al.*, 2017). Elevated Troponin T has been found to predict heart failure, coronary heart disease and cardiovascular mortality (Saunders *et al.*, 2011; McEvoy *et al.*, 2015; McEvoy *et al.*, 2016; Stephen *et al.*, 2017). Individuals with periodontal disease are more likely to suffer from oral infections and it has been reported that bacteria from mouth lesions can travel through the circulatory system and cause bacterial endocarditis, which is a heart infection caused by bacteria entering the bloodstream (Cahill *et al.*, 2017; Carrizales-Sepúlveda *et al.*, 2018). Moreover, periodontal disease induces a similar inflammatory response to diseases such as cardiovascular disease (Carrizales-Sepúlveda *et al.*, 2018), and can contribute to atherosclerosis and thrombus formation (James *et al.*, 2001). This evidence offers support for the observed association of periodontal disease with high levels of hsTnT. Elevated Troponin T may possibly explain the association between periodontal disease and coronary heart disease.

Moreover, partial tooth loss was associated with increased levels of NT-proBNP. NT-proBNP is a marker of left ventricular stress and a tool for the diagnosis of heart failure in older people (Eggers *et al.*, 2009). It has been found that levels of NT-proBNP increase with age (Wang *et al.*, 2002). A previous study in individuals with stable coronary disease found that tooth loss was associated with high levels of NT-proBNP (Vedin *et al.*, 2017). It was suggested that tooth loss may be linked to baseline cardiac dysfunction (Vedin *et al.*, 2017). Additionally, in a meta-analysis, tooth loss was associated with 34% increased risk of developing coronary heart disease (Humphrey *et al.*, 2008). However, the studies included in this meta-analysis, consisted of young and middle-aged adults. It is possible that tooth loss as a result of periodontal disease or a marker of life stressors can be associated with high levels of cardiac biomarkers, including hsTnT and NT-proBNP and therefore contribute to the burden of chronic diseases in older people.

5.6.3. Strengths and limitations

5.6.3.1. Strengths of this study

This is one of the first studies examining the associations between a range of objective and subjective oral health problems with not only systemic inflammatory markers (CRP, IL-6) but also with haemostatic and cardiac biomarkers in older community-dwelling people. Few studies have examined the associations between subjective oral health problems and inflammation in older people. Furthermore, this study provided much needed evidence on the relationship between poor oral health and biomarkers of cardiovascular and coronary heart diseases. In this study, I was also able to investigate whether the accumulation of oral health problems, an important indicator of the burden of poor oral health, was associated with several markers of inflammation.

5.6.3.2. Possible bias and limitations

A limitation of this study is that analyses were cross-sectional, and causal relationships, or the direction of associations observed cannot be established. Subjective oral health problems, such as dry mouth, were self-reported by participants which can be a source of bias (Ikebe *et al.*, 2007). Nonetheless, these self-reported measures are important in measuring the impact that oral health problems have on individuals because they can negatively influence quality of life.

Both studies were comparable in terms of comprising older people, but certain differences in the assessment of oral health measures (periodontal disease, dry mouth) and markers of inflammation were present. In the BRHS inflammatory, haemostatic, and cardiac biomarkers were measured and available for analysis, whereas in the HABC Study only inflammatory markers (CRP, IL-6) were assessed in Year 2, and therefore analysis was performed for these two markers.

In terms of population characteristics, both cohorts may not be representative of the whole population of older people (Shaper *et al.*, 1981; Walker *et al.*, 2004). In the HABC Study, at baseline, individuals with any functional disability were excluded from the study, and therefore participants may be healthier than the rest of the community-dwelling older population (Yaffe *et al.*, 2003). In both studies it is highly

possible that the individuals who did not answer the questionnaires or did not attend the examinations were older, and with poorer health outcomes in comparison to the respondents. Therefore, selection bias may be present, and the reported associations for poor oral health and levels of inflammation may be underestimating the true level of associations because respondents may have had lower levels of inflammation and better oral health than non-respondents.

For the purpose of this study, a number of associations between oral health problems and inflammatory, haemostatic, and cardiac biomarkers were investigated. As a result, multiple comparisons were performed in both studies. Hence, there is a risk of reporting false-positive results. As the number of hypothesis testing increases, so does the risk of observing false-positive results (Lindquist and Mejia, 2015). Additionally, analyses were adjusted for a number of covariates, but it is possible that other uncontrolled or unmeasured confounders may have affected the reported results and introduced residual confounding (Liang *et al.*, 2014).

5.7. Conclusions

The results of Chapter 5 show that poor oral health is associated with high levels of inflammatory, haemostatic, and cardiac biomarkers in two studies of community-dwelling older people. Tooth loss was associated with high levels of CRP, fibrin d-dimer, hsTnT, and NT-proBNP. Periodontal disease was associated with increased levels of hsTnT. For subjective oral health problems, fair/poor self-reported oral health was associated with high levels of t-PA. Additionally, cumulative oral health problems was associated with increased levels of CRP, IL-6, and vWF in older people. In the presence of dental problems, food habits and diet quality can be influenced and as a result levels of inflammation can also be affected. Establishing associations between oral health and increased inflammation and poor diet quality, will help in examining the causal pathways implicated in the association of oral health with health, and particularly onset of disability. In the next Chapter, Chapter 6, the associations of objective and subjective oral health problems with diet quality and dietary intake in community-dwelling older people living in the UK and USA will be examined.

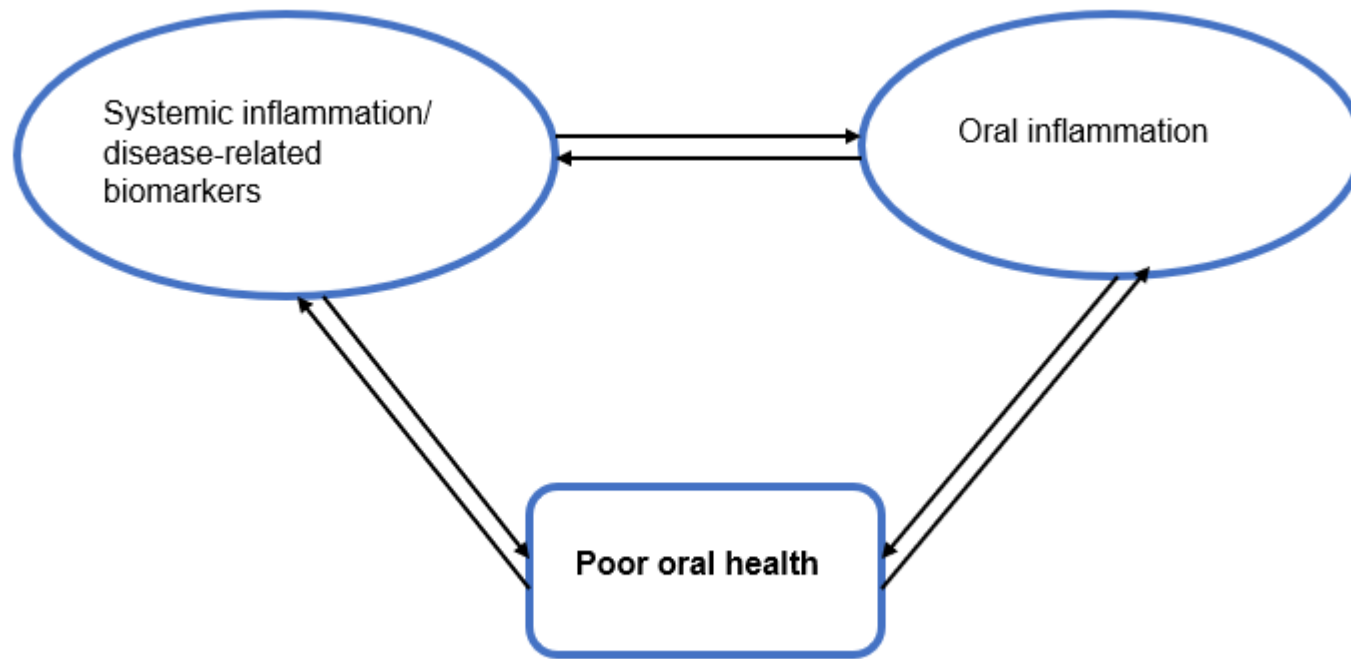


Figure 5.1. Bi-directional associations between poor oral health and inflammation.

Table 5.1. Odds ratios (95%CI) for the associations of oral health problems with top tertiles of CRP, and IL-6 in British men aged 71-92 years in the BRHS.

Oral Health Problems	Top tertile of CRP ^a (n=535, 33%)			Top tertile of IL-6 ^a (n=539, 33%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss		<i>N=1544</i>	<i>N=1431</i>		<i>N=1560</i>	<i>N=1448</i>
≥21 teeth	154 (27)	1.00	1.00	157 (28)	1.00	1.00
15-20 teeth	108 (35)	1.38 (1.02, 1.86)	1.35 (0.99, 1.85)	108 (34)	1.27 (0.94, 1.72)	1.29 (0.94, 1.77)
8-14 teeth	83 (34)	1.31 (0.95, 1.92)	1.13 (0.80, 1.61)	90 (36)	1.35 (0.98, 1.86)	1.20 (0.85, 1.70)
1-7 teeth	38 (33)	1.24 (0.80, 1.92)	1.11 (0.70, 1.77)	42 (37)	1.31 (0.85, 2.02)	1.18 (0.75, 1.88)
0 teeth	133 (43)	1.90 (1.41, 2.56)	1.52 (1.09, 2.13)	124 (40)	1.47 (1.09, 1.99)	1.22 (0.87, 1.71)
Complete tooth loss						
≥1 teeth	383 (31)	1.00	1.00	397 (32)	1.00	1.00
0 teeth	133 (43)	1.61 (1.24, 2.09)	1.35 (1.01, 1.80)	124 (40)	1.26 (0.97, 1.64)	1.06 (0.79, 1.43)
Partial tooth loss						
≥21 teeth	154 (27)	1.00	1.00	157 (28)	1.00	1.00
<21 teeth	362 (37)	1.49 (1.18, 1.87)	1.31 (1.02, 1.68)	364 (37)	1.35 (1.08, 1.70)	1.23 (0.96, 1.59)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=1170</i>	<i>N=1096</i>		<i>N=1181</i>	<i>N=1108</i>
≤20%	254 (28)	1.00	1.00	259 (29)	1.00	1.00
>20%	97 (35)	1.33 (1.00, 1.78)	1.34 (0.99, 1.81)	102 (37)	1.39 (1.04, 1.85)	1.32 (0.97, 1.78)
Self-rated oral health		<i>N=1530</i>	<i>N=1427</i>		<i>N=1548</i>	<i>N=1446</i>
Good or excellent	327 (32)	1.00	1.00	319 (31)	1.00	1.00
Fair or poor	189 (37)	1.18 (0.94, 1.48)	1.13 (0.89, 1.43)	194 (37)	1.23 (0.98, 1.54)	1.24 (0.98, 1.58)
Dry mouth symptoms		<i>N=1527</i>	<i>N=1427</i>		<i>N=1543</i>	<i>N=1445</i>
0	186 (32)	1.00	1.00	194 (36)	1.00	1.00
1-2	167 (33)	1.04 (0.81, 1.34)	1.01 (0.77, 1.33)	163 (31)	0.92 (0.71, 1.19)	0.84 (0.65, 1.11)
≥3	160 (37)	1.19 (0.92, 1.55)	1.20 (0.91, 1.59)	152 (35)	0.99 (0.76, 1.29)	0.96 (0.73, 1.27)

^a values for top tertile of CRP= 2.24-239.8 mg/L, reference group= <2.24 mg/L; values for top tertile of IL-6 = 3.90-30 pg/ml, reference group= <3.90 pg/ml

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

Table 5.1 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with top tertiles of CRP, and IL-6 in British men aged 71-92 years in the BRHS.

Oral Health Problems	Top tertile of CRP ^a (n=535, 33%)			Top tertile of IL-6 ^a (n=539, 33%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Cumulative oral health problems^c		<i>N=1601</i>	<i>N=1484</i>		<i>N=1618</i>	<i>N=1502</i>
0	90 (28)	1.00	1.00	89 (28)	1.00	1.00
1	255 (34)	1.28 (0.96, 1.71)	1.11 (0.81, 1.51)	265 (35)	1.31 (0.98, 1.75)	1.23 (0.90, 1.68)
2	129 (35)	1.33 (0.96, 1.84)	1.17 (0.82, 1.66)	134 (36)	1.36 (0.98, 1.89)	1.21 (0.85, 1.72)
≥3	61 (39)	1.54 (1.03, 2.31)	1.37 (0.89, 2.12)	51 (32)	1.07 (0.70, 1.63)	1.07 (0.68, 1.68)

^a values for top tertile of CRP= 2.24-239.8 mg/L, reference group= <2.24 mg/L; values top tertile IL-6 = 3.90-30 pg/ml, reference group= <3.90 pg/ml

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

^c <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 5.2. Odds ratios (95%CI) for the associations of oral health problems with top tertiles of CRP, and IL-6 in American men and women aged 71-80 years in the HABC Study.

Oral Health Problems	Top tertile of CRP ^a (n=924, 33%)			Top tertile of IL-6 ^a (n=912, 33%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Tooth loss		<i>N=1936</i>	<i>N=1901</i>		<i>N=1936</i>	<i>N=1901</i>
≥21 teeth	238 (26)	1.00	1.00	251 (27)	1.00	1.00
15-20 teeth	128 (36)	1.65 (1.27, 2.15)	1.39 (1.05, 1.84)	115 (33)	1.30 (1.00, 1.70)	1.05 (0.79, 1.39)
8-14 teeth	102 (37)	1.67 (1.25, 2.22)	1.26 (0.92, 1.72)	115 (41)	1.88 (1.42, 2.48)	1.45 (1.07, 1.96)
1-7 teeth	75 (41)	2.02 (1.45, 2.82)	1.52 (1.07, 2.18)	71 (39)	1.74 (1.25, 2.43)	1.27 (0.89, 1.82)
0 teeth	78 (39)	1.89 (1.37, 2.60)	1.57 (1.10, 2.25)	74 (37)	1.56 (1.13, 2.15)	1.24 (0.87, 1.78)
Complete tooth loss						
≥1 teeth	543 (31)	1.00	1.00	552 (32)	1.00	1.00
0 teeth	78 (39)	1.42 (1.05, 1.92)	1.28 (0.92, 1.78)	74 (37)	1.26 (0.93, 1.71)	1.10 (0.79, 1.53)
Partial tooth loss						
≥21 teeth	238 (26)	1.00	1.00	251 (27)	1.00	1.00
<21 teeth	383 (38)	1.76 (1.45, 2.15)	1.40 (1.13, 1.75)	375 (37)	1.58 (1.30, 1.91)	1.22 (0.98, 1.51)
Periodontal disease (% of sites with loss of attachment ≥3 mm)		<i>N=1117</i>	<i>N=1107</i>		<i>N=1117</i>	<i>N=1107</i>
≤20%	113 (28)	1.00	1.00	109 (27)	1.00	1.00
>20%	215 (30)	1.18 (0.90, 1.55)	1.08 (0.80, 1.44)	228 (32)	1.30 (0.99, 1.71)	1.11 (0.83, 1.48)
Self-rated oral health		<i>N=2683</i>	<i>N=2670</i>		<i>N=2683</i>	<i>N=2670</i>
Good or excellent	593 (32)	1.00	1.00	565 (30)	1.00	1.00
Fair or poor	299 (37)	1.23 (1.04, 1.47)	1.03 (0.85, 1.24)	301 (37)	1.34 (1.13, 1.59)	1.17 (0.97, 1.41)
Dry mouth		<i>N=2684</i>	<i>N=2671</i>		<i>N=2684</i>	<i>N=2671</i>
No	851 (33)	1.00	1.00	828 (32)	1.00	1.00
Yes	41 (39)	1.28 (0.86, 1.91)	1.10 (0.72, 1.66)	42 (40)	1.39 (0.93, 2.07)	1.29 (0.85, 1.95)

^a values for top tertile of CRP= 4.96-141 ug/ml, reference group= <4.96 ug/ml; values for top tertile of IL-6= 3.29-32.87 pg/ml, reference group= <3.29 pg/ml

^b adjusted for age, gender, race, education, smoking, history of CVD and diabetes, BMI

Table 5.2 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with top tertiles of CRP, and IL-6 in American men and women aged 71-80 years in the HABC Study.

Oral Health Problems	Top tertile of CRP ^a (n=535, 33%)			Top tertile of IL-6 ^a (n=539, 33%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Cumulative oral health problems^c		<i>N=2720</i>	<i>N=2681</i>		<i>N=2720</i>	<i>N=2681</i>
0	198 (26)	1.00	1.00	204 (27)	1.00	1.00
1	467 (35)	1.50 (1.24, 1.83)	1.25 (1.01, 1.55)	461 (34)	1.43 (1.18, 1.74)	1.18 (0.96, 1.46)
2	149 (38)	1.76 (1.35, 2.28)	1.43 (1.09, 1.89)	122 (31)	1.24 (0.95, 1.62)	1.05 (0.79, 1.39)
≥3	91 (41)	1.97 (1.44, 2.70)	1.42 (1.01, 1.99)	96 (43)	2.12 (1.55, 2.89)	1.65 (1.19, 2.31)

^a values for top tertile of CRP= 4.96-141 ug/ml, reference group= <4.96 ug/ml; values for top tertile of IL-6= 3.29-32.87 pg/ml, reference group= <3.29 pg/ml

^b adjusted for age, gender, race, education, smoking, history of CVD and diabetes, BMI

^c <21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 5.3. Odds ratios (95%CI) for the associations of oral health problems with top tertiles of fibrin d-dimer, and vWF in British men aged 71-92 years in the BRHS.

Oral Health Problems	Top tertile of fibrin d-dimer ^a (n=537, 33%)			Top tertile of vWF ^a (n=537, 33%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Tooth loss		<i>N=1552</i>	<i>N=1435</i>		<i>N=1552</i>	<i>N=1435</i>
≥21 teeth	145 (26)	1.00	1.00	175 (31)	1.00	1.00
15-20 teeth	96 (30)	1.17 (0.85, 1.60)	1.17 (0.84, 1.62)	95 (30)	0.92 (0.68, 1.25)	0.88 (0.64, 1.21)
8-14 teeth	80 (33)	1.24 (0.88, 1.74)	1.19 (0.83, 1.72)	84 (34)	1.11 (0.80, 1.52)	1.02 (0.72, 1.44)
1-7 teeth	52 (46)	1.93 (1.26, 2.97)	1.93 (1.22, 3.05)	48 (42)	1.48 (0.98, 2.25)	1.44 (0.93, 2.23)
0 teeth	141 (45)	1.83 (1.35, 2.49)	1.64 (1.16, 2.30)	109 (35)	1.08 (0.80, 1.46)	0.91 (0.65, 1.28)
Complete tooth loss						
≥1 teeth	373 (30)	1.00	1.00	402 (32)	1.00	1.00
0 teeth	141 (45)	1.57 (1.20, 2.05)	1.38 (1.03, 1.85)	109 (35)	1.04 (0.79, 1.35)	0.89 (0.66, 1.19)
Partial tooth loss						
≥21 teeth	145 (26)	1.00	1.00	175 (31)	1.00	1.00
<21 teeth	369 (37)	1.45 (1.15, 1.84)	1.37 (1.05, 1.77)	336 (34)	1.07 (0.86, 1.34)	0.98 (0.77, 1.25)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=1169</i>	<i>N=1093</i>		<i>N=1169</i>	<i>N=1093</i>
≤20%	258 (29)	1.00	1.00	283 (32)	1.00	1.00
>20%	86 (32)	1.05 (0.77, 1.42)	0.98 (0.71, 1.36)	105 (39)	1.32 (0.99, 1.75)	1.17 (0.87, 1.58)
Self-rated oral health		<i>N=1540</i>	<i>N=1433</i>		<i>N=1540</i>	<i>N=1433</i>
Good or excellent	325 (32)	1.00	1.00	314 (31)	1.00	1.00
Fair or poor	185 (35)	1.08 (0.86, 1.36)	1.06 (0.83, 1.36)	197 (38)	1.31 (1.05, 1.64)	1.24 (0.98, 1.57)
Dry mouth symptoms		<i>N=1534</i>	<i>N=1431</i>		<i>N=1534</i>	<i>N=1431</i>
0	178 (31)	1.00	1.00	192 (33)	1.00	1.00
1-2	163 (32)	1.07 (0.82, 1.40)	1.11 (0.84, 1.46)	157 (31)	0.90 (0.69, 1.16)	0.90 (0.69, 1.18)
≥3	167 (38)	1.24 (0.94, 1.64)	1.24 (0.93, 1.66)	168 (38)	1.20 (0.92, 1.56)	1.27 (0.97, 1.67)

^a values for top tertile of fibrin d-dimer= 277.27-2000 ng/ml, reference group= <277.27 ng/ml; values for top tertile of vWF= 132.69-433.17 IU/dl, reference group= <132.69 IU/dl

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

Table 5.3 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with top tertiles of fibrin d-dimer, vWF in British men aged 71-92 years in the BRHS.

Oral Health Problems	Top tertile of fibrin d-dimer ^a (n=537, 33%)			Top tertile of vWF ^a (n=537, 33%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Cumulative oral health problems^c		<i>N=1610</i>	<i>N=1489</i>		<i>N=1610</i>	<i>N=1489</i>
0	87 (27)	1.00	1.00	90 (28)	1.00	1.00
1	244 (32)	1.14 (0.84, 1.54)	1.09 (0.79, 1.50)	244 (32)	1.19 (0.89, 1.58)	1.16 (0.85, 1.58)
2	145 (39)	1.48 (1.06, 2.07)	1.38 (0.97, 1.98)	142 (38)	1.51 (1.09, 2.08)	1.49 (1.05, 2.09)
3	61 (38)	1.35 (0.89, 2.06)	1.23 (0.78, 1.94)	61 (38)	1.49 (1.00, 2.24)	1.49 (0.97, 2.30)

^a values for top tertile of fibrin d-dimer= 277.27-2000 ng/ml, reference group= <277.27 ng/ml; values for top tertile of vWF= 132.69-433.17 IU/dl, reference group= <132.69 IU/dl

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

^c <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 5.4. Odds ratios (95%CI) for the associations of oral health problems with the top tertile of t-PA in British men aged 71-92 years in the BRHS.

Oral Health Problems	Top tertile of t-PA ^a (n=537, 33%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Tooth loss		<i>N=1552</i>	<i>N=1435</i>
≥21 teeth	180 (32)	1.00	1.00
15-20 teeth	95 (30)	0.90 (0.67, 1.22)	0.93 (0.67, 1.28)
8-14 teeth	87 (35)	1.16 (0.84, 1.59)	1.13 (0.80, 1.60)
1-7 teeth	41 (36)	1.18 (0.77, 1.81)	1.08 (0.68, 1.71)
0 teeth	114 (37)	1.22 (0.90, 1.64)	1.08 (0.76, 1.52)
Complete tooth loss			
≥1 teeth	403 (32)	1.00	1.00
0 teeth	114 (37)	1.19 (0.91, 1.55)	1.06 (0.78, 1.43)
Partial tooth loss			
≥21 teeth	180 (32)	1.00	1.00
<21 teeth	337 (34)	1.09 (0.87, 1.36)	1.03 (0.80, 1.33)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=1169</i>	<i>N=1093</i>
≤20%	276 (31)	1.00	1.00
>20%	93 (34)	1.17 (0.87, 1.56)	1.12 (0.82, 1.52)
Self-rated oral health		<i>N=1540</i>	<i>N=1433</i>
Good or excellent	317 (31)	1.00	1.00
Fair or poor	196 (37)	1.31 (1.05, 1.63)	1.27 (1.00, 1.61)
Dry mouth symptoms		<i>N=1534</i>	<i>N=1431</i>
0	189 (33)	1.00	1.00
1-2	176 (34)	1.08 (0.84, 1.39)	1.06 (0.81, 1.39)
≥3	149 (34)	1.04 (0.80, 1.36)	0.95 (0.71, 1.27)
Cumulative oral health problems^c		<i>N=1610</i>	<i>N=1489</i>
0	102 (32)	1.00	1.00
1	238 (32)	0.98 (0.74, 1.30)	0.97 (0.71, 1.32)
2	140 (37)	1.28 (0.93, 1.75)	1.11 (0.78, 1.56)
3	57 (36)	1.18 (0.79, 1.76)	1.16 (0.74, 1.80)

^a values for top tertile t-PA= 10.63-50 ng/ml, reference group= <10.63 ng/ml

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

^c <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 5.5. Odds ratios (95%CI) for the associations of oral health problems with top tertiles of hsTnT and NT-proBNP in British men aged 71-92 years in the BRHS.

Oral Health Problems	Top tertile of hsTnT ^a (n=534, 33%)			Top tertile of NT-proBNP ^a (n=534, 33%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Tooth loss		<i>N=1547</i>	<i>N=1434</i>		<i>N=1547</i>	<i>N=1434</i>
≥21 teeth	148 (26)	1.00	1.00	166 (29)	1.00	1.00
15-20 teeth	101 (32)	1.24 (0.90, 1.72)	1.33 (0.94, 1.87)	114 (36)	1.30 (0.96, 1.77)	1.40 (1.01, 1.94)
8-14 teeth	85 (34)	1.27 (0.90, 1.80)	1.24 (0.85, 1.81)	80 (32)	1.00 (0.71, 1.40)	1.08 (0.75, 1.56)
1-7 teeth	48 (42)	1.44 (0.92, 2.25)	1.31 (0.81, 2.12)	40 (35)	0.95 (0.61, 1.48)	0.95 (0.59, 1.53)
0 teeth	129 (42)	1.42 (1.03, 1.96)	1.40 (0.98, 2.02)	121 (40)	1.15 (0.84, 1.57)	1.09 (0.76, 1.55)
Complete tooth loss						
≥1 teeth	382 (31)	1.00	1.00	400 (32)	1.00	1.00
0 teeth	129 (42)	1.23 (0.93, 1.63)	1.19 (0.87, 1.63)	121 (40)	1.08 (0.82, 1.42)	0.99 (0.73, 1.34)
Partial tooth loss						
≥21 teeth	148 (26)	1.00	1.00	166 (29)	1.00	1.00
<21 teeth	363 (37)	1.33 (1.04, 1.70)	1.32 (1.01, 1.74)	355 (36)	1.13 (0.90, 1.43)	1.17 (0.91, 1.52)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=1173</i>	<i>N=1099</i>		<i>N=1173</i>	<i>N=1099</i>
≤20%	240 (27)	1.00	1.00	273 (30)	1.00	1.00
>20%	107 (39)	1.64 (1.21, 2.23)	1.49 (1.08, 2.07)	98 (36)	1.16 (0.86, 1.56)	1.12 (0.81, 1.54)
Self-rated oral health		<i>N=1532</i>	<i>N=1429</i>		<i>N=1532</i>	<i>N=1429</i>
Good or excellent	310 (31)	1.00	1.00	323 (32)	1.00	1.00
Fair or poor	191 (37)	1.23 (0.97, 1.57)	1.20 (0.93, 1.56)	178 (34)	1.04 (0.82, 1.32)	1.07 (0.83, 1.38)
Dry mouth symptoms		<i>N=1529</i>	<i>N=1429</i>		<i>N=1529</i>	<i>N=1429</i>
0	184 (32)	1.00	1.00	168 (29)	1.00	1.00
1-2	157 (31)	0.96 (0.73, 1.27)	0.87 (0.65, 1.16)	173 (34)	1.29 (0.99, 1.69)	1.20 (0.90, 1.59)
≥3	162 (37)	1.12 (0.84, 1.48)	1.00 (0.74, 1.35)	165 (38)	1.37 (1.04, 1.81)	1.25 (0.93, 1.68)

^avalues for top tertile of hsTnT= 14.34-407.10 ng/l, reference group= <14.34 ng/l; for NT-proBNP= 226-15899 ng/l, reference group= <226 ng/l

^badjusted for age, social class, smoking, history of CVD and diabetes, BMI

Table 5.5 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with top tertiles of hsTnT and NT-proBNP in British men aged 71-92 years in the BRHS.

Oral Health Problems	Top tertile of hsTnT ^a (n=534, 33%)			Top tertile of NT-proBNP ^a (n=534, 33%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Cumulative oral health problems^c		<i>N=1603</i>	<i>N=1486</i>		<i>N=1603</i>	<i>N=1486</i>
0	86 (27)	1.00	1.00	101 (31)	1.00	1.00
1	248 (33)	1.18 (0.86, 1.60)	1.17 (0.84, 1.63)	229 (30)	0.84 (0.63, 1.13)	0.81 (0.59, 1.12)
2	140 (38)	1.41 (1.00, 2.00)	1.33 (0.91, 1.93)	147 (40)	1.26 (0.91, 1.75)	1.16 (0.81, 1.66)
≥3	60 (38)	1.31 (0.85, 2.03)	1.31 (0.82, 2.10)	57 (37)	1.01 (0.66, 1.53)	1.03 (0.65, 1.62)

^a values for top tertile of hsTnT= 14.34-407.10 ng/l, reference group= <14.34 ng/l; for NT-proBNP= 226-15899 ng/l, reference group= <226 ng/l

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

^c <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Chapter 6. Cross-Sectional Associations of Oral Health Problems with Diet Quality and Dietary Intake in Older People in the UK and USA

6.1. Summary

Oral health problems in older age may influence food habits and diet quality. Diet quality has been implicated in the pathway linking poor oral health with disability in older people. However, recent studies have provided inconsistent findings for the association between objective oral health problems and diet. Furthermore, less attention has been given to subjective oral health problems. This Chapter examines the cross-sectional associations of objective and subjective oral health problems with diet quality and dietary intake in community-dwelling older people. Furthermore, the association between change in diet quality over a period of 10 years and oral health problems later in life was investigated. Data from two population-based studies were used. The British Regional Heart Study (BRHS) included data from a) 4252 older British men aged 60-79 years (first time point) and b) 2147 individuals aged 71-92 years (second time point). The Health, Aging, and Body Composition (HABC) Study comprised 3075 older men and women aged 71-80 years (only one time point) living in Pittsburgh and Memphis, USA. Objective oral health problems included number of natural teeth (tooth loss), and periodontal disease (loss of attachment, pocket depth). Subjective problems consisted of self-rated oral health, dry mouth, difficulty eating, sensitivity to hot/cold/sweets (BRHS), and limitation of food because of gum problems (HABC Study). A composite variable for accumulation of oral health problems was also created. Logistic and ordinal regressions were conducted to test these associations. Tooth loss, fair/poor self-rated oral health, and cumulative oral health problems were associated with poor diet quality in the BRHS (odds ratio (OR)=1.57, 95% CI 1.05-2.34; OR=1.51, 95% CI 1.14-1.99; OR=1.83, 95% CI 1.11-3.01, respectively). Persistent poor diet quality (60-79 to 71-92 years) was associated with tooth loss and cumulative oral health problems at 71-92 years in the BRHS. Both objective and subjective oral health problems were associated with high intakes of calories, saturated and trans-fatty acids, and processed meat as well as

low intakes of fruits and vegetables, and vitamins after adjusting for confounders. Cumulative oral health problems were also associated with high/low intakes of several nutrients (total calories, saturated fat, processed meat, fruits and vegetables, α -tocopherol, and vitamin D). In summary, poor oral health was associated with greater odds of poor diet quality and poor dietary intake in older people in the UK and USA.

6.2. Introduction

In previous Chapters it has been established that poor oral health is associated cross-sectionally with disability (Chapter 4) and several markers of inflammation (Chapter 5). As mentioned in Chapter 2 (sub-section 2.5.2), oral conditions have also been found to be associated with poor diet quality and low intakes of specific nutrients, in a number of cross-sectional studies (Ritchie *et al.*, 2002; Hung *et al.*, 2005; Zhu and Hollis, 2014; Iwasaki *et al.*, 2016a; Hamasaki *et al.*, 2017). However, these studies have reported inconsistent results, with some studies observing associations, while others failed to report any (Ervin and Dye, 2009; Gaewkhiew *et al.*, 2017). The majority of studies have focused on the associations of tooth loss and periodontal disease (objective) with diet quality and intake of specific nutrients. As a result, there is limited evidence on the cross-sectional associations between subjective measures of oral health, including dry mouth and self-rated oral health (Iwasaki *et al.*, 2016a). In particular, for dry mouth, information is lacking about the relationship with diet quality, and intakes of various nutrients in older people. Dry mouth may lead to the consumption of fewer nutritious foods (Iwasaki *et al.*, 2016a) and therefore it could be associated with poor diet quality in older populations. Moreover, few studies have examined the relationships of the accumulation of oral problems, and subsequent oral health burden, with diet quality and intake of nutrients.

Previous studies (Chapter 2, sub-section 2.5.2) have also indicated that poor diet quality can influence oral health status, suggesting a bi-directional association (Iwasaki *et al.*, 2011a; Iwasaki *et al.*, 2018a) (see Figure 6.1, page 169). However, few oral health problems have been studied (tooth loss, periodontal disease), while the associations with subjective oral health problems remain unknown. Establishing bi-directional associations can highlight (a) the importance of oral health in

maintaining good health as well as (b) the need to promote diet intervention programmes for the improvement of oral health.

Furthermore, few studies have included a wide range of nutrients, including intake of proteins, fruits and vegetables, saturated and trans-fatty acids, and vitamins. Further research is required to clarify the associations of poor oral health with diet quality and nutrient intake, and the potential bidirectionality of these associations in older community-dwelling people. Establishing these associations can help understand the ways that diet influences not only oral health and vice versa, but also pinpoint the exact diet components which are implicated in the pathway connecting oral health with chronic conditions, particularly disability, in older people.

6.3. Aim and Objectives

This Chapter aims to investigate the associations of objective and subjective oral health problems with diet quality and dietary intake in older people. The specific objectives of this Chapter are:

- I. To investigate the cross-sectional associations of objective and subjective oral health problems with diet quality and dietary intake in community-dwelling older people.
- II. To investigate the associations between change in diet quality and objective and subjective oral health problems in community-dwelling older people in the BRHS only.

6.4. Methods

Analyses on this Chapter are based on data from the BRHS and HABC Study. An overview of both studies has been presented in Chapter 3 (sections 3.2 and 3.5). Relevant data for the analyses of this Chapter's objectives will be described below.

6.4.1. Subjects and methods of data collection

In the BRHS, cross-sectional data from the 30-year re-examination in 2010-2012 were used, where participants aged 71-92 years. To calculate change in diet quality, data from the 20-year re-examination (1998-2000) were also utilised, where 4252 participants (77% response rate) aged 60-79 years completed postal questionnaires and took part in the physical examination. Information on diet was provided by Food Frequency Questionnaires (FFQ). More details are provided in Chapter 3 (sections 3.2 and 3.3).

In the HABC Study, cross-sectional data from Year 2 in 1998-1999 were used, where participants aged 71-80 years. Information on diet was derived from FFQs. Further details are presented in Chapter 3 (sections 3.5 and 3.6).

6.4.2. Oral health

6.4.2.1. Objective oral health problems

Number of teeth and periodontal disease were assessed by trained professionals in both studies. Tooth loss was classified as a 5-level variable (0, 1-7, 8-14, 15-20, ≥ 21 teeth). Having ≥ 21 teeth indicated a functional dentition (Hobdell *et al.*, 2003). Periodontal disease was measured according to Extent and Severity Index (Carlos *et al.*, 1986) and included loss of attachment and pocket depth. Then it was grouped in two binary variables according to percentage of sites affected ($>20\%$ sites affected vs. $\leq 20\%$ sites). Further details can be found in Chapter 3 (sub-sections 3.3.1 and 3.6.1).

6.4.2.2. Subjective oral health problems

Data from questionnaires were used to assess dry mouth, self-rated oral health, difficulty eating, sensitivity to hot/cold/sweets, limitation of food due to problems with teeth or dentures. More details on these markers can be found in Chapter 3 (sub-sections 3.3.1. and 3.6.1).

6.4.3. Dietary Intake

In the BRHS, dietary Intake was measured at two time points: at the 20-year (1998-2000) and at the 30-year re-examination in 2010-2012 through a self-administered postal FFQ which assessed frequency (1, 2, 3, 4, 5, 6, or 7 days per week, monthly, or rarely/never) of consuming 86 food and drink items, as detailed in Chapter 3 (sub-section 3.3.6) (see Appendix E, page 329 for a copy of the FFQ). The total macro- and micronutrient intakes were calculated by a validated computer programme which is based on UK food composition tables (Holland *et al.*, 1991; Atkins *et al.*, 2014). Caloric intake was then calculated according to the intakes of macro- and micronutrients. In this Chapter, dietary intake included protein, fruits and vegetables, calories from total and saturated fat, vitamin C, and α -tocopherol. All nutrients, excluding protein, were divided into quartiles.

In the HABC Study, dietary intake was assessed at Year 2 via a 108-item, interviewer-administered modified version of the Block FFQ (Block Dietary Data Systems) (Hengeveld *et al.*, 2018). This FFQ was designed for the HABC Study according to 24-h recall data from the NHANES III for >65 years old African-American and white adults (Hengeveld *et al.*, 2018), as described in Chapter 3 (sub-section 3.6.6) (see Appendix H, page 347 for a copy of the FFQ). Frequency of food consumption was assessed through the following responses: never, 1-11 times/year, once/month, 2-3 times/month, once/week, twice/week, 3-4 times/week, 5-6 times/week, and every day. The intakes of energy, macronutrients, and food groups were calculated by Block Dietary Data Systems (Berkeley, California) (Hengeveld *et al.*, 2018). Dietary intake consisted of protein, fruits and vegetables, percentage of calories from total, saturated, and trans-fatty acids, percentage of energy from sweets and sodas, and vitamin D. All nutrients, excluding protein, were divided into quartiles.

In both studies, in order to further examine the association between poor oral health and fat intake, a variable about the frequency of consumption of processed meat was created. In the BRHS, processed meat comprised consumption of bacon, salami, tinned meat, corned beef, pork and beef sausages, meat pie and pasties

were used to create this variable. In the HABC Study, it consisted of ham, bacon, sausage, bologna, and fried chicken. This variable was then categorised as: monthly/rarely (low), 1 type of processed meat ≥ 2 times per week (moderate), 2 types of processed meat ≥ 2 times per week (high). Additionally, protein intake was defined as g/kg body weight/day. In the BRHS, protein intake was classified as low (<0.75 g/kg/d) and high (≥ 0.75 g/kg/d) (Department of Health, 1991). In the HABC Study, were grouped as low (<0.8 g/kg/d) and high (≥ 0.80 g/kg/d) (Institute of Medicine, 2005).

6.4.4. Diet quality

Diet quality was measured by using two dietary predefined diet scores – the Elderly Dietary Index (EDI) in the BRHS, and the Health Eating Index (HEI) in the HABC Study.

6.4.4.1. The Elderly Dietary Index

The EDI was developed to assess adherence to nutritional recommendations, according to the US Modified MyPyramid for Older Adults (Kourlaba *et al.*, 2009). The EDI score includes 9 food components: meat, fish and seafood, legumes, fruit, vegetables, cereals, bread, olive oil and dairy. According to the frequency of consumption each of these components is assigned a 4-point scoring system, resulting to a score ranging from 9 to 36 points (Atkins *et al.*, 2014). The frequency of olive oil consumption was not available so scoring was adapted by using the quantity of weekly consumption (1 = never/rarely consumed; 2-4 = tertiles 1-3 of intake for those who did consume olive oil) (Atkins *et al.*, 2014). For fruits, vegetables, cereals and olive oil, the highest consumption was assigned a score equal to 4. However, score 4 was assigned for moderate consumption (1-2 days/week) for meat, fish/seafood, and legumes. For dairy, score 4 was assigned for low fat milk and cheese intake. For bread intake, individuals were assigned a score 4 when they consumed only whole grain bread (Atkins *et al.*, 2014). High EDI scores represent a healthy diet. In this study, EDI scores were divided to quartiles, with the lowest

quartile indicating poor diet quality and the highest indicating good diet quality. Change in EDI scores over a 10-year follow up time (60-79 to 71-92 years) was calculated as 1=persistent poor EDI score, 2=decrease in score, 3= improvement of score, 4=persistent good score.

6.4.4.2. *The Healthy Eating Index (HEI)*

In the HABC Study, diet quality was measured via the HEI, which was developed to assess adherence to the Dietary Guidelines for Americans of 1995 and the Food Pyramid of 1992 (Kennedy *et al.*, 1995; Bowman *et al.*, 1998; Hengeveld *et al.*, 2018). The HEI score consists of 10 components; 9 food components (grains, vegetables, fruit, milk, and meat, intakes of percentages of calories from total and saturated fat, total cholesterol, and total sodium) and 1 component which assess diet variety. The first five components (grains, vegetables, fruits, milk, and meat) measure how well the individual adheres to the age- and sex-specific serving recommendations, as specified in the Food Guide Pyramid; the next four show how well the individual follows the dietary recommendations for intakes of total and saturated fat (percentages of caloric intake), total cholesterol, and total sodium; while the last component assesses variety of diet (Hengeveld *et al.*, 2018). Each of these 10 components is assigned a score ranging from 1 to 10, resulting in a total HEI score from 0-100 (Hengeveld *et al.*, 2018). Similar to EDI score, high HEI score reflects good diet quality, whereas low score represents poor diet quality. In this Chapter, HEI scores were categorised into 3 groups: poor (<51), needs improvement (51-80), and good (>80) (Bowman *et al.*, 1998).

In nutritional research, it is common practice to divide dietary variables in quartiles. Quartiles can be applied to data that are not symmetrically distributed and those which have outliers and can also reflect low and high intakes of nutrients. Generally, quartiles are useful in observing the extreme values of available data, particularly values which are in the first (0-25%) or fourth percentiles (75-100%). Extreme values can represent adverse intakes of nutrients which can be detrimental to health.

6.4.5. Socio-demographic, lifestyle factors, and chronic diseases

In both studies, information on socioeconomic status, smoking, alcohol, history of cardiovascular disease (CVD), and history of diabetes were measured through questionnaires. BMI (weight/height²) was classified as normal, overweight, and obese. Caloric intake was calculated from FFQs and was defined as kcal/day. Information on the number of prescribed medications causing xerostomia was also used. More details can be found in Chapter 3 (sub-sections 3.3.2 and 3.6.2).

6.4.6. Statistical Analysis

For each study separate logistic and ordinal regressions were performed. These regression models assessed the associations of objective and subjective oral health problems with diet quality and dietary intake in older people. For the intakes of percentage of calories from saturated, trans-fatty acids, and soda and sweets the top quartiles were the outcomes in the logistic regression models and the rest of the quartiles were combined in one group. For vitamins C, D, and α -tocopherol the bottom quartiles were the outcome measure in logistic regression. Categories of high and low fruits and vegetables intake were created based on the recommended values of fruits and vegetables. In the BRHS individuals with intake smaller than 5 portions/day and in the HABC Study participants with intake smaller than 6 portions/day were classified as having low intake of fruits and vegetables (Food Standards Agency, 2016; U.S. Department of Health and Human Services and U.S. Department of Agriculture, December 2015). In the HABC study, for diet quality, poor HEI score (<51) was the outcome of interest, and the other two groups were combined. In the BRHS, the bottom quartile of EDI score was the outcome, and the other three quartiles were combined. Ordinal regression was performed to examine the associations between poor oral health and processed meat. In both studies, the first category of processed meat (0, consuming processed meat monthly/rarely- indicating low intake) was the reference in ordinal regression. Ordinal and logistic regression were conducted to study the associations between change in EDI scores (60-79 to 71-92 years) and oral health problems at age 71-92 years. For all analyses odds ratios (OR) and their 95% CIs were reported. In the BRHS, regression models

were adjusted for age, social class, smoking, alcohol, history of CVD and diabetes, BMI. Some of the models were further adjusted for caloric intake (continuous). In the HABC Study, age, gender, race, education, smoking, alcohol, history of CVD and diabetes, and BMI were entered in the models as confounders. Again, some of these models were further adjusted for caloric intake (continuous).

6.5. Results

Prevalence of oral health problems and population characteristics has been presented in Chapter 4 (Table 4.1).

6.5.1. Associations of oral health problems with diet quality

Table 6.1 shows the odds ratios (OR) with 95% confidence intervals (CI) for the association of objective and subjective oral health problems with poor diet quality in the BRHS and HABC Study.

In the BRHS, having 0, 1-7, 8-14, and 15-20 teeth when compared to ≥ 21 teeth were associated with the bottom quartile of EDI score (poor diet quality), in the age adjusted model (n=1496). After adjusting for age, social class, smoking, alcohol, history of CVD and diabetes, BMI, and caloric intake (n=1335), only the association for 8-14 teeth remained (OR=1.57, 95% CI 1.05-2.34). Fair/poor self-rated oral health was associated with the bottom quartile of EDI score in both age (n=1841) and fully adjusted models (n=1343) (OR=1.56, 95% CI 1.25-1.94; OR=1.51, 95% CI 1.14-1.99, respectively). Dry mouth symptoms were not associated with poor diet quality. Lastly, ≥ 3 oral health problems was associated with poor diet quality after adjustment for confounders (n=1388) (OR=1.83, 95% CI 1.11-3.01).

In the HABC Study, having 0, 1-7 and 15-20 teeth when compared to ≥ 21 teeth were associated with poor HEI score (<51), in the age adjusted models (n=1938) (OR=1.78, 95% CI 1.03-3.08; OR=2.17, 95% CI 1.27-3.70; OR=1.74, 95% CI 1.11-2.74, respectively). These associations did not remain after adjusting for age, gender, race, education, smoking, alcohol, history of CVD and diabetes, and BMI

(n=1908). Periodontal disease was associated with poor diet quality in the age adjusted model (n=1127) (OR=2.21, 95% CI 1.33-3.70), but did not remain after adjustment (n=1110) (OR=1.69, 95% CI 0.98-2.94). Fair/poor self-rated oral health (n=2709), dry mouth (n=2708), and cumulative oral health problems (n=2720) (2 vs. 0 oral health problems) were associated with poor diet quality only in the age adjusted models (OR=1.68, 95% CI 1.26-2.24; OR=1.84, 95% CI 1.03-3.29; OR=1.64, 95% CI 1.03-2.63).

6.5.2. Associations of oral health problems with dietary intake

Table 6.2 presents the ORs and 95% CIs for the association between objective and subjective oral health problems and high intakes of calories, and percentage of calories from saturated fat. The associations between poor oral health and low intake of fruits and vegetables in the BRHS are presented in Table 6.3.

Having 15-20 teeth (vs. ≥ 21 teeth) was associated with the top quartile of caloric intake in the fully adjusted model (n=1413) (OR=1.54, 95% CI 1.11-2.16). Additionally, having 0 teeth (vs. ≥ 21 teeth) was associated with low intake of fruits and vegetables after adjusting for confounders (n=1413) (OR=1.04, 95% CI 1.04-2.78). Periodontal disease was not associated with high caloric intake, high intake of percentage of calories from saturated fat, or low intake of fruits and vegetables. Fair/poor self-rated oral health was associated with the top quartile of percentage of calories from saturated fat (n=1291) and low intake of fruits and vegetables (n=1420) after full adjustment (OR=1.34, 95% CI 1.02-1.77; OR=1.66, 95% CI 1.16-2.37, respectively). Having ≥ 3 dry mouth symptoms was associated with the top quartile of caloric intake in both age (n=1889) and fully adjusted models (n=1422) (fully adjusted, OR=1.58, 95% CI 1.17-2.13). Having ≥ 3 oral health problems was associated with top quartiles of caloric (n=1469) and saturated fat intakes (n=1336) in the fully adjusted models.

Table 6.4 shows ORs and 95% CIs for the associations of objective and subjective oral health problems and high intakes of calories, and percentage of calories from saturated fat in the HABC Study. Table 6.3 shows the associations between poor oral health and low intake of fruits and vegetables in the HABC study. Having 0 teeth

when compared to ≥ 21 teeth was associated with the top quartile of caloric intake (n=1944) and low intake of fruits and vegetables (n=1973) in the age adjusted models. After adjustment (n=1913) only the association for low fruit and vegetables consumption remained (OR= 1.56, 95% CI 1.03-2.34). Having 1-7 teeth (vs. ≥ 21 teeth) was associated with top quartiles of caloric (n=1944) and percentage of energy from saturated fat (n=1930) intakes in the age adjusted models, but did not remain after adjusting for confounders. Having 8-14 teeth (vs. ≥ 21 teeth) was associated with high caloric intake only in the age adjusted model (n=1944). Similarly, 15-20 teeth was associated with increased intake of saturated fat only in the age adjusted model (n=1930). Periodontal disease (loss of attachment) was associated with high intake of percentage of calories from saturated fat after adjusting for confounders (n=1112) (OR= 1.48, 95% CI 1.09-2.01), whereas pocket depth was associated with high caloric intake in the fully adjusted model (n=1121) (OR=1.75, 95% CI 1.29-2.37). Fair/poor self-rated oral health was associated with high caloric intake only in the age adjusted model (n=2718). No associations were reported for dry mouth. Furthermore, ≥ 3 oral health problems was associated with high caloric intake in both age (n=2732) and fully adjusted models (n=2706) (fully adjusted, OR=1.49, 95% CI 1.04-2.15).

The associations between oral health problems and processed meat in the BRHS can be found in Table 6.5. Having 0, and 15-20 teeth (vs. ≥ 21 teeth) were associated with high intake of processed meat (≥ 2 types of processed meat ≥ 2 times per week) after adjusting for age, social class, smoking, alcohol, history of CVD and diabetes, and BMI (n=1504) (fully adjusted, OR= 1.63, 95% CI 1.06-2.49; OR=1.51, 95% CI 1.01-2.27, respectively). Periodontal disease was associated with high intake of processed meat only in the age adjusted model (n=1245). Fair/poor self-rated oral health was not associated with high consumption of processed meat. Having ≥ 3 dry mouth symptoms was associated with high intake of processed meat only in the age adjusted model (n=2034) (OR=1.38, 95% CI 1.03-1.85). Furthermore, ≥ 3 oral health problems was associated with high consumption of processed meat after adjustment for confounders (n=1561) (OR=2.16, 95% CI 1.22-3.18). When caloric intake was entered in the fully adjusted models, associations for tooth loss, and cumulative oral health problems did not remain.

Associations between oral health problems and processed meat in the HABC study are presented in Table 6.6. Having 0, 1-7, and 8-14 teeth when compared to ≥ 21 teeth was associated with high intake of processed meat in the age adjusted models (n=1973), but these associations did not remain after adjustment for confounders (n=1926). Periodontal disease was associated with high intake of processed meat in the fully adjusted model (n= 1121) (OR=1.70, 95% CI 1.17-2.46). Fair/poor self-rated oral health and dry mouth were not associated with increased consumption of processed meat. Cumulative oral health problems were associated with moderate consumption of processed meat but not with high after adjustment for confounders (n=2706) (moderate consumption, ≥ 3 problems vs. 0, OR=1.80, 95% CI 1.24-2.60).

Table 6.7 presents the ORs and 95% CIs for the associations of objective and subjective oral health problems with percentages of calories from trans-fatty acids and sweets and sodas in the HABC study. These variables were available only in the HABC Study. Having 0, and 1-7 teeth when compared to ≥ 21 teeth were associated with high intake of trans-fatty acids in both age (n=1930) and fully adjusted models (n=1913) (fully adjusted, OR= 1.73, 95% CI 1.20-2.50; OR=1.69, 95% CI 1.16-2.47, respectively). For 1-7 teeth (vs. ≥ 21 teeth) borderline associations with high intake of energy from sweets and soda were observed in both age (n=1944) and fully adjusted models (n=1926) (fully adjusted, OR= 1.47, 95% CI 1.00-2.16). Periodontal disease was associated with high intake of energy from sweets and soda only in the age adjusted model (n=1132). No associations were observed for fair/poor self-rated oral health. Moreover, a borderline association was reported for dry mouth (yes vs. no) and high intake of energy from sweets and soda in the fully adjusted model (n=2696) (OR=1.53, 95% CI 1.00-2.34). Cumulative oral health problems (≥ 3 problems vs. 0) were associated with high intake of sweets and soda in the fully adjusted model (n=2706) (OR= 1.65, 95% CI 1.15-2.36).

Table 6.8 shows the ORs and 95%CI for the association between oral health problems and protein intake in the BRHS and HABC Study. In the BRHS, having 15-20 teeth was associated with low intake of protein after adjusting for confounders (n=1413) (OR=1.90, 95% CI 1.19-3.04). No further associations were reported in the BRHS. In the HABC Study no associations were observed for oral health problems and protein intake.

Associations between oral health problems and intakes of a-tocopherol and vitamin C in the BRHS and intake of vitamin D in HABC Study are presented in Table 6.9. In the BRHS, having 0, 1-7, 8-14, 15-20 teeth (vs. ≥ 21 teeth) were associated with the bottom quartile of a-tocopherol intake in the age adjusted models (n=1363) and with the exception of 8-14 teeth, these associations remained after adjusting for confounders (n=1256) (0 teeth, OR=2.20, 95% CI 1.40-3.46; 1-7 teeth, OR=2.08, 95% CI 1.13-3.86; 15-20 teeth, OR=1.71, 95% CI 1.12-2.60). Periodontal disease was associated with the bottom quartile of a-tocopherol in both age (n=1049) and fully adjusted models (n=972) (fully adjusted, OR=1.67, 95% CI 1.12-2.49). Fair/poor self-rated oral health was associated with the bottom quartile of vitamin C in both age (n=2007) and fully adjusted models (n= 1420) (fully adjusted, OR=1.38, 95% CI 1.04-1.84). No associations were observed for dry mouth. Lastly, cumulative oral health problems were associated with the bottom quartile of a-tocopherol intake in the fully adjusted model (n=1306) (≥ 3 problems vs. 0, OR= 2.06, 95% CI 1.10-3.87).

In the HABC Study, complete tooth loss (0 teeth vs. ≥ 21 teeth) was associated with the bottom quartile of vitamin D, in the age adjusted model (n=1944) but did not remain after adjustment for confounders (n=1913). No associations were observed for periodontal disease, fair/poor self-rated oral health, and dry mouth. Having at least 3 oral health problems was associated with low intake of vitamin D in both age (n=2732) and fully adjusted (n=2688) models (fully adjusted, OR=1.77, 95% CI 1.21-2.58).

6.5.3. Change in EDI score and prevalence of oral health problems (10 years follow up)

Table 6.10 presents the ORs and 95% CIs for the association of change in EDI scores over a 10-year follow-up (age 60-79 to 71-92 years) with poor oral health at 71-92 years. This analysis was performed only in the BRHS. Groups which did not have good EDI scores at both time points (improved score over 10 years, decreased score over 10 years, low score at both time points vs. good score at both time points) were associated with partial tooth loss (<21 teeth vs. ≥ 21 teeth) in the age adjusted model (n=980). After adjustment (n=924) only the association between having low EDI score at both time points and partial tooth loss remained (OR=1.66, 95% CI

1.09-2.52). Furthermore, improvement of EDI score over 10 years and low score at both time points when compared to good EDI score at both time points were associated with periodontal disease at 71-92 years in the age adjusted model (n=754), but these associations did not remain after full adjustment (n=715). Low EDI score at both time points was associated with fair/poor self-rated oral health only in the age adjusted model (n=1178) (OR=1.44, 95% CI 1.03-2.01). Decrease in diet quality over 10 years (vs. good EDI score at both time points) was associated with ≥ 3 dry mouth symptoms in the age adjusted model (n=1179) (OR= 1.65, 95% CI 1.11-2.43), but did not remain in the fully adjusted model (n=1111). Decrease in EDI score, and persistent low EDI score over 10 years were associated with cumulative oral health problems at 71-92 years in the age adjusted model (n=1217), with the associations for 2 oral problems remaining after adjusting for confounders (n=1149) (2 problems vs. 0, OR=1.81, 95% CI 1.08-3.03; OR=1.96, 95% CI 1.07-3.56, respectively).

6.6. Discussion

6.6.1. Summary of findings

In this Chapter, the cross-sectional associations of objective and subjective oral health problems with diet quality and dietary intake were investigated in two population-based studies of older people living in the UK and USA. In the BRHS, tooth loss, fair/poor self-rated oral health, and cumulative oral health problems were associated with poor diet quality, whereas in the HABC study no associations were reported after full adjustment. Additionally, in the BRHS persistent low and declining diet quality were associated with tooth loss and cumulative oral health problems at age 71-92 years. Oral health problems were also associated with high intakes of total energy, calories from saturated and trans-fatty acids, processed meat, calories from sweets and soda, and low intake of fruits and vegetables. In the BRHS, partial tooth loss was associated with low protein intake, whereas no associations were observed in the HABC Study. Furthermore, in the BRHS fair/poor self-rated oral health was associated with low intake of vitamin C; tooth loss, periodontal disease,

and cumulative oral health problems with low intake of α -tocopherol (BRHS); and in the HABC Study cumulative oral problems with low intake of vitamin D.

6.6.2. Comparison with previous studies

6.6.2.1. Oral health problems and diet quality

In the BRHS, partial tooth loss, fair/poor self-rated oral health, and cumulative oral health problems were associated with poor diet quality (bottom quartile of EDI scores). Previous studies have reported similar findings (Ritchie *et al.*, 2002; Zhu and Hollis, 2014). Chewing ability is interrelated with tooth loss, and particularly tooth loss can affect perceived chewing ability of individuals (Moynihan and Bradbury, 2001). Older individuals suffering from tooth loss and subsequent chewing difficulties have been found to be more likely to lose their appetite and be malnourished which subsequently influences their diet quality (Dion *et al.*, 2007).

A relationship between fair/self-rated oral health and diet quality was also reported. Previous studies have not examined this specific association. However, one study reported that chewing disability which is a result of tooth loss, can significantly impact oral health related quality of life in older people, which can reflect poor self-rated oral health (Bortoluzzi *et al.*, 2012). Therefore, fair/poor self-rated health as a consequence of incremental tooth loss and chewing difficulties may influence further food choices and diet quality. Moreover, the association between cumulative oral health problems and poor diet quality indicates that the presence of more than one oral conditions can impact diet quality in older people. Interestingly, no associations were observed in the HABC Study for diet quality, after adjusting for confounders. Nevertheless, the small number of individuals in the low HEI score group, may have influenced these results. It is possible that poor diet can have mediating effects on the association of oral health problems, including tooth loss, periodontal disease, and dry mouth with development of disability in older people (Bauer *et al.*, 2014). The mediating role of diet quality in the association between oral health problems and risk of developing disability will be examined in Chapter 7.

6.6.2.2. Oral health problems and dietary intake

Tooth loss was associated with high intake of total energy, percentages of calories from trans-fatty acids, and sweets and soda, increased consumption of processed meat, and low intake of α -tocopherol. These findings are supported by previous studies in adults (Joshi *et al.*, 1996; Hung *et al.*, 2005; Iwasaki *et al.*, 2016b). Chewing difficulties which are caused by tooth loss can lead to (a) avoidance of hard to chew food groups, including carrots and apples, solid bread, (b) lower consumption of fibre and many vitamins but also increased consumption of unhealthy foods (easier to chew), for example those high in fat (Joshi *et al.*, 1996; Sheiham *et al.*, 2001; Ritchie *et al.*, 2002; Bradbury *et al.*, 2008). However, a recent meta-analysis did not report any associations between complete tooth loss and nutritional status (Toniazzi *et al.*, 2018). Periodontal disease was also associated with increased intake of total energy, high consumption of calories from saturated fat, sweets and soda, and processed meat, as well as low intake of α -tocopherol. Previous studies have indicated that those with periodontal disease consumed more fatty acids (Jauhiainen *et al.*, 2016) and had lower levels of vitamin E (Najeeb *et al.*, 2016). Periodontal disease and tooth loss are closely linked, and tooth loss can be the result of periodontal disease, dental caries or accumulation of oral conditions (Friedman and Lamster, 2016). Periodontal disease is associated with high levels of inflammation, and it has been shown that diets rich in antioxidants can significantly improve the progression of this disease (Iwasaki *et al.*, 2011a; Najeeb *et al.*, 2016).

Fair/poor self-rated oral health was associated with high intake of saturated fat, and low intakes of fruits and vegetables and vitamin C. Again, self-rated oral health as an indicator of the general oral health status shows that poor oral health is associated with unhealthier dietary patterns. Furthermore, dry mouth was associated with high intake of total calories. Dry mouth, can cause difficulties in chewing and swallowing (Iwasaki *et al.*, 2016a) because it is an important factor in the process of food (Gupta *et al.*, 2006). Earlier research suggested an association between hyposalivation and low intake of fruits and vegetables (Iwasaki *et al.*, 2016a). It can be hypothesised that individuals with dry mouth symptoms similar to those with tooth loss avoid consumption of foods rich in nutrients and consume foods high in calories. Finally,

accumulation of oral health problems was associated with high intakes of total energy, saturated fat, processed meat, and low intakes of fruits and vegetables, α-tocopherol, and vitamin D. These findings support the suggested hypothesis that a compromised oral health status in older people can significantly impact food choices.

It should be mentioned that in both studies, there was high consumption of meat and fish, cakes/cookies/desserts as well as high intake of liquid and solid fats.

Additionally, mean intakes of percentages of energy from saturated and trans-fat were above the current recommendations (Institute of Medicine, 2005). For protein intake the only association observed was with partial tooth loss in the BRHS. The lack of other associations may be explained by the fact that in both populations mean intake of protein was above recommended levels (Department of Health, 2001; Institute of Medicine, 2005). Disentangling these associations between poor oral health and specific nutrients can help in designing programmes which are focused on improving oral health by targeting specific components of an individual's diet. These programmes can also help ameliorate the combined effect of diet and poor oral health on other health outcomes, such as disability and mortality.

6.6.2.3. Change in EDI score over 10 years and prevalence of oral health problems at age 71-92 years

Persistent poor diet quality was associated with tooth loss and cumulative oral health problems. This finding shows that poor diet quality is associated with higher prevalence of oral health problems later in life in older people. It has been reported that when a diet rich in antioxidants and vitamins, and low in saturated fatty acids was followed, fewer teeth were lost over time (Kotsakis *et al.*, 2018). Poor oral health, can influence eating behaviours and food preferences and choices and lead to poor diet quality, but at the same time a compromised diet can cause the development or deterioration of oral health problems (Moynihan, 2005).

6.6.3. Strengths and limitations

6.6.3.1. Strengths of this study

One of the strengths of this Chapter is that the associations between objective and subjective oral health problems with a range of nutrients were examined in two studies of older community-dwelling people. Furthermore, associations between diet quality and poor oral health later in life were investigated. Another important strength is that this Chapter provides information about the associations of subjective oral health problems (dry mouth, self-rated oral health) and diet quality and dietary intake, as previous studies have focused on tooth loss and periodontal disease.

6.6.3.2. Possible bias and limitations

The majority of analyses in this study were cross-sectional and therefore causal relationships could not be established. Furthermore, certain differences in the measurement of oral health problems (periodontal disease, dry mouth) were present between the two studies. Additionally, some dietary variables, such as calories from trans-fatty acids and sweets and soda, vitamin D, were not available in both studies. Additionally, different associations for oral health and diet quality were observed between the two studies. Diet quality was measured by using the EDI score in the BRHS and the HEI score in the HABC Study. It is possible that these different measures may explain the differences in reported results. Also, when the associations for tooth loss were examined, the use of dentures was not considered. Individuals with tooth loss who are wearing dentures may experience fewer eating problems because of the presence of dentures. However, ill-fitting dentures can significantly impact and exacerbate eating problems which are caused by tooth loss (Jones *et al.*, 2003; Nowjack-Raymer and Sheiham, 2003). Additionally, self-reported measures of oral health, may be prone to response bias (Ikebe *et al.*, 2007).

When dietary intake is assessed by self-reported measures, including the FFQ method, it can lead to misreporting of intakes and this can introduce bias in the form of measurement error (Livingstone and Black, 2003; Poslusna *et al.*, 2009). This can influence the estimation of energy and micronutrient intakes (Livingstone and Black, 2003; Poslusna *et al.*, 2009). Moreover, it is possible that higher rates of non-response in older populations may have contributed to further misreporting, and

particularly underreporting (Bussolotto *et al.*, 1999). Nevertheless the FFQs used in this study have been validated in the British and US populations (Yarnell *et al.*, 1983; Ahluwalia *et al.*, 2016; Hengeveld *et al.*, 2018). Additionally, FFQs were answered at one time point and thus it is not certain whether participants followed the same dietary habits throughout the entire study period. However, this Chapter assessed changes in diet quality over 10 years of follow-up and reported associations with oral health problems later in life in the BRHS.

Furthermore, as mentioned in Chapters 4 and 5, the populations that participated in the BRHS and HABC Study may not be representative of the whole older population of the UK and USA respectively. Moreover, individuals who attended the examinations and answered questionnaires may be healthier than those who did not provide data during this time point, and this may have resulted in underestimation of the reported results.

All associations were adjusted for a number of confounders in this study. Nevertheless, it is possible that other variables influencing these associations were not entered in the models, or were not measured, and therefore residual confounding may be present. Finally, a number of associations between poor oral health and diet were examined in this study, and therefore there is the potential of a risk of reporting false-positive results. As the number of hypothesis testing increases, so does the risk of observing false-positive results (Lindquist and Mejia, 2015).

6.7. Conclusions

Tooth loss, fair/poor self-rated oral health and cumulative oral health problems were associated with poor diet quality. In the BRHS, change in diet quality over 10 years was associated with tooth loss and cumulative oral health problems later in life.

Tooth loss, periodontal disease, fair/poor self-rated oral health, and cumulative oral health problems were associated with excess/inadequate intakes of nutrients.

Finally, diet quality, as well as high levels of inflammation have been implicated in the causal pathway linking oral health with disability in older people. Establishing these indirect effects will improve our understanding of the ways that oral health may influence important health outcomes in older people.

In the next Chapter, the associations of objective and subjective oral health problems with incidence of disability as well as the mediating effects of inflammation and diet will be examined.

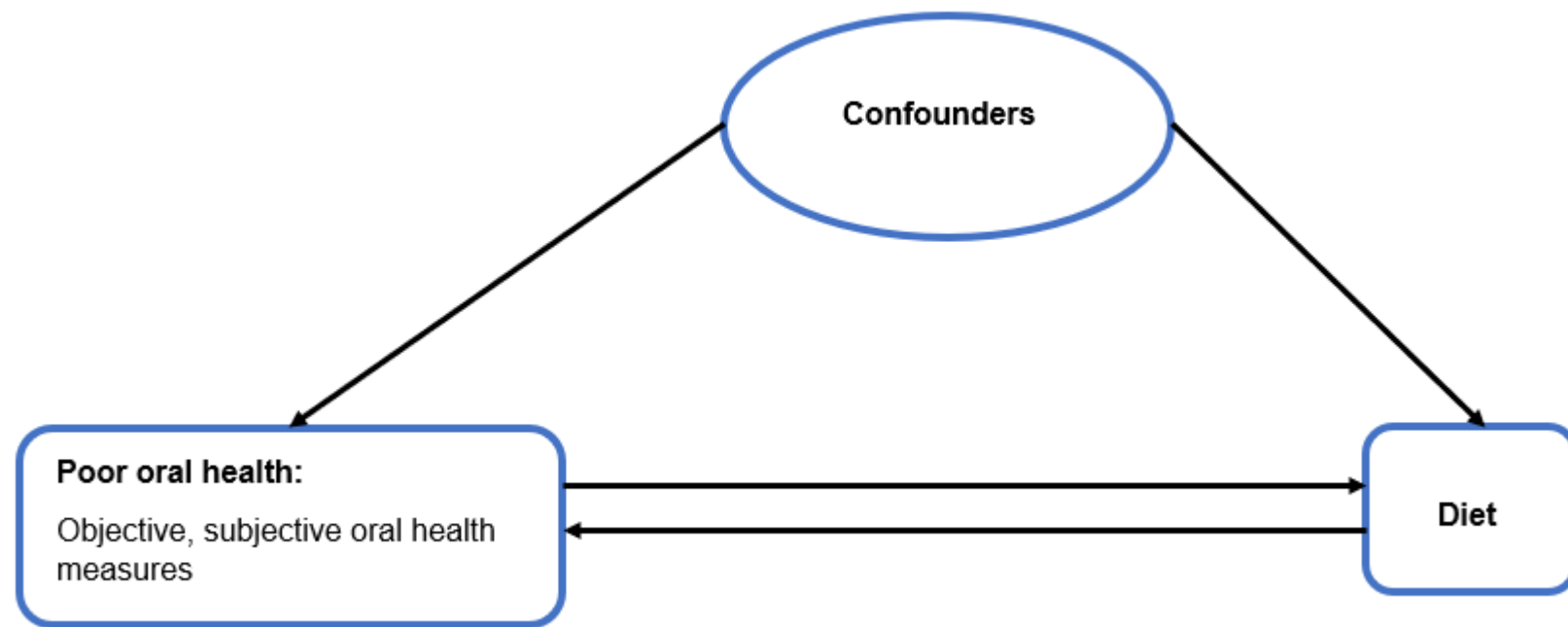


Figure 6.1. Bi-directional associations between poor oral health and diet

Table 6.1 Odds ratios (95%CI) for the associations of oral health problems with Elderly Dietary Index (EDI) and Healthy Eating Index (HEI) scores in older British men aged 71-92 years (BRHS) and older American men and women aged 71-80 years (HABC study).

BRHS				HABC Study			
Bottom quartile of EDI score (11-22) ^a (n=470; 25%)				Low HEI score (<51) ^a (n=216; 8%)			
Oral Health Problems		Age adjusted	Fully adjusted ^b	Oral Health Problems		Age adjusted	Fully adjusted ^c
	N (%)	OR (95% CI)	OR (95% CI)		N (%)	OR (95% CI)	OR (95% CI)
Tooth loss		<i>N=1496</i>	<i>N=1335</i>	Tooth loss		<i>N=1938</i>	<i>N=1908</i>
≥21 teeth	90 (16)	1.00	1.00	≥21 teeth	53 (6)	1.00	1.00
15-20 teeth	69 (23)	1.47 (1.03, 2.08)	1.30 (0.89, 1.90)	15-20 teeth	34 (10)	1.74 (1.11, 2.74)	1.18 (0.72, 1.94)
8-14 teeth	65 (27)	1.84 (1.28, 2.65)	1.57 (1.05, 2.34)	8-14 teeth	24 (9)	1.57 (0.95, 2.60)	0.99 (0.57, 1.73)
1-7 teeth	28 (26)	1.74 (1.07, 2.85)	1.54 (0.90, 2.62)	1-7 teeth	21 (12)	2.17 (1.27, 3.70)	1.19 (0.65, 2.17)
0 teeth	79 (27)	1.76 (1.24, 2.49)	1.34 (0.90, 2.01)	0 teeth	19 (10)	1.78 (1.03, 3.08)	0.87 (0.46, 1.64)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=1135</i>	<i>N=1026</i>	Periodontal disease (% of sites with loss of attachment ≥3 mm)		<i>N=1127</i>	<i>N=1110</i>
≤20%	167 (19)	1.00	1.00	≤20%	20 (5)	1.00	1.00
>20%	67 (24)	1.33 (0.96, 1.84)	1.28 (0.89, 1.82)	>20%	71 (10)	2.21 (1.33, 3.70)	1.69 (0.98, 2.94)
Self-rated oral health		<i>N=1841</i>	<i>N=1343</i>	Self-rated oral health		<i>N=2709</i>	<i>N=2668</i>
Excellent or good	255 (21)	1.00	1.00	Excellent or good	126 (7)	1.00	1.00
Fair or poor	189 (30)	1.56 (1.25, 1.94)	1.51 (1.14, 1.99)	Fair or poor	89 (11)	1.68 (1.26, 2.24)	1.29 (0.94, 1.77)
Dry mouth symptoms		<i>N=1841</i>	<i>N=1344</i>	Dry mouth		<i>N=2708</i>	<i>N=2667</i>
0	165 (24)	1.00	1.00	No	201 (8)	1.00	1.00
1-2	140 (23)	0.93 (0.71, 1.20)	0.85 (0.61, 1.17)	Yes	14 (13)	1.84 (1.03, 3.29)	1.63 (0.86, 3.10)
≥3	141 (25)	1.02 (0.79, 1.33)	1.09 (0.79, 1.52)				

^a BRHS: reference group values= 23-33; HABC Study: reference group values= 51-99

^b age, social class, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^c age, gender, race, education, smoking, alcohol, history of CVD and diabetes, BMI

Table 6.1 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with Elderly Dietary Index (EDI) and Healthy Eating Index (HEI) scores in older British men aged 71-92 years (BRHS) and older American men and women aged 71-80 years (HABC study).

BRHS				HABC Study			
Bottom quartile of EDI score (11-22) ^a (n=470; 25%)				Low HEI score (<51) ^a (n=216; 8%)			
Oral Health Problems		Age adjusted	Fully adjusted ^b	Oral Health Problems		Age adjusted	Fully adjusted ^c
	N (%)	OR (95% CI)	OR (95% CI)		N (%)	OR (95% CI)	OR (95% CI)
Cumulative oral health problems^d		<i>N=1907</i>	<i>N=1388</i>	Cumulative oral health problems^e		<i>N=2720</i>	<i>N=2677</i>
0	53 (17)	1.00	1.00	0	42 (6)	1.00	1.00
1	234 (26)	1.64 (1.17, 2.28)	1.12 (0.78, 1.62)	1	122 (9)	1.70 (1.19, 2.45)	1.12 (0.75, 1.67)
2	120 (25)	1.55 (1.08, 2.22)	0.97 (0.64, 1.48)	2	34 (9)	1.64 (1.03, 2.63)	0.91 (0.54, 1.56)
≥3	63 (31)	2.06 (1.35, 3.15)	1.83 (1.11, 3.01)	≥3	18 (8)	1.49 (0.84, 2.65)	0.73 (0.38, 1.38)

^a BRHS: reference group values= 23-33; HABC Study: reference group values= 51-99

^b age, social class, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^c age, gender, race, education, smoking, alcohol, history of CVD and diabetes, BMI

^d <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

^e <21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problem

Table 6.2. Odds ratios (95%CI) for the associations of oral health problems with top quartiles of caloric intake, and percentage of energy from saturated fat in older British men aged 71-92 years in the BRHS.

Oral Health Problems	Top quartile of caloric intake (2,274-4,965 kcal/day) ^a (n=490; 25%)			Top quartile of % of calories from saturated fat (14.14-32.5%kcal/day) ^a (n=446; 25%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Tooth loss		<i>N=1539</i>	<i>N=1413</i>		<i>N=1399</i>	<i>N=1283</i>
≥21 teeth	117 (21)	1.00	1.00	107 (21)	1.00	1.00
15-20 teeth	92 (29)	1.59 (1.16, 2.18)	1.54 (1.11, 2.16)	63 (22)	1.03 (0.72, 1.46)	0.95 (0.65, 1.37)
8-14 teeth	68 (28)	1.46 (1.03, 2.06)	1.43 (0.99, 2.07)	62 (28)	1.37 (0.95, 1.98)	1.32 (0.89, 1.96)
1-7 teeth	28 (26)	1.33 (0.83, 2.15)	1.26 (0.75, 2.10)	30 (32)	1.62 (1.00, 2.64)	1.41 (0.83, 2.40)
0 teeth	76 (25)	1.29 (0.92, 1.80)	1.12 (0.77, 1.63)	58 (21)	0.89 (0.62, 1.29)	0.71 (0.47, 1.08)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=1169</i>	<i>N=1082</i>		<i>N=1063</i>	<i>N=985</i>
≤20%	213 (24)	1.00	1.00	177 (22)	1.00	1.00
>20%	79 (28)	1.21 (0.89, 1.64)	1.19 (0.86, 1.63)	72 (28)	1.32 (0.96, 1.81)	1.27 (0.90, 1.79)
Self-rated oral health		<i>N=1888</i>	<i>N=1420</i>		<i>N=1715</i>	<i>N=1291</i>
Excellent or good	311 (25)	1.00	1.00	261 (23)	1.00	1.00
Fair or poor	166 (26)	1.04 (0.83, 1.29)	1.10 (0.85, 1.42)	169 (29)	1.38 (1.10, 1.74)	1.34 (1.02, 1.77)
Dry mouth symptoms		<i>N=1889</i>	<i>N=1422</i>		<i>N=1715</i>	<i>N=1291</i>
0	153 (22)	1.00	1.00	156 (24)	1.00	1.00
1-2	160 (26)	1.27 (0.99, 1.64)	1.27 (0.95, 1.70)	134 (24)	0.97 (0.74, 1.26)	0.95 (0.69, 1.31)
≥3	167 (30)	1.57 (1.21, 2.02)	1.58 (1.17, 2.13)	143 (28)	1.20 (0.92, 1.56)	1.29 (0.93, 1.78)
Cumulative oral health problems^c		<i>N=1962</i>	<i>N=1469</i>		<i>N=1785</i>	<i>N=1336</i>
0	65 (20)	1.00	1.00	56 (19)	1.00	1.00
1	224 (24)	1.26 (0.93, 1.72)	1.26 (0.90, 1.77)	208 (24)	1.32 (0.94, 1.83)	1.18 (0.81, 1.70)
2	129 (26)	1.45 (1.03, 2.03)	1.28 (0.87, 1.88)	121 (27)	1.50 (1.05, 2.15)	1.31 (0.87, 1.98)
≥3	72 (35)	2.18 (1.46, 3.23)	2.32 (1.46, 3.67)	61 (32)	1.90 (1.24, 2.91)	1.68 (1.01, 2.78)

^a reference group values for caloric intake= 406.2-2,272.8 kcal/day; reference group values for calories from saturated fat= 3.54-14.13% kcal/day

^b age, social class, smoking, alcohol, history of CVD and diabetes, and BMI

^c <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 6.3 Odds ratios (95%CI) for the associations of oral health problems with low fruits and vegetables intakes in older British men aged 71-92 years (BRHS) and in older American men and women aged 71-80 years (HABC study).

BRHS				HABC Study			
Oral Health Problems		Low fruits and vegetables intake (<5 portions/day) (n=231; n= 11%)		Oral Health Problems		Low fruits and vegetables intake (<6 portions/day) (n= 1789; 58%)	
		N (%)	Age adjusted OR (95% CI)			N (%)	Age adjusted OR (95% CI)
Tooth loss			N=1660	Tooth loss			N=1973
≥ 21 teeth		45 (8)	1.00	≥ 21 teeth		584 (62)	1.00
15-20 teeth		40 (12)	1.62 (1.04, 2.54)	15-20 teeth		223 (62)	1.02 (0.79, 1.31)
8-14 teeth		30 (11)	1.55 (0.95, 2.53)	8-14 teeth		192 (68)	1.31 (0.99, 1.74)
1-7 teeth		11 (9)	1.19 (0.59, 2.38)	1-7 teeth		112 (61)	0.95 (0.69, 1.31)
0 teeth		48 (14)	2.01 (1.29, 3.11)	0 teeth		150 (72)	1.60 (1.15, 2.22)
Periodontal disease (% of sites with loss of attachment >5.5 mm)			N=1246	Periodontal disease (% of sites with loss of attachment ≥ 3 mm)			N=1133
$\leq 20\%$		79 (8)	1.00	$\leq 20\%$		261 (63)	1.00
$>20\%$		32 (12)	1.52 (1.00, 2.30)	$>20\%$		473 (64)	1.11 (0.86, 1.43)
Self-rated oral health			N=2039	Self-rated oral health			N=2718
Excellent or good		121 (9)	1.00	Excellent or good		1213 (64)	1.00
Fair or poor		97 (13)	1.55 (1.16, 2.06)	Fair or poor		565 (68)	1.19 (1.00, 1.42)
Dry mouth symptoms			N=2034	Dry mouth			N=2719
0		87 (11)	1.00	No		1713 (66)	1.00
1-2		68 (10)	0.88 (0.63, 1.23)	Yes		69 (64)	0.95 (0.64, 1.42)
≥ 3		66 (11)	0.95 (0.68, 1.34)				N=2677

^a age, social class, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^b age, gender, race, education, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

Table 6.3 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with low fruits and vegetables intakes in older British men aged 71-92 years (BRHS) and in older American men and women aged 71-80 years (HABC study).

Oral Health Problems	BRHS			HABC Study		
	Low fruits and vegetables intake (<5 portions/day) (n=231; n= 11%)			Low fruits and vegetables intake (<6 portions/day) (n= 1789; 58%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)		Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Cumulative oral health problems^c		<i>N=2147</i>	<i>N=1469</i>	Cumulative oral health problems^d	<i>N=2761</i>	<i>N=2688</i>
0	30 (9)	1.00	1.00	0	485 (62)	1.00
1	118 (11)	1.32 (0.87, 2.02)	1.08 (0.67, 1.75)	1	882 (65)	1.09 (0.91, 1.31)
2	53 (10)	1.13 (0.70, 1.81)	1.03 (0.59, 1.78)	2	270 (69)	1.31 (1.01, 1.70)
≥ 3	30 (13)	1.58 (0.92, 2.72)	1.60 (0.84, 3.07)	≥ 3	152 (68)	1.28 (0.93, 1.76)

^a age, social class, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^b age, gender, race, education, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^c <21 teeth, ≥ 3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

^d <21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 6.4. Odds ratios (95%CI) for the associations of oral health problems with top quartiles of caloric intake, and percentage of energy from saturated fat in older American men and women aged 71-80 years in the HABC Study.

Oral Health Problems	Top quartile of caloric intake (2,270-8,456 kcal/day) ^a (n=678; 25%)			Top quartile of % of calories from saturated fat (11.15-23%) ^a (n=678; 25 %kcal/day)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Tooth loss		<i>N=1944</i>	<i>N=1926</i>		<i>N=1930</i>	<i>N=1913</i>
≥21 teeth	195 (21)	1.00	1.00	186 (20)	1.00	1.00
15-20 teeth	91 (26)	1.30 (0.97, 1.73)	1.14 (0.84, 1.54)	96 (27)	1.38 (1.04, 1.84)	1.26 (0.93, 1.70)
8-14 teeth	76 (27)	1.42 (1.05, 1.93)	1.20 (0.86, 1.67)	74 (27)	1.32 (0.96, 1.81)	1.18 (0.85, 1.65)
1-7 teeth	56 (31)	1.70 (1.19, 2.41)	1.34 (0.92, 1.97)	55 (31)	1.51 (1.05, 2.17)	1.32 (0.90, 1.94)
0 teeth	57 (29)	1.53 (1.08, 2.16)	1.16 (0.79, 1.70)	59 (30)	1.36 (0.96, 1.95)	1.08 (0.73, 1.60)
Periodontal disease						
% of sites with loss of attachment						
≥3 mm		<i>N=1129</i>	<i>N=1118</i>		<i>N=1123</i>	<i>N=1112</i>
≤20%	94 (23)	1.00	1.00	97 (24)	1.00	1.00
>20%	186 (26)	1.20 (0.90, 1.60)	1.00 (0.74, 1.36)	187 (26)	1.48 (1.09, 2.01)	1.48 (1.09, 2.01)
% of sites with pocket depth ≥3 mm		<i>N=1132</i>	<i>N=1121</i>		<i>N=1126</i>	<i>N=1115</i>
≤20%	89 (18)	1.00	1.00	91 (18)	1.00	1.00
>20%	191 (31)	2.05 (1.54, 2.72)	1.75 (1.29, 2.37)	193 (31)	1.43 (1.08, 1.88)	1.26 (0.94, 1.69)
Self-rated oral health		<i>N=2718</i>	<i>N=2695</i>		<i>N=2699</i>	<i>N=2677</i>
Excellent or good	447 (24)	1.00	1.00	450 (24)	1.00	1.00
Fair or poor	227 (27)	1.22 (1.01, 1.46)	1.00 (0.81, 1.22)	225 (27)	0.82 (0.67, 1.01)	0.82 (0.67, 1.01)
Dry mouth		<i>N=2719</i>	<i>N=2696</i>		<i>N=2700</i>	<i>N=2678</i>
No	645 (25)	1.00	1.00	645 (25)	1.00	1.00
Yes	29 (27)	1.13 (0.73, 1.75)	1.15 (0.73, 1.82)	29 (27)	1.05 (0.67, 1.66)	1.05 (0.67, 1.66)
Cumulative oral health problems^c		<i>N=2732</i>	<i>N=2706</i>		<i>N=2713</i>	<i>N=2688</i>
0	148 (19)	1.00	1.00	146 (19)	1.00	1.00
1	359 (27)	1.51 (1.22, 1.88)	1.33 (1.06, 1.67)	368 (27)	1.20 (0.96, 1.50)	1.20 (0.96, 1.50)
2	103 (26)	1.48 (1.11, 1.97)	1.24 (0.92, 1.69)	99 (25)	0.94 (0.69, 1.28)	0.94 (0.69, 1.28)
≥3	68 (30)	1.83 (1.30, 2.56)	1.49 (1.04, 2.15)	64 (29)	1.06 (0.73, 1.52)	1.06 (0.73, 1.52)

^a reference group values for caloric intake= 111.5-2,270 kcal/day; reference group values for calories from saturated fat= 0.80-11.1% kcal/day

^badjusted for age, gender, race, education, smoking, alcohol, history of CVD and diabetes, BMI

^c<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 6.5. Odds ratios (95%CI) for the associations of oral health problems with intake of processed meat in older British men aged 71-92 years in the BRHS.

	Processed meat intake					
	Monthly/Rarely (n=903; 42%)	1 type of processed meat ≥2 times per week (n=823; 38%)	≥2 types of processed meat ≥2 times per week (n=421; 20%)	Monthly/Rarely (n=903; 42%)	1 type of processed meat ≥2 times per week (n=823; 38%)	≥2 types of processed meat ≥2 times per week (n=421; 20%)
Oral Health Problems		Age adjusted OR (95% CI)	Age adjusted OR (95% CI)		Fully adjusted ^a OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss		N=1660			N=1504	
≥21 teeth	1.00	1.00	1.00	1.00	1.00	1.00
15-20 teeth	1.00	1.12 (0.83, 1.50)	1.64 (1.12, 2.38)	1.00	1.17 (0.86, 1.60)	1.51 (1.01, 2.27)
8-14 teeth	1.00	1.01 (0.73, 1.39)	1.35 (0.89, 2.04)	1.00	1.05 (0.74, 1.49)	1.23 (0.78, 1.94)
1-7 teeth	1.00	0.89 (0.57, 1.38)	1.48 (0.87, 2.52)	1.00	0.93 (0.58, 1.50)	1.25 (0.70, 2.23)
0 teeth	1.00	1.14 (0.84, 1.55)	2.03 (1.40, 2.95)	1.00	1.13 (0.80, 1.59)	1.63 (1.06, 2.49)
Periodontal disease (% sites with pocket depth >3.5mm)		N=1245			N=1140	
≤20%	1.00	1.00	1.00	1.00	1.00	1.00
>20%	1.00	1.08 (0.82, 1.42)	1.47 (1.05, 2.05)	1.00	1.05 (0.78, 1.40)	1.36 (0.94, 1.95)
Self-rated oral health		N=2039			N=1502	
Excellent or good	1.00	1.00	1.00	1.00	1.00	1.00
Fair or poor	1.00	0.96 (0.79, 1.18)	1.27 (0.99, 1.62)	1.00	0.93 (0.73, 1.19)	1.12 (0.83, 1.51)
Dry mouth symptoms		N=2034			N=1504	
0	1.00	1.00	1.00	1.00	1.00	1.00
1-2	1.00	0.91 (0.72, 1.15)	1.07 (0.81, 1.43)	1.00	0.93 (0.71, 1.21)	1.08 (0.77, 1.52)
≥3	1.00	1.21 (0.95, 1.54)	1.38 (1.03, 1.85)	1.00	1.26 (0.95, 1.68)	1.27 (0.89, 1.82)
Cumulative oral health problems^b		N=2147			N=1561	
0	1.00	1.00	1.00	1.00	1.00	1.00
1	1.00	1.00 (0.77, 1.31)	1.65 (1.14, 2.40)	1.00	1.05 (0.78, 1.42)	1.49 (0.98, 2.26)
2	1.00	1.26 (0.94, 1.71)	2.11 (1.41, 3.16)	1.00	1.19 (0.85, 1.67)	1.48 (0.93, 2.36)
≥3	1.00	1.15 (0.79, 1.68)	2.26 (1.40, 3.64)	1.00	1.36 (0.87, 2.13)	2.16 (1.22, 3.18)

^aage, social class, smoking, alcohol, history of CVD and diabetes, and BMI

^b<21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 6.6. Odds ratios (95%CI) for the associations of oral health problems with intake of processed meat in older American men and women aged 71-80 years (HABC study).

	Processed meat intake					
	Monthly/Rarely (n=1771; 58%)	1 type of processed meat ≥2 times per week (n=734; 24%)	≥2 types of processed meat ≥2 times per week (n=570; 18%)	Monthly/Rarely	1 type of processed meat ≥2 times per week	≥2 types of processed meat ≥2 times per week
Oral Health Problems		Age adjusted OR (95% CI)	Age adjusted OR (95% CI)		Fully adjusted ^a OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss	<i>N=1973</i>			<i>N=1926</i>		
≥21 teeth	1.00	1.00	1.00	1.00	1.00	1.00
15-20 teeth	1.00	1.23 (0.92, 1.64)	1.40 (1.00, 1.97)	1.00	1.02 (0.76, 1.38)	0.90 (0.62, 1.30)
8-14 teeth	1.00	1.34 (0.97, 1.84)	2.23 (1.58, 3.13)	1.00	1.09 (0.78, 1.53)	1.25 (0.85, 1.83)
1-7 teeth	1.00	1.23 (0.84, 1.82)	2.23 (1.50, 3.31)	1.00	0.96 (0.63, 1.45)	1.13 (0.73, 1.76)
0 teeth	1.00	1.73 (1.20, 2.49)	3.12 (2.14, 4.54)	1.00	1.35 (0.90, 2.02)	1.34 (0.87, 2.07)
Periodontal disease (% sites with pocket depth ≥3mm)	<i>N=1136</i>			<i>N=1121</i>		
≤20%	1.00	1.00	1.00	1.00	1.00	1.00
>20%	1.00	1.31 (0.99, 1.72)	2.60 (1.86, 3.65)	1.00	1.12 (0.84, 1.51)	1.70 (1.17, 2.46)
Self-rated oral health	<i>N=2718</i>			<i>N=2695</i>		
Excellent or good	1.00	1.00	1.00	1.00	1.00	1.00
Fair or poor	1.00	1.30 (1.07, 1.58)	1.57 (1.28, 1.93)	1.00	1.11 (0.91, 1.37)	0.95 (0.75, 1.20)
Dry mouth	<i>N=2719</i>			<i>N=2696</i>		
No	1.00	1.00	1.00	1.00	1.00	1.00
yes	1.00	1.02 (0.65, 1.62)	1.05 (0.64, 1.73)	1.00	1.00 (0.62, 1.60)	0.87 (0.51, 1.50)
Cumulative oral health problems^b	<i>N=2761</i>			<i>N=2706</i>		
0	1.00	1.00	1.00	1.00	1.00	1.00
1	1.00	1.28 (1.03, 1.58)	1.83 (1.43, 2.34)	1.00	1.09 (0.87, 1.37)	1.12 (0.85, 1.47)
2	1.00	1.73 (1.30, 2.30)	2.36 (1.71, 3.26)	1.00	1.43 (1.06, 1.94)	1.29 (0.90, 1.84)
≥3	1.00	2.24 (1.58, 3.19)	2.97 (2.01, 4.38)	1.00	1.80 (1.24, 2.60)	1.34 (0.86, 2.06)

^a adjusted for age, gender, race, education, smoking, alcohol, history of CVD and diabetes, BMI

^b <21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 6.7. Odds ratios (95%CI) for the associations of oral health problems with top quartiles of percentages of calories from trans-fatty acids and sweets and soda in older American men and women aged 71-80 years in the HABC Study.

	Top quartile of % of energy intake from trans-fat (3.91-10.2 %kcal/day) ^a (n=678; 25%)			Top quartile of % of caloric intake from sweets and soda (18.4-70.6 %kcal/day) ^a (n=678; 25%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Oral health Problems						
Tooth loss		N=1930	N=1913		N=1944	N=1926
≥21 teeth	187 (20)	1.00	1.00	195 (21)	1.00	1.00
15-20 teeth	95 (27)	1.11 (0.83, 1.48)	1.15 (0.85, 1.56)	91 (26)	1.29 (0.98, 1.72)	1.36 (1.01, 1.82)
8-14 teeth	71 (26)	1.27 (0.93, 1.73)	1.34 (0.97, 1.86)	76 (27)	1.24 (0.91, 1.69)	1.32 (0.95, 1.83)
1-7 teeth	57 (32)	1.58 (1.11, 2.25)	1.69 (1.16, 2.47)	56 (31)	1.43 (1.00, 2.05)	1.47 (1.00, 2.16)
0 teeth	56 (28)	1.69 (1.21, 2.36)	1.73 (1.20, 2.50)	57 (29)	1.34 (0.94, 1.90)	1.38 (0.94, 2.02)
Periodontal disease (% of sites with pocket depth ≥3 mm)		N=1126	N=1115		N=1132	N=1121
≤20%	91 (18)	1.00	1.00	89 (18)	1.00	1.00
>20%	162 (26)	1.14 (0.85, 1.52)	1.17 (0.86, 1.58)	191 (31)	1.35 (1.02, 1.79)	1.28 (0.94, 1.73)
Self-rated oral health		N=2699	N=2677		N=2718	N=2695
Excellent or good	451 (24)	1.00	1.00	447 (24)	1.00	1.00
Fair or poor	226 (27)	1.06 (0.88, 1.28)	1.06 (0.87, 1.30)	227 (27)	0.96 (0.79, 1.16)	0.95 (0.78, 1.16)
Dry mouth		N=2700	N=2678		N=2719	N=2696
No	643 (25)	1.00	1.00	645 (25)	1.00	1.00
Yes	34 (32)	1.27 (0.83, 1.95)	1.26 (0.81, 1.95)	29 (27)	1.44 (0.95, 2.18)	1.53 (1.00, 2.34)
Cumulative oral health problems^c		N=2713	N=2688		N=2732	N=2706
0	142 (19)	1.00	1.00	148 (19)	1.00	1.00
1	362 (27)	1.24 (1.01, 1.53)	1.21 (0.97, 1.51)	359 (27)	1.29 (1.04, 1.59)	1.28 (1.03, 1.60)
2	105 (27)	1.26 (0.95, 1.67)	1.23 (0.91, 1.65)	103 (26)	1.13 (0.85, 1.51)	1.12 (0.83, 1.52)
≥3	70 (31)	1.45 (1.03, 2.03)	1.43 (1.00, 2.04)	68 (31)	1.61 (1.16, 2.25)	1.65 (1.16, 2.36)

^a reference group values for calories from trans-fat= 0- 3.9 %kcal/day; reference group values for % calories from sweets/soda= 0-18.3 %kcal/day

^b adjusted for age, gender, race, education, smoking, alcohol, history of CVD and diabetes, BMI

^c<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 6.8. Odds ratios (95%CI) for the associations of oral health problems with protein intake in older British men aged 71-92 years (BRHS) and in older American men and women aged 71-80 years (HABC study).

BRHS				HABC study			
		Low protein Intake (<0.75 g/kg/day) (n=296; 18%)				Low protein Intake(<0.80 g/kg/day) (n=1200; n=44%)	
Oral Health Problems	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	Oral Health Problems	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Tooth loss		<i>N=1603</i>	<i>N=1413</i>	Tooth loss		<i>N=1930</i>	<i>N=1913</i>
≥21 teeth	94 (16)	1.00	1.00	≥21 teeth	390 (42)	1.00	1.00
15-20 teeth	69 (21)	1.36 (0.96, 1.92)	1.90 (1.19, 3.04)	15-20 teeth	152 (43)	1.05 (0.82, 1.35)	0.99 (0.68, 1.42)
8-14 teeth	51 (20)	1.29 (0.88, 1.88)	1.37 (0.80, 2.34)	8-14 teeth	128 (46)	1.19 (0.91, 1.56)	1.06 (0.70, 1.60)
1-7 teeth	14 (12)	0.72 (0.39, 1.32)	0.51 (0.20, 1.29)	1-7 teeth	78 (44)	1.07 (0.78, 1.48)	0.92 (0.55, 1.52)
0 teeth	57 (17)	1.10 (0.73, 1.65)	1.28 (0.75, 2.16)	0 teeth	90 (46)	1.16 (0.85, 1.59)	0.91 (0.55, 1.51)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=1205</i>	<i>N=1082</i>	Periodontal disease (% of sites with loss of attachment ≥3 mm)		<i>N=1123</i>	<i>N=1112</i>
≤20%	151 (17)	1.00	1.00	≤20%	167 (41)	1.00	1.00
>20%	60 (20)	1.30 (0.91, 1.85)	1.25 (0.78, 2.01)	>20%	317 (45)	1.20 (0.93, 1.53)	1.31 (0.89, 1.91)
Self-rated oral health		<i>N=1602</i>	<i>N=1420</i>	Self-rated oral health		<i>N=2699</i>	<i>N=2677</i>
Excellent or good	174 (17)	1.00	1.00	Excellent or good	820 (44)	1.00	1.00
Fair or poor	110 (20)	1.27 (0.98, 1.66)	0.97 (0.67, 1.40)	Fair or poor	373 (45)	1.08 (0.91, 1.27)	0.92 (0.72, 1.19)
Dry mouth symptoms		<i>N=1606</i>	<i>N=1422</i>	Dry mouth		<i>N=2700</i>	<i>N=2678</i>
0	107 (18)	1.00	1.00	No	1146 (44)	1.00	1.00
1-2	98 (18)	1.05 (0.78, 1.42)	1.06 (0.69, 1.64)	Yes	50 (48)	1.15 (0.78, 1.70)	1.43 (0.79, 2.61)
≥3	79 (17)	0.99 (0.72, 1.36)	1.18 (0.76, 1.82)				
Cumulative oral health problems^c		<i>N=1664</i>	<i>N=1469</i>	Cumulative oral health problems^d		<i>N=2713</i>	<i>N=2688</i>
0	57 (17)	1.00	1.00	0	331 (43)	1.00	1.00
1	139 (18)	1.05 (0.73, 1.51)	1.08 (0.69, 1.70)	1	588 (44)	1.01 (0.85, 1.21)	1.01 (0.77, 1.31)
2	76 (19)	1.15 (0.79, 1.68)	1.30 (0.78, 2.16)	2	183 (47)	1.17 (0.92, 1.50)	1.12 (0.77, 1.63)
≥3	24 (14)	0.81 (0.48, 1.37)	1.18 (0.57, 2.45)	≥3	98 (44)	1.03 (0.76, 1.39)	1.23 (0.77, 1.97)

^aage, social class, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^bage, gender, race, education, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^c<21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

^d<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 6.9. Odds ratios (95%CI) for the associations of oral health problems with bottom quartiles of vitamin C, a-tocopherol and vitamin D in older British men aged 71-92 years (BRHS) and in older American men and women aged 71-80 years (HABC study).

BRHS					HABC Study		
Oral Health Problems	Bottom quartile of vitamin C (5.5-51.90 mg/day) ^a (n=523; 25%)		Bottom quartile of a-tocopherol (0.60-4.60 mg/day) ^a (n=427, 25%)		Oral Health Problems	Bottom quartile of vitamin D (0-110.3 IU/day) ^a (n=678; 25%)	
	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)		Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)
Tooth loss	<i>N=1622</i>	<i>N=1412</i>	<i>N=1363</i>	<i>N=1256</i>	Tooth Loss	<i>N=1944</i>	<i>N=1913</i>
≥21 teeth	1.00	1.00	1.00	1.00	≥21 teeth	1.00	1.00
15-20 teeth	0.98 (0.70, 1.37)	0.98 (0.66, 1.44)	1.47 (1.04, 2.08)	1.71 (1.12, 2.60)	15-20 teeth	1.17 (0.88, 1.55)	1.12 (0.81, 1.54)
8-14 teeth	1.15 (0.81, 1.64)	0.99 (0.65, 1.50)	1.54 (1.06, 2.24)	1.61 (1.00, 2.57)	8-14 teeth	1.11 (0.81, 1.52)	1.03 (0.71, 1.47)
1-7 teeth	1.38 (0.87, 2.17)	1.22 (0.72, 2.09)	1.87 (1.14, 3.08)	2.08 (1.13, 3.86)	1-7 teeth	1.31 (0.91, 1.88)	1.18 (0.77, 1.82)
0 teeth	1.28 (0.93, 1.77)	1.02 (0.68, 1.52)	1.69 (1.18, 2.41)	2.20 (1.40, 3.46)	0 teeth	1.44 (1.02, 2.03)	1.14 (0.75, 1.72)
Periodontal disease (% of sites with loss of attachment >5.5 mm)	<i>N=1216</i>	<i>N=1082</i>	<i>N=1049</i>	<i>N=972</i>	Periodontal disease (% of sites with loss of attachment ≥3 mm)	<i>N=1129</i>	<i>N=1112</i>
≤20%	1.00	1.00	1.00	1.00	≤20%	1.00	1.00
>20%	1.22 (0.90, 1.66)	1.12 (0.78, 1.61)	1.40 (1.02, 1.94)	1.67 (1.12, 2.49)	>20%	1.03 (0.77, 1.37)	1.00 (0.72, 1.38)
Self-rated oral health	<i>N=2007</i>	<i>N=1420</i>	<i>N=1675</i>	<i>N=1269</i>	Self-rated oral health	<i>N=2718</i>	<i>N=2677</i>
Excellent or good	1.00	1.00	1.00	1.00	Excellent or good	1.00	1.00
Fair or poor	1.47 (1.19, 1.81)	1.38 (1.04, 1.84)	1.10 (0.87, 1.39)	1.10 (0.79, 1.51)	Fair or poor	1.12 (0.93, 1.35)	1.00 (0.80, 1.24)
Dry mouth symptoms	<i>N=2005</i>	<i>N=1421</i>	<i>N=1677</i>	<i>N=1271</i>	Dry mouth	<i>N=2719</i>	<i>N=2678</i>
0	1.00	1.00	1.00	1.00	No	1.00	1.00
1-2	0.85 (0.67, 1.08)	0.73 (0.53, 1.01)	1.03 (0.79, 1.34)	0.96 (0.67, 1.36)	Yes	1.37 (0.90, 2.09)	1.47 (0.91, 2.36)
≥3	0.72 (0.56, 0.93)	0.94 (0.67, 1.32)	0.93 (0.70, 1.22)	1.27 (0.88, 1.85)			

^a BRHS: reference group values for vitamin C= 52-221.10mg/day, for a-tocopherol = 4.70-40.70 mg/day; HABC Study: reference group values for vitamin D= >110.44-1279.15 IU/day

^b age, social class, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^c age, sex, race, education, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

Table 6.9 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with bottom quartiles of vitamin C, a-tocopherol and vitamin D in older British men aged 71-92 years (BRHS) and in older American men and women aged 71-80 years (HABC study).

BRHS					HABC Study		
		Bottom quartile of vitamin C (5.5-51.90 mg/day) ^a (n=523; 25%)		Bottom quartile of a-tocopherol (0.60-4.60 mg/day) ^a (n=427, 25%)		Bottom quartile of vitamin D (0-110.3 IU/day) ^a (n=678; 25%)	
		Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	Age adjusted OR (95% CI)	Fully adjusted ^c OR (95% CI)
Cumulative oral health problems ^d		N=2089	N=1468	N=1729	N=1306	Cumulative oral health problems ^e	
0	1.00		1.00	1.00	1.00	0	1.00
1	1.51 (1.11, 2.05)		1.13 (0.78, 1.63)	1.95 (1.38, 2.75)	2.15 (1.41, 3.26)	1	1.10 (0.89, 1.36)
2	1.31 (0.94, 1.83)		1.24 (0.82, 1.88)	1.82 (1.25, 2.65)	2.20 (1.37, 3.53)	2	1.17 (0.88, 1.56)
≥3	1.14 (0.75, 1.73)		1.07 (0.62, 1.87)	1.34 (0.83, 2.14)	2.06 (1.10, 3.87)	≥3	1.65 (1.19, 2.29)

^a BRHS: reference group values for vitamin C= 52-221.10mg/day, for a-tocopherol = 4.70-40.70 mg/day; HABC Study: reference group values for vitamin D= >110.44-1279.15 IU/day

^b age, social class, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^c age, sex, race, education, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^d <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

^e <21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 6.10. Odds ratios (95%CI) for the associations of change in dietary quality (EDI scores) over 10 years (age 60-79 to 71-92 years) and the association with having oral health problems at 71-92 years in the BRHS.

	Tooth loss (< 21 teeth) (n=933; 64%)		Loss of attachment (>20% sites affected) (n=265; 24%)		Self-rated oral health (fair/poor) (n=609; n=34%)				
EDI change over 10 years (60-79 yrs to 71-92 yrs)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)			
	<i>N=980</i>	<i>N=924</i>	<i>N=754</i>	<i>N=715</i>	<i>N=1178</i>	<i>N=1111</i>			
	Good score at both time points	1.00	1.00	1.00	1.00	1.00			
	Score improved over 10 years	1.70 (1.20, 2.40)	1.41 (0.97, 2.06)	1.69 (1.06, 2.69)	1.46 (0.90, 2.37)	1.16 (0.83, 1.63)	1.17 (0.82, 1.66)		
	Score decreased over 10 years	1.91 (1.32, 2.75)	1.61 (1.08, 2.38)	1.60 (0.98, 2.62)	1.33 (0.80, 2.21)	1.17 (0.84, 1.64)	1.08 (0.76, 1.54)		
Low score at both time points	2.35 (1.61, 3.42)	1.66 (1.09, 2.52)	1.77 (1.08, 2.88)	1.34 (0.78, 2.29)	1.44 (1.03, 2.01)	1.31 (0.91, 1.88)			
	Cumulative oral health problems ^b								
	Age adjusted OR (95% CI)		Fully adjusted ^a OR (95% CI)						
EDI change over 10 years (60-79 yrs to 71-92 yrs)	0	1 (n=883; 46%)	2 (n=471; 25%)	≥3 (n=188; 10%)	0	1	2	≥3	
	<i>N=1217</i>				<i>N=1149</i>				
	Good score at both time points	1.00	1.00	1.00	1.00	1.00	1.00	1.00	
	Score improved over 10 years	1.00	1.35 (0.89, 2.03)	1.51 (0.96, 2.39)	1.79 (0.97, 3.32)	1.00	1.13 (0.73, 1.76)	1.22 (0.74, 2.01)	1.35 (0.70, 2.61)
	Score decreased over 10 years	1.00	1.94 (1.25, 3.02)	2.24 (1.38, 3.63)	2.50 (1.33, 4.69)	1.00	1.66 (1.04, 2.63)	1.81 (1.08, 3.03)	1.82 (0.93, 3.56)
Low score at both time points	1.00	3.62 (2.21, 5.94)	2.95 (1.71, 5.09)	3.17 (1.59, 6.34)	1.00	2.60 (1.52, 4.45)	1.96 (1.07, 3.56)	2.04 (0.96, 4.33)	

^a age, social class, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

^b <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 6.10 (*continued*). Odds ratios (95%CI) for the associations of change in dietary quality (EDI scores) over 10 years (age 60-79 to 71-92 years) and the association with having oral health problems at 71-92 years in the BRHS.

EDI change over 10 years (60-79 yrs to 71-92 yrs)	Dry mouth symptoms					
	Age adjusted OR (95% CI)			Fully adjusted ^a OR (95% CI)		
	<i>N</i> =1179			<i>N</i> =1111		
	0	1-2 (<i>n</i> =666; 32.7%)	≥3 (<i>n</i> =606; 29.8%)	0	1-2	≥3
Good score at both time points	1.00	1.00	1.00	1.00	1.00	1.00
Score improved over 10 years	1.00	1.15 (0.80, 1.67)	1.13 (0.76, 1.67)	1.00	0.88 (0.59, 1.33)	0.79 (0.50, 1.25)
Score decreased over 10 years	1.00	1.23 (0.84, 1.80)	1.65 (1.11, 2.43)	1.00	0.99 (0.64, 1.53)	1.13 (0.71, 1.80)
Low score at both time points	1.00	1.25 (0.86, 1.82)	1.18 (0.79, 1.76)	1.00	1.03 (0.66, 1.62)	0.85 (0.52, 1.40)

^a age, social class, smoking, alcohol, history of CVD and diabetes, BMI, caloric intake

Chapter 7. Prospective Associations of Oral Health Problems with Risk of Incident Disability in Older People in the UK and USA: Do Inflammation and Diet Quality Mediate this Relationship?

7.1. Summary

Oral health problems and disability co-exist in older people. As described in Chapter 4, poor oral health is associated cross-sectionally with different measures of disability. However, the prospective associations between oral health problems and risk of developing disability are not well-established. Additionally, it has been proposed that inflammation and diet are potential mediators explaining the association between poor oral health and risk of developing disability but the evidence confirming their role is lacking. In this Chapter, the prospective associations of objective and subjective oral health problems with risk of disability were examined. Additionally, causal mediation analysis was performed to investigate the mediating effects of inflammation and diet quality underlying the association between poor oral health and risk of incident mobility limitations (measure of disability). Data from the British Regional Heart Study (BRHS) and the US Health, Aging, and Body Composition (HABC) Study were used. Oral health problems were assessed through (1) a dental examination (tooth loss, periodontal disease-objective) and (2) questionnaires (dry mouth, self-rated oral health, difficulty eating, sensitivity to hot/cold/sweets and limitation of food due to gum problems-subjective). Measures of disability consisted of mobility limitations, Activities of Daily Living (ADL), and Instrumental Activities of Daily Living (IADL). To assess incidence of disability, individuals were followed-up for 4 years. In the BRHS, markers of inflammation comprised CRP, IL-6, and fibrin d-dimer, whereas in the HABC Study CRP, and IL-6 were available. In the BRHS, the Elderly Dietary Index (EDI) was used to assess diet quality, and in the HABC Study diet quality was measured via the Healthy Eating Index (HEI). For prospective analyses, logistic regression was performed. For causal mediation analysis, the Karlson/Holm/Breen method of decomposition of total, direct and indirect effects was used to assess mediating effects of diet and inflammation in separate models. Tooth loss, and dry mouth were

associated with increased risk of incident mobility limitations and ADL difficulties. Periodontal disease was associated with greater risk of incident mobility limitations (OR= 1.75, 95% CI 1.04-2.95). Fair/poor self-rated oral health was associated with risk of developing ADL and IADL difficulties (OR=1.42, 95% CI 1.04-1.94; OR= 2.09, 95% CI 1.34-3.26, respectively). Cumulative oral health problems were associated with greater risk of developing ADL difficulties (≥ 3 problems vs. 0, OR= 2.53, 95% CI 1.14-5.61). In summary, poor oral health was associated with greater risk of incident disability in older people. Markers of inflammation and diet quality did not appear to mediate the association between oral health problems and risk of incident mobility limitations in both studies.

7.2. Introduction

Ageing is characterised by increased prevalence of oral health problems, as well as high rates of disability, which negatively affect quality of life (Marcenes *et al.*, 2013; Ramsay *et al.*, 2015b; James *et al.*, 2018). In Chapter 4, it was reported that oral health problems are cross-sectionally associated with different measures of disability (mobility limitations, ADL and IADL difficulties). However, whether oral health problems influence the development of disability later in life is not well understood. The majority of studies have examined the prospective associations of poor oral health with future deterioration of physical function, and few have focused on risk of developing disability (Hämäläinen *et al.*, 2004; Holm-Pedersen *et al.*, 2008; Tsakos *et al.*, 2015; Welmer *et al.*, 2017). Additionally, in some studies nationwide standards (as first certification of long-term care insurance for those conducted in older Japanese populations) were used for the measurement of disability (Komiya *et al.*, 2016). Hence, existing studies have assessed disability in different ways and few studies have used measures of disability, including mobility limitations, ADL and IADL difficulties. Being able to be mobile, perform activities which are necessary for the management of basic physical needs but also activities which correspond to being independent within a community are crucial in maintaining functional independence and good quality of life in older people (Katz, 1983; Chen and Wilmoth, 2004; Mlinac and Feng, 2016; James *et al.*, 2018). Additionally, more evidence is needed for the associations of periodontal disease, dry mouth, self-rated

oral health, and cumulative oral health problems with incident disability. Subjective dental problems can be assessed quicker and easier and are important indicators of poor oral health status (Chen *et al.*, 2013; Han *et al.*, 2015). Establishing how oral health problems influence the development of disability in older people as well as which domains of functional activities are influenced by oral health can help design interventions to improve oral health status of older people and potentially improving functional independence of older people later in life.

In addition to establishing the prospective associations between poor oral health and incidence of disability, it is important to also pinpoint the causal pathway(s) which underpin these associations. In other words, it is crucial to understand whether dental problems are associated directly with the development of disability or whether other factors, including diet quality and inflammation, are responsible for this association. In Chapters 5, and 6 it was established that oral health problems are associated with increased inflammation and poor diet quality. It has been suggested that inflammatory markers such as CRP, and IL-6, and diet quality/eating problems act as potential pathways connecting oral health with disability, physical function, and chronic diseases (Ritchie *et al.*, 2002; Welmer *et al.*, 2017; Carrizales-Sepúlveda *et al.*, 2018; Yin *et al.*, 2020). Likewise, fibrin d-dimer has been highlighted as an important biomarker of ageing and it is possible that it could also mediate these associations (Kotronia *et al.*, 2020). However, only one study has performed causal mediation to examine the mediating roles of one of the aforementioned factors, particularly that of eating problems, and observed that eating problems mediated the association between tooth loss and incidence of disability (ADL, IADL) (Yin *et al.*, 2020). To my knowledge, no other studies have performed causal mediation analysis to investigate the mediating effects of inflammation or diet quality on these prospective associations. Disentangling the pathway linking oral health with disability can assist to better understand how poor oral health influences the development of chronic conditions, and help establish its role as an important modifiable risk factor in improving health and alleviating the burden of diseases in older people.

7.3. Aim and Objectives

This Chapter aims to investigate the prospective associations between oral health problems and risk of incident disability in older people. Moreover, it aims to investigate the pathways linking poor oral health with the incidence (new cases) of disability. Therefore, the objectives of this Chapter are:

- I. To examine the prospective associations between objective and subjective oral health problems and risk of incident mobility limitations, ADL, and IADL in older people.
- II. To explore the mediating effects of CRP, IL-6, and fibrin d-dimer on the association between oral health problems and risk of incident mobility limitations in older people in the BRHS.
- III. To explore the mediating effects of CRP and IL-6 on the association between oral health problems and risk of incident mobility limitations in older people in the HABC Study.
- IV. To explore the mediating effect of diet quality on the association between oral health problems and risk of incident mobility limitations in older people in both studies.

7.4. Methods

Analyses in this Chapter are based on data from the BRHS and HABC Study. Details on both the BRHS and HABC Study, including selection of participants, data collection and data verifications can be found in Chapter 3 (Sections 3.2 and 3.5). This section (section 7.4) focuses on data used for the analyses presented in this Chapter.

7.4.1. Subjects and methods of data collection

In the BRHS, data are based on the 20-year (1998-2000), 30-year (2010-2012) re-examinations, and follow-up in 2014. At the 20- and 30-year re-examinations men completed questionnaires, and attended a physical examination. In 2014, only postal questionnaires were completed by participants. Participants were followed

prospectively for disability from 2010-2012 to 2014. Attrition and response rates are detailed in Chapter 3 (sub-section 3.8.1, Figure 3.4).

In the HABC Study, data are based on Year 1 (1997-1998), Year 2 (1998-1999) and Year 5 (2001-2002) examinations. Individuals answered questionnaires and attended physical examinations in all three different time points. Participants were followed prospectively for disability from Year 2 (1998-1999) to Year 5 (2001-2002). Attrition and response rates are described in Chapter 3 (sub-section 3.8.1, Figure 3.5).

7.4.2. Oral health

In the BRHS, oral health problems were measured at 2010-2012, when participants aged 71-92 years. In the HABC Study, oral health was assessed at 1998-1999 when participants aged 71-80 years.

7.4.2.1. Objective oral health problems

Number of teeth and periodontal disease were assessed by trained professionals in both studies. Tooth loss was classified as: 5-level group (0, 1-7, 8-14, 15-20, ≥ 21 teeth), and two binary (<21 teeth vs. ≥ 21 teeth; 0 teeth vs. ≥ 1 teeth). Having ≥ 21 teeth indicated a functional dentition (Hobdell *et al.*, 2003). Periodontal disease was measured according to Extent and Severity Index (Carlos *et al.*, 1986) and included loss of attachment and pocket depth. It was grouped in two binary variables according to percentage of sites affected (>20% sites affected vs. $\leq 20\%$ sites). Further details can be found in Chapter 3 (sub-sections 3.3.1 and 3.6.1).

7.4.2.2. Subjective oral health problems

Questionnaires were used to assess dry mouth, self-rated oral health, difficulty eating, sensitivity to hot/cold/sweets, limitation of food due to problems with teeth or dentures. More details on these markers can be found in Chapter 3 (sub-sections 3.3.1 and 3.6.1).

7.4.3. Disability

In the BRHS disability was assessed through mobility limitations, ADL and IADL, as detailed in Chapter 4 (sub-section 4.4.3). In the HABC Study, mobility limitations and ADL were used to assess disability, as described in Chapter 4 (sub-section 4.4.3). In the BRHS, participants were followed-up from 2010-2012 to 2014. Similarly, in the HABC Study, participants were followed from 1998-1999 to 2001-2002. In both studies, new cases of disability identified only at follow-up were used to calculate incidence of disability. In the BRHS, to assess only new cases of disability, those who reported disability at baseline (2010-2012) (n=564) and those who did not answer any disability-related questions were excluded (n=44). Likewise, in the HABC Study, those who reported disability at baseline (1998-1999) were excluded from the analysis (n=882).

7.4.4. Mediators for causal analysis

For the causal mediation analysis, data on mediators were used from 30-year (2010-2012) in the BRHS, and from Year 2 (1998-1999) in the HABC Study.

7.4.4.1. Markers of inflammation

In the BRHS, inflammatory markers included CRP, IL-6, and fibrin d-dimer. In the HABC Study, CRP and IL-6 were available. More details about the measurements are presented in Chapter 3 (sub-sections 3.3.4 and 3.6.4). For the purpose of causal mediation analysis, markers of inflammation were log-transformed and used as continuous variables.

7.4.4.2. Diet quality

In both studies, diet quality was assessed through validated Food Frequency Questionnaires (FFQ), as described in Chapter 6 (sub-section 6.4.3). In the BRHS,

diet quality was measured by the Elderly Dietary Index (EDI), whereas in the HABC Study the Healthy Eating Index (HEI) was used. More details are presented in Chapter 6 (sub-section 6.4.4). For the purpose of causal mediation analysis, diet quality was used as a continuous variable. An increasing score of HEI or EDI represent better diet quality. Diet quality was chosen as the mediator because it is a marker of overall nutritional status.

7.4.5. Socio-demographic, lifestyle factors, and chronic diseases

In both studies, information on socioeconomic status, smoking, alcohol, physical activity, history of cardiovascular disease (CVD), history of diabetes was collected through questionnaires. BMI (weight/height²) was classified as normal, overweight, and obese. Information on the number of prescribed medications causing dry mouth (xerostomia) was also used. More details can be found in Chapter 3 (sections 3.3 and 3.6).

For prospective analyses between oral health problems and incident disability, confounders were assessed at 2010-2012 in the BRHS, and at 1998-1999 in the HABC Study.

For causal mediation analysis, data from an earlier time point was used to allow assessing confounders prior to measurement of exposures (VanderWeele, 2019). In the BRHS confounders were measured at 20-year (1998-2000), and in the HABC Study covariates were assessed at Year 1 (1997-1998).

7.4.6. Statistical Analysis

7.4.6.1. Prospective associations of poor oral health with risk of incident disability

Separate logistic regression models was performed to calculate the odds ratios (OR) and 95% CIs for the associations between objective and subjective oral health problems and risk of incident disability in both studies. Having any mobility limitation, any difficulty or needing help with ADL or IADL were the binary outcome variables for disability. In the BRHS, regression models were adjusted for age, social class (2 levels), smoking (3 levels), alcohol (5 levels), physical activity (5 levels), history of

CVD and diabetes, and BMI (3 levels). In the HABC Study, the fully adjusted model included age (continuous), gender, race (2 levels), education (3 levels), smoking (3 levels), alcohol (4 levels), physical activity (continuous), history of CVD and diabetes, and BMI (3 levels).

7.4.6.2. Causal mediation

Causal mediation analysis can determine whether the association between an exposure (oral health) and an outcome (mobility limitations) is due to the influence of the exposure or the mediator (diet quality, inflammation). This section aims to decompose the effect of oral health problems on mobility limitations into total effect (TE) (effect estimate of the association between exposure and outcome-excluding the mediator), natural direct effect (NDE) (effect estimate of the association between exposure and outcome- including the mediator) and natural indirect effect (NIE) (effect of the mediator on the association between exposure and outcome) through inflammation and diet quality as potential mediators. Further details on TE, NDE, and NIE can be found in Chapter 3 (sub-section 3.9.3). The effect of each mediator will be tested separately.

To calculate TE, NDE, and NIE the Karlson/Holm/Breen (khab) method was performed (Breen *et al.*, 2013). This method can perform causal mediation analysis when the outcome measure is binary and provide robust effect estimates (Breen *et al.*, 2013). The construction of the causal mediation models was guided by the longitudinal analysis on the association between oral health problems with risk of incident disability. Mobility limitations was chosen as the disability outcome. Mobility limitations can influence the ability to perform ADL and IADL and can be an indirect indicator of decreased muscle strength and subsequent decreased physical function (Chen and Wilmoth, 2004; Visser *et al.*, 2005; Reid and Fielding, 2012).

Causal mediation analysis was performed only for oral health problems that were associated longitudinally with mobility limitations after adjustment for confounders. Thus, causal analysis was conducted in the BRHS, with tooth loss (2 levels), periodontal disease (2 levels) and dry mouth (3 levels) as independent/exposure

variables, and in the HABC Study, with complete tooth loss the only exposure. For inflammation in the BRHS, CRP, IL-6, and fibrin d-dimer were tested as mediators, and in the HABC Study, CRP and IL-6 were included as potential mediators. In both studies, mediation through diet was assessed via diet quality. Furthermore, causal mediation models were adjusted for the same set of confounders as in the simple longitudinal analysis. As a result, two causal diagrams were created: 1 for markers of inflammation and diet quality in the BRHS (Figure 7.1, page 206), and one causal diagram for both mediators in the HABC Study (Figure 7.2, page 207).

After exploring patterns of missingness of data used, low percentage of missing data was observed (see Chapter 3, sub-section 3.8.2). Therefore, complete case analyses was performed. Standard errors were clustered to account for the cohort study design.

7.4.6.3. Sensitivity analysis

First to check for the robustness of indirect effects of inflammation and diet quality in causal mediation analyses, interactions between mediators and exposure variables were tested. In the presence of interactions, indirect effects can be biased to the null (VanderWeele, 2016). Second, significant and strong associations between the mediator and confounders can influence reported indirect effects of the mediator and lead to biased results (mask effect of mediator). Therefore, the associations between confounders and mediators were also explored in both studies. Confounders which were associated with the mediators were excluded from the models to examine whether this would significantly change the indirect effect of each mediator. Finally, simple longitudinal analysis, similar to the one described in sub-section 7.4.6.1 was performed, but this time regression models were adjusted for confounders measured prior to exposure and mediators. This was done to test whether the TE's from khb analysis were the same as the odds ratios provided by the simple longitudinal analysis.

7.5. Results

7.5.1. Prospective associations of oral health problems with risk of incident disability

Population characteristics and prevalence of objective and subjective oral health problems at baseline (BRHS 2010-2012; HABC Study 1998-1999) were presented in Chapter 4.

7.5.1.1. Prospective associations of oral health problems with risk of incident mobility limitations

The odds ratios (OR) and 95% CIs for the association between oral health problems and risk of incident mobility limitations, and ADL difficulties in the BRHS are presented in Table 7.1. Having 0, 1-7, 8-14, and 15-20 when compared to ≥ 21 teeth were associated with greater risk of incident mobility limitations in the age adjusted model (n=970). After adjusting for age, social class, smoking, alcohol, physical activity, history of CVD and diabetes, and BMI only the associations for 8-14, and 15-20 teeth remained (n=855) (OR=2.05, 95% CI: 1.10-3.81; OR= 1.96, 95% CI: 1.12-3.43, respectively). Additionally, <21 teeth (vs. ≥ 21 teeth) was associated with greater risk of mobility limitations after adjusting for confounders (n=855) (OR=1.86, 95% CI: 1.16-3.01). Periodontal disease was also associated with higher risk of incident mobility limitations in the fully adjusted model (n=677) (OR= 1.75, 95% CI: 1.04-2.95). Having ≥ 3 dry mouth symptoms (vs. 0 symptoms) was associated with higher risk of mobility limitations after full adjustment (n=859) (OR= 2.08, 95% CI 1.27-3.42). A borderline significant association was observed for fair/poor self-rated oral health with risk of developing mobility limitations in the age adjusted model (n=1106), which was further attenuated and did not remain after adjusting for confounders (n=860). Cumulative oral health problems (2 vs. 0, and ≥ 3 vs. 0 problems) were associated with greater risk of mobility limitations only in the age adjusted model (n=978).

Odds ratios (OR) and 95% CIs for the association between oral health problems and risk of incident mobility limitations, and ADL difficulties in the HABC Study are

presented in Table 7.2. Having 0, and 8-14 teeth when compared to ≥ 21 teeth were associated with greater risk of developing mobility limitations in the age adjusted models (n=1333). After adjusting for age, gender, race, education, smoking, alcohol, physical activity, history of CVD and diabetes, and BMI (n=1309), only the association for complete tooth loss (0 vs. ≥ 21 teeth) remained (OR=1.86, 95% CI 1.13-3.06). No associations were observed between periodontal disease and risk of mobility limitations. In the age adjusted model (n=1805), fair/poor self-rated oral health was associated with higher risk of incident mobility limitations (OR=1.34, 95% CI 1.03-1.73), but this association did not remain after adjustment (n=1792). No associations were observed for dry mouth and risk of mobility limitations. Cumulative oral health problems (2 vs. 0, and ≥ 3 vs. 0 problems) were associated with greater risk of incident mobility limitations in the age adjusted model (n=1825) (≥ 3 problems, OR= 2.12, 95% CI 1.29-3.50). These associations did not remain in the fully adjusted model (n=1796).

7.5.1.2. Prospective associations of oral health problems with incident ADL difficulties

As presented in Table 7.1, in the BRHS, having 8-14 teeth when compared to ≥ 21 teeth was associated with greater risk of incident ADL difficulties in the age adjusted model (n=1070) (OR=2.19, 95% CI 1.24-3.84), but this association was attenuated and did not remain after full adjustment (n=944). Partial tooth loss (<21 teeth vs. ≥ 21 teeth) was associated with greater risk of incident ADL difficulties in both age (n=1070) and fully adjusted (n=944) models (fully adjusted, OR=1.68, 95% CI 1.02-2.73). Periodontal disease was not associated with risk of developing ADL difficulties. Fair/poor self-rated oral health was associated with increased risk of incident ADL difficulties only in the age adjusted model (n=1215) (OR=1.63, 95% CI 1.14-2.32). Having ≥ 3 dry mouth symptoms was associated with greater risk of developing ADL difficulties after adjusting for confounders (n=946) (OR=1.73, 95% CI 1.03-2.90). Cumulative oral health problems (2 vs. 0, and ≥ 3 vs. 0 problems) were associated with increased risk of incident ADL difficulties in both age (n=1269) and fully adjusted (n=980) models (fully adjusted, (2 vs. 0) OR=2.16, 95% CI 1.12-4.18; (≥ 3 vs. 0) OR=2.47, 95% CI 1.10-5.55).

As presented in Table 7.2, in the HABC Study, no associations between tooth loss, periodontal disease and risk of incident ADL difficulties were observed in both age and fully adjusted models. Fair/poor self-rated oral health was associated with greater risk of developing ADL difficulties in both age (n=1834) and fully adjusted (n=1821) models (fully adjusted, OR= 1.42, 95% CI 1.04-1.94). No associations were observed for dry mouth, cumulative oral health problems and risk of incident ADL difficulties.

7.5.1.3. Prospective associations of oral health problems with incident IADL difficulties (BRHS)

IADL difficulties were not assessed in the HABC Study, and therefore this analysis was only performed in the BRHS. The ORs and 95% CIs for the association of oral health problems with risk of incident IADL problems in the BRHS are presented in Table 7.3. Having 0 teeth when compared to ≥ 21 teeth was associated with greater risk of incident IADL difficulties in the age adjusted model (n=1095) (OR=2.02, 95% CI 1.20-3.40), but did not remain after adjustment (n=965). Likewise, partial tooth loss (<21 teeth vs. ≥ 21 teeth) was associated with increased risk of IADL problems in the age adjusted model (n=1095) (OR=1.56, 95% CI 1.03-2.37), but did not remain in the fully adjusted model (n=965). No significant associations were observed between periodontal disease and risk of IADL difficulties. Fair/poor self-rated oral health was associated with greater risk of developing IADL difficulties after full adjustment (n=968) (OR=2.09, 95% CI 1.34-3.26). No associations were observed for dry mouth symptoms and risk of IADL problems. Finally, cumulative oral health problems (2 vs. 0, and ≥ 3 vs. 0 problems) were associated with greater risk of incident IADL difficulties in the age adjusted model (n=1298) (≥ 3 vs. 0, OR= 2.40, 95% CI 1.19-4.85), but these associations did not remain after adjusting for confounders (n=1003).

7.5.2. Mediating effects of inflammation and diet quality

7.5.2.1. Inflammatory markers (CRP, IL-6, fibrin d-dimer)

The TE, NDE, NIE, and proportion of mediation for the association of partial tooth loss, and periodontal disease with risk of incident disability through inflammation in the BRHS are presented in Table 7.4. TE, NDE, and NIE are presented as odds ratios (OR), and only estimates from the fully adjusted models are presented.

Partial tooth loss and risk of incident mobility limitations (BRHS)

When CRP was considered as a mediator (n=799), the TE of partial tooth loss on development of mobility limitations was equal to 1.90 (95% CI 1.17-3.09).

Additionally, the NIE through CRP was 1.03 (95% CI 0.98-1.07). When IL-6 was considered (n=793), TE was equal to 1.80 (95% CI 1.09-2.97), whereas the NIE was not significant. For fibrin d-dimer (n=793), the TE of partial tooth loss was 1.79 (1.08, 2.94). The NIE through fibrin d-dimer was 1.00, and thus no mediation was observed.

Periodontal disease and risk of incident mobility limitations (BRHS)

The TE of periodontal disease with CRP as the mediator (n=641) was 1.78 (95% CI 1.03-3.07). The NIE for CRP was not significant. In the model testing the mediating effect of IL-6 (n=635), the TE of periodontal disease was 1.80 (95% CI 1.04-3.13), whereas the NIE through IL-6 was again not significant. For fibrin d-dimer (n=641), the TE of periodontal disease on mobility limitations was 1.78 (95% CI 1.03-3.07), and the NIE was not significant.

Dry mouth symptoms and risk of incident mobility limitations (BRHS)

The TE, NDE, NIE, and proportion of mediation for the association of dry mouth with risk of incident mobility limitations through inflammation in the BRHS are presented

in Table 7.5. When CRP was considered (n=800), the OR of the TE of ≥ 3 dry mouth symptoms was 2.29 (95% CI 1.34-3.90). Moreover, the NIE was 1.03 (95% CI 0.96-1.10). In the model with IL-6 as the mediator (n=795), the TE for ≥ 3 dry mouth symptoms was 2.24 (95% CI 1.30-3.89), and the NIE was 1.00. When fibrin d-dimer was considered (n=795), TE of ≥ 3 dry mouth symptoms was 2.24 (95% CI 1.30-3.88). Additionally, the NIE through fibrin d-dimer was 1.00.

Complete tooth loss and risk of incident mobility limitations (HABC Study)

The TE, NDE, NIE, and proportion of mediation for the association of complete tooth loss with risk of incident mobility limitations through inflammation in the HABC Study are presented in Table 7.6. TE, NDE, and NIE are included in the form of odds ratios (OR), and only estimates from the fully adjusted models are presented. When CRP was considered (n=1305), TE of complete tooth loss on incident mobility limitations was 1.92 (95% CI 1.19-3.08). Furthermore, the NIE was 1.00. When IL-6 was considered (n=1285), the TE of complete tooth loss was 1.88 (95% CI 1.17-3.03), whereas the NIE through IL-6 was not significant.

7.5.2.2. Diet quality (EDI, HEI scores)

The TE, NDE, NIE, and proportion of mediation for the association of partial tooth loss (n=773), periodontal disease (n=620), and dry mouth (n=867) with risk of mobility limitations through diet quality in the BRHS are presented in Table 7.7. TE, NDE, and NIE are included in the form of odds ratios (OR), and only estimates from the fully adjusted models are presented.

The TE of partial tooth loss on mobility limitations was 2.03 (95% CI 1.22-3.37). Furthermore, the NIE through diet quality (EDI score) was 1.03 (0.99, 1.08). The TE of periodontal disease on risk of mobility limitations was 1.82 (95% CI 1.10-3.02), whereas the NIE was not significant. The TE of ≥ 3 dry mouth symptoms on risk of incident mobility limitations was 2.41 (1.45-4.01), whereas the NIE was 1.00.

The TE, NDE, NIE, and proportion of mediation for the association of complete tooth loss, with risk of mobility limitations through diet quality (HEI score) (n=1305) in the HABC Study are presented in Table 7.8. TE, NDE, and NIE are included in the form of odds ratios (OR), and only estimates from the fully adjusted models are presented. The TE of complete tooth loss on risk of incident mobility limitations was 2.02 (95% CI 1.27-3.22), whereas the NIE was 1.03 (0.98-1.08).

In these results, that there was no evidence for mediation through inflammation and diet quality for the association between oral health and incidence of mobility limitations in older people in both studies.

7.5.3. Sensitivity analysis

First, when interactions between exposures and mediators were tested. In the BRHS, a significant interaction was observed between tooth loss and CRP, showing that tooth loss and CRP are correlated. Additionally, in both studies, a significant interaction between periodontal disease and CRP was observed. No other interactions were observed between oral health problems and IL-6 or fibrin d-dimer (BRHS). For diet quality, no significant interactions were observed.

Second, the results for significant interactions between mediators and confounders will now be presented. In both studies, indirect effects through inflammation did not change significantly after excluding confounders which were highly correlated with markers of inflammation. For diet quality, in the BRHS excluding specific confounders from the decomposition models did not lead to any significant changes in the indirect effects. However, in the HABC Study, when race and smoking were excluded separately from the models testing mediating effect of diet quality, the indirect effects did not change substantially but the odds ratios did become statistically significant.

Finally, total effects provided by causal mediation analysis were similar to the odds ratios reported by the simple longitudinal analysis which was adjusted for confounders measured prior to the exposure and mediators (results presented in Appendix L, Table L2).

7.6. Discussion

7.6.1. Summary of main findings

This Chapter examined the prospective associations of objective and subjective oral health problems with risk of incident disability. Additionally, the mediating effects of inflammatory markers (CRP, IL-6, fibrin d-dimer) and diet quality on the association between poor oral health and risk of incident mobility limitations were investigated.

Tooth loss, and dry mouth were associated with risk of incident mobility limitations and ADL difficulties. Periodontal disease was associated with risk of developing mobility limitations. Self-rated oral health was associated with risk of incident ADL and IADL difficulties. Cumulative oral health problems were associated with greater risk of ADL difficulties. Furthermore, the association between oral health problems and risk of incident mobility limitations did not appear to be mediated by CRP, or IL-6 in both studies. In the BRHS, these associations also did not appear to be mediated by fibrin d-dimer. Likewise, diet quality did not appear to mediate the relationship between poor oral health and risk of incident mobility limitations in older community-dwelling people.

7.6.2. Comparison with previous studies

7.6.2.1. Prospective associations of oral health problems with risk of incident disability

Tooth loss was associated with greater risk of developing mobility limitations and ADL difficulties. This is in accordance with previous studies which observed associations between tooth loss and risk of developing disability (Holm-Pedersen *et al.*, 2008; Aida *et al.*, 2012; Komiyama *et al.*, 2016; Sato *et al.*, 2016; Zhang *et al.*, 2018; Yin *et al.*, 2020). However, only two of these studies used ADL to measure disability (Zhang *et al.*, 2018; Yin *et al.*, 2020). Additionally, none of these studies examined the association between tooth loss and incidence of mobility limitations. Tooth loss, through its impact on chewing ability and food choices can influence

muscle strength and consequently the development of disability (Bradbury *et al.*, 2008; Bortoluzzi *et al.*, 2012; Hruby *et al.*, 2018).

Furthermore, in this study, periodontal disease was associated with higher risk of developing mobility limitations in older community-dwelling people. This is one of the first studies establishing the relationship between periodontal disease and risk of developing disability in older people. Periodontal disease is one of the leading causes of tooth loss in older age (Kinane *et al.*, 2017), and is associated with high levels of oral and systemic inflammation (Carrizales-Sepúlveda *et al.*, 2018; Kotronia *et al.*, 2020). High levels of inflammation are associated with onset of disability in older people (Cesari *et al.*, 2012; Dekker *et al.*, 2017). Therefore, periodontal disease-related inflammation, and diet changes could potentially explain this association in older people.

Fair/poor self-rated oral health was associated with greater risk of developing ADL and IADL difficulties in older age. In one previous study, self-rated oral health was associated with decline in ADL (Zhang *et al.*, 2018). Self-rated oral health can be influenced by tooth loss, periodontal disease and it can be linked to untreated oral disease (Northridge *et al.*, 2012). This association establishes a relationship between self-perception of oral health status and development of disability in later life and that poor self-rated oral status could be indicative of future health problems. Furthermore, having ≥ 3 dry mouth symptoms was associated with greater risk of incident mobility limitations and ADL difficulties. As described previously (Chapter 4) dry mouth can exacerbate already existing oral conditions, including tooth loss and periodontal disease (Han *et al.*, 2015). Additionally, dry mouth is associated with oral inflammation and compromised diet, and could therefore be linked to the development of disability in older people (Walls and Steele, 2004; Han *et al.*, 2015). Dry mouth can also be caused by medications prescribed for common conditions such as diabetes, and thus being an indirect indicator of health status (Thomson, 2015). However, when the associations were further adjusted for medications causing xerostomia (dry mouth), no significant changes were observed. Finally, having at least 3 oral health problems was associated with greater risk of ADL difficulties, which again highlights that the presence of more than one oral condition can significantly impact functional ability in community-dwelling older people.

Confirming the proposed mediating effects of inflammation and diet on the association of poor oral health with development of disability can lead to the development of intervention programmes which are designed to improve these specific components and eventually ameliorate the burden of diseases.

7.6.2.2. Causal mediation – Mediating effects of inflammation and diet quality

In the BRHS, CRP, IL-6 and fibrin d-dimer did not mediate the relationship between oral health problems (partial tooth loss, periodontal disease, dry mouth) and risk of developing mobility limitations. Likewise, CRP and IL-6 did not appear to have any mediating effects on the relationship between complete tooth loss and risk of incident mobility limitations in the HABC Study. In the sensitivity analyses it was observed that there was significant interaction between tooth loss, and periodontal disease with CRP. Moreover, potential multicollinearity bias in confounders in addition to interaction between exposure and mediator may have masked any significant indirect effects of CRP on the association of oral health problems with risk of incident mobility limitations. Also, it is possible that changes in markers of inflammation over time may be more useful in establishing the mediating effects of inflammation on this association.

Even though, there was lack of significant mediating effects of diet and inflammation these variables may still mediate the association between oral health and onset of disability. CRP, IL-6, and fibrinogen have been found to predict disability and poor physical function in later life (Wannamethee *et al.*, 2014; Friedman and Shorey, 2019). The production of CRP is triggered by elevations in cytokines, including IL-6 and there is a number of conditions which can lead to increases in levels of CRP including, viral infections, periodontal disease, cardiac conditions, increasing age (Singh and Newman, 2011; Bray *et al.*, 2016). CRP is sensitive to the intensity of the acute inflammation and as a result levels can fall significantly once inflammation recedes (Bray *et al.*, 2016). Moreover, levels of IL-6 increase with age, independent of the presence of acute infection (Singh and Newman, 2011). Likewise, levels of fibrin d-dimer also increase with age (Tita-Nwa *et al.*, 2010) and can influence the

production of IL-6 (Robson *et al.*, 1994). It is possible therefore that these variables may act synergistically as mediators.

In previous studies using causal mediation, inflammatory markers have been included as a latent variable, which accounts for measurement error and the interconnectedness of these markers (Friedman *et al.*, 2015). Nevertheless, there are some limitations in the use of latent variables. In particular, if they are not correctly specified, they can lead to biased estimates and findings which cannot be generalised (Jeon, 2015). Moreover, the variables used to construct a latent variable should be correlated, and in this study, inflammatory markers were weakly correlated (Zhang, 2017). Additionally, due to the binary nature of the outcome measure of disability, the khb method was performed which does not support the use of latent variables (Breen *et al.*, 2013). As a result separate models for CRP, IL-6, and fibrin d-dimer were created. Generally, it is hard to define inflammation in the human body, and probably using only CRP, IL-6 and fibrin d-dimer does not reflect inflammation appropriately.

In both studies, no mediating effects of diet quality were observed. A previous study indicated that eating problems, which can be viewed as a precursor of compromised diet, mediated the association of tooth loss with incidence of ADL disability (Yin *et al.*, 2020). The lack of significant mediating effects of diet quality in this Chapter does not indicate that diet does not mediate this relationship. It is possible that a bi-directional association between oral health and diet exists, which may have led to misspecification of the causal model, contributing to biased effect estimates (see Figure 7.3, page 210). Moreover, diet may be influencing this association through impacting other conditions, such as obesity, chronic diseases, muscle function (Savoca *et al.*, 2010; Hruby *et al.*, 2018; Parsons *et al.*, 2019). Furthermore, diet was measured at one time point, through an FFQ, and it is highly possible that the reported diet quality could change or fluctuate throughout the years.

If we were to think of poor oral health as a condition which represents the accumulation of life-stressors throughout the years, and therefore an indicator or result of poor general health it is highly possible that a combination of factors may mediate the association of oral health with risk of chronic diseases, disability, and eventually mortality. As a result, more complex mediation models are needed, which

will take into consideration the connectedness of factors such as inflammation, diet, and other health behaviours to establish the potential pathways. In addition it is important to demonstrate the relationships of oral health with other chronic diseases and mortality, which are undesirable endpoints in older people. Establishing more links between dental conditions/diseases and health outcomes will reinforce the notion that by improving oral health, general health status can be improved as well. Therefore, the associations between poor oral health and all- and specific cause mortality will be examined in Chapter 8.

7.6.3. Strengths and limitations

7.6.3.1. Strengths of this study

A major strength of this study is that causal mediation analysis was performed to examine the mediating effects of inflammation and diet quality. It is an important first step in identifying the factors that are implicated in the pathway linking oral health problems with the risk of developing disability in later life. Moreover, in the BRHS, mediation analysis was focused on more than one dental conditions, and therefore mediating effects were examined for both objective and subjective oral health problems. Furthermore, in the analyses of this Chapter various measures of disability were included, providing additional details on which components of daily life are influenced by oral health problems. This Chapter also provides much needed evidence on the associations between periodontal disease, self-rated oral health, dry mouth, and cumulative oral health problems with incidence of different measures of disability in older people.

7.6.3.2. Possible bias and limitations

There were some differences in the availability of disability and inflammation variables between the two studies. In the HABC Study, IADL was not available, and ADL was measured slightly different from BRHS. In addition, fibrin d-dimer was not available in the HABC Study. Moreover, self-reported measures of oral health may be sensitive to response bias (Ikebe *et al.*, 2007).

Causal mediation analysis rests on a number of strong assumptions about no confounding between exposure, mediator, and outcome (VanderWeele, 2016). Even though models were adjusted for confounders, it is possible that measured or unmeasured confounders may have influenced the reported effect estimates. Also, in causal mediation confounders should be measured prior to exposure and mediators to better estimate their effect on both exposure and mediators (VanderWeele, 2019). However, it cannot be ascertained that confounders did precede the presence of oral health problems because information on history of oral health was not available in both studies. Furthermore, significant interactions were observed between oral health and CRP. This can lead to biased indirect effects, particularly biased towards the null (VanderWeele and Vansteelandt, 2010). Therefore, the presented indirect effects of CRP may be underestimated. Nevertheless, no other interactions between exposure(s) and other mediators were observed. Additionally, in the HABC Study, for the model examining the mediating effect of diet quality (associations of tooth loss with risk of mobility limitations), when race and smoking were excluded separately from regression models, the indirect effects of diet quality were statistically significant but did not change much from those where race and smoking were included in the model. However, race and smoking were included as confounders in the models because these factors are important covariates influencing the exposure, mediators, and outcome.

In this study, a latent variable for inflammation was not constructed due to the limitations of latent variables and the performed method of causal mediation analysis. However, it is possible that inflammatory markers act synergistically, and this may explain the lack of significant indirect effects of inflammation. Furthermore, inflammation and diet quality were not included in the same causal model, and no sequential mediation analysis was performed. Sequential mediation analysis accounts for the direction of associations between mediators (VanderWeele and Vansteelandt, 2014). Diet and inflammation are linked and can influence each other (see Figure 7.3, page 210), and the reported estimates did not take account of the joint effect of these two mediators. However, the relationship between diet and inflammation can be bi-directional and therefore it would have been impossible to make assumptions in the direction of causality between these two mediators.

Diet quality was measured through FFQ's in both studies. Self-reported dietary intake can lead to misreporting of intakes, and this can introduce bias in the form of measurement error, as described in Chapter 6 (sub-section 6.6.3.2).

Attrition may have influenced reported results, with healthier individuals attending the examinations, and this may have contributed to underestimation of reported effect estimates. Finally, in simple longitudinal analyses, the issue of residual confounding still remains.

7.7. Conclusions

Tooth loss, periodontal disease, fair/poor self-rated oral health, dry mouth, and cumulative oral health problems were associated with risk of incident disability, after adjusting for confounders in older community-dwelling people. CRP, IL-6, and fibrin d-dimer did not appear to mediate the association between oral health problems and risk of incident mobility limitations. Additionally, diet quality also did not mediate the same association. More studies are needed in establishing prospective associations between poor oral health and incidence of disability, chronic diseases, and mortality. This will assist in adding valuable evidence about the impact of dental problems on older people's health. Further research should also investigate the causal pathways linking oral health with chronic conditions in older people and account for the complexity of bi-directional mediating effects. The association between oral health problems and all-cause, CVD and respiratory mortality will be examined in Chapter 8.

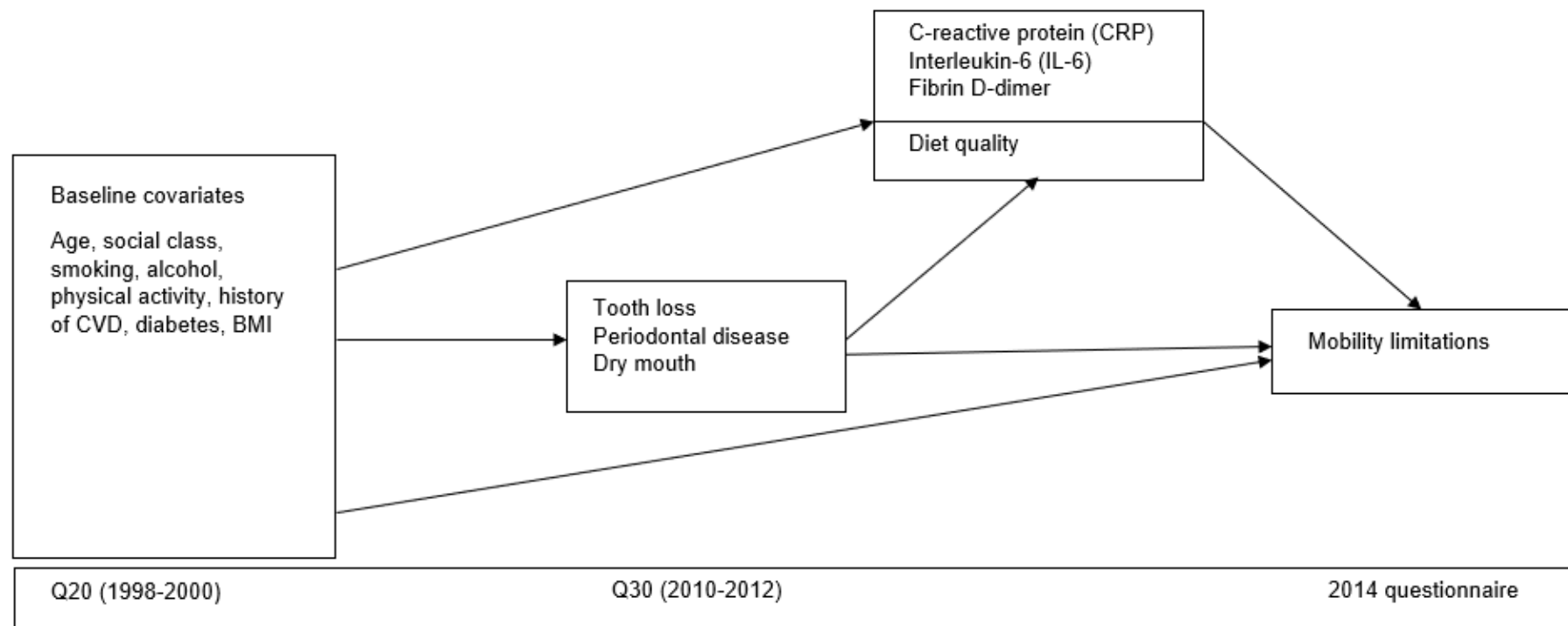


Figure 7.1. Causal diagram illustrating causal relationships between oral health problems and mobility limitations in the BRHS (inflammation, diet quality).

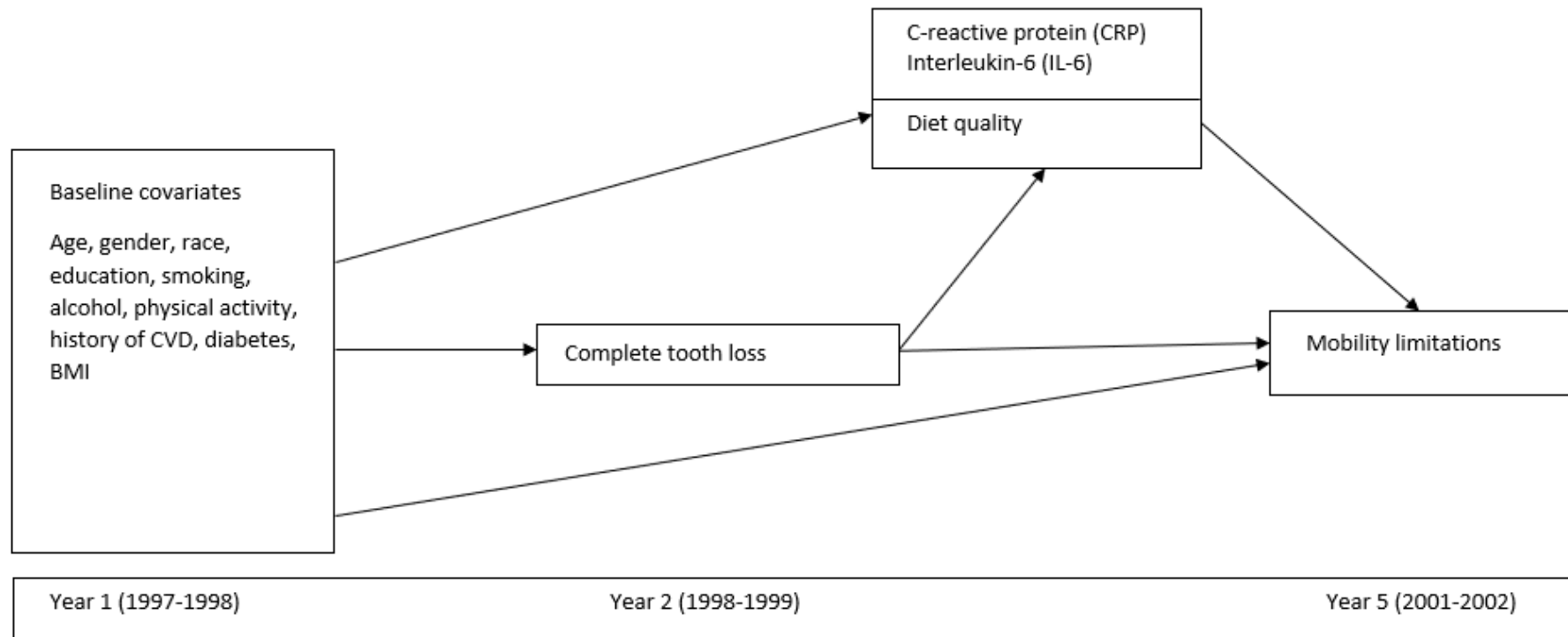


Figure 7.2. Causal diagram illustrating causal relationships between oral health problems and mobility limitations in the HABC Study (inflammation and diet quality).

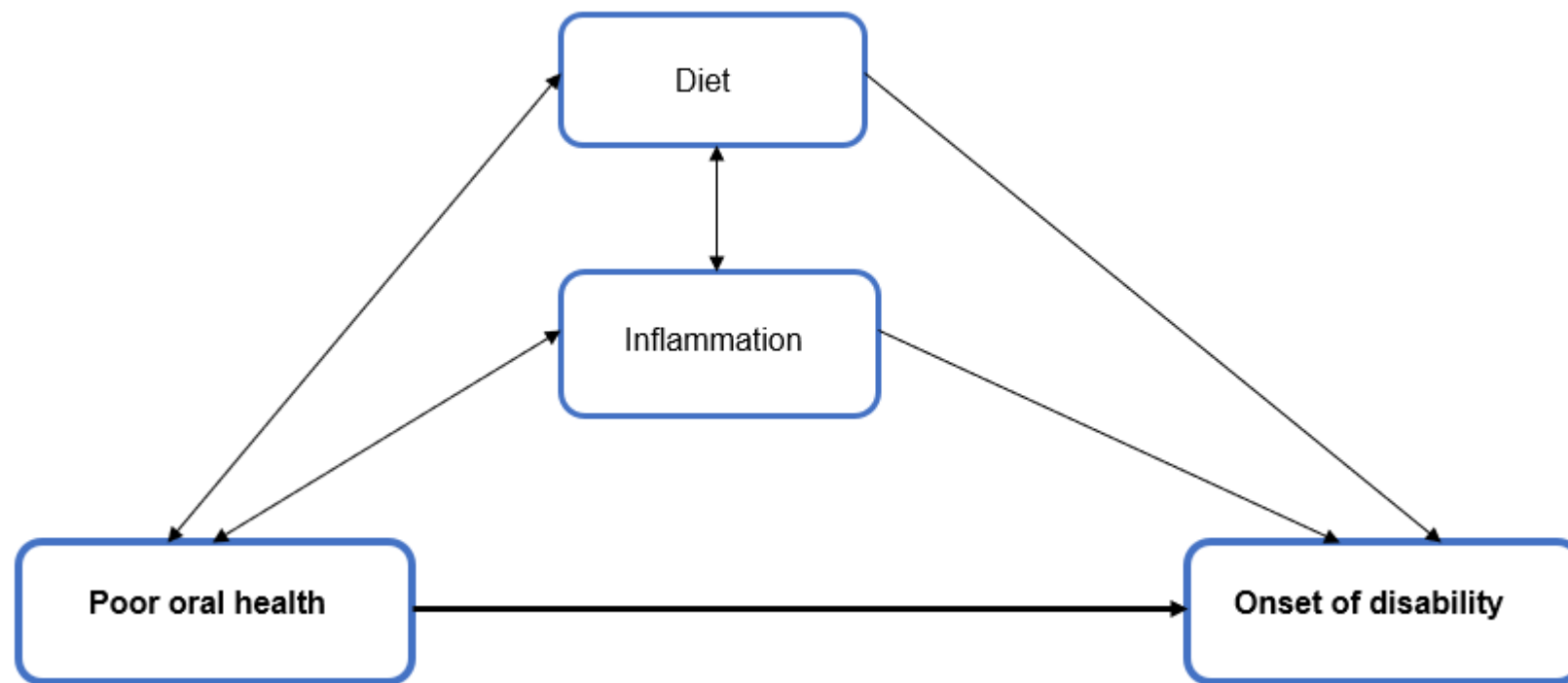


Figure 7.3. Causal diagram for poor oral health and onset of disability, showing bi-directional associations between mediators, and exposure and mediators.

Table 7.1. Odds ratios (95% CI) for the associations between oral health problems and risk of incident mobility limitations and Activities of Daily Living (ADL) difficulties in older British men aged 71-92 years at baseline in the BRHS.

Oral Health Problems	Incident Mobility Limitations (n=175; 15%)			Incident ADL (n=122; 11%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	N (%)	Age-adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss		<i>N=970</i>	<i>N=855</i>		<i>N=1070</i>	<i>N=944</i>
≥21 teeth	34 (9%)	1.00	1.00	31 (7%)	1.00	1.00
15-20 teeth	35 (17%)	2.02 (1.21, 3.36)	1.96 (1.12, 3.43)	29 (12%)	1.70 (0.99, 2.91)	1.68 (.0.93, 3.03)
8-14 teeth	33 (22%)	2.75 (1.62, 4.66)	2.05 (1.10, 3.81)	26 (16%)	2.19 (1.24, 3.84)	1.75 (0.91, 3.36)
1-7 teeth	13 (21%)	2.22 (1.08, 4.56)	2.03 (0.94, 4.37)	10 (14%)	1.76 (0.81, 3.83)	1.62 (0.70, 3.77)
0 teeth	30 (18%)	2.02 (1.18, 3.47)	1.49 (0.80, 2.77)	26 (14%)	1.64 (0.93, 2.89)	1.60 (0.84, 3.01)
Partial tooth loss						
≥21 teeth	34 (9%)	1.00	1.00	31 (7%)	1.00	1.00
<21 teeth	111 (19%)	2.22 (1.47, 3.36)	1.86 (1.16, 3.01)	91 (14%)	1.81 (1.17, 2.79)	1.68 (1.02, 2.73)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=768</i>	<i>N=677</i>		<i>N=838</i>	<i>N=739</i>
<20%	71 (12%)	1.00	1.00	63 (10%)	1.00	1.00
≥20%	38 (21%)	1.82 (1.17, 2.83)	1.75 (1.04, 2.95)	29 (15%)	1.50 (0.93, 2.43)	1.08 (0.61, 1.91)
Self-rated oral health		<i>N=1106</i>	<i>N=860</i>		<i>N=1215</i>	<i>N=946</i>
Excellent or good	104 (14%)	1.00	1.00	84 (10%)	1.00	1.00
Fair or poor	67 (19%)	1.41 (1.00, 1.97)	0.97 (0.64, 1.49)	63 (16%)	1.63 (1.14, 2.32)	1.16 (0.76, 1.80)
Dry mouth symptoms		<i>N=1107</i>	<i>N=859</i>		<i>N=1269</i>	<i>N=946</i>
0	49 (11%)	1.00	1.00	44 (9%)	1.00	1.00
1-2	62 (16%)	1.52 (0.91, 2.53)	1.36 (0.84, 2.20)	48 (11%)	1.25 (0.81, 1.94)	1.02 (0.61, 1.71)
≥3	59 (22%)	2.50 (1.45, 4.30)	2.08 (1.27, 3.42)	51 (16%)	1.90 (1.23, 2.93)	1.73 (1.03, 2.90)
Cumulative oral health problems^b		<i>N=978</i>	<i>N=889</i>		<i>N=1269</i>	<i>N=980</i>
0	21 (9%)	1.00	1.00	20 (8%)	1.00	1.00
1	78 (14%)	1.54 (0.93, 2.57)	1.38 (0.79, 2.43)	59 (10%)	1.18 (0.69, 2.01)	1.15 (0.61, 2.14)
2	53 (21%)	2.52 (1.46, 4.35)	1.50 (0.80, 2.83)	49 (17%)	2.35 (1.35, 4.08)	2.16 (1.12, 4.18)
≥3	23 (24%)	3.01 (1.57, 5.79)	2.34 (1.06, 5.17)	22 (20%)	2.63 (1.36, 5.08)	2.47 (1.10, 5.55)

^a adjusted for age, social class, smoking, alcohol, physical activity, history of CVD and diabetes, BMI

^b <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 7.2. Odds ratios (95% CI) for the association between oral health problems and incident mobility limitations and Activities of Daily Living (ADL) difficulties in older American men and women aged 71-80 years at baseline in the HABC Study.

Oral Health Problems	Incident mobility limitations (n=380; 20%)			Incident ADL (n=250; 13%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss		<i>N=1333</i>	<i>N=1309</i>		<i>N=1345</i>	<i>N=1324</i>
≥21 teeth	111 (16%)	1.00	1.00	84 (12%)	1.00	1.00
15-20 teeth	42 (17%)	1.05 (0.71, 1.55)	0.86 (0.57, 1.31)	31 (12%)	1.01 (0.65, 1.58)	0.80 (0.50, 1.28)
8-14 teeth	40 (23%)	1.52 (1.01, 2.29)	1.05 (0.67, 1.66)	23 (14%)	1.15 (0.70, 1.89)	0.89 (0.52, 1.52)
1-7 teeth	17 (15%)	0.90 (0.52, 1.56)	0.56 (0.30, 1.02)	11 (9%)	0.70 (0.36, 1.36)	0.58 (0.29, 1.15)
0 teeth	38 (31%)	2.33 (1.51, 3.60)	1.86 (1.13, 3.06)	17 (13%)	1.05 (0.60, 1.84)	0.77 (0.41, 1.44)
Complete tooth loss						
≥1 teeth	210 (17%)	1.00	1.00	149 (12%)	1.00	1.00
0 teeth	38 (31%)	2.12 (1.40, 3.22)	1.99 (1.25, 3.16)	17 (13%)	1.07 (0.62, 1.83)	0.90 (0.50, 1.61)
Periodontal disease (% of sites with loss of attachment ≥3 mm)		<i>N=807</i>	<i>N=797</i>		<i>N=812</i>	<i>N=805</i>
<20%	49 (16%)	1.00	1.00	31 (10%)	1.00	1.00
≥20%	73 (15%)	0.92 (0.62, 1.37)	0.85 (0.56, 1.31)	54 (10%)	0.99 (0.62, 1.58)	0.90 (0.55, 1.49)
Self-rated oral health		<i>N=1805</i>	<i>N=1792</i>		<i>N=1834</i>	<i>N=1821</i>
Excellent or good	238 (18%)	1.00	1.00	146 (11%)	1.00	1.00
Fair or poor	106 (22%)	1.34 (1.03, 1.73)	1.09 (0.83, 1.45)	81 (16%)	1.59 (1.19, 2.14)	1.42 (1.04, 1.94)
Dry mouth		<i>N=1801</i>	<i>N=1788</i>		<i>N=1835</i>	<i>N=1822</i>
No	331 (19%)	1.00	1.00	218 (12%)	1.00	1.00
Yes	13 (27%)	1.63 (0.85, 3.13)	1.45 (0.73, 2.89)	9 (16%)	1.41 (0.68, 2.92)	1.31 (0.62, 2.77)
Cumulative oral health problems^b		<i>N=1825</i>	<i>N=1796</i>		<i>N=1857</i>	<i>N=1827</i>
0	87 (15%)	1.00	1.00	66 (12%)	1.00	1.00
1	174 (19%)	1.28 (0.97, 1.70)	0.98 (0.72, 1.33)	109 (12%)	1.02 (0.74, 1.42)	0.83 (0.58, 1.17)
2	62 (25%)	1.85 (1.28, 2.68)	1.35 (0.91, 2.02)	36 (15%)	1.33 (0.86, 2.07)	1.08 (0.68, 1.71)
3	27 (28%)	2.12 (1.29, 3.50)	1.50 (0.87, 2.57)	21 (18%)	1.68 (0.98, 2.87)	1.27 (0.72, 2.26)

^aadjusted for age, gender, race, education, smoking, alcohol, physical activity, history of CVD and diabetes, BMI

^b<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 7.3. Odds ratios (95% CI) for the associations between oral health problems and incident Instrumental Activities of Daily Living (IADL) difficulties in older British men aged 71-92 years at baseline in the BRHS.

Oral Health Problems	Incident IADL (n=159; 12%)		
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Tooth loss		<i>N=1095</i>	<i>N=965</i>
≥21 teeth	36 (8%)	1.00	1.00
15-20 teeth	28 (12%)	1.39 (0.82, 2.35)	1.51 (0.83, 2.74)
8-14 teeth	24 (14%)	1.60 (0.92, 2.80)	1.48 (0.77, 2.84)
1-7 teeth	8 (11%)	1.10 (0.48, 2.51)	0.88 (0.33, 2.32)
0 teeth	34 (18%)	2.02 (1.20, 3.40)	1.56 (0.84, 2.91)
Partial tooth loss			
≥21 teeth	36 (8%)	1.00	1.00
<21 teeth	93 (14%)	1.56 (1.03, 2.37)	1.44 (0.88, 2.35)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=865</i>	<i>N=768</i>
<20%	62 (9%)	1.00	1.00
≥20%	27 (13%)	1.35 (0.82, 2.20)	1.47 (0.85, 2.56)
Self-rated oral health		<i>N=1244</i>	<i>N=968</i>
Excellent or good	83 (10%)	1.00	1.00
Fair or poor	72 (18%)	2.02 (1.43, 2.86)	2.09 (1.34, 3.26)
Dry mouth symptoms		<i>N=1249</i>	<i>N=970</i>
0	54 (11%)	1.00	1.00
1-2	57 (13%)	1.39 (0.92, 2.08)	1.21 (0.73, 2.01)
≥3	45 (14%)	1.45 (0.94, 2.24)	1.33 (0.78, 2.27)
Cumulative oral health problems^b		<i>N=1298</i>	<i>N=1003</i>
0	18 (7%)	1.00	1.00
1	87 (14%)	1.91 (1.12, 3.27)	1.27 (0.68, 2.35)
2	38 (13%)	1.90 (1.05, 3.44)	1.30 (0.65, 2.60)
≥3	18 (16%)	2.40 (1.19, 4.85)	1.81 (0.78, 4.23)

^a adjusted for age, social class, smoking, alcohol, physical activity, history of CVD and diabetes, BMI

^b <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table 7.4. Total effect (TE), natural direct effect (NDE), and natural indirect effect (NIE) of partial tooth loss and periodontal disease on incident mobility limitations, with mediation through C-reactive protein (CRP), interleukin-6 (IL-6), and fibrin d-dimer in the BRHS.

Partial tooth loss (<21 teeth vs. ≥ 21 teeth)			
	CRP (n=799)	IL-6 (n=793)	Fibrin d-dimer (n=793)
	Fully adjusted ^a OR (95% CI)	Fully adjusted ^a OR (95% CI)	Fully adjusted ^a OR (95% CI)
TE	1.90 (1.17, 3.09)	1.80 (1.09, 2.97)	1.79 (1.08, 2.94)
NDE	1.85 (1.13, 3.03)	1.81 (1.10, 2.98)	1.78 (1.08, 2.94)
NIE	1.03 (0.98, 1.07)	1.00 (0.98, 1.01)	1.00 (0.99, 1.01)
Percentage of proportion mediated	4.2%	-0.4%	0.15%
Periodontal disease (loss of attachment; >20% sites vs. ≤20% sites affected)			
	CRP (n=641)	IL-6 (n=635)	Fibrin d-dimer (n=641)
	Fully adjusted ^a OR (95% CI)	Fully adjusted ^a OR (95% CI)	Fully adjusted ^a OR (95% CI)
TE	1.78 (1.03, 3.07)	1.80 (1.04, 3.13)	1.78 (1.03, 3.07)
NDE	1.75 (1.02, 3.03)	1.78 (1.03, 3.09)	1.75 (1.02, 3.03)
NIE	1.02 (0.96, 1.07)	1.01 (0.97, 1.05)	1.02 (0.96, 1.07)
Percentage of proportion mediated	2.8%	1.8%	2.8%

^aage, social class, smoking, alcohol, physical activity, history of CVD and diabetes, BMI

Table 7.5. Total effect (TE), natural direct effect (NDE), and natural indirect effect (NIE) of dry mouth on incident mobility limitations, with mediation through C-reactive protein (CRP), interleukin-6 (IL-6), and fibrin d-dimer in the BRHS.

	Dry mouth symptoms ^a		1-2	≥3	1-2	≥3
	1-2	≥3				
	CRP (n=800)	IL-6 (n=795)				
	Fully adjusted ^b OR (95% CI)	Fully adjusted ^b OR (95% CI)	Fully adjusted ^b OR (95% CI)	Fully adjusted ^b OR (95% CI)	Fully adjusted ^b OR (95% CI)	Fully adjusted ^b OR (95% CI)
TE	1.50 (0.92, 2.47)	2.29 (1.34, 3.90)	1.58 (0.96, 2.60)	2.24 (1.30, 3.89)	1.57 (0.95, 2.59)	2.24 (1.30, 3.88)
NDE	1.51 (0.92, 2.48)	2.22 (1.31, 3.79)	1.57 (0.95, 2.60)	2.24 (1.29, 3.88)	1.57 (0.95, 2.59)	2.25 (1.30, 3.90)
NIE	1.00 (0.94, 1.06)	1.03 (0.96, 1.10)	1.00 (0.98, 1.02)	1.00 (0.98, 1.02)	1.00 (0.99, 1.01)	1.00 (0.97, 1.03)
Percentage of proportion mediated	-0.6%	3.4%	0.4%	0.4%	0.1%	-0.4%

^a0 dry mouth symptoms was the reference category for dry mouth

^bage, social class, smoking, alcohol, physical activity, history of CVD and diabetes, BMI

Table 7.6. Total effect (TE), natural direct effect (NDE), and natural indirect effect (NIE) of complete tooth loss on incident mobility limitations, with mediation through C-reactive protein (CRP), and Interleukin-6 (IL-6) in the HABC Study.

	Complete tooth loss (0 teeth vs. ≥ 1 teeth)	
	CRP (n=1305)	IL-6 (n=1285)
	Fully adjusted ^a OR (95% CI)	Fully adjusted ^a OR (95% CI)
TE	1.92 (1.19, 3.08) ²	1.88 (1.17, 3.03) ³
NDE	1.91 (1.19, 3.06)	1.86 (1.15, 2.99)
NIE	1.00 (0.98, 1.03)	1.01 (0.98, 1.04)
Percentage of proportion mediated	0.75%	2.1%

^aage, gender, race, education, smoking, alcohol, physical activity, history of CVD and diabetes, BMI

Table 7.7. Total effect (TE), natural direct effect (NDE), and natural indirect effect (NIE) of partial tooth loss, periodontal disease, and dry mouth on incident mobility limitations, with mediation through diet quality in the BRHS.

	Partial tooth loss (<21 teeth vs. ≥ 21 teeth)	Periodontal disease (pocket depth; >20% sites vs. ≤20% sites affected)	Dry mouth symptoms 1-2 vs. 0 ≥3 vs. 0	
	Diet quality (EDI score) (n=773)	Diet quality (EDI score) (n=620)	Diet quality (EDI score) (n=867)	
	Fully adjusted ^a OR (95% CI)	Fully adjusted ^a OR (95% CI)	Fully adjusted ^a OR (95% CI)	Fully adjusted ^a OR (95% CI)
TE	2.03 (1.22, 3.37)	1.82 (1.10, 3.02)	1.60 (0.99, 2.59)	2.41 (1.45, 4.01)
NDE	1.97 (1.18, 3.28)	1.83 (1.10, 3.04)	1.60 (0.99, 2.60)	2.40 (1.45, 3.99)
NIE	1.03 (0.99, 1.08)	0.99 (0.97, 1.03)	0.99 (0.96, 1.03)	1.00 (0.97, 1.04)
Percentage of proportion mediated	4.3 %	-0.8%	-1.0%	0.5%

^aage, social class, smoking, alcohol, physical activity, history of CVD and diabetes, BMI

Table 7.8. Total effect (TE), natural direct effect (NDE), and natural indirect effect (NIE) of complete tooth loss on incident mobility limitations, with mediation through diet quality in the HABC Study.

	Complete tooth loss (0 teeth vs. ≥ 1 teeth)
	Diet quality (HEI score) (n=1305)
	Fully adjusted ^a OR (95% CI)
TE	2.02 (1.27, 3.22)
NDE	1.96 (1.23, 3.12)
NIE	1.03 (0.98, 1.08)
Percentage of proportion mediated	4.3%

¹age, gender, race, education, smoking, alcohol, physical activity, history of CVD and diabetes, BMI

Chapter 8. Associations of Oral Health Problems with Risk of All-Cause, Cardiovascular Disease, and Respiratory Mortality in Older People in the UK and USA

8.1. Summary

Poor oral health is prevalent in older age. Oral diseases can influence a number of age-related health conditions. As described in previous Chapters, oral health problems were associated with increased inflammation, poor diet quality, disability, and poor physical function. In addition, poor oral health has also been found to be associated with increased risk of mortality. However, associations between oral health problems and cause-specific mortality are not well established. Moreover, the associations between subjective oral health problems and all- and cause-specific mortality in older people still remain unclear. In this Chapter, the associations of objective and subjective oral health problems with all-cause, cardiovascular disease (CVD), and respiratory mortality were examined. Data from the British Regional Heart Study (BRHS) and the Health, Aging, and Body Composition (HABC) Study were used. Oral health problems were assessed through (1) a dental examination (tooth loss, periodontal disease-objective) and (2) questionnaires (dry mouth, self-rated oral health, difficulty eating, sensitivity to hot/cold/sweets and limitation of food due to gum problems-subjective). In the BRHS, participants were followed up from re-examination at 2010-2012 through to June 2019, and in the HABC Study individuals were followed-up from Year 2 at 1998-1999 until September 2014. Cox proportional hazards models were used to assess associations of oral health problems with risk of all-cause mortality and estimates will be presented as hazard ratios (HR) and 95% CIs. Competing risks analysis was used to examine associations of oral health problems with risk of CVD mortality and estimates will be presented as subdistribution hazard ratios (SHR) and 95% CIs. Accelerated failure time models were performed to assess the associations between poor oral health and respiratory mortality and estimates will be presented as time ratios (TR) and 95% CIs. For objective oral health problems, tooth loss was associated with greater risk of all-cause and high respiratory mortality. Periodontal disease was associated

with greater risk of CVD mortality, while accounting for the competing risk of non-CVD deaths (SHR=1.49, 95% CI 1.01-2.20). Dry mouth was associated with increased risk of all-cause mortality (HR=1.46, 95% CI 1.15-1.84), and accumulation of oral health problems was associated with greater risk of all-cause (≥ 3 vs. 0 problems, HR= 1.27, 95% CI 1.04-1.55) and high respiratory mortality (2 vs. 0 problems, TR=0.77, 95% CI 0.61-0.97) in older people. In summary, some oral health problems (both objective and subjective) were associated with greater risk of all-cause and CVD mortality, as well as increased respiratory mortality in older people.

8.2. Introduction

Life expectancy can reflect burden of disease and population's health (Nunes *et al.*, 2016). The prevalence of oral health problems in older people is relatively high, and has been found to influence several health outcomes, including disability, CVD, and pneumonia (Terpenning *et al.*, 2001; Holm-Pedersen *et al.*, 2008; Cheng *et al.*, 2018; Lee *et al.*, 2019; Manabe *et al.*, 2019). Additionally, studies have suggested associations between oral health problems and increased risk of mortality, as discussed in Chapter 2 (section 2.7) (Holm-Pedersen *et al.*, 2008; Ansai *et al.*, 2010; Chen *et al.*, 2015; Hirotomi *et al.*, 2015; Iwasaki *et al.*, 2018b; Goto *et al.*, 2020). The majority of studies have focused on specific oral health problems, particularly tooth loss and periodontal disease (objective), and the associations with all-cause mortality. Nevertheless, findings for the associations between tooth loss, periodontal disease, and all-cause mortality in older people, remain inconsistent.

There is also paucity of studies examining the associations of subjective oral health problems (dry mouth, self-rated oral health) and accumulation of oral health problems with risk of all-cause mortality in community-dwelling older populations, with one study conducted in middle-aged and another one in older people living in nursing homes. Moreover, fewer studies have examined the associations of poor oral health with risk of CVD and respiratory mortality in older people. Identifying risk factors of CVD mortality is very important because CVD is one of the most common causes of death in older people, even if rates have declined the past years (Bhatnagar *et al.*, 2016). Poor oral health has been suggested as a risk factor of

CVD in older people (Alpert, 2017). However, the associations between objective and subjective oral health problems and risk of CVD mortality in older people are not well-established, especially for subjective oral health problems. Additionally, to my knowledge there are no studies performing competing risks analysis to investigate the relationship between oral health problems and risk of CVD mortality. Competing risks analysis calculates the risk of CVD mortality in the presence of other causes of death which can influence effect estimates and provide biased results if not considered (Austin *et al.*, 2016).

Additionally, in the UK, respiratory (any respiratory disease, flu, infectious diseases) mortality rates still remain high, even after improvements in care and decrease of smoking (Saliccioli *et al.*, 2018). Previous research, as mentioned in Chapter 2 (sub-section 2.7.3), has linked oral health problems, mainly tooth loss and periodontal disease with greater risk of respiratory mortality. However, a number of studies in older people have focused on mortality from pneumonia, rather than focusing on the association of poor oral health with total respiratory mortality. Moreover, few studies have been conducted in older populations, with the majority including non-Western adult and middle-aged populations.

8.3. Aim and Objectives

This Chapter aims to investigate the associations of objective and subjective oral health problems with risk of all-cause, CVD, and respiratory mortality in older people. The objectives of this Chapter are:

- I. To examine the associations of objective and subjective oral health problems with risk of all-cause mortality in older people.
- II. To investigate the associations of objective and subjective oral health problems with risk of CVD mortality, while accounting for the competing risk of non-CVD deaths in older people.
- III. To estimate the associations of objective and subjective oral health problems with respiratory mortality in older people.

8.4. Methods

Analyses in this Chapter are based on data from the BRHS and HABC Study. Details on both the BRHS and HABC Study, including selection of participants, data collection and data verifications can be found in Chapter 3 (Sections 3.2 and 3.5). This section (section 8.4) focuses on data used for the analyses presented in this Chapter.

8.4.1. Subjects and methods of data collection

In the BRHS, data are based on the 30-year re-examination in 2010-2012 when participants aged 71-92 years. At the 30-year re-examination men completed a questionnaire, and attended a physical examination. Participants were followed up prospectively for mortality from re-examination (2010-2012) through to June 2019. Information on mortality data collection is detailed in Chapter 3 (sub-section 3.2.4).

In the HABC Study, data are based on Year 2 examination in 1998-1999 when participants aged 71-80 years. At Year 2, individuals answered questionnaires and attended a physical examination. Participants were followed up prospectively for mortality from Year 2 (1998-1999) through to September 2014. Details on mortality data collection are described in Chapter 3 (sub-section 3.5.4).

8.4.2. Oral health

8.4.2.1. Objective oral health problems

Number of teeth and periodontal disease were assessed by trained professionals in both studies. Tooth loss was classified as having 0, 1-7, 8-14, 15-20, and ≥ 21 teeth. Having ≥ 21 teeth indicated a functional dentition (Hobdell *et al.*, 2003). Periodontal disease was measured according to Extent and Severity Index (Carlos *et al.*, 1986) and included loss of attachment and pocket depth. It was grouped in two binary variables according to percentage of sites affected ($>20\%$ sites affected vs. $\leq 20\%$ sites). Further details can be found in Chapter 3 (sub-sections 3.3.1 and 3.6.1).

8.4.2.2. Subjective oral health problems

Questionnaires were used to assess dry mouth, self-rated oral health, difficulty eating, sensitivity to hot/cold/sweets, limit of food due to problems with teeth or dentures. More details on these markers can be found in Chapter 3 (sections 3.3.1, and 3.6.1).

8.4.3. Mortality

The main outcomes examined in both studies were all-cause, CVD and respiratory mortality. In the BRHS, CVD mortality was defined as all fatal CVD events (ICD-9 codes 390-459). Respiratory mortality was defined as all fatal respiratory events (ICD-9 codes 461-5198). In the HABC, all fatal events were defined according to the adjudication protocol as described in sub-section 3.6.2. In the BRHS individuals were censored at the date of the failure event or end of study, whereas in the HABC Study censoring was performed for those who were alive, at the last day of contact.

8.4.4. Socio-demographic, lifestyle factors, biomarkers, and chronic diseases

In both studies, information on socioeconomic status, smoking, alcohol, history of CVD, and history of diabetes were measured through questionnaires (Weyant *et al.*, 2004; Lennon *et al.*, 2015). Diet quality was assessed by a Food Frequency questionnaire. BMI, blood pressure, forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC), respiratory rate, total blood cholesterol, total blood triglycerides, blood high-density lipoprotein cholesterol (HDL-C), C-reactive protein (CRP), interleukin-6 (IL-6), fibrin d-dimer, and high sensitivity Troponin T (hsTnT) were measured at the physical examinations. More details are provided in Chapter 3 (sections 3.3 and 3.6).

8.4.5. Statistical analysis

In both studies, cox proportional hazards regression was used to calculate the hazard ratios (HR) with 95% CIs for the association of objective and subjective oral

health problems with risk of all-cause mortality. To examine the association of poor oral health with risk of CVD mortality, competing risks analysis was performed. To estimate the cumulative hazard function the Fine-Grey subdistribution hazard model was used (Fine and Gray, 1999). Estimates from the Fine and Gray model are presented as subdistribution hazard ratios (SHR) with 95% CIs. The SHR represents the change in the rate of occurrence of the outcome of interest (i.e. mortality) due to the exposure in the presence of competing risks; a SHR which is greater than 1 shows an increase in mortality rate or in other words increased risk of mortality due to the exposure while considering the competing risk (Austin and Fine, 2017). In the analysis for the associations of oral health problems with respiratory mortality, the proportional hazard (PH) assumption was violated. As a result, Accelerated Failure Time (AFT) regression was performed. In this analysis, an acceleration factor was added to the hazard function of the model (Coppini *et al.*, 2000). Additionally, the Weibull distribution was chosen for data used in this study. Estimates are presented at time ratios (TR) with 95% CI. When performing AFT analysis effect estimates cannot be interpreted as risk ratios, but rather as time ratios reflecting whether the exposure leads to a decrease or increase in survival time without calculating the risk of dying from the outcome of interest. In particular, a time ratio smaller than 1 indicates that the exposure is harmful and there is decreased survival.

In the BRHS, models examining the associations of poor oral health with all-cause and CVD mortality were adjusted for age, social class, smoking, alcohol, physical activity, history of CVD and diabetes, BMI, diet quality, hypertension, triglycerides, HDL, CRP, IL-6, fibrin d-dimer and hsTnT. In the HABC Study, models for all-cause and CVD mortality were adjusted for age, gender, race, smoking, alcohol, physical activity, history of CVD and diabetes, diet quality, hypertension, total blood cholesterol, CRP, and IL-6. For respiratory mortality, in the BRHS, AFT models were further adjusted for FEV1/FVC ratio, whereas in the HABC Study, respiratory rate was added to the fully adjusted models.

8.5. Results

Prevalence of objective and subjective oral health problems and distribution of population characteristics has been presented in Chapter 4, Table 4.1. In the BRHS median survival time was 7.75 years and in the HABC study 12.6 years.

8.5.1. Associations of oral health problems with risk of all-cause mortality

HRs and 95% CIs for the associations between objective and subjective oral health problems and risk of all-cause mortality in older people in both studies are presented in Table 8.1. In the BRHS, 0, 1-7, and 8-14 teeth when compared to ≥ 21 teeth were associated with greater risk of all-cause mortality in the age adjusted models (n=1660). After adjusting for confounders (n=1185), only the association for 8-14 teeth remained (HR=1.59, 95% CI 1.09-2.31). Periodontal disease was associated with greater risk of all-cause mortality in the age adjusted model (n=1246) (HR=1.45, 95% CI 1.16-1.81), but this association was attenuated and did not remain after adjustment for confounders (n=914). No associations were observed for self-rated oral health. Experiencing ≥ 3 dry mouth symptoms was associated with increased risk of all-cause mortality only in the age adjusted model (n=2034) (HR=1.32, 95% CI 1.11-1.56). Likewise, cumulative oral health problems was associated with greater risk of all-cause mortality only in the age adjusted models (n=2147) (≥ 3 vs. 0 problems, HR= 1.79, 95% CI 1.34-2.38).

In the HABC Study, 0, 1-7, and 8-14 teeth when compared to ≥ 21 teeth were associated with greater risk of all-cause mortality in the age adjusted model (n=1973). After adjusting for confounders (n=1814), associations remained for 0, and 1-7 teeth (HR=1.33, 95% CI 1.06-1.65; HR=1.33, 95% CI 1.08-1.63, respectively). A borderline significant association was observed for periodontal disease and all-cause mortality in the age adjusted model (n=1136) (HR=1.17, 95% CI 1.00-1.48), which did not remain after adjustment for confounders (n=1066). No associations were observed for self-rated oral health. Dry mouth was associated with greater risk of all-cause mortality in both age (n=2718) and fully adjusted (n=2536) models (fully adjusted, HR=1.46, 95% CI 1.15-1.84). Likewise, having ≥ 3 oral health problems

was associated with all-cause mortality in both age (n=2760) and fully adjusted (n=2545) models (fully adjusted, HR=1.27, 95% CI 1.04-1.55).

8.5.2. Associations of oral health problems with risk of CVD mortality

Subdistribution hazard ratios (SHRs) and 95% CIs for the associations of objective and subjective oral health problems with risk of CVD mortality in both studies are presented in Table 8.2. In the BRHS, 1-7, and 8-14 teeth (vs. ≥ 21 teeth) were associated with greater risk of CVD mortality while considering the competing risk of non-CVD deaths in the age adjusted model (n=1660) (SHR=2.11, 95% CI 1.27-3.51; SHR=1.92, 95% CI 1.24-2.95, respectively). These associations were attenuated and did not remain statistically significant after adjustment for confounders (n=1185). For the association between periodontal disease and CVD mortality, in the fully adjusted model (n=914), a non-significant SHR equal to 1.50 (95% CI 0.93-2.40) was observed. No significant associations were present between fair/poor self-rated oral health, dry mouth symptoms and risk of CVD mortality. In the age adjusted model (n=2147), for the association between 2 oral health problems (vs. 0 problems) and risk of CVD mortality, the SHR was 1.49 (95% CI 0.98-2.26) and was further attenuated after adjustment for confounders (n=1232).

In the HABC Study, no significant associations were observed between tooth loss and CVD mortality in both age (n=1973) and fully adjusted (n=1814) models (0 vs. ≥ 21 teeth, SHR=1.49, 95% CI 0.95-2.26, fully adjusted). Periodontal disease was associated with greater risk of CVD mortality while considering the competing risk of non-CVD deaths after adjusting for confounders (n=1066) (SHR=1.49, 95% CI 1.01-2.20). No significant associations were observed for self-rated oral health, dry mouth, and accumulation of oral health problems with risk of CVD mortality.

8.5.3. Associations of oral health problems with respiratory mortality

Time ratios (TR) and 95% CIs for the associations of objective and subjective oral health problems with respiratory mortality in both studies are presented in Table 8.3. In the BRHS, having 0, and 1-7 teeth (vs. ≥ 21 teeth) was associated with higher

mortality from respiratory causes in the age adjusted models (n=1660) (TR=0.56, 95% CI 0.36-0.87; TR=0.46, 95% CI 0.27-0.78, respectively). After adjusting for confounders (n=1101), these associations were attenuated and did not remain significant. Periodontal disease was not associated with respiratory mortality. No associations were observed between self-rated oral health, dry mouth and increased respiratory mortality. For the associations between cumulative oral health problems and respiratory mortality TRs for 2 and ≥ 3 oral problems (vs. 0 problems) were identical but not significant in the age adjusted models (n=2147) (TR=0.65, 95% CI 0.40-1.04; TR=0.65, 95% CI 0.38-1.12, respectively). These estimates were further attenuated after adjustment (n=1147).

In the HABC Study, complete tooth loss when compared to ≥ 21 teeth was associated with high respiratory mortality in both age (n=1972) and fully adjusted (n=1813) models (fully adjusted, TR= 0.73, 95% CI 0.55-0.97). Likewise, having 1-7 teeth when compared to ≥ 21 teeth was associated with increased respiratory mortality after adjusting for confounders (n=1813) (TR=0.73, 95% CI 0.54-0.98). Periodontal disease was not associated with respiratory mortality. Likewise, fair/poor self-rated oral health was not associated with high respiratory mortality. Dry mouth was associated with increased mortality from respiratory causes in the age adjusted model (n=2718) (TR=0.71, 95% CI 0.52-0.96). After adjustment (n=2535) the effect estimate did not change but was no longer significant. Cumulative oral health problems were associated with increased respiratory mortality in both age (n=2760) and fully adjusted (n=2544) models (2 vs. 0 problems, TR= 0.77, 95% CI 0.61-0.97; ≥ 3 vs. 0 problems, TR= 0.76, 95% CI 0.58-1.01).

8.6. Discussion

8.6.1. Summary of main findings

This Chapter examined the associations of objective and subjective oral health problems with all-cause, CVD, and respiratory mortality in older people. Partial and complete tooth loss were associated with greater risk of all-cause mortality in older people. In the HABC Study, dry mouth and accumulation of oral health problems were associated with greater risk of all-cause mortality. Additionally, in the HABC

Study, periodontal disease was associated with increased risk of CVD mortality, while considering the competing risk of non-CVD deaths. Finally, in the HABC Study, partial, and complete tooth loss and accumulation of oral health problems were associated with increased respiratory mortality.

8.6.2. Comparison with previous studies

8.6.2.1. Associations of oral health problems with risk of all-cause mortality

In both studies, tooth loss was associated with greater risk of all-cause mortality, which is in accordance with previous research in older people (Fukai *et al.*, 2007; Holm-Pedersen *et al.*, 2008; Hayasaka *et al.*, 2013; Hu *et al.*, 2015). First, one possible explanation of this association is that tooth loss influences survival through its impact on chewing ability and consequently food choices and diet quality (Moynihan, 2007; Atkins *et al.*, 2014; de Souza *et al.*, 2015). In support of the intermediate role of diet, a recent study in older Japanese individuals suggested that nutritional status, measured by levels of serum albumin, mediated the association between tooth loss and all-cause mortality (Hiratsuka *et al.*, 2019). Second, tooth loss as a consequence of chronic periodontal disease, may be characterised by increased levels of oral inflammation (Ebersole *et al.*, 2016). Oral inflammation can contribute to elevated systemic inflammation which has long been implicated to increased risk of mortality in older populations (Ebersole *et al.*, 2016; Friedman and Shorey, 2019; Hiratsuka *et al.*, 2019). However, in this Chapter diet quality and inflammatory markers were included as confounders. It is possible that other measures of diet quality and/or inflammation that were not included as confounders may influence these associations. Third, the observed association of tooth loss with greater risk of all-cause mortality, may be due to the complex relationship that exists between tooth loss and general health, with tooth loss reflecting declining health and comorbidities (Friedman and Lamster, 2016; Gill *et al.*, 2020). In particular, tooth loss is associated with conditions including osteoporosis and cognitive impairment, two conditions which are closely related with mortality and are highly prevalent in older people (Friedman and Lamster, 2016). In other words, tooth loss may be a consequence of ageing and comorbidities, which then adds to the burden of chronic diseases and increases the risk of mortality.

Dry mouth and accumulation of oral health problems were also associated with greater risk of all-cause mortality. Previously, one study in an older Japanese population observed that older individuals with low production of saliva were at greater risk of all-cause mortality (Iwasaki *et al.*, 2018b). However, hyposalivation is not an indicator of self-perceived dry mouth; therefore the findings of this Chapter provide valuable evidence about the association of dry mouth and greater risk of all-cause mortality in older populations. Dry mouth can be a consequence of medications commonly prescribed for chronic diseases, such as diabetes and medications prescribed for CVD (Turner and Ship, 2007). However, in the analyses presented in this Chapter associations were not influenced by medication use, showing an independent association between dry mouth and risk of all-cause mortality. Furthermore, dry mouth can reflect presence of other dental problems including periodontal disease, caries, chewing problems, speech difficulty as well as sleep problems and comorbidities (Turner and Ship, 2007). Hence, the influence of dry mouth on mortality may be a consequence of a chronic poor general and oral health status.

8.6.2.2. Associations of oral health problems with risk of CVD mortality

In the HABC Study periodontal disease was associated with greater risk of CVD mortality, while taking account of the competing risk of non-CVD deaths. Similar effect estimates were observed in the BRHS but were not statistically significant. This may be due to a smaller sample size in the BRHS than the HABC Study. In the HABC Study, the association persisted even after adjusting for inflammation. In both studies, inflammation was assessed at one time point, which may not reflect the influence of chronic inflammation on this association. Also, as mentioned in sub-section 8.6.2.1. it is possible that different markers of inflammation may influence the reported association between periodontal disease and CVD mortality. Many studies have reported positive associations between periodontal disease and CVD and biomarkers related to CVD (Beck and Offenbacher, 2005; Belstrøm *et al.*, 2012). In periodontal disease, oral bacteria are concentrated in the infected area around the tooth, which then leads to inflammation and swelling of the surrounding tissue (Belstrøm *et al.*, 2012). Previous research has reported that the most frequent

bacteria found in atherosclerotic plaques come from the oral microflora (Amar *et al.*, 2009; Belstrøm *et al.*, 2012). It has also been indicated that bacteria related to periodontal disease can contribute to thrombus formation, pointing to a relationship between oral bacteria and platelets (Herzberg *et al.*, 1983). Clinical symptoms of periodontal disease are also affected by immune response, with high levels of inflammation increasing the immune response which can then lead to atherosclerotic changes (Beck and Offenbacher, 2005; Belstrøm *et al.*, 2012). Therefore, periodontal disease through its positive association with CVD, could contribute to an increased risk of CVD mortality.

8.6.2.3. Associations of oral health problems with increased respiratory mortality

In the HABC Study, partial, and complete tooth loss, and cumulative oral health problems were associated with increased mortality from respiratory causes. Similar magnitude of associations was observed between tooth loss and respiratory mortality in the BRHS; however, the associations were non-significant. Again, this may be a result of smaller sample size in the BRHS compared to the HABC Study. A previous study showed that those with missing teeth and eating problems had an increased risk of respiratory mortality when compared to those with a functional dentition (Aida *et al.*, 2011). Tooth loss related eating difficulties are associated with poor diet quality, which is characterised by low intakes of fruits and vegetables, and therefore low consumption of antioxidants (Moynihan, 2005). It has been found that those with periodontal disease, a major cause of tooth loss, were more likely to have low intake of antioxidants and vitamins (Iwasaki *et al.*, 2012b). Furthermore, treatments with vitamins have been found to be preventative of pneumonia and therefore can influence respiratory mortality (Hemilä, 2017). Additionally, tooth loss and respiratory mortality have been linked with low levels of vitamin D, and it is possible that vitamin D may play a role in increased respiratory mortality (Zhan *et al.*, 2014; Holter *et al.*, 2016). Moreover, oral bacteria have been found in the lungs of patients with pneumonia, highlighting that the associations between tooth loss and respiratory mortality could be due to periodontal disease related infections (D'Aiuto *et al.*, 2004). However, in this study we did not observe associations between periodontal disease and respiratory mortality. It is likely that in both studies, teeth

with severe periodontal disease may have already been lost with the healthier ones remaining and being assessed for periodontal disease. Finally, the association between accumulation of oral health problems with increased mortality shows that poor oral health status can impact survival in older people, and increase mortality rates from respiratory causes, something especially important for hospitalised older people, in whom rates of pneumonia and oral health problems are higher than community-dwelling individuals.

8.6.3. Strengths and limitations

8.6.3.1. Strengths of this study

This is one of the first studies investigating the associations of oral health problems with risk of CVD mortality, while considering the competing risks of non-CVD deaths. This analysis provides more reliable results, when competing risks are present. Additionally, this study offers much needed evidence for the associations of subjective oral health problems (dry mouth, self-rated oral health), and accumulation of oral health problems with all-cause, CVD and respiratory mortality in older people. Also, it further establishes associations between objective oral health problems and cause-specific mortality in older age. Finally, both studies, included comparable oral health data, both objectively and subjectively assessed.

8.6.3.2. Possible bias and limitations

Differences existed in the measurement of certain oral health problems (i.e. periodontal disease, dry mouth) and follow-up was shorter in the BRHS than the HABC Study. However, similar associations were observed for some oral health problems with mortality in both studies. Moreover, self-reported measures of oral health may be sensitive to response bias (Ikebe *et al.*, 2007).

Furthermore, in both studies findings may not be generalisable to the whole older population of the UK and USA. Additionally, healthier individuals may have attended the physical examinations and answered questionnaires, and thus associations between oral health and mortality may have been underestimated. In the analysis

presented in this Chapter, CVD mortality may have been a competing risk in the association between oral health problems and respiratory mortality. However, due to the violation of PH assumption for respiratory mortality, it was not possible to perform competing risks analysis for this outcome. In both studies, most of the observed associations of poor oral health and all-cause and cause-specific mortality were reported for objective oral health problems, including tooth loss and periodontal disease. For subjective oral health problems, only dry mouth was associated with risk of all-cause mortality after adjusting for confounders and only in the HABC Study. This raises the issue of the validity of self-reported measures of oral health as predictors of mortality in older populations. Finally, there is still the risk of residual confounding, even if adjustment for several confounders was conducted.

8.7. Conclusions

Tooth loss was associated with increased risk of all-cause mortality in both studies. Dry mouth and cumulative oral health problems were associated with greater risk of all-cause mortality in the HABC Study. Periodontal disease was associated with greater risk of CVD mortality, while taking account of competing risks of non-CVD deaths in older people in the HABC Study. Moreover, in the HABC Study, tooth loss, and cumulative oral health problems were associated with increased respiratory mortality in older individuals. These findings highlight the role of poor oral health as a risk factor of shortened longevity. Modifying and improving oral health in older people can have a significant effect in survival through its impact on disease prognosis. Future research should focus on the pathways that underpin these associations, to better understand which behaviours or health components influence the relationship between oral health and mortality. This will also clarify the mechanistic pathways involved in the associations of poor oral health with chronic diseases since similar factors have been implicated as mediating factors (i.e. inflammation, diet). Moreover, more studies are needed on the association between (a) subjective oral health problems and risk of mortality and (b) poor oral health and other causes of death, including cancer as well as how different combinations of oral health problems influence risk of mortality.

Table 8.1. Hazard ratios (HR) and 95% confidence intervals (CI) for the association between oral health problems and risk of all-cause mortality in older people in the BRHS after 9 years of follow-up and in the HABC Study after 15 years of follow-up.

BRHS				HABC Study			
Oral Health Problems	All-cause mortality			Oral Health Problems	All-cause mortality		
	N (%)	Age adjusted HR (95% CI)	Fully adjusted ^a HR (95% CI)		N (%)	Age adjusted HR (95% CI)	Fully adjusted ^b HR (95% CI)
Tooth loss		<i>N=1660</i>	<i>N=1185</i>	Tooth loss		<i>N=1973</i>	<i>N=1814</i>
≥21 teeth	144 (26)	1.00	1.00	≥21 teeth	544 (58)	1.00	1.00
15-20 teeth	99 (29)	1.14 (0.88, 1.47)	0.97 (0.71, 1.32)	15-20 teeth	220 (61)	1.11 (0.95, 1.30)	0.98 (0.83, 1.16)
8-14 teeth	96 (36)	1.40 (1.08, 1.82)	1.06 (0.76, 1.47)	8-14 teeth	181 (64)	1.22 (1.03, 1.44)	1.08 (0.90, 1.30)
1-7 teeth	60 (49)	1.71 (1.26, 2.32)	1.59 (1.09, 2.31)	1-7 teeth	121 (66)	1.48 (1.21, 1.81)	1.33 (1.06, 1.65)
0 teeth	156 (46)	1.71 (1.36, 2.15)	1.16 (0.85, 1.57)	0 teeth	157 (75)	1.47 (1.23, 1.76)	1.33 (1.08, 1.63)
Periodontal disease (% of sites with loss of attachment >5.5 mm)		<i>N=1246</i>	<i>N=914</i>	Periodontal disease (% of sites with pocket depth ≥ 3 mm)		<i>N=1136</i>	<i>N=1066</i>
≤20%	249 (26)	1.00	1.00	≤20%	270 (53)	1.00	1.00
>20%	116 (38)	1.45 (1.16, 1.81)	1.24 (0.94, 1.63)	>20%	378 (60)	1.17 (1.00, 1.48)	1.09 (0.92, 1.29)
Self-rated oral health		<i>N=2039</i>	<i>N=1191</i>	Self-rated oral health		<i>N=2717</i>	<i>N=2536</i>
Excellent or good	472 (36)	1.00	1.00	Excellent or good	1168 (62)	1.00	1.00
Fair or poor	297 (41)	1.15 (0.99, 1.33)	1.10 (0.89, 1.36)	Fair or poor	544 (66)	1.11 (1.00, 1.23)	0.99 (0.89, 1.11)
Dry mouth symptoms		<i>N=2034</i>	<i>N=1200</i>	Dry mouth		<i>N=2718</i>	<i>N=2536</i>
0	258 (34)	1.00	1.00	No	1630 (62)	1.00	1.00
1-2	232 (35)	1.07 (0.89, 1.28)	1.10 (0.85, 1.42)	Yes	86 (80)	1.52 (1.23, 1.90)	1.46 (1.15, 1.84)
≥ 3	274 (45)	1.32 (1.11, 1.56)	1.22 (0.94, 1.57)				
Cumulative oral health problems^c		<i>N=2147</i>	<i>N=1232</i>	Cumulative oral health problems^d		<i>N=2760</i>	<i>N=2545</i>
0	85 (25)	1.00	1.00	0	442 (57)	1.00	1.00
1	393 (38)	1.48 (1.17, 1.88)	1.23 (0.90, 1.67)	1	886 (65)	1.30 (1.16, 1.45)	1.15 (1.02, 1.30)
2	239 (44)	1.74 (1.35, 2.23)	1.29 (0.92, 1.82)	2	258 (65)	1.25 (1.07, 1.46)	1.08 (0.92, 1.28)
≥3	105 (46)	1.79 (1.34, 2.38)	1.32 (0.88, 1.97)	≥3	157 (70)	1.45 (1.21, 1.74)	1.27 (1.04, 1.55)

^aage, social class, smoking, alcohol, physical activity, history of CVD and diabetes, BMI, EDI score, hypertension, triglycerides, HDL, CRP, IL-6, fibrin d-dimer, hsTnT

^bage, gender, race, education, smoking, alcohol, physical activity, history of CVD and diabetes, BMI, HEI score, hypertension, blood cholesterol, CRP, IL-6

^c<21 teeth, ≥3 symptoms of dry mouth, difficulty eating, sensitivity hot/cold/sweet

^d<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 8.2. Competing risk analysis (subdistribution hazard ratios (SHR) and 95% confidence intervals (CI)) for the association between oral health problems and risk of CVD mortality in older people in the BRHS after 9 years of follow-up and in the HABC Study after 15 years of follow-up.

BRHS				HABC Study			
		CVD mortality				CVD mortality	
Oral Health Problems	N (%)	Age adjusted SHR (95% CI)	Fully adjusted ^a SHR (95% CI)	Oral Health Problems	N (%)	Age adjusted SHR (95% CI)	Fully adjusted ^b SHR (95% CI)
Tooth loss		<i>N=1660</i>	<i>N=1185</i>	Tooth loss		<i>N=1973</i>	<i>N=1814</i>
≥21 teeth	41 (7)	1.00	1.00	≥21 teeth	123 (13)	1.00	1.00
15-20 teeth	30 (9)	1.14 (0.72, 1.80)	0.99 (0.56, 1.73)	15-20 teeth	43 (12)	0.91 (0.65, 1.29)	0.91 (0.62, 1.32)
8-14 teeth	38 (14)	1.92 (1.24, 2.95)	1.53 (0.86, 2.71)	8-14 teeth	47 (17)	1.31 (0.93, 1.83)	1.25 (0.85, 1.82)
1-7 teeth	22 (18)	2.11 (1.27, 3.51)	1.67 (0.82, 3.40)	1-7 teeth	22 (12)	0.93 (0.59, 1.46)	0.87 (0.52, 1.47)
0 teeth	42 (12)	1.33 (0.86, 2.07)	1.04 (0.59, 1.85)	0 teeth	37 (18)	1.37 (0.95, 1.98)	1.46 (0.95, 2.26)
Periodontal disease (% of sites with pocket depth >3.5 mm)		<i>N=1245</i>	<i>N=914</i>	Periodontal disease (% of sites with pocket depth ≥ 3 mm)		<i>N=1136</i>	<i>N=1066</i>
≤20%	77 (9)	1.00	1.00	≤20%	49 (10)	1.00	1.00
>20%	39 (11)	1.27 (0.88, 1.85)	1.50 (0.93, 2.40)	>20%	87 (14)	1.54 (1.08, 2.19)	1.49 (1.01, 2.20)
Self-rated oral health		<i>N=2039</i>	<i>N=1191</i>	Self-rated oral health		<i>N=2065</i>	<i>N=1926</i>
Excellent or good	61 (5)	1.00	1.00	Excellent or good	270 (14)	1.00	1.00
Fair or poor	49 (7)	1.21 (0.94, 1.57)	1.14 (0.77, 1.69)	Fair or poor	128 (15)	1.09 (0.88, 1.35)	1.12 (0.90, 1.40)
Dry mouth symptoms		<i>N=2034</i>	<i>N=1193</i>	Dry mouth		<i>N=2066</i>	<i>N=1927</i>
0	32 (4)	1.00	1.00	No	378 (14)	1.00	1.00
1-2	35 (5)	1.14 (0.83, 1.56)	1.12 (0.69, 1.81)	Yes	20 (19)	1.32 (0.84, 2.07)	1.39 (0.86, 2.23)
≥3	43 (7)	1.33 (0.97, 1.80)	1.31 (0.81, 2.12)				
Cumulative oral health problems^c		<i>N=2147</i>	<i>N=1232</i>	Cumulative oral health problems^d		<i>N=2103</i>	<i>N=1933</i>
0	18 (5)	1.00	1.00	0	102 (13)	1.00	1.00
1	49 (5)	0.98 (0.66, 1.46)	0.68 (0.40, 1.18)	1	206 (15)	1.18 (0.93, 1.50)	1.16 (0.90, 1.51)
2	36 (6)	1.49 (0.98, 2.26)	1.10 (0.62, 1.94)	2	63 (16)	1.23 (0.90, 1.68)	1.27 (0.91, 1.78)
≥3	14 (6)	1.40 (0.86, 2.28)	0.97 (0.50, 1.92)	≥3	30 (13)	1.05 (0.70, 1.58)	1.10 (0.70, 1.71)

^aage, social class, smoking, alcohol, physical activity, history of CVD and diabetes, BMI, EDI, hypertension, triglycerides, HDL, CRP, IL-6, fibrin d-dimer, hsTnT

^bage, gender, race, education, smoking, alcohol, physical activity, history of CVD and diabetes, BMI, HEI score, hypertension, blood cholesterol, CRP, IL-6

^c<21 teeth, ≥3 symptoms of dry mouth, difficulty eating, sensitivity hot/cold/sweet

^d<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table 8.3. Accelerated failure time analysis (Time Ratios (TR) and 95% confidence intervals (CI)) for the association between oral health problems and respiratory mortality in older people in the BRHS after 9 years of follow-up and the HABC Study after 15 years of follow-up.

BRHS				HABC Study			
Oral Health Problems		Respiratory mortality		Oral Health Problems		Respiratory mortality	
		Age adjusted TR (95% CI)	Fully adjusted ^a TR (95% CI)			Age adjusted TR (95% CI)	Fully adjusted ^b TR (95% CI)
		N (%)				N (%)	
Tooth loss				Tooth loss			
			<i>N=1660</i>				<i>N=1972</i>
			<i>N=1101</i>				<i>N=1813</i>
≥21 teeth	18 (3)	1.00	1.00	≥21 teeth	55 (6)	1.00	1.00
15-20 teeth	16 (5)	0.76 (0.47, 1.23)	0.89 (0.53, 1.50)	15-20 teeth	26 (7)	0.87 (0.69, 1.11)	0.95 (0.74, 1.21)
8-14 teeth	14 (5)	0.72 (0.43, 1.18)	1.15 (0.60, 2.22)	8-14 teeth	20 (7)	0.86 (0.66, 1.12)	0.88 (0.68, 1.14)
1-7 teeth	13 (11)	0.46 (0.27, 0.78)	0.85 (0.41, 1.75)	1-7 teeth	15 (8)	0.76 (0.57, 1.02)	0.73 (0.54, 0.98)
0 teeth	28 (8)	0.56 (0.36, 0.87)	0.72 (0.44, 1.19)	0 teeth	18 (9)	0.74 (0.56, 0.97)	0.73 (0.55, 0.97)
Periodontal disease (% of sites with loss of attachment >5.5 mm)				Periodontal disease (% of sites with loss of attachment ≥ 3 mm)			
			<i>N=1246</i>				<i>N=1133</i>
			<i>N=889</i>				<i>N=1064</i>
≤20%	36 (4)	1.00	1.00	≤20%	23 (6)	1.00	1.00
>20%	16 (5)	0.85 (0.59, 1.23)	1.04 (0.65, 1.64)	>20%	54 (7)	0.83 (0.65, 1.07)	0.90 (0.70, 1.16)
Self-rated oral health				Self-rated oral health			
			<i>N=2039</i>				<i>N=2717</i>
			<i>N=1108</i>				<i>N=2535</i>
Excellent or good	76 (6)	1.00	1.00	Excellent or good	126 (7)	1.00	1.00
Fair or poor	54 (8)	0.85 (0.66, 1.09)	1.02 (0.71, 1.45)	Fair or poor	68 (8)	0.87 (0.75, 1.02)	0.97 (0.83, 1.14)
Dry mouth symptoms				Dry mouth			
			<i>N=2034</i>				<i>N=2718</i>
			<i>N=1114</i>				<i>N=2535</i>
0	42 (5)	1.00	1.00	No	184 (7)	1.00	1.00
1-2	42 (6)	0.89 (0.66, 1.21)	1.05 (0.71, 1.55)	Yes	12 (11)	0.71 (0.52, 0.96)	0.75 (0.55, 1.02)
≥3	47 (8)	0.84 (0.62, 1.12)	1.24 (0.81, 1.90)				
Cumulative oral health problems^c				Cumulative oral health problems^d			
			<i>N=2147</i>				<i>N=2760</i>
			<i>N=1147</i>				<i>N=2544</i>
0	11 (3)	1.00	1.00	0	41 (5)	1.00	1.00
1	75 (7)	0.61 (0.39, 0.96)	0.93 (0.56, 1.54)	1	99 (7)	0.79 (0.65, 0.96)	0.85 (0.70, 1.03)
2	38 (7)	0.65 (0.40, 1.04)	1.11 (0.62, 1.96)	2	36 (9)	0.70 (0.55, 0.90)	0.77 (0.61, 0.97)
≥3	16 (7)	0.65 (0.38, 1.12)	1.38 (0.64, 3.00)	≥3	23 (10)	0.64 (0.49, 0.84)	0.76 (0.58, 1.01)

^aage, social class, smoking, alcohol, physical activity, history of CVD and diabetes, BMI, EDI, FEV1/FVC, hypertension, triglycerides, HDL, CRP, IL-6, fibrin d-dimer, hsTnT

^bage, gender, race, education, smoking, alcohol, physical activity, history of CVD and diabetes, BMI, HEI, respiration rate, hypertension, blood cholesterol, CRP, IL-6

^c<21 teeth, ≥3 symptoms of dry mouth, difficulty eating, sensitivity hot/cold/sweet

^d<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Chapter 9. Implications and Conclusions

9.1. Summary

This Chapter describes the implications of the findings of this thesis for public health and future epidemiological research. Overall, the results showed that poor oral health was associated cross-sectionally with disability, poor physical function, increased inflammation and poor diet quality and dietary intake in older people. Additionally, it was found that poor oral health is a potential risk factor for onset of disability, and risk of all-cause, cardiovascular disease (CVD), and increased respiratory mortality, while poor diet quality and increased inflammation did not seem to mediate the association between poor oral health and onset of disability. Public health implications consist of the need to: a) improve the assessment of oral health to better predict the risk of developing disability and the risk of shortened survival in older individuals; b) prevent accumulation of oral health problems to improve prognosis of age-related health outcomes; c) improve guidance on appropriate management and treatment of dental problems in older adults while incorporating them in community programmes aiming to protect general health; d) target improvement of dental health in young and middle-aged adults and e) improve oral health through targeted dietary intervention programmes in community settings f) address impact of social determinants of oral health and design upstream and community-based strategies to improve oral health throughout the life course. These findings also have implications for future epidemiological studies which include the need: i) to carry out larger epidemiological studies in diverse community-dwelling older populations examining the associations between poor oral health and risk of disability, all-cause, and cause-specific mortality; ii) to focus on a homogeneous definition of poor oral health-using similar assessment tools measuring both oral diseases and self-reported measures which represent the influence of dental problems on quality of life; iii) for more studies on the associations of poor oral health with haemostatic and cardiac biomarkers in older people to replicate and confirm findings presented in this thesis; iv) to examine further how oral health problems are related to diet quality and nutritional intake, as well as how changes in oral health affect changes in diet quality over time; and v) for more research on the mediating

roles of diet and inflammation in the prospective association between poor oral health and risk of developing disability in older adults.

9.2. Introduction

9.2.1. Key findings

The research in this thesis has addressed the following objectives examining (a) the cross-sectional associations of objective and subjective oral health problems with disability, physical function, diet quality and nutritional intake, and inflammatory, haemostatic and cardiac biomarkers in older people; (b) the prospective associations of objective and subjective oral health problems with the risk of developing disability, and with all-cause, CVD and respiratory mortality as well as investigating pathways underpinning the association between oral health and risk of developing disability. To address these objectives, data from two population-based cohort studies of older people were used; the British Regional Heart Study (BRHS) which included older British men aged 71-92 years and the Healthy, Aging and Body Composition (HABC) Study which comprised older US men and women aged 71-80 years.

Chapter 4 indicated that both objective (tooth loss) and subjective (self-rated oral health, dry mouth) oral health problems were cross-sectionally associated with mobility limitations, difficulties with activities of daily living (ADL) and instrumental activities of daily living (IADL). Additionally, it showed that presence of more than one health problem was associated with all three measures of disability.

Furthermore, Chapter 4 suggested that oral health problems including, periodontal disease and dry mouth were associated with weak handgrip strength, whereas poor self-rated oral health and dry mouth were associated with slow walking speed.

Findings from Chapter 5 revealed that oral health problems are linked to high levels of inflammation; particularly tooth loss was associated with elevated inflammatory (CRP, IL-6), haemostatic (fibrin d-dimer), and cardiac biomarkers (hsTnT, NT-proBNP), whereas accumulation of oral health problems was associated with high levels of inflammatory (CRP, IL-6), and haemostatic (vWF) biomarkers. Chapter 6 showed that individuals with objective and subjective oral health problems were more likely to have poor diet quality, but also individuals with persistent poor diet

quality over the years (~10yrs) were at greater risk of experiencing oral health problems later in life. In particular, in this Chapter tooth loss, fair/poor self-rated oral health, and cumulative oral health problems were associated with poor diet quality. Additionally, both objective and subjective oral health problems were associated with increased intakes of total energy, calories from saturated and trans-fatty acids, processed meat, calories from sweets and soda, low intake of fruits and vegetables, and low intakes of vitamins/antioxidants.

Findings from Chapter 7 provided evidence on the role of various oral health problems as determinants of the onset of disability in older age. In particular, tooth loss, and dry mouth seem to be strong risk factors of mobility limitations and ADL difficulties in older age. Additionally, periodontal disease was associated with higher risk of developing mobility limitations, whereas fair/poor self-rated oral health predicted onset of ADL and IADL difficulties. Additionally, accumulation of oral health problems, which reflects burden of poor oral health, was associated with greater risk of developing IADL difficulties. In Chapter 7, findings from the causal mediation analyses, did not suggest any mediating effects by inflammatory markers (CRP, IL-6, fibrin d-dimer) and poor diet quality on the association between poor oral health and risk of disability. However, these results do not rule out the potential role of diet and inflammation as mediators. Finally, Chapter 8 showed that poor oral health could be a determinant of shortened longevity. In particular, tooth loss was associated with increased risk of all-cause mortality, while periodontal disease was associated with greater risk of cardiovascular disease (CVD) mortality while considering the competing risk of non-CVD deaths. Additionally, tooth loss and accumulation of oral health problems were associated with increased mortality from respiratory causes. Findings from both Chapters 7 and 8 highlight that improving oral health through targeted treatments and community programs can potentially delay onset of disability and reduce the risk of mortality in older people.

9.2.2. Novelty of findings

Although there is evidence suggesting that poor oral health is associated with several health outcomes, such as disability, nutritional deficiencies, and oral inflammation in older age (Sheiham *et al.*, 2002; Hämäläinen *et al.*, 2003; Janket *et*

al., 2008; Carramolino-Cuellar *et al.*, 2014; Tsakos *et al.*, 2015; Friedman and Lamster, 2016; Scannapieco and Cantos, 2016; Son *et al.*, 2020), the relationships between various oral health problems (objective and subjective) with disability, physical function, increased inflammation, diet quality, and risk of mortality are still not well-established, as discussed in Chapter 2. The results in Chapter 4 have provided evidence that a range of oral health problems, both objective (tooth loss) and subjective (dry mouth, fair/poor self-rated oral health) as well as accumulation of oral problems are associated with greater odds of disability (mobility limitations, ADL and IADL difficulties). In addition, previous studies have suggested that older individuals with tooth loss are also more likely to have poor physical function, with limited evidence for other oral health problems. Chapter 4 showed that periodontal disease as well as subjective oral health problems (dry mouth, poor self-rated oral health) were associated with poor physical function (weak handgrip strength, slow walking speed). These findings suggest that not only tooth loss, but also other oral health problems, including dry mouth, poor self-rated oral health, as well as accumulation of oral health problems are related to impaired physical independence through presence of disability and poor physical function in older age.

Previously, it has also been suggested that oral health problems can predict onset of mobility limitations, ADL and IADL difficulties (Chapter 2, section 2.3) in older people. However, most studies have assessed poor oral health through tooth loss, with limited evidence on measures, including periodontal disease, dry mouth, self-rated oral health as well as accumulation of oral health problems. Likewise, few studies have assessed onset of disability through mobility limitations, ADL, and IADL difficulties (Holm-Pedersen *et al.*, 2008; Zhang *et al.*, 2018; Yin *et al.*, 2020). Chapter 7 validated the associations between tooth loss and risk of disability (mobility limitations), and further demonstrated that those with periodontal disease, dry mouth, and those who reported fair/poor self-rated oral health were at greater risk of developing disability (mobility limitations, ADL, IADL difficulties). Additionally, it established accumulation of oral health problems (burden of oral health) as a risk factor of developing disability in older age.

Chapter 5 highlighted associations between tooth loss and high levels of C-reactive protein (CRP), interleukin-6 (IL-6), fibrin d-dimer, Troponin T, and N-terminal pro brain natriuretic peptide (NT-proBNP). Additionally, presence of more than one oral

health problems was associated with increased systemic and CVD-related inflammation (CRP, IL-6, and vWF). These findings showed that older individuals with poor oral health are more likely to have high levels of several markers of inflammation, which are linked to chronic diseases and overall health. Previous studies investigated these associations in middle-aged populations, therefore these relationships remained unclear in older populations. Moreover, these novel findings suggested oral health is associated with CVD-related biomarkers (haemostatic and cardiac biomarkers), hence supporting previous findings of associations between poor oral health and CVD.

Chapter 6 provided evidence on the associations between subjective oral health problems, and accumulation of oral health markers with poor diet quality and intakes of several nutrients. Additionally, in this study, those following a poor diet at both time points (60-79yrs to 71-92yrs) were at greater odds of tooth loss, and experiencing 2 oral health problems later in life, highlighting the potential impact of a compromised diet on oral health of older people. These findings provide insight on the dietary patterns of two different populations of older people, and suggested that older people with poor oral health are more likely to consume processed meat, saturated and trans-fatty acids, and fewer fruits and vegetables. Previously, findings of associations between oral health problems and diet quality have been inconsistent, with most studies focusing on tooth loss and periodontal disease and ignoring self-reported measures of oral health.

Diet and inflammation have been suggested as potential mediators in the associations between poor oral health and risk of disability in older people. However the mediating patterns are still unknown and to my knowledge there are no studies using causal mediation analysis to examine mediation through these two particular factors (Yin *et al.*, 2020). Chapter 7 did not provide significant findings about the mediating roles of CRP, IL-6, fibrin d-dimer and diet quality in the associations between poor oral health and risk of developing mobility limitations. Although this Chapter provided non-significant results and therefore absence of mediating effects through diet and inflammation, this does not necessarily mean that there is absence of mediation through these two factors.

Finally, as discussed in Chapter 2 (section 2.7), inconsistent findings have been reported about the associations between objective oral health problems (tooth loss, periodontal disease) with all-cause, CVD, and respiratory mortality in older people, while associations for subjective oral health problems remain unclear. Findings from Chapter 8 showed that those with poor oral health are in greater risk of all-cause, CVD, as well as increased respiratory mortality in older age, highlighting the importance of oral health status in improving life expectancy in older populations.

The strengths and limitations as well as the consonance of these findings in respect to existing literature were discussed in each of the results Chapters. In the following sections, the implications for public health as well as the implications for future epidemiological research will be discussed.

9.3. Public Health Implications of Findings

9.3.1. Poor oral health as a determinant of disability, all-cause, CVD, and respiratory mortality in older age

This thesis has shown that poor oral health is associated with onset of disability, and risk of all-cause, CVD, and respiratory mortality in older people. These findings carry significant public health implications which include the importance of i) assessing and monitoring several oral health problems in older people to reduce the risk of adverse outcomes in older age and particularly the risk of developing disability and improve survival, and ii) that prevention programmes should focus on preventing accumulation of oral health problems in older people.

Given the preventable and treatable nature of oral health problems and the several associations with chronic diseases, the need to monitor and improve oral health status has been highlighted by previous research as a fundamental goal in itself (Dörfer *et al.*, 2017). However in order to improve surveillance and treatment of oral health there is a need for a more comprehensive definition of oral health; one that encompasses all potential manifestations of poor oral health (Glick *et al.*, 2016), particularly tailored to older adults. The use of a common definition can assist in strengthening the role that oral health has in overall well-being, as different components of oral health can affect health differently. Previously, the definition of

oral health was the absence of disease (Glick *et al.*, 2016). However, there are also other parts of oral health which are also characteristics of poor oral health (Glick *et al.*, 2016). Therefore, it has been proposed that the definition of oral health should include a combination of oral diseases and other self-reported functions, taking account of the influence that external health factors have on oral disease progression and self-perception of oral health (Locker and Allen, 2007; Glick *et al.*, 2016). This definition promotes the notion that oral health is embedded in general health, and should not be viewed as an isolated health problem (Glick *et al.*, 2016). However, to date, few studies have focused on the role of multiple dental conditions in age-related health outcomes. The use of a common definition of poor oral health in future epidemiologic studies, but also in intervention programs in community settings can address current limitations of poor oral health definition in studies, but also contribute to better predictions of the risk of disability and mortality in older adults with poor oral health. A further discussion of the implications of the assessment of poor oral health in future studies will be described in sub-section 9.4.1.

9.3.2. Strategies to treat and improve poor oral health in older populations

Findings from this thesis established associations between poor oral health and disability, poor physical function (Chapter 4), increased inflammation (Chapter 5), poor diet quality (Chapter 6), and increased risk of all-cause, CVD and respiratory mortality (Chapter 8), highlighting the impact that dental problems have on important age-related health outcomes in older people.

Globally, prevention and treatment efforts of oral health problems have been inadequate (Peres *et al.*, 2019). Higher percentage of older people now retain their natural teeth which leads to an increase in need of restorative care (Dye *et al.*, 2015; Peres *et al.*, 2019). Several strategies have been proposed for maintaining natural teeth longer or retaining a functional dentition. Generally, appropriate dental hygiene has been suggested as one of the most efficient ways in improving oral health and reducing its burden on chronic diseases, disability, and mortality (Hayasaka *et al.*, 2013; Bando *et al.*, 2017; Hyde *et al.*, 2017; Park *et al.*, 2018; Manabe *et al.*, 2019). Research has shown that the use of fluoride toothpaste accompanied by daily

toothbrushing or use of fluoride varnish in combination with toothbrushing can protect oral health (Public Health England, 2018).

Additionally, to maintain a functional dentition, removable or fixed prostheses (dentures, dental implants) are among the most common strategies of reducing the impact that tooth loss can have in older people (Peres and Lalloo, 2020). Well-fitting dentures can improve chewing in older people, and therefore have a positive effect on food preparation and food choices (De Marchi *et al.*, 2011; Gonçalves *et al.*, 2014). However, retaining of natural teeth with no need for use of dentures or implants is significantly better for oral function and better oral health (Gonçalves *et al.*, 2014; Watson *et al.*, 2019; Peres and Lalloo, 2020). Nevertheless, these particular treatment options for tooth loss are costly for older individuals, and rely on access to dental services and health insurance of the individual (Peres *et al.*, 2019; Peres and Lalloo, 2020). More details on access to dental services will be described in sub-section 9.3.3.

Also, it is well-established that tooth loss can be a consequence of periodontal disease and dental caries, and therefore treatment of both periodontal disease and caries could potentially reduce the number of teeth being lost (Petersen and Ogawa, 2012). However, there is not enough evidence on whether such treatment approach can reduce tooth loss (Hyde *et al.*, 2017). Nevertheless, early prevention and treatment particularly of dental caries from childhood with continued support throughout the life course could significantly reduce the burden of tooth loss on oral health and potential effects on other aspects of health (Heilmann A *et al.*, 2015). Overall, for treatment of periodontal disease and caries (dental plaque) in older people, a combination of adequate tooth brushing (particularly targeting infected areas) and use of antimicrobial mouth rinse have been found to be effective (Schiffner *et al.*, 2007; Hyde *et al.*, 2017).

Dry mouth has a number of different causes and therefore strategies to improve this condition should be adapted according to the health status of older individuals (Gil-Montoya *et al.*, 2016). When dry mouth is a result of medications causing xerostomia, studies have suggested the use of malic acid with fluoride and xylitol, both spray and tablets, for the treatment of dry mouth symptoms and increase of volume of saliva (Da Mata *et al.*, 2009; Gómez-Moreno *et al.*, 2013a; Gómez-Moreno

et al., 2013b). In other cases, specific pharmaceutical strategies have been utilised however these studies had short follow-up periods and it is unknown whether the observed improvement applies for longer periods (Gil-Montoya *et al.*, 2016). Overall, for most oral health problems a combination of dental hygiene and pharmaceutical treatments have been indicated as the most appropriate.

Finally, research has highlighted the need for targeted dental treatment not only in older age but also throughout adult life (Hyde *et al.*, 2017). Most importantly, improvement of oral health in older people, which can prove challenging due to comorbidities, plays an important role in avoiding accumulation of oral conditions, which can increase the risk of health complications in older age (Hyde *et al.*, 2017). As a result it is necessary to prevent deterioration of dental problems starting from young and middle-aged adults to protect oral health in older age.

9.3.3. Access to dental services for older adults and related costs

Access to dental services is one of the most important factors which can impact oral health and oral disease progression (Peres *et al.*, 2019). In order for older individuals to get dental treatments, as mentioned in sub-section 9.3.2., access to adequate dental services is a prerequisite (Ástvaldsdóttir *et al.*, 2018; Peres *et al.*, 2019). However, a significant number of older people (almost 50%) do not go to the dentist (Raphael, 2017). In the USA, almost 70% of older individuals do not have dental insurance, while Medicare does not include coverage of routine dental care (Raphael, 2017). Likewise, older British people are also less likely to frequently visit the dentist (Tickle *et al.*, 2015). Furthermore, access to dental services can be further impacted by physical status of an individual, with older people with functional disability facing more difficulties in accessing dental services and practising good oral hygiene (Ástvaldsdóttir *et al.*, 2018). In older community-dwelling people where individuals are responsible for managing their dental appointments and commuting to the dentist complications due to other diseases or residence in non-urban areas can also impede access to treatment (Hyde *et al.*, 2017; Chávez *et al.*, 2018). Furthermore, the cost of dental services is a burden for both the individual and healthcare system (Raphael, 2017; Peres *et al.*, 2019). In the UK, in 2014, £3.4 billion were spent for NHS dentistry for all ages, whereas £2.3 billion were spent

additionally in private dentists (NHS England, 2014; Public Health England, 2018). In 2014-2015, costs for the NHS for tooth removal carried out in older individuals admitted at hospitals were estimated to be around 57 million pounds, which represents an additional cost to health services (Public Health England, 2018). Seeking private dental treatments can be an extra financial burden for the individual. Moreover, oral health can also increase healthcare spending indirectly because dental problems may contribute to admissions due to other conditions including dehydration and malnutrition (Public Health England, 2018). Moreover, older adults are usually in need of complex dental procedures which can be quite costly and especially in the USA not covered by health insurance (Raphael, 2017).

To address the complexity of dental services for older individuals, there has been a call to identify oral health as an integral part of health in older age (Raphael, 2017), with more campaigns and outreach programmes for oral care in older community-dwelling people (Raphael, 2017; Public Health England, 2018). In the USA, oral health was included in the Older Americans Reauthorization Act in 2016, and it included provision of funding to ageing public health (state and local) agencies to carry out oral health screenings in the community, as part of disease prevention in populations of older people (114th Congress, 2015-2016). Such policies which provide sufficient financial support to community dental services, with the additional help of appropriately-designed needs assessment plans can contribute to the prevention of future deterioration of oral health. This can result in better access to dental services and reduced costs of dental treatments (Public Health England, 2015; Raphael, 2017). Finally, due to the special health needs of older people, a multidisciplinary oral care plan is needed, with collaboration between different health professionals, highlighting the interrelation between poor oral health and systemic diseases (Hyde *et al.*, 2017; Public Health England, 2018).

9.3.4. Targeting predictors of poor oral health in older age

Poor oral health and systemic diseases share common risk factors, including diet, and increased inflammation. It has been suggested that for the prevention of dental problems, intervention programs should target risk factors of poor oral health (Helal *et al.*, 2019; Gugnani and Gugnani, 2020). In this thesis, oral health problems were

cross-sectionally associated with both high levels of inflammatory markers and poor diet quality in two populations of older people. In addition to this finding, several studies have highlighted the role of diet and inflammatory markers as determinants of the progression of oral conditions, such as periodontal disease (Iwasaki *et al.*, 2011a; Iwasaki *et al.*, 2011b; Iwasaki *et al.*, 2012a; Iwasaki *et al.*, 2012b; Chapple *et al.*, 2017; Kotsakis *et al.*, 2018). In this thesis, it was also observed that having a compromised diet over 10 years was associated with poor oral health later in life.

Through an improved diet, a reduction in levels of inflammation can be achieved, which can then significantly impact oral health but also systemic health (Barbaresko *et al.*, 2013; Kotsakis *et al.*, 2018). A recent Public Health England report on oral health, pointed out that public health prevention efforts should focus on diet improvement in older people in community settings (Public Health England, 2018). However, there is lack of prevention programs in community settings for older people, and there is a substantial paucity of intervention studies focusing on how diet can help improve oral health in older age (Public Health England, 2018).

In older people, studies have focused on epidemiological associations between diet components and oral diseases. In particular, studies have suggested that diets which are characterised by low levels of antioxidants, including ascorbic acid, α -tocopherol, vitamin C and β -carotene, and high intake of saturated fatty-acids are associated with greater incidence of periodontal disease in older Japanese populations (Iwasaki *et al.*, 2011a; Iwasaki *et al.*, 2012a; Iwasaki *et al.*, 2012b). Likewise, a pro-inflammatory diet which is based on the consumption of nutrients which are related to increased levels of inflammatory markers including IL-6 and CRP, increased the risk of tooth loss in adults (Kotsakis *et al.*, 2018). These findings can be the foundation of public health prevention programs, where a diet rich in fruits and vegetables, and low in fat and sugar consumption can be promoted and supported, in combination with appropriate dental treatment and dental hygiene to address needs of older people.

Additionally, the role of sugar in oral health should be highlighted in public health efforts to improve oral health or prevent deterioration of dental conditions. Sugar consumption is a well-known risk factor of dental conditions, including caries and subsequent tooth loss, but also of other health conditions such as diabetes and

obesity (Peres *et al.*, 2019). Particularly, it has been shown that increased prevalence of dental caries is linked to increased consumption of sugary drinks (Popkin and Hawkes, 2016; Peres *et al.*, 2019). Therefore, it is of paramount importance to limit consumption of products high in sugar, and promote public health policies targeting the sugar industry, which will limit the advertising, marketing and availability of these products but also their influence on decision making (Peres *et al.*, 2019).

In a report by the World Dental Federation, advocacy campaigns about the interrelation of oral health and non-communicable diseases (NCDs) were highlighted. It was suggested that previous campaigns to improve NCDs which promoted (i) reduction of sugars in foods and drinks, (ii) limiting salt intake, (iii) replacement of saturated fats with polyunsaturated fats and (iv) the benefits of diet and physical activity can also be used for the improvement of oral health in adults (FDI World Dental Federation, 2020).

In the UK, there have been public health efforts to promote better diet quality in older people as a way to improve general health through the National Service Framework for Older People (Department of Health, 2001), but this policy targeted the general population and did not focus on older people. There have been a few policy recommendations on how to improve diet in older individuals (Clegg and Williams, 2018). First, changes in palatability, through enhancement of food flavour have been found to contribute to increases in energy and protein intake in older age (Dermiki *et al.*, 2015). Second, especially in older people with chewing problems, increased consumption of liquid meals which are high in nutrient density, protein, and rich in taste can also assist in improving diet quality (Nieuwenhuizen *et al.*, 2010; Clegg and Williams, 2018). Third, in older community-dwelling individuals living alone preparation of meals can be impacted by any inability to buy foods, cook, and eat and therefore pre-packaged meals can be a very effective solution in improving diet quality (Kronl *et al.*, 2008). Pre-packaged meals in the form of home-delivered meals can improve quality of life and reduce risk of mortality and disability (Campbell *et al.*, 2015). However, a recent systematic review showed that few older individuals have access to home-delivered meals and identified that expansion of such public health programs should be supported and a potential integration within other health services may be beneficial (Campbell *et al.*, 2015).

Finally, in this thesis, the impact of social determinants of health on the associations between oral health and age-related health outcomes was not examined. Nevertheless, social and economic factors can have a substantial impact on health, and particularly can lead to accumulating effects throughout life (Tellez *et al.*, 2014). Oral health shares social determinants with general health and NCDs which further highlights the importance of addressing these factors in public health prevention efforts (Heilmann A *et al.*, 2015). Determinants including housing and working conditions, social capital, psychosocial factors such as stress and social support, and access to health care can influence dental disease prevention and progression (Peres *et al.*, 2019). It has been established that people from low socioeconomic areas with higher deprivation have worse oral health outcomes (Tellez *et al.*, 2014; Ramsay *et al.*, 2018a). Additionally, experiencing loneliness can have a negative impact on oral health, while being socially active and having social support can alleviate the burden of dental conditions (Rouxel *et al.*, 2015; Rouxel *et al.*, 2017). To address social determinants upstream and community-based policies are needed (Watt, 2007; Peres *et al.*, 2019). In upstream policies, the primary causes of causes of disease are targeted, including social determinants of oral health throughout the life course (Watt, 2007). However dental practices and oral health care are primarily based on individualistic approaches (individual's behaviour and biological risk factors) (Watt, 2007; Peres *et al.*, 2019). Therefore, future health policies should shift focus to a more integrated approach, where oral health is part of NCDs prevention programmes targeting several age groups (childhood to older populations), while promoting oral health through appropriate legislation, regulation and economic incentives at any level (local, national, international) (Watt, 2007).

9.4. Implications for Future Epidemiological Research

This thesis has addressed several questions on the associations of various oral health problems with disability (both cross-sectional and prospective), poor physical function, diet quality, increased inflammation, and all-cause, CVD, and respiratory mortality in two population-based studies of older individuals living in the UK and USA. However, due to the multidimensional nature of oral health and its different links to age-related health outcomes, there are still questions that need to be

answered. Limitations of this thesis have already been addressed in previous Chapters, and therefore implications for future epidemiological studies will be discussed in this section.

9.4.1. Investigating associations of poor oral health with the risk of disability and all-cause and cause-specific mortality

This thesis has investigated the cross-sectional associations between objective and subjective oral health problems with disability and poor physical function (Chapter 4), as well as the prospective associations of poor oral health with risk of disability (Chapter 7) and all-cause, CVD, and respiratory mortality (Chapter 8). This study has numerous strengths such as using data from two large population-based studies (BRHS and HABC Study) of community dwelling older people. Therefore, it was possible to examine the associations in two diverse samples of older people, with high follow-up rates (Walker *et al.*, 2004; Lennon *et al.*, 2015), in contrast to previous studies which focused on young and middle-aged adults. Both studies had comparable oral health data, where objective measures were assessed by trained professionals and subjective measures were assessed through questionnaires. Additionally, information on a number of risk factors, such as socioeconomic status, smoking, history of CVD and diabetes, and BMI were available. However there are still limitations and implications of this thesis' findings which should be applied in future research in older populations.

Findings from this thesis may not be representative of the whole population of older people in the UK and USA. The BRHS recruited at baseline only white men living across the UK but not in urban centres where there is increased mobility, and in the HABC Study white and African-American men and women living in only two USA cities participated in the data collection. Furthermore, previous research has reported gender differences in observed associations, with women having higher rates of poor oral health and disability, potentially as a result of prolonged longevity (Moriya *et al.*, 2012). Additionally, it has been suggested that racial differences exist in the prevalence of oral health problems in older people with black people having higher rates of tooth loss, and poor self-rated oral health compared to older white individuals (Quandt *et al.*, 2009; Bomfim *et al.*, 2021). Likewise, racial/minority

groups were also more likely to experience higher odds of age-related adverse health outcomes, including ADL difficulties when compared to white US older people (Ng *et al.*, 2014). In this thesis, only the HABC Study included both white and African-American men and women while the BRHS consisted of older white men. Therefore potential gender and race differences could only be examined in one of the two studies included in this thesis (HABC Study). However there was no effect modification by gender or race for the majority of associations in the HABC Study. To further develop findings from this thesis and to produce findings which can be generalised to all older community-dwelling people, future studies should recruit a large population of both men and women, from diverse backgrounds, living in both urban and suburban areas across the country. Replication of findings between studies can show whether the associations observed between poor oral health and disease-related biomarkers, diet quality, risk of disability and mortality are consistent in older populations.

One of the key challenges in research about the associations of poor oral health with age-related health outcomes is defining poor oral health. As mentioned in sub-section 9.3.1. a multidimensional definition of poor oral health is needed. In this thesis a comprehensive set of oral health problems was utilised, objective and self-reported. Studies included in the literature review (Chapter 2) usually examined only one dental problem, and the majority of them focused on tooth loss and periodontal disease. However, poor oral health in older adults is not characterised by only these two conditions. It has been proposed that a definition comprising of three core elements should be used in epidemiologic studies (Glick *et al.*, 2016). Those elements include severity or progression of oral disease, physiological factors such as ability to speak, smile, chew and psychosocial factors which refer to the influence of dental problems on mental health including ability to interact in social situations without feeling embarrassed (Glick *et al.*, 2016). In other words, it is important to focus on different aspects of oral health and use various dental problems which are better suited to describe the complexity of oral health. In this thesis, differences existed in associations with health outcomes between different measures of oral health, highlighting the need of incorporating more than one dental problems when defining poor oral health. Nevertheless, one limitation of this thesis is that dental caries were not included as an oral health problem. Dental caries are another

prevalent dental problem in older age, and can significantly influence tooth loss and oral health status in older people, as well as adverse health outcomes (Dye *et al.*, 2015; Tonetti *et al.*, 2017). Due to the chronic nature of dental caries and various implications to oral health and connections with NCD's establishing associations with age-related health outcomes should be a priority in future research. Particularly, studies should investigate associations between dental caries and disability, physical function, inflammation, diet, and mortality in older adults. Additionally, it is crucial for future studies to utilise various assessments of oral health, including both oral diseases and self-reported measures (chewing problems, frequency of brushing teeth), to address the question of how poor oral health (a) influences risk of disability and all-cause, CVD and respiratory mortality, and subsequently its role in preventing disability and reducing mortality rates in older individuals.

9.4.2. Investigating associations with diet quality and inflammation as well as mediating pathways of associations of poor oral health with onset of disability in older age

In this thesis, the cross-sectional associations between poor oral health and poor diet quality (Chapter 6) and high levels of inflammatory, haemostatic, and cardiac biomarkers (Chapter 5), and the mediating roles of diet and inflammation in the association of poor oral health with risk of disability (Chapter 7) were examined in older community-dwelling people in both studies. Strengths of this study were that it established associations between poor oral health and increased levels of haemostatic and cardiac biomarkers in older people, while providing evidence for the associations between subjectively assessed oral health problems with poor diet quality and dietary intake. Furthermore, this was one of the first studies to explore, through causal mediation the mediating roles of poor diet quality, CRP, IL-6, and fibrin d-dimer (BRHS) in the association between oral health and risk of incident mobility limitations in older people.

Findings from this thesis further supported associations between poor oral health and CVD, based on the associations observed between tooth loss, poor self-rated oral health and cumulative oral health problems with high levels of haemostatic and cardiac biomarkers. Future research should replicate these findings in large

population-based studies of older community-dwelling people. Furthermore, to develop further the findings of this thesis, the prospective associations of poor oral health on levels of inflammation over time should be investigated. Both objective and subjective oral health problems were associated with poor diet quality and several adverse intakes of nutrients. Currently, there are contradictory findings between studies for intakes of specific nutrients, including fat and energy, as well as different ways to measure diet quality. It is necessary therefore to utilise similar diet scores across studies in order to compare findings and validate results of this thesis. Moreover, due to regional differences in diet (da Silva *et al.*, 2009; Imamura *et al.*, 2015), findings can only be representative of ageing populations in the UK and USA. Therefore, studies from different countries are needed to clarify the associations between poor oral health and diet quality globally. Furthermore, in this thesis, associations were established between changes in diet quality over time and prevalence of oral health problems later showing that deterioration or persistent poor diet quality can lead to oral health problems. Hence, assessing changes in oral health (improvement or deterioration) and how these changes are related with changes in diet will also add valuable evidence about the bi-directionality of associations and develop findings from this thesis further.

Finally, this thesis did not observe any mediating effects of diet quality or inflammation in the association between poor oral health and risk of disability in both studies. However, this finding does not necessarily rule out mediation. As mentioned in Chapter 7, the potential bi-directional associations between oral health and inflammation and diet, the interrelation of inflammation and diet as well as methodological considerations of causal mediation analysis can potentially explain the lack of associations (Minihane *et al.*, 2015; VanderWeele, 2016; Alpert, 2017). Diet and inflammation are implicated in almost every pathway underpinning associations of poor oral health with age-related health outcomes (Bailey *et al.*, 2004; Moynihan, 2007; Berkey and Scannapieco, 2013); therefore future studies should explore further mediation through these factors. In this thesis certain inflammatory markers and diet measurements were tested as mediators; however it was not possible to examine all inflammatory markers and diet components which may act as mediators. In particular, tumour necrosis factor-alpha (TNF- α) or white blood cell count are inflammatory markers which increase with age and have been

found to be associated with chronic diseases, disability, and mortality (Cheng *et al.*, 2004; Singh and Newman, 2011; Nilsson *et al.*, 2014). Similarly, for diet quality, biomarkers of diet quality, including plasma levels of vitamins or other nutrients should also be considered as mediators, since they are more reliable markers of diet quality than intakes resulting from food frequency questionnaires (Neuhouser *et al.*, 2003; Cheong *et al.*, 2020). Although it was not possible to use this variable in this thesis, future studies could potentially utilise diet-borne systemic inflammation as a way to incorporate the effects of diet and inflammation in one measure. Diet-borne systemic inflammation can be assessed through the Dietary Inflammatory Index (DII) which was created to address the relationship between diet and inflammation and how this influences health outcomes (Shivappa *et al.*, 2014; Hébert *et al.*, 2019). Interestingly, diet borne inflammation has been found to be associated with higher prevalence of tooth loss in older people in the USA (Kotsakis *et al.*, 2018). Additionally, older adults with higher DII scores were more likely to experience functional limitations and ADL difficulties in a population-based study in the USA (Wang *et al.*, 2021). These findings suggest that further exploration of the mediating role of DII score on the association of poor oral health and risk of disability in older age could be beneficial. Moreover, more complex models could also be designed where the bi-directionality of diet and inflammation is taken into consideration, by introducing interaction terms in the models (Aitken *et al.*, 2018) or using more complex causal mediation analyses including the 4-way decomposition model by VanderWeele (VanderWeele, 2014). More complex models, including sequential mediation analysis, as well as using mediators such as the DII can further develop our understanding of the mediation pathways which underlie the associations between poor oral health and age-related health outcomes. Additionally, in causal mediation models, social determinants of health could be added as mediators, to highlight the impact that these factors have on the associations of oral health and health outcomes in older populations.

Finally, there are few intervention studies seeking to improve oral health through diet, but these studies have focused on periodontal disease/gingival bleeding, had a small sample size, and recruited young and middle-aged adults (18-65 years) (Baumgartner *et al.*, 2009; Kondo *et al.*, 2014; Zare Javid *et al.*, 2014; Woelber *et al.*, 2016; Woźniewicz *et al.*, 2018; Woelber *et al.*, 2019). As a result, it is unknown if the

same interventions can be beneficial for older populations, who have considerably worse oral health, comorbidities and take various medications which can influence dental health. Furthermore, future intervention studies need to focus on overall improvement of oral health, and not only on a specific oral condition, since oral health in older adults is a multidimensional health condition characterised by a set of problems (Glick *et al.*, 2016). Dietary intervention studies in older populations should also focus on the impact on levels of inflammation as well as oral health status over a long period of time (>6 months), because oral and general health can change constantly in older people due to new medications, or disease diagnosis/prognosis.

9.5. Concluding Statement

There is a steady increase of ageing populations worldwide. In the UK, the population over 75 years is projected to rise between 2014 and 2039 from 5.2 to 9.9 million (Government Office for Science, 2016). Additionally, the US Department of Health and Human Services indicated that the ≥ 65 years population increased by 34% between 2007 and 2017, with the population ≥ 85 years estimated to rise by 134% by 2040 (Administration for Community Living, 2018). Poor oral health is a common health condition in older people, and is closely associated with chronic diseases and overall well-being (Alpert, 2017). Results from this thesis have demonstrated that older individuals with oral health problems are more likely to experience disability and poor physical function, have a compromised diet, and have high levels of inflammatory, haemostatic, and cardiac biomarkers. Additionally, poor oral health appears to be a predictor of greater incidence of disability, all-cause, CVD, and respiratory mortality in two population-based studies of older people in the UK and USA. Finally, diet quality and inflammation (CRP, IL-6, fibrin d-dimer) did not appear to mediate the association between poor oral health and onset of disability. The findings of this thesis highlight the need to improve oral health through targeted intervention programs in community settings and improved dental treatment, in order to decrease risk of disability and prolong survival in older adults.

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Appendix A Thesis Publications

Three first-author papers, based on this thesis objectives, have been published in peer-reviewed journals (Kotronia *et al.*, 2019; Kotronia *et al.*, 2020; Kotronia *et al.*, 2021). These publications are listed below.

1. Kotronia, E., Brown, H., Papacosta, A.O., Lennon, L.T., Weyant, R.J., Whincup, P.H., Wannamethee, S.G. and Ramsay, S.E. (2021) 'Poor oral health and the association with diet quality and intake in older people in two studies in the UK and USA', *British Journal of Nutrition*, pp. 1-13.
2. Kotronia, E., Wannamethee, S.G., Papacosta, A.O., Whincup, P.H., Lennon, L.T., Visser, M., Kapila, Y.L., Weyant, R.J. and Ramsay, S.E. (2020) 'Poor Oral Health and Inflammatory, Hemostatic, and Cardiac Biomarkers in Older Age: Results From Two Studies in the UK and USA', *The Journals of Gerontology: Series A*, 76(2), pp. 346-351.
3. Kotronia, E., Wannamethee, S.G., Papacosta, A.O., Whincup, P.H., Lennon, L.T., Visser, M., Weyant, R.J., Harris, T.B. and Ramsay, S.E. (2019) 'Oral Health, Disability and Physical Function: Results From Studies of Older People in the United Kingdom and United States of America', *Journal of the American Medical Directors Association*, 20(12), pp. 1654.e1-1654.e9.

Authorship Contributions

Study concept and design: EK, SER, SGW, AOP, PHW.

Acquisition of data: SER, SGW, AOP, PHW, LTL, RJW.

Analysis: EK

Interpretation of data: All authors.

Drafting of the manuscript: first draft by EK, with contributions from all authors.

Critical revision of the manuscript for important intellectual content: All authors.

Appendix B. Conference Oral Presentations (Peer-Reviewed Abstracts)

1. **Kotronia E**, Wannamethee SG, Papacosta AO, Whincup PH, Lennon LT, Visser M, Weyant RJ, Harris TB, Ramsay SE. Oral health, disability and physical function: results from studies of older people in the UK and USA. Society for Social Medicine and International Epidemiological Association (Glasgow, September 2019).
2. **Kotronia E**, Wannamethee SG, Papacosta AO, Whincup PH, Lennon LT, Visser M, Kapila YL, Weyant RJ, Ramsay SE. The association of poor oral health with a range of inflammatory markers: results from two population-based studies of older people in the UK and USA. Society for Social Medicine (Glasgow, September 2019).
3. **Kotronia E**, Wannamethee SG, Papacosta AO, Whincup PH, Lennon LT, Visser M, Weyant RJ, Ramsay SE. Poor oral health and incidence of disability: results from studies of older people in the UK and USA. World Congress on Public Health (online event, 2020).

Appendix C. Conference Poster Presentations (Peer-Reviewed Abstracts)

1. **Kotronia E**, Wannamethee SG, Papacosta AO, Whincup PH, Lennon LT, Visser M, Weyant RJ, Harris TB, Ramsay SE. Oral health, disability and physical function: results from studies of older people in the UK and USA. 10th Annual Alliance for Healthy Aging (Hexham, 2019).
2. **Kotronia E**, Brown H, Papacosta AO, Lennon LT, Weyant RJ, Whincup PH, Wannamethee SG, Ramsay SE. Poor oral health and the association with diet quality and intake in older people in two studies in the UK and USA. Society for Social Medicine (online event, 2020).
3. **Kotronia E**, Brown H, Papacosta AO, Lennon LT, Weyant RJ, Whincup PH, Wannamethee SG, Ramsay SE. Poor oral health and incidence of disability: results from studies of older people in the UK and USA. Society for Epidemiologic Research (online event, 2020).

Appendix D. Data Sheet from Physical Examination in 2010-2012 at 30-Year Re-Examination.

DATASHEET : UCL LONDON British Regional Heart Study 2010-2012

Batch / Study #	Name	Please amend your details if necessary:
DOB:	Age:	
Tel:		
GP:		

STATION 1	Observer		Initials,		Time			(24 hr)
Sit/Stand 5 times	No reas		ref=1 dis=2			secs	N at 30sec?	
Walk 3 metres	No reas		ref=1 dis=2			secs	Incompl at 30 sec	
Height (cm)							Problem?	
Weight							(kg)	Problem?
Pacemaker?	No	→ TANITA BODY COMPOSITION						Problem?
	Yes	→ SCALES						Problem?
1. Waist circ 1 (cm)			3. Waist circ 2			Problem?		
2. Hip circ 1 (cm)			4. Hip circ 2			Problem?		
Arm circ R (cm)						Problem?		
1. Triceps R1 (mm)			3. Triceps R2			Problem?		
2. Subscap R1 (mm)			4. Subscap R2			Problem?		
Cuff size	Arm circ < 22 cm = 1 (small) 22-32 cm = 2 (medium) >32 cm = 3 (large)							

Blood pressure R	SITTING 1	SITTING 2	STANDING 1	STANDING 2
Systolic (mmHg)				
Diastolic (mmHg)				
Heart rate (per min)				

Cuff		Instr		Problem?		P/T	Faintness		Y = 1	Breathless?		Y = 1
Room temp (°C)				Ethnicity	WE = 1 BAC = 2 SA = 3							
				Ch/J/O = 4 Other = 5								
Spirometry	Instr		Inhal 24hr		Y = 1	Time 24hr						
	BTV %			CI		Y = 1				Problem?		P/T

Grip Instr									
Grip strength (R)					Dom		P/T	Problem?	
Grip strength (L)					Dom		P/T	Problem?	

P = Participant T = Technical

STAPLED DATA RECORDS

SPIROMETRY DATA

Ref number			
N blows			BTV %
FVC			
FEV1			
FEV0.5			
PEF			
FEF25-75%			
FEF75-85%			
FEF25%			
FEF50%			
FEF75%			

BIOIMPEDANCE DATA (TANITA)

TANITA BODY COMPOSITION ANALYSER

Date DD MM YYYY Time (24hr)

Body type Standard=1/Athletic=2 ☐
Gender Female=1/Male=2 ☐

Age
Height cm
Weight kg
BMI kg/m²
BMR kJ
 Kcal
Fat % %
Fat mass kg
FFM kg
TBW kg
Visceral fat rating

IMPEDANCE

Whole Body
Right leg
Left leg
Right arm
Left arm

Segmental Analysis

Right leg
Fat % %
Fat mass kg
FFM kg
Predicted Muscle Mass kg

Left leg
Fat % %
Fat mass kg
FFM kg
Predicted Muscle Mass kg

Right arm
Fat % %
Fat mass kg
FFM kg
Predicted Muscle Mass kg

Left arm
Fat % %
Fat mass kg
FFM kg
Predicted Muscle Mass kg

Trunk
Fat % %
Fat mass kg
FFM kg
Predicted Muscle Mass kg

DATASHEET: CARDIFF UNIVERSITY
British Regional Heart Study 2010-2012

Batch / Study #	Date
DOB:	

BIOIMPEDANCE

Pacemaker?

☐

No = 2 Both Bio impedance measurements

YES = 1 → NO BIOIMPEDANCE MEASUREMENTS GO DIRECT TO BLOOD TEST

NO Pacemaker: BOTH BIOIMPEDANCE MEASUREMENTS

1. Bodystat Instrument ☐ Reading

STATION 2: Observer ID. ROOM TEMP °C SKIN TEMP °C

RIGHT SIDE

Comments

RCCA ☐

RDist ☐

PLAQUE ☐ Y=1

RCCA ☐ RCCB ☐ RICA ☐ RECA ☐

Cuff size (Arm circ < 22 cm = 1 (small), 22-32 cm = 2 (medium), >32 cm = 3 (large))

RBP1 Sys Dia HR

RBP2 Sys Dia HR

Left side

Comments

LCCA ☐

LDist ☐

PLAQUE ☐ Y=1

LCCA ☐ LCB ☐ LICA ☐ LECA ☐

LBP1 Sys Dia HR

LBP2 Sys Dia HR

Observer ID

Comments

APBI (PPG)

1.Sys BP R brachial

2.Sys BP R brachial

3.Sys BP R brachial

1.Sys BP L brachial

2.Sys BP L brachial

3.Sys BP L brachial

Sys BP R toe

Sys BP R toe

Sys BP R toe

Sys BP L toe

Sys BP L toe

Sys BP L toe

RABPI

RABPI

RABPI

LABPI

LABPI

LABPI

STATION 3 Observer ID

Comments

PWA (Sphyg)

R BP Sys Dia HR

R BP Sys Dia HR

Reading 1 Augmentation (mmHg) Alx (%)

Reading 2 Augmentation (mmHg) Alx (%)

PWA (Vicorder)

R BP Sys Dia HR

Reading 1 Augmentation (mmHg) Alx (%)

Reading 2 Augmentation (mmHg) Alx (%)

Comments

R BP1 Sys Dia HR

R BP2 Sys Dia HR

PWV (Sphyg)

Accepted

1 CAR-FEM Dis Prox (mm) . ± m/s ☐

2 CAR-FEM Dis Prox (mm) . ± m/s ☐

3 CAR-FEM Dis Prox (mm) . ± m/s ☐

4 CAR-FEM Dis Prox (mm) . ± m/s ☐

PWV (Vicorder)

1 CAR-FEM Dis . Prox . (cm) . m/s

2 CAR-FEM Dis . Prox . (cm) . m/s

STATION 4 Observer ID ☐ Refusal=1 ☐ Prob =1 ORAL HEALTH

I. TOTAL NUMBER OF NATURAL TEETH:

Upper

Lower

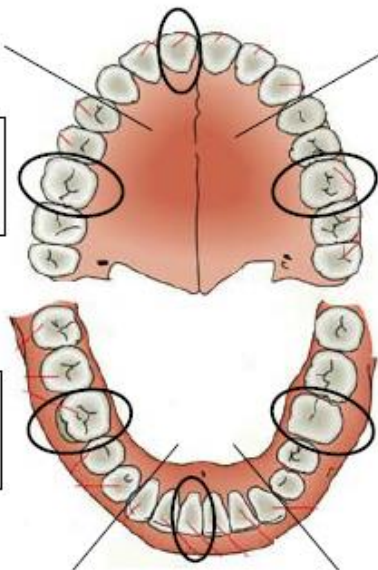
Batch No:

II. PERIODONTAL POCKET

2. Mesial =
Distal =

1. Mesial =
Distal =

6. Mesial =
Distal =



3. Mesial =
Distal =

4. Mesial =
Distal =

5. Mesial =
Distal =

Score -

0 = Up to 3.5 mm (first probe band)

1 = 4 to 5.5 mm (first dark band)

2 = 6 to 8.5 mm (between two dark bands)

3 = 9 to 11.5 mm (second dark band)

8 = Unscorable

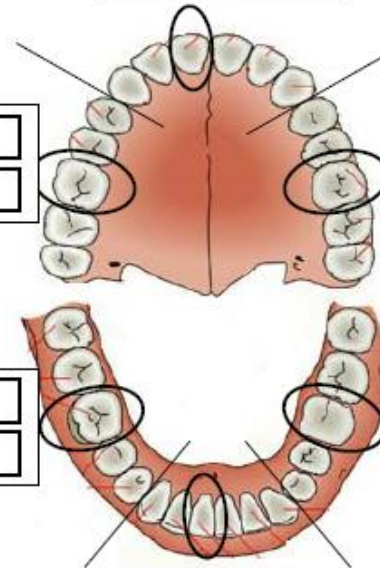
9 = Missing

III. GINGIVAL BLEEDING

2. Mesial =
Distal =

1. Mesial =
Distal =

6. Mesial =
Distal =



3. Mesial =
Distal =

4. Mesial =
Distal =

5. Mesial =
Distal =

Score -

Yes = 1

No = 0

Missing = 9

BLOODS

Blood test Success? ☐ Full = 2 Part = 1
None = 0

Problem? ☐ Refusal = 1
Technical = 2

Time (blood test) (24 hour)

Fasting instructions followed? ☐ Yes= 1 No=2
Diabetes =3

Time last eaten? (24 hour)

Day last eaten ☐ Today = 1, Yesterday = 2

ID

AFFIX BLOOD LABEL HERE

Incomplete sample – mark completed tubes with 1

☐	☐	☐	☐	☐	☐	☐	☐	☐

A B C DE FJ K LN PS T

ECG

Electrocardiogram ☐ Yes= 1 No=2

Ankle oedema: Left ☐ Right ☐ Yes= 1 No=2

PHYSICAL ACTIVITY SURVEY

Would you be prepared to wear this small monitor (which will measure how much activity you do) around your waist for the next week or so and then post it back to us?

Actigraph? ☐ Yes= 1 No =2 Tel Number: _____ (if not already
recorded on the front of the datasheet)

If activity survey has not been **prepacked**, please use a spare and record the Monitor Serial number below. Ensure the participant ID is recorded on the questionnaire, diary & monitor.
If no telephone number is provided, the participant will be unable to take part in the Activity Survey.

ID:

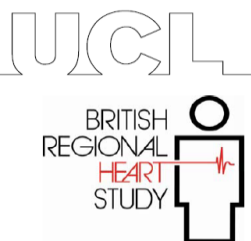
AFFIX BLOOD LABEL HERE

M	A	T	2	C	0												

Appendix E. Questionnaire in 2010-2012 at 30-Year Re-Examination in the BRHS.

(only those which apply to this study)

Study Number:



BRITISH REGIONAL HEART STUDY 30 YEAR FOLLOW UP SURVEY

Thank you very much for taking the time to complete this questionnaire, which will bring us up to date with your present health and lifestyle. All the information will be treated as **strictly confidential** and will only be seen by the Research Team.

Most questions can be answered by ticking the correct box ☒

Please check that you have answered as many questions as you can and return it to us in the envelope provided – you do not need to use a stamp.

If you have any trouble answering the questions, or would like a large-print copy, please phone us on 020 7830 2335 and give us your telephone number. We will then call you back to answer your query.

THANK YOU FOR YOUR HELP

Department of Primary Care & Population Health
UCL Medical School
Royal Free Campus
Rowland Hill Street
London NW3 2PF

Dates

1.0 Please enter today's date 20

1.1 Please give your Date of Birth 19

(This information is necessary for us to ensure that you are the correct recipient).

Conditions affecting the heart or circulation

2.0 Have you **ever** been told by a doctor that you have or have had any of the following conditions? If **yes**, please give the year this last happened.

		Yes	No	Year of last occurrence
a	Angina	☐	☐	
b	Aortic Aneurysm	☐	☐	
c	Atrial Fibrillation	☐	☐	
d	Deep Vein Thrombosis (clot in the deep leg vein)	☐	☐	
e	Heart attack (coronary thrombosis or myocardial infarction)	☐	☐	
f	Heart failure	☐	☐	
g	High blood cholesterol	☐	☐	
h	High blood pressure	☐	☐	
i	Narrowing or hardening of the leg arteries (including claudication)	☐	☐	
j	Other heart trouble	☐	☐	
k	Pulmonary Embolism (clot on the lung)	☐	☐	

2.1 Do you have any other problems of the heart and circulation

Yes	No	Year
☐	☐	

Office Use

a If **yes** please give details

Stroke

		Yes	No	Year of last occurrence
3.0	Have you ever been told by a doctor that you have had a stroke?	☐	☐	
	If yes ,			
a	Did the symptoms last for more than 24 hours?	☐	☐	
b	Have you made a complete recovery from your stroke?	☐	☐	
c	Following your stroke, do you still need any help in carrying out everyday activities?	☐	☐	

Investigations and special treatment for conditions affecting your heart and circulation				
4.0	Have you ever had one of the following?	Yes	No	Year of last occurrence
a	A referral to a heart specialist	☐	☐	_____
b	A referral to a chest pain clinic	☐	☐	_____
c	An exercise ECG ("stress" or "treadmill") test	☐	☐	_____
d	Angiogram or X-ray of coronary arteries (using a dye)	☐	☐	_____
e	Angioplasty (balloon treatment of coronary artery for angina)	☐	☐	_____
f	Coronary artery bypass graft operation ("heart bypass" or "CABG")	☐	☐	_____
g	Other tests, investigations or operations on your heart, arteries or veins?	☐	☐	_____
h	If yes, please give details:			Office Use ☐

Diabetes				
5.0	Have you ever been told by a doctor that you <u>have or have had</u> diabetes?	Yes	No	Year of diagnosis
		☐	☐	_____
5.1	If yes, Do you have any complications of diabetes affecting your: (please tick whichever apply)			
	feet	☐	₁	
	kidneys	☐	₁	
	eyes	☐	₁	
	nerves	☐	₁	

Cancer				
6.0	Have you ever been told by a doctor that you <u>have or have had</u> cancer?	Yes	No	Year of diagnosis
		☐	☐	_____
6.1	If yes, please give the Cancer Site (parts of the body affected)			Office Use
	_____			☐
	_____			☐

Other medical conditions					
7.0	Have you ever been told by a doctor that you <u>have or have had</u> any of the following conditions?			Yes	No
a	Anaemia	☐	☐		
b	Asthma	☐	☐		
c	Bronchitis	☐	☐		
d	Cataract	☐	☐		
e	Chronic Kidney disease	☐	☐		
f	Crohn's disease	☐	☐		
g	Depression	☐	☐		
h	Emphysema	☐	☐		
i	Gall bladder disease	☐	☐		
j	Gastric, peptic or duodenal ulcer	☐	☐		
k	Glaucoma	☐	☐		
l	Gout	☐	☐		
m	Liver disease, cirrhosis or hepatitis	☐	☐		
n	Macular degeneration	☐	☐		
o	Osteoporosis	☐	☐		
p	Parkinson's disease	☐	☐		
q	Pneumonia	☐	☐		
r	Prostate trouble	☐	☐		
s	Shingles	☐	☐		
t	Ulcerative colitis	☐	☐		
u	Other conditions, please give details			Office Use	
	_____			☐	
	_____			☐	

Arthritis				
8.0	Have you ever been told by a doctor that you <u>have or have had</u> arthritis?	Yes	No	Year of diagnosis
		☐	☐	_____
8.1	If yes, please give the type of arthritis if known,:			
	Osteoarthritis	☐	₁	
	Rheumatoid arthritis	☐	₂	
	Other (please give details)	☐	₃	Office Use
	_____			☐
8.2	Which joints are affected: (Please tick whichever apply)			
	Knees	☐	₁	Back ☐
	Hips	☐	₁	Neck ☐
	Feet	☐	₁	Shoulders ☐
	Hands and / or wrists	☐	₁	Other (please specify) ☐
	_____			Office Use
	_____			☐

Weight

19.0 What is your present weight (indoor clothes, without shoes)?
 _____ Stones _____ Pounds or _____ Kilograms

19.1 If you have no scales and have made an estimate please tick here ☐

19.2 Have you tried to lose weight in the **last four years**? Yes ☐ No ☐

19.3 If **yes**, did you: (Please tick whichever apply)
 Change your diet? ☐
 Take more exercise? ☐

19.4 Has your weight changed in the **last four years**?
 Not changed ☐
 Increased ☐
 Decreased ☐
 Both increased and decreased ☐
 Don't know ☐

If your weight has changed in the last four years:

19.5 was this change intentional? Yes ☐ No ☐
 (Please tick whichever apply)

19.6 was it the result of Personal choice ☐
 Medical advice ☐
 Illness or ill health ☐

Smoking

Cigarette smoking

20.0 Do you smoke cigarettes at present? Yes ☐ No ☐

20.1 If **yes**, How many cigarettes a day do you smoke at present _____

20.2 Have you changed your cigarette smoking habits during the past four years?
 No ☐
 Yes, increased ☐
 Yes, cut down ☐
 Yes, given up ☐

Pipe and cigar smoking

20.3 Do you currently smoke a pipe? Yes ☐ No ☐

20.4 Do you currently smoke cigars? ☐ ☐

Alcohol Intake

21.0 Would you describe your present alcohol intake as
 Daily/most days ☐
 Weekends only ☐
 Occasionally once or twice a month ☐
 Special occasions only ☐
 None ☐

One drink is **HALF A PINT** of beer/lager/cider, a **SINGLE** whisky, gin, etc. or **ONE GLASS** of wine or sherry

21.1 How much do you usually drink on the days when you drink alcohol?
 More than 6 drinks ☐
 5-6 drinks ☐
 3-4 drinks ☐
 1-2 drinks ☐

21.2 How many alcoholic drinks do you have during an average week? _____

21.3 What type of drink do you usually take?
 Beers, Lagers ☐
 Wines, Sherry ☐
 Spirits ☐
 Combination of Beers, Wines or Spirits ☐
 Low alcohol drinks ☐

21.4 Do you drink white wine Yes ☐ No ☐ If **yes**, number of glasses per week _____

21.5 Do you drink red wine ☐ ☐ _____

21.6 Is the alcohol which you drink usually taken..... (Please tick whichever apply)
 before meals ☐
 with meals ☐
 after meals ☐
 separate from meals ☐

21.7 Have you reduced your alcohol intake in the last four years? Yes ☐ No ☐

21.8 If **yes**, was this due to: (please tick whichever apply)
 Personal choice ☐
 Doctor's advice ☐
 Illness or ill-health ☐
 Other reasons ☐

21.9 Have you ever felt you ought to cut down on your drinking? Yes ☐ No ☐

21.10 Have people annoyed you by criticizing your drinking? ☐ ☐

21.11 Have you ever felt bad or guilty about your drinking? ☐ ☐

21.12 Have you had a drink first thing in the morning (eye-opener) to steady your nerves or get rid of a hangover? ☐ ☐

Physical activity

22.0 Do you make regular journeys every day or most days either walking or cycling?

No ☐ 1
Walk ☐ 2
Cycle ☐ 3
Both ☐ 4

22.1 How many hours do you normally spend walking e.g. on errands or for leisure in an average week? _____ hours

22.2 Which of the following best describes your usual walking pace?

Slow ☐ 1
Steady average ☐ 2
Fast ☐ 3

22.3 How long do you spend cycling in an average week? _____ hours

22.4 Compared with a man who spends two hours on most days on activities such as: walking, gardening, household chores, DIY projects, how physically active would you consider yourself?

Much more active ☐ 1
More active ☐ 2
Similar ☐ 3
Less active ☐ 4
Much less active ☐ 5

22.5 Do you take active sporting physical exercise such as running, swimming, dancing, golf, tennis, squash, jogging, bowls, cycling, hiking, etc.?

No ☐ 1
Occasionally less than once a month ☐ 2
Frequently once a month or more ☐ 3

22.6 If you ticked **frequently** please state type of activities:

Office Use
☐ ☐

How many times a **month** on average do you take part in these activities?

(please give overall total)

22.7 _____ Times

22.8 In winter _____ Times
In summer _____ times

22.9 Do you engage in exercises to increase muscle strength and endurance such as lifting weights, doing push-ups, using exercise machines?

Yes ☐ No ☐

22.10 If **yes**, on average how many **hours per week** do you engage in these exercises?

_____ Hours

23.0 **General health** Excellent ☐₁
Good ☐₂
Fair ☐₃
Poor ☐₄

23.1 **Pain/discomfort** I have no pain or discomfort ☐₁
I have moderate pain or discomfort ☐₂
I have extreme pain or discomfort ☐₃

23.2 **Usual activities** (eg work, study, housework, family or leisure activities):
I have no problems with performing my usual activities ☐₁
I have some problems with performing my usual activities ☐₂
I am unable to perform my usual activities ☐₃

23.3 **Mobility** I have no problems in walking about ☐₁
I have some problems in walking about ☐₂
I am confined to a chair/wheelchair ☐₃

23.5 **Anxiety/depression** I am not anxious or depressed ☐₁
I am moderately anxious and/or depressed ☐₂
I am extremely anxious and/or depressed ☐₃

23.5 **Health scale**
We have drawn a health scale (rather like a thermometer) on which perfect health is 100 and very poor health is 0. Please put a cross (X) on the scale to reflect how good or bad your health is today.

Worst Imaginable Health State

Best Imaginable Health State

0 10 20 30 40 50 60 70 80 90 100

Office use

24.0	Do you have any long-standing illness, disability or infirmity?		☐	☐
"long-standing" means anything which has troubled you over a period of time or is likely to do so				
a	If yes ,	does this illness or disability limit your activities in any way?	Yes ☐	No ☐
b		do you receive a disability allowance?	☐	☐
24.1	Do you currently have difficulty carrying out any of the following activities on your own as a result of a long term health problem?			
a		Going up or down stairs	Yes ☐	No ☐
b		Bending down	☐	☐
		Straightening up	☐	☐
d		Keeping your balance	☐	☐
e		Going out of the house	☐	☐
f		Walking 400 yards	☐	☐
24.2	Is your present state of health causing problems with any of the following:-			
a		Job at work paid employment	Yes ☐ ₁	No ☐ ₂
b		Household chores	☐	☐
c		Social life	☐	☐
d		Interests and hobbies	☐	☐
e		Holidays and outings	☐	☐
			Does not apply ☐ ₃	

Activities of daily living

The following questions will help us to understand difficulties people may have with various everyday activities

- 25.0 What is the furthest you can walk on your own without stopping and without discomfort?
 200 yards or more ☐ ₁
 More than a few steps but less than 200 yards ☐ ₂
 Only a few steps ☐ ₃
- 25.1 Can you walk up and down a flight of 12 stairs without resting?
 Yes ☐ ₁
 Only if I hold on and take a rest ☐ ₂
 Not at all ☐ ₃
- 25.2 Can you, when standing, bend down and pick up a shoe from the floor? Yes ☐ No ☐

- 26.0 Please indicate if you have difficulty doing any of the following activities:
- | | No Difficulty ₁ | Some difficulty ₂ | Unable to do or need help ₃ |
|--|----------------------------|------------------------------|--|
| a Reaching or extending your arms above shoulder level | ☐ | ☐ | ☐ |
| b Pulling or pushing large objects like a living room chair | ☐ | ☐ | ☐ |
| c Walking across a room | ☐ | ☐ | ☐ |
| d Getting in and out of bed on your own | ☐ | ☐ | ☐ |
| e Getting in and out of a chair on your own | ☐ | ☐ | ☐ |
| f Dressing and undressing yourself on your own | ☐ | ☐ | ☐ |
| g Bathing or showering | ☐ | ☐ | ☐ |
| h Feeding yourself, including cutting food | ☐ | ☐ | ☐ |
| i Getting to and using the toilet on your own | ☐ | ☐ | ☐ |
| j Lifting and carrying something as heavy as 10 lbs. (eg a bag of groceries) | ☐ | ☐ | ☐ |
| k Shopping for personal items such as toilet items or medicine by yourself | ☐ | ☐ | ☐ |
| l Doing light housework (eg washing up) | ☐ | ☐ | ☐ |
| m Preparing your own meals by yourself | ☐ | ☐ | ☐ |
| n Using the telephone by yourself | ☐ | ☐ | ☐ |
| o Taking medications by yourself | ☐ | ☐ | ☐ |
| p Managing money (e.g. paying bills etc) | ☐ | ☐ | ☐ |
| q Using public transport on your own | ☐ | ☐ | ☐ |
| r Driving a car on your own | ☐ | ☐ | ☐ |
| s Gripping with hands (eg. opening a jam jar) | ☐ | ☐ | ☐ |

Snoring

- 29.6 Do you snore while asleep? Yes, regularly ☐ ₁
 Yes, occasionally ☐ ₂
 No, never ☐ ₃
 Don't know ☐ ₄
- 29.7 If yes, do you snore loudly? Yes ☐ No ☐ Don't Know ☐
- 29.8 Have you ever been told that you hold your breath during sleep? (stop breathing for at least 10 seconds) ☐ ☐
- 29.9 Have you ever woken short of breath during sleep? ☐ ☐

Dental Health (mouth, teeth and or dentures)

- General Dental Health** Please tick **only one box**
- 30.0 Would you say that your dental health is: Excellent ☐ ₁
 Good ☐ ₂
 Fair ☐ ₃
 Poor ☐ ₄
- 30.1 Please indicate which of the following statements applies to you:
 I have
 ...only natural teeth ☐ ₁
 ...both natural teeth and dentures ☐ ₂
 ...no natural teeth, and wear dentures ☐ ₃
 ...neither natural teeth or dentures ☐ ₄
- 30.2 How many of your own (natural) teeth do you have? Don't Know ☐

- 30.3 How many of your own (natural) teeth have you lost in the last five years? _____ ☐
- Pain/ discomfort**
- In the past 6 months:** Yes No
- 30.4 Have you experienced toothache or severe discomfort with your teeth? ☐ ☐
- 30.5 How often were your teeth or gums sensitive to hot or cold or sweets? Never ☐ ₁
 Hardly ever ☐ ₂
 Occasionally ☐ ₃
 Fairly often ☐ ₄
 Very often ☐ ₅
- In the past 6 months:**
- 30.6 Which of the following dental conditions have caused difficulties or problems? (please tick all that apply)
- a Toothache, sensitive tooth, tooth decay (hole in tooth) ☐ ₁
- b Loose tooth, gum problems (bleeding, receding, swelling, abscess), bad breath ☐ ₁
- c Bad position of teeth (eg. crooked or gap), deformity of mouth ☐ ₁
- d Fractured tooth, loose or ill fitting dentures ☐ ₁
- e Colour, shape or size of teeth ☐ ₁
- f Or any other reason, please specify _____ ☐ ₁

In the past 6 months:

30.7 Have any problems with mouth, teeth or dentures caused any of the following difficulty or problem effecting your daily life?

(please tick all that apply)

a Difficulty eating food ☐

b Difficulty speaking clearly ☐

c Difficulty going out, for example to shop or visit someone ☐

d Difficulty relaxing (including sleeping) ☐

e Problems with smiling, laughing and showing teeth without embarrassment ☐

f Emotional problems eg becoming more easily upset than usual ☐

g Problems enjoying the company of others eg. family, friends or neighbours ☐

h None of these ☐

31.0 **Dry Mouth**

The following statements will help assess the extent to which you have dryness of mouth
Please tick which of the statements that apply to you over the last 4 weeks.

	Never	Hardly ever	Occasionally	Fairly often	Very often
a My mouth feels dry	☐	☐	☐	☐	☐
b I have difficulty in eating dry foods	☐	☐	☐	☐	☐
c I get up at night to drink	☐	☐	☐	☐	☐
d My mouth feels dry when eating a meal	☐	☐	☐	☐	☐
e I sip liquids to aid in swallowing food	☐	☐	☐	☐	☐
f I suck sweets to relieve dry mouth	☐	☐	☐	☐	☐
g I have difficulties swallowing certain foods	☐	☐	☐	☐	☐
h The skin of my face feels dry	☐	☐	☐	☐	☐
i My eyes feel dry	☐	☐	☐	☐	☐
j My lips feel dry	☐	☐	☐	☐	☐
k The inside of my nose feels dry	☐	☐	☐	☐	☐

Dental service use

32.0 In general do you go to the dentist for?

Regular check-up ☐

Occasional check up ☐

Only when having trouble ☐

Never go to the dentist ☐

32.1 How long has it been since you had your last dental visit?

12 months or less ☐

12 months to 2 years ☐

2 years to 5 years ☐

5 years or more ☐

Never ☐

Medications

Details of ALL medicines

45.0 Please write down details of all medicines– including tablets, injections, inhalers, eye-drops etc – which you take regularly. Please also include any medications which you buy for yourself.

	Name of medicine	Reason for taking (if known)	Year started	Is this prescribed?		Office Use
				Yes	No	
1				☐	☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
2				☐	☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
3				☐	☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
4				☐	☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
5				☐	☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
6				☐	☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
7				☐	☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
8				☐	☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
9				☐	☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
10				☐	☐	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Please use the back of the questionnaire if more space is needed to record this information.

Vitamins, minerals and complementary therapies								
46.0	Do you regularly (at least once a week or more) take any vitamins, minerals and complementary therapies?	Yes	No					
		☐	☐					
46.1	Do you take any <u>multi vitamin & minerals</u> ?	☐	☐					
46.2	If yes , how often to you take them?							
	Daily	☐						
	1-6 times per week	☐						
	Less than once per week	☐						
46.3	How long have you been taking them?							
	Less than one year	☐						
	Between 1-5 years	☐						
	More than 5 years	☐						
46.4	Please give the brand name/ preparation:	Office Use ☐						

46.5	Not counting multi vitamins, do you take any of the following vitamin/ minerals?							
	Name of vitamin/ mineral	Yes	How often do you take them?			How long have you been taking them?		
			Daily	1-6 times per week	Less than once per week	Less than one year	Between 1-5 years	More than 5 years
a	Vitamin A	☐	☐	☐	☐	☐	☐	☐
b	Vitamin B	☐	☐	☐	☐	☐	☐	☐
c	Vitamin C	☐	☐	☐	☐	☐	☐	☐
d	Vitamin D	☐	☐	☐	☐	☐	☐	☐
e	Vitamin E	☐	☐	☐	☐	☐	☐	☐
f	Calcium	☐	☐	☐	☐	☐	☐	☐
g	Cod liver Oil	☐	☐	☐	☐	☐	☐	☐
h	Fish oil	☐	☐	☐	☐	☐	☐	☐
i	Garlic	☐	☐	☐	☐	☐	☐	☐
j	Glucosamine	☐	☐	☐	☐	☐	☐	☐
k	Magnesium	☐	☐	☐	☐	☐	☐	☐
l	Selenium	☐	☐	☐	☐	☐	☐	☐
46.6	Other, please give details: (please include homeopathic and herbal treatments)							
	Name of vitamin/ mineral		How often do you take them?			How long have you been taking them?		
			Daily	1-6 times per week	Less than once per week	Less than one year	Between 1-5 years	More than 5 years
		☐	☐	☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐	☐	☐

PART II : YOUR DIET

How to fill in the diet questionnaire	
The following questions are mostly about how often you USUALLY eat different sorts of food each week.	
If you usually eat a food every day , ring 7 days a week.	
If you usually eat a food on three days a week , ring 3, and so on.	
For foods which you eat less than once a week :-	
Ring M if you eat it at least once a month.	
Ring R if you eat it less than once a month, or if you never eat it at all.	
Please ring one answer for each of the foods listed. Remember to circle R if you never eat a food.	

EXAMPLE		Number of days each week							Monthly	Rarely / Never
Food eaten every day	7 days a week	7	6	5	4	3	2	1	M	R
Food eaten on three days a week		7	6	5	4	3	2	1	M	R
Food eaten less often than once a week but at least once a month		7	6	5	4	3	2	1	(M)	R
Food eaten never or less than once a month		7	6	5	4	3	2	1	M	(R)

Diet		Yes	No	Office Use
D1.0	Are you on any special diet eg vegetarian, low fat, diabetic?	☐	☐	☐
D1.1	If yes , please give details:			

Meat		Number of days each week							Monthly	Rarely / Never
D2.0	Beef including minced beef, beef burgers	7	6	5	4	3	2	1	M	R
D2.1	Lamb	7	6	5	4	3	2	1	M	R
D2.2	Pork, bacon, ham, salami	7	6	5	4	3	2	1	M	R
D2.3	Chicken, turkey, other poultry	7	6	5	4	3	2	1	M	R
D2.4	Tinned meat all types, corned beef, etc	7	6	5	4	3	2	1	M	R
D2.5	Pork Sausages	7	6	5	4	3	2	1	M	R
D2.6	Beef Sausages	7	6	5	4	3	2	1	M	R
D2.7	Meat Pie, Pasties	7	6	5	4	3	2	1	M	R
D2.8	Liver, kidney, heart	7	6	5	4	3	2	1	M	R

Fish		Number of days each week							Monthly	Rarely / Never
D3.0	White fish cod, haddock, hake, plaice, fish fingers, etc	7	6	5	4	3	2	1	M	R
D3.1	Kippers, herrings, pilchards, tuna, sardines, salmon, mackerel including tinned	7	6	5	4	3	2	1	M	R
D3.2	Shellfish	7	6	5	4	3	2	1	M	R

Please remember to circle **R** if you never eat a food

Please remember to circle ® if you never eat a food									
Vegetables		fresh, tinned, dried, frozen	Number of days each week	Monthly	Rarely / Never				
D4.0	Potatoes:	boiled, baked, mashed	7 6 5 4 3 2 1	M	R				
D4.1		chips or fried from shop	7 6 5 4 3 2 1	M	R				
D4.2		chips or fried cooked at home	7 6 5 4 3 2 1	M	R				
D4.3		roast potatoes	7 6 5 4 3 2 1	M	R				
D4.4		Green vegetables, salads	7 6 5 4 3 2 1	M	R				
D4.5		Carrots	7 6 5 4 3 2 1	M	R				
D4.6		Parsnips, swedes, turnips, beetroot, And other root vegetables	7 6 5 4 3 2 1	M	R				
D4.7		Baked or butter beans, lentils, peas, chickpeas, sweetcorn	7 6 5 4 3 2 1	M	R				
D4.8		Onions cooked, raw, pickled	7 6 5 4 3 2 1	M	R				
D4.9		Garlic	7 6 5 4 3 2 1	M	R				
D4.10		Spaghetti and other pasta	7 6 5 4 3 2 1	M	R				
D4.11		Rice all types except pudding rice	7 6 5 4 3 2 1	M	R				
D4.12		Tomatoes fresh, tinned, pureed	7 6 5 4 3 2 1	M	R				
How often do you eat fresh vegetables in:									
D4.13		summer	7 6 5 4 3 2 1	M	R				
D4.14		winter	7 6 5 4 3 2 1	M	R				

Fresh Fruit		Number of days each week	Monthly	Rarely / Never
How often do you eat fresh fruit in :				
D5.0	summer	7 6 5 4 3 2 1	M	R
D5.1	winter	7 6 5 4 3 2 1	M	R
D5.2	Number of apples eaten a week _____			
D5.3	Number of pears eaten a week _____			
D5.4	Number of oranges or grapefruit eaten a week _____			
D5.5	Number of bananas eaten a week _____			
D5.6	Number of other fruits eaten a week (please give name and quantity)			
NAME OF FRUIT		QUANTITY	Office Use	

Please remember to circle ® if you never eat a food

Please remember to circle ® if you never eat a food									
Cheese		Number of days each week	Monthly	Rarely / Never					
D6.0	Full-fat cheese eg Cheddar, Leicester, Stilton, Brie, soft cheeses	7 6 5 4 3 2 1	M	R					
D6.1	Low-fat cheese eg Edam, Cottage cheese, reduced fat cheeses	7 6 5 4 3 2 1	M	R					
Bread		Number of days each week	Monthly	Rarely / Never					
D7.0	White bread	7 6 5 4 3 2 1	M	R					
D7.1	Brown bread	7 6 5 4 3 2 1	M	R					
D7.3	Wholemeal	7 6 5 4 3 2 1	M	R					
D7.4	Bread rolls	7 6 5 4 3 2 1	M	R					
D7.5	Crispbread Ryvita, cream crackers, etc	7 6 5 4 3 2 1	M	R					
D7.6	please give name of crispbread etc: _____								
Further details about your bread									
How many slices/ Rolls per day?		Are the slices thick, medium or thin? Please circle your answer.							
D7.7	White Bread	_____	THICK ₁	MEDIUM ₂ THIN ₃					
D7.8	Brown Bread	_____	THICK ₁	MEDIUM ₂ THIN ₃					
D7.9	Wholemeal Bread	_____	THICK ₁	MEDIUM ₂ THIN ₃					
D7.10	Bread Rolls	_____	LARGE ₁	MEDIUM ₂ SMALL ₃					
Breakfast Cereals		Number of days each week	Monthly	Rarely / Never					
D8.0	Grapenuts, Porridge, Ready Brek, Special K, Sugar Puffs, Rice Crispies	7 6 5 4 3 2 1	M	R					
D8.1	Cornflakes, Muesli, Shredded Wheat, Sultana Bran, Weetabix	7 6 5 4 3 2 1	M	R					
D8.2	Bran Flakes, Puffed wheat	7 6 5 4 3 2 1	M	R					
D8.3	All Bran, Wheat Bran	7 6 5 4 3 2 1	M	R					
D8.4	Another Cereal	7 6 5 4 3 2 1	M	R					
please give name: _____									
Biscuits, puddings and sweets		Number of days each week	Monthly	Rarely / Never					
D9.0	Digestive biscuits, plain biscuits	7 6 5 4 3 2 1	M	R					
D9.1	Sweet biscuits, sponge cakes, scones, buns	7 6 5 4 3 2 1	M	R					
D9.2	Ice cream, sweet yoghurts, trifle	7 6 5 4 3 2 1	M	R					
D9.3	Fruit cake, fruit bread, plum pudding	7 6 5 4 3 2 1	M	R					
D9.4	Fruit tart, jam tart, fruit crumble	7 6 5 4 3 2 1	M	R					
D9.5	Milk puddings rice, tapioca	7 6 5 4 3 2 1	M	R					
D9.6	Tinned fruit, jellies	7 6 5 4 3 2 1	M	R					
D9.7	Sweet sauces, chocolate, custard	7 6 5 4 3 2 1	M	R					
D9.8	Chocolate, chocolate bars, sweets all types	7 6 5 4 3 2 1	M	R					

Please remember to circle ® if you never eat a food

Please remember to circle ® if you never eat a food										
Eggs		Number of days each week					Monthly	Rarely / Never		
D10.0	Eggs boiled, poached, fried, scrambled	7	6	5	4	3	2	1	M	R
D10.1	Eggs in baked dishes eg flans, quiches, soufflés, egg custard, etc	7	6	5	4	3	2	1	M	R

Other foods		Number of days each week					Monthly	Rarely / Never		
D11.0	Soups all kinds, home-made, tinned, packet	7	6	5	4	3	2	1	M	R
D11.1	Nuts, nut butter eg salted or unsalted peanuts	7	6	5	4	3	2	1	M	R
D11.2	Savoury snacks eg potato crisps, corn chips, crackers	7	6	5	4	3	2	1	M	R
D11.3	Chutney, brown sauce, tomato sauce	7	6	5	4	3	2	1	M	R
D11.4	Sweet spreads eg jam, honey, marmalade chocolate spread	7	6	5	4	3	2	1	M	R

Drinks and Juices non-alcoholic		Number of days each week					Monthly	Rarely / Never		
D12.0	Natural fruit juices including tomato juice	7	6	5	4	3	2	1	M	R
D12.1	Fizzy drinks and Non-diet squashes	7	6	5	4	3	2	1	M	R
D12.2	Low calorie (diet) squashes and fizzy drinks	7	6	5	4	3	2	1	M	R

Milk	
D13.0	What type of milk do you usually drink? Cow's Milk ☐₁ Soya Milk ☐₂ Other, please give details _____ ☐ Office Use
D13.1	Roughly how much milk do you drink a day in tea, coffee, milky drinks or cereals? none at all ☐₁ half pint or less ☐₂ between half and one pint ☐₃ more than one pint ☐₄
D13.2	What kind of milk do you usually use? full fat milk, fresh or dried ☐₁ semi-skimmed milk, fresh or dried ☐₂ fully skimmed milk, fresh or dried ☐₃ other kinds of milk, eg condensed, evaporated ☐₄

Salt	
D14.0	How much salt is added to your food in cooking? a lot ☐₁ a little ☐₂ none ☐₃
D14.1	How much salt is added to your food on your plate? a lot ☐₁ a little ☐₂ none ☐₃

Fats	
D15.0	What do you usually spread on bread? butter ☐₁ full-fat soft margarine ☐₁ low-fat soft margarine ☐₁ hard margarine ☐₁ Give brand name _____ Office Use ☐
D15.1	How do you normally spread the fat? thinly ☐₁ average ☐₂ thickly ☐₃ How often do you eat home-fried food including chips, cooked with :- Lard, dripping, solid vegetable oil Number of days each week 7 6 5 4 3 2 1 Monthly M Rarely / Never R Give brand name and type _____ Office Use ☐
D15.2	Liquid vegetable oil 7 6 5 4 3 2 1 M R Give brand name and type _____ Office Use ☐
D15.3	Liquid vegetable oil 7 6 5 4 3 2 1 M R Give brand name and type _____ Office Use ☐

Your household	
D16.0	How many people normally eat in your household? Number of adults including yourself _____ Number of children 5 to 16 years old _____ Number of children 1 to 4 years old _____ Number of babies under 1 year old _____ How much of the following foods does your household use on average each week including cooking and baking? If you live on your own, please give the amounts which you yourself eat a week.
D16.1	Butter _____ lbs _____ ozs or _____ grams
D16.2	Margarine _____ lbs _____ ozs or _____ grams
D16.3	Lard and solid vegetable oil _____ lbs _____ ozs or _____ grams
D16.4	Liquid vegetable oil eg Sunflower, Corn, Groundnut oil _____ ozs or _____ ml
D16.5	Olive Oil _____ ozs or _____ ml
D16.6	Cream _____ ozs or _____ ml
D16.7	Full-fat cheese eg Cheddar, Leicester, Stilton, Brie, & soft cheeses _____ lbs _____ ozs or _____ grams
D16.8	Low-fat cheese eg reduced fat cheddar, reduced fat soft cheeses, Edam _____ lbs _____ ozs or _____ grams
D16.9	Sugar _____ lbs _____ ozs or _____ grams

Hot drinks	
Coffee	
D17.0	How many cups of coffee do you have a day? _____ Cups per day
D17.1	Is this: Ground coffee ☐ ₁ Instant coffee ☐ ₂
D17.2	Is it decaffeinated: Yes ☐ ₁ No ☐ ₂
D17.3	How many teaspoons of sugar do you take in each cup? _____ Teaspoons Do not count artificial sweeteners
Tea	
D17.4	How many cups of tea do you have a day? _____ Cups per day
D17.5	How many teaspoons of sugar do you take in each cup? _____ Teaspoons Do not count artificial sweeteners
Other Hot Drinks	
D17.7	How many cups of other hot drinks (e.g. hot chocolate, malted milk, Horlicks) do you have a day? _____ Cups per day

Alcoholic Drinks					
D18.0	Have you ever consumed alcoholic drinks?	Yes ☐	No ☐	Seldom ☐	
D18.1	Do you take alcoholic drinks at present?	☐ ₁	☐ ₂	☐ ₃	
Think back carefully over the last seven days. Please write the number of alcoholic drinks you have consumed on each day during the past week. It may help if you try to remember where you were and who you were with on each day. For each day, write in how much you have drunk:					
(i) the number of half pints of non-alcoholic beer, lager, etc (ii) the number of half pints of low-alcohol beer, lager, etc (iii) the number of half pints of beer, lager, shandy, cider, stout, etc (iv) the number of single glasses of whisky, vodka, gin, rum, etc (v) the number of single glasses of wine, sherry, martini, port, etc					
	Half-pints of non-alcoholic beer	Half-pints of low-alcohol beer	Half-pints of beer, lager, shandy	Single glasses of Spirits	Single glasses of wine
Monday					
Tuesday					
Wednesday					
Thursday					
Friday					
Saturday					
Sunday					
D18.2	Would you say last week was fairly typical of what you usually have to drink in one week?		Yes ☐ ₁	No ☐ ₂	
D18.3	If last week was not typical, would you normally drink more or less in a week?		More ☐ ₁	Less ☐ ₂	

Appendix F. Follow-up Questionnaire for Disability in 2014 at 30-Year Re-Examination in the BRHS.

Study Number:




BRITISH REGIONAL HEART STUDY 2014

Thank you very much for taking the time to complete this questionnaire, which will bring us up to date with your present health and circumstances. All the information will be treated as **strictly confidential** and will only be seen by the Research Team.

Most questions can be answered by ticking the correct box ☒

Please check that you have answered as many questions as you can and return it to us in the envelope provided – you do not need to use a stamp.

If you have any trouble answering the questions, or would like a large-print copy, please phone us on 020 7830 2335 and give us your telephone number. We will then call you back to answer your query.

THANK YOU FOR YOUR HELP

Professor Peter Whincup & Ms Lucy Lennon
on behalf of the British Regional Heart Study research team

Department of Primary Care & Population Health
UCL Medical School
Royal Free Campus
Rowland Hill Street
London NW3 2PF

Disability

29.1 Do you currently have difficulty carrying out any of the following activities on your own as a result of a long term health problem?

	Yes	No
a Going up or down stairs	☐	☐
b Bending down	☐	☐
c Straightening up	☐	☐
d Keeping your balance	☐	☐
e Going out of the house	☐	☐
f Walking 400 yards	☐	☐

29.2 Is your present state of health causing problems with any of the following:-

	Yes	No	Does not apply
a Job at work paid employment	☐ ₁	☐ ₂	☐ ₃
b Household chores	☐	☐	
c Social life	☐	☐	
d Interests and hobbies	☐	☐	
e Holidays and outings	☐	☐	

29.3 Do you have any difficulties getting about outdoors? (Tick one box only)

No difficulty	☐ ₁
Slight	☐ ₂
Moderate	☐ ₃
Severe	☐ ₄
Unable to do	☐ ₅

Activities of daily living

The following questions will help us to understand difficulties people may have with various everyday activities

30.0 What is the furthest you can walk on your own without stopping and without discomfort?

200 yards or more	☐ ₁
More than a few steps but less than 200 yards	☐ ₂
Only a few steps	☐ ₃

30.1 Can you walk up and down a flight of 12 stairs without resting?

Yes	☐ ₁
Only if I hold on and take a rest	☐ ₂
Not at all	☐ ₃

30.2 When standing, can you bend down and pick up a shoe from the floor?

Yes	☐
No	☐

31.0	Please indicate if you have difficulty doing any of the following activities:			
		No Difficulty 1	Some difficulty 2	Unable to do or need help 3
a	Reaching or extending your arms above shoulder level	☐	☐	☐
b	Pulling or pushing large objects like a living room chair	☐	☐	☐
c	Walking across a room	☐	☐	☐
d	Getting in and out of bed on your own	☐	☐	☐
e	Getting in and out of a chair on your own	☐	☐	☐
f	Dressing and undressing yourself on your own	☐	☐	☐
g	Bathing or showering	☐	☐	☐
h	Feeding yourself, including cutting food	☐	☐	☐
i	Getting to and using the toilet on your own	☐	☐	☐
j	Lifting and carrying something as heavy as 10 lbs, (eg a bag of groceries)	☐	☐	☐
k	Shopping for personal items such as toilet items or medicine by yourself	☐	☐	☐
l	Doing light housework (eg washing up)	☐	☐	☐
m	Preparing your own meals by yourself	☐	☐	☐
n	Using the telephone by yourself	☐	☐	☐
o	Taking medications by yourself	☐	☐	☐
p	Managing money (e.g. paying bills etc)	☐	☐	☐
q	Using public transport on your own	☐	☐	☐
r	Driving a car on your own	☐	☐	☐
s	Gripping with hands (eg. opening a jam jar)	☐	☐	☐

Appendix G. Questionnaire in 1998-1999 at Year 2.

(only those which apply to this study)



PHYSICAL FUNCTION

4. Because of a health or physical problem, do you have any difficulty walking a quarter of a mile, that is about 2 or 3 blocks? *(Interviewer Note: If the participant responds "Don't do," probe to determine whether this is because of a health or physical problem. If the participant doesn't walk because of a health or physical problem, check "Yes." If the participant doesn't walk for other reasons, check "Don't do.")* **BCDWQMYN**

☐ 1 Yes
 ☐ 0 No
 ☐ 8 Don't know
 ☐ 7 Refused
 ☐ 9 Don't do

☐ 0 No → Go to Question #4c
☐ 7 Refused → Go to Question #4b

a. How much difficulty do you have? *(Interviewer Note: Read response options.)* **BCDWQMDF**

☐ 1 A little difficulty
☐ 2 Some difficulty
☐ 3 A lot of difficulty
☐ 4 Or are you unable to do it?
☐ 8 Don't know

b. What is the main reason that you have difficulty? Is it because of arthritis, shortness of breath, heart disease, or some other reason?
(Interviewer Note: If "some other reason," probe for response. Do NOT read response options. Mark only ONE answer.) **BCMNRS**

☐ 1 Arthritis ☐ 2 Back pain ☐ 3 Balance problems/unsteadiness on feet ☐ 4 Cancer ☐ 5 Chest pain/discomfort ☐ 6 Circulatory problems ☐ 7 Diabetes ☐ 8 Fatigue/tiredness (no specific disease) ☐ 9 Fall ☐ 10 Heart disease (including angina, congestive heart failure, etc.) ☐ 11 High blood pressure/hypertension	☐ 12 Hip fracture ☐ 13 Injury (Please specify _____) ☐ 14 Joint pain ☐ 15 Lung disease (asthma, chronic bronchitis, emphysema, etc.) ☐ 16 Old age (no mention of a specific condition) ☐ 17 Osteoporosis ☐ 18 Shortness of breath ☐ 19 Stroke ☐ 1 Other symptom (Please specify _____) BCMNRS4 ☐ 2 Multiple conditions/symptoms given; unable to determine MAIN reason ☐ 8 Don't know

Go to Question #5



HABC Enrollment ID #	Acrostic	Date Form Completed	Staff ID #
H		/ /	
BCID	BCACROS	BCDATE Month Day Year	BCSTFID

YEAR 2 QUESTIONNAIRE

Date of 6-month Follow-up Contact Interview: / /
(Interviewer Note: Refer to Data From Baseline Visit Form.)

1. In general, how would you say your health is? **BCHSTAT**
(Interviewer Note: Read response options.)

☐ 1 Excellent ☐ 2 Very good ☐ 3 Good ☐ 4 Fair	☐ 5 Poor ☐ 8 Don't know ☐ 7 Refused

2. Since your last phone interview about 6 months ago, did you stay in bed all or most of the day because of an illness or injury? Please include days that you were a patient in a hospital. Please include days in bed. **BCBED12**

☐ 1 Yes
 ☐ 0 No
 ☐ 8 Don't know
 ☐ 7 Refused

About how many days did you stay in bed all or most of the day because of an illness or injury? Please include days that you were a patient in a hospital.
(Interviewer Note: If necessary, probe - "If you are unsure, please make your best guess.")

days **BCBEDDAY**

3. Since your last phone interview about 6 months ago, did you cut down on the things you usually do, such as going to work or working around the house, because of an illness or injury? Please include days in bed. **BCCUT12**

☐ 1 Yes
 ☐ 0 No
 ☐ 8 Don't know
 ☐ 7 Refused

How many days did you cut down on the things you usually do because of illness or injury? Please include days in bed.
(Interviewer Note: If necessary, probe - "If you are unsure, please make your best guess.")

days **BCCUTDAY**

5c. How easy is it for you to walk up 10 steps without resting?
(Interviewer Note: Read response options.)

- ☐ 1 Very easy
- ☐ 2 Somewhat easy
- ☐ 3 Or not that easy
- ☐ 8 Don't know/Don't do

BCDW10EZ

5d. Do you get tired when you walk up 10 steps without resting?

- ☐ 1 Yes
- ☐ 0 No
- ☐ 8 Don't know/Don't do

BCDW10WX

6. Do you have to use a cane, walker, crutches, or other special equipment to help you get around?

BCEQUIP ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

8. Do you have any difficulty stooping, crouching or kneeling?
(Interviewer Note: "Difficulty" refers to difficulty getting down AND/OR getting back up.)

BCDIFSCK ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

How much difficulty do you have?
(Interviewer Note: Read response options.)

- ☐ 1 A little difficulty
- ☐ 2 Some difficulty
- ☐ 3 A lot of difficulty
- ☐ 4 Or are you unable to do it?
- ☐ 8 Don't know

BCDSCKAM

How easy is it for you to stoop, crouch, or kneel?
(Interviewer Note: Read response options.)

- ☐ 1 Very easy
- ☐ 2 Somewhat easy
- ☐ 3 Or not that easy
- ☐ 8 Don't know

BCEZSCK

9. Because of a health or physical problem, do you have any difficulty getting in and out of bed or chairs?

BCDIOYN ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

How much difficulty do you have?
(Interviewer Note: Read response options.)

- ☐ 1 A little difficulty
- ☐ 2 Some difficulty
- ☐ 3 A lot of difficulty
- ☐ 4 Or are you unable to do it?
- ☐ 8 Don't know

BCDIODIF

Do you usually receive help from another person when you get in and out of bed or chairs?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know

BCDIORHY

10. Do you have any difficulty bathing or showering? BCBATHYN

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

How much difficulty do you have?
(Interviewer Note: Read response options.)

- ☐ 1 A little difficulty
- ☐ 2 Some difficulty
- ☐ 3 A lot of difficulty
- ☐ 4 Or are you unable to do it?
- ☐ 8 Don't know

BCBATHDF

Do you usually receive help from another person in bathing or showering?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know

BCBATHRH

11. Because of a health or physical problem, do you have any difficulty dressing?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

BCDDYN

How much difficulty do you have?
(Interviewer Note: Read response options.)

- ☐ 1 A little difficulty
- ☐ 2 Some difficulty
- ☐ 3 A lot of difficulty
- ☐ 4 Or are you unable to do it?
- ☐ 8 Don't know

Do you usually receive help from another person in dressing?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know

BCDDRHYN

DENTAL HISTORY

BZID

BZACROS

- 42.** How would you rate your overall oral health (teeth, gums, inside of mouth)?
(Interviewer Note: Read response options.)

- ☐ 1 Excellent
☐ 3 Good
☐ 4 Fair
☐ 5 Poor
☐ 8 Don't know
☐ 7 Refused

BZDHSTAT

- 43.** How often do you brush your teeth in an average day?

- ☐ 0 Not at all
☐ 1 One time
☐ 2 Two times
☐ 3 Three or more times
☐ 8 Don't know
☐ 7 Refused

BZDHBRSH

- 44.** How often do you use dental floss in an average week?

- ☐ 0 Not at all
☐ 1 One time
☐ 2 Two times
☐ 3 Three or more times
☐ 8 Don't know
☐ 7 Refused

BZDHFLOS

- 45.** How often do you go to your dentist for a check-up?

- ☐ 1 2 times or more per year
☐ 2 Once per year
☐ 3 Less than once per year
☐ 8 Don't know
☐ 7 Refused

BZDHDENT

- 46.** Have you ever been told by a dentist or periodontist that you have gum (periodontal) disease?

- ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

BZDHGUMD

When were you last treated for gum disease?

- ☐ 0 Never
☐ 1 Within the past 12 months
☐ 2 More than 1 year ago
☐ 8 Don't know/Don't remember

BZDH

- 47.** Have you ever lost any teeth because of gum disease?

- ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

BZDHLOST

How old were you when you lost your first tooth because of gum disease?

years old

- ☐ -1 Don't know
BZDHLARF

BZDHLAGE

48. Do you limit the kinds or amounts of food you eat because of problems with your teeth or dentures?
Would you say...? (Interviewer Note: Read response options.)

☐ 4 Always
☐ 3 Often
☐ 2 Sometimes
☐ 1 Seldom
☐ 0 Never
☐ 8 Don't know
☐ 7 Refused

BZDHUMT

49. Do you have trouble biting or chewing any kinds of food, such as firm meat or apples?
(Interviewer Note: Read response options.)

☐ 4 Always
☐ 3 Often
☐ 2 Sometimes
☐ 1 Seldom
☐ 0 Never
☐ 8 Don't know
☐ 7 Refused

BZDHCHEW

50. Does the amount of saliva in your mouth seem to be...?
(Interviewer Note: Read response options.)

☐ 1 Too little
☐ 2 Too much
☐ 3 Don't notice
☐ 8 Don't know
☐ 7 Refused

BZDHSALV

51. Does your mouth feel dry when eating? BZDHMDRY

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

52. During the past 3 months, how much pain have you had in your gums or teeth?
(Interviewer Note: Read response options.)

☐ 3 A great deal or pain
☐ 2 Some pain
☐ 1 A little pain
☐ 0 No pain at all
☐ 8 Don't know
☐ 7 Refused

BZDHPAIN

53. During the past 3 months, how often have you had trouble chewing food or eating because of
problems with your teeth or gums? (Interviewer Note: Read response options.)

☐ 3 Most of the time
☐ 2 Some of the time
☐ 1 A little of the time
☐ 0 None of the time
☐ 8 Don't know
☐ 7 Refused

BZDHPCHW

54. During the past 3 months, how much of the time have problems with the way your teeth or gums look
caused you to avoid conversation with people? (Interviewer Note: Read response options.)

☐ 3 Most of the time
☐ 2 Some of the time
☐ 1 A little of the time
☐ 0 None of the time
☐ 8 Don't know
☐ 7 Refused

BZDHLOOK

Now I'm going to ask you about some medical problems that you might have had since your last clinic visit about 12 months ago.

Since your last clinic visit about 12 months ago, has a doctor told you that you had...?

66. Hypertension or high blood pressure? **BZHCHBP**
☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

67. Diabetes or sugar diabetes? **BZSGDIAB**
☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

Since your last clinic visit about 12 months ago...

68. Have you fallen and landed on the floor or ground? **BZAJFALL**
☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

Please go to Question #69

How many times have you fallen in the past 12 months?
If you are unsure, please make your best guess.

☐ 1 One **BZAJFNUM**
☐ 2 Two or three
☐ 4 Four or five
☐ 6 Six or more
☐ 8 Don't know

Now I'm going to ask you about any medical problems you might have had since your last phone interview about 6 months ago.

72. Since your last phone interview about 6 months ago, has a doctor told you that you had a heart attack, angina, or chest pain due to heart disease? **BZHCMANI**

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

Were you hospitalized overnight for this problem? **BZHOSMI**

☐ 1 Yes ☐ 0 No

Complete a Health ABC Event Form(s),
Section I, for each overnight hospitalization.
Record reference #'s below:

a. **BZREF9A**
b. **BZREF9B**
c. **BZREF9C**

Go to Question #73

73. Since your last phone interview about 6 months ago, has a doctor told you that you had a stroke, mini-stroke, or TIA? **BZHCCVA**

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

Were you hospitalized overnight for this problem? **BZHOSMI2**

☐ 1 Yes ☐ 0 No

Complete a Health ABC Event Form(s),
Section I, for each overnight hospitalization.
Record reference #'s below:

a. **BZREF10A**
b. **BZREF10B**
c. **BZREF10C**

Go to Question #74

74. Since your last phone interview about 6 months ago, has a doctor told you that you had cancer?
We are specifically interested in hearing about a cancer that your doctor diagnosed for
the first time since your last phone interview.

BZCHMGMT

1

Yes

0

No

8

Don't know

7

Refused

Complete a Health ABC Event Form(s),
Section II, for each event.
Record reference #'s below:

a.

BZREF11A

b.

BZREF11B

c.

BZREF11C

(only those which apply to this study)

Section A Medication Reception

Collect all prescription and over-the-counter medications (including pills, dermal patches, eye drops, creams, salves, and injections) used in the previous two weeks. Record the complete drug name exactly as written on the container label.

Are these all the prescription and over-the-counter medications that you took during the last two weeks? We are also interested in drugs not usually prescribed by a doctor, such as supplements, vitamins, pain medications, laxatives or bowel medicines, cold medications, cough medications, antacids or stomach medicines, and ointments or salves?

MAMEDS	☐ Yes	☐ No	☐ Took no prescription or non-prescription medicines

MATOTAL	Total number brought in:	Did examiner call participant to complete MIF?	☐ Yes	☐ No	MACALL

Section B Prescription Medication.

Copy the name of the prescription, the strength in milligrams (mg) or other units, the total number of doses taken per day, week or month. Indicate whether the medication is taken on an "as needed" basis, and whether or not the container was actually seen. In addition, record reason for use, date started, and formulation code.

Medication Name (Generic Name or Trade Name)	Strength	Units	Indicate Number Used	PRN?	Container Seen?
			Circle Day, Week or Month	Check "X" Yes or No	Check "X" Yes or No
1. MIFNAME	MIF STREN	MIFUNIT	MIFDWM D W M	MIFPRN ☐ Y ☐ N	MIFSEEN ☐ Y ☐ N
Reason for use: _____	MIFREAS	MIFNMUS 1 2 3	MIFMONTH/MIFYEAR	Formulation Code: MIFFORM	☐ Rx ☐ Non Rx
Date Started: _____	Month Year				
2.			D W M	☐ Y ☐ N	☐ Y ☐ N
Reason for use: _____			Month Year	Formulation Code: _____	☐ Rx ☐ Non Rx
3.			D W M	☐ Y ☐ N	☐ Y ☐ N
Reason for use: _____			Month Year	Formulation Code: _____	☐ Rx ☐ Non Rx
4.			D W M	☐ Y ☐ N	☐ Y ☐ N
Reason for use: _____			Month Year	Formulation Code: _____	☐ Rx ☐ Non Rx
5.			D W M	☐ Y ☐ N	☐ Y ☐ N
Reason for use: _____			Month Year	Formulation Code: _____	☐ Rx ☐ Non Rx

YEAR 2 CLINIC VISIT PROCEDURE CHECKLIST

Page Numbers		Please check if done		Comments
1. Medication Inventory Update	2	☐ Yes	☐ No	B1MI
2. Weight	7	☐ Yes	☐ No	B1WT
3. Radial Pulse, Respiratory Rate & Temperature	7	☐ Yes	☐ No	B1RP
4. Blood Pressure	8	☐ Yes	☐ No	B1BP
5. Food Frequency Questionnaire	9	☐ Yes	☐ No	B1FFQ
6. Grip Strength	17	☐ Yes	☐ No	B1GRIP
7. 20-meter Walk	18	☐ Yes	☐ No	B120M
8. Long Distance Corridor Walk	19	☐ Yes	☐ No	B1LD
9. Ultrasound	24	☐ Yes	☐ No	B1ULTRA
10. Bone Density Scan (DXA)	26	☐ Yes	☐ No	B1DXA
11. Periodontal Eligibility Assessment	28	☐ Yes	☐ No	B1PERIOD
12. Dental Examination	31	☐ Yes	☐ No	B1DENT
13. Isokinetic Strength (Kin-Com)	32	☐ Yes	☐ No	B1ISO
14. Joint (OA) Evaluation	35	☐ Yes	☐ No	B1JOINT
15. Knee X-ray Tracking	43	☐ Yes	☐ No	☐ 5 Not Applicable B1KNXR
16. Knee MRI Eligibility and Tracking	44	☐ Yes	☐ No	☐ 5 Not Applicable B1KNMRI
17. Energy Expenditure (Visit 1)	46	☐ Yes	☐ No	☐ 5 Not Applicable B1EE
18. Phlebotomy	48	☐ Yes	☐ No	B1PHL
19. Laboratory Processing	49	☐ Yes	☐ No	B1LAB
20. Was the Year 2 Questionnaire administered?		☐ Yes	☐ No	B1Y2ADM

Memphis Only: **B1DOC**
Would you like us to send a copy of your test results to your doctor? ☒ Yes ☐ No

WEIGHT, RADIAL PULSE, RESPIRATORY RATE, AND TEMPERATURE

WEIGHT

① B1WTK kg B1STFD1 Staff ID#

RADIAL PULSE

②

Measurement 1	B1PULSE beats per minute	←	<i>Clinic Use Only</i> Measurement 1 B1PLSSM1 beats per 30 seconds x 2 Measurement 2 B1PLSMS2 beats per 30 seconds x 2
Measurement 2	B1PULSE2 beats per minute	←	
Total (Measurement 1 + Measurement 2)			
	B1PLSTOT		
	÷ 2		
=	Average beats per minute		
	B1PLSAV		(Examiner Note: Record Radial Pulse on Long Distance Corridor Walk Eligibility Assessment Form, page 19, Question #2a.)

RESPIRATORY RATE

③ B1RESP
inspirations per 30 seconds B1STFD5 Staff ID#

TEMPERATURE

④ ° F B1TEMP B1STFD3 Staff ID#

BLOOD PRESSURE

BLOOD PRESSURE

① Cuff Size ☒ Small ☐ Regular ☐ Large ☐ Thigh B1OCUF
 ② Arm Used ☒ Right ☐ Left → Please explain why right arm was not used:
 (Examiner Note: Refer to Data from Baseline Visit Form.) B1ARMRL

Pulse Obliteration Level

③ Palpated Systolic B1POPS mmHg * Add +30 to Palpated Systolic to obtain
 Maximal Inflation Level.
 Add 30*
 ④ Maximal Inflation Level (MIL) B1POMX mmHg + If MIL is ≥ 300 mmHg, repeat the MIL. If MIL
 is still ≥ 300 mmHg, terminate blood pressure
 measurements.
 ⑤ Was blood pressure measurement terminated because MIL ≥ 300 mmHg after second reading?
☒ Yes ☐ No B1BPYN

Sitting Blood Pressure Measurement #1

⑥ Systolic mmHg Comments (required for missing or unusual values):
 B1SYS
 ⑦ Diastolic mmHg B1DIA

Sitting Blood Pressure Measurement #2

⑧ Systolic mmHg Comments (required for missing or unusual values):
 B1SY2
 ⑨ Diastolic mmHg B1DIA2

Standing Blood Pressure Measurement

Examiner Note:
 a) Perform Standing Blood Pressure Measurement after
 participant has been standing for one minute.
 ⑩ Systolic B1SY3 mmHg
 b) Record these measurements on Long Distance
 Corridor Walk Eligibility Assessment Form
 (page 19, Question #2b).
 ⑪ Diastolic B1DIA3 mmHg

FOOD FREQUENCY QUESTIONNAIRE

Food Introduction

Now I'd like to ask you some questions about the foods you usually eat. There are no right or wrong answers, and it is very important that we learn what you actually eat, not what you think you should eat.

This section is about your usual eating habits over the past year or so. This includes all meals or snacks, at home or in a restaurant or carry-out.

Please tell me how often, on average, you eat each food. For example, twice a week, three times a month, and so forth.

Interviewer Note: REQUIRED - Show Card A

Also, please tell me how much you usually eat of each food. Sometimes I'll ask "how much" as number of pieces, such as 1 egg, 2 eggs, etc. Sometimes I'll ask you to tell me the portion size you usually eat, using these models (**Interviewer Note: Show models**).

Type of Food	How often? →									How much each time?			
	Never	1-11 times per year	Once per mon.	2-3 times per mon.	Once per week	Twice per week	3-4 times per week	5-6 times per week	Every Day	Portion Size			
Please tell me how often you eat each of the following foods.													
Bananas B2BANA	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many each time? B2BANASZ ① 1/2 ② 1 ③ 2 ④ 3			
Fresh apples or pears B2APPL	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many? B2APPLSZ ① 1 ② 2 ③ 3			
Oranges or tangerines, not including juice B2ORAN	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many? B2ORANSZ ① 1 ② 2 ③ 3			
Grapefruit, not including juice B2GFRU	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many? B2GFRUSZ ① 1 ② 2 ③ 3			
Cantaloupe B2CANT	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2CANTSZ ① 1/4 ② 1/2 ③ 1			
Raw peaches, apricots, nectarines, in season B2PEAC	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many? B2PEACSZ ① 1 ② 2 ③ 3			
Applesauce, fruit cocktail, canned pears B2APA	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2APASZ ① B ② C ③ D			
Canned, frozen or stewed peaches or apricots B2CNPC	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2CNPCSZ ① B ② C ③ D			
Any other fruit, like grapes, honeydew, pineapple, strawberries B2OTH	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2OTHSZ ① A ② B ③ C ④ D			



FOOD FREQUENCY QUESTIONNAIRE

Type of Food	How often? →									How much each time?			
	Never	1-11 times per year	Once per mon.	2-3 times per mon.	Once per week	Twice per week	3-4 times per week	5-6 times per week	Every Day	Portion Size			
How often do you eat...? Eggs, including biscuit sandwiches, and Egg McMuffins B2EGGS	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many eggs each time? B2EGGSSZ ① 1 ② 2 ③ 3 ④ 4			
Bacon B2BACN	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many pieces? B2BACNSZ ① 1 ② 2 ③ 3 ④ 4			
Breakfast sausage, including sausage biscuits B2SAUS	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many pieces? B2SAUSSZ ① 1 ② 2 ③ 3 ④ 4			
Pancakes, waffles, or French toast B2PANC	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many pieces? B2PANCsz ① 1 ② 2 ③ 3 ④ 4			
Cooked cereals like oatmeal, cream of wheat, or grits B2OATM	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (bowl) B2OATMSZ ① B ② C ③ D			
Any kind of cold cereal (Interviewer Note: If "Never" skip to Cottage Cheese) B2CERE	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (bowl) B2CERESZ ① B ② C ③ D			
How often do you eat Fiber or bran cereals? B2FIBR	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (bowl) B2FIBRSZ ① B ② C ③ D			
How often do you eat Product 19, Just Right or Total cereal? B2TOTL	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (bowl) B2TOTLSZ ① B ② C ③ D			
How often do you eat other cold cereals like Corn Flakes, Cheerios, Special K? B2SPEK	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (bowl) B2SPEKSZ ① B ② C ③ D			
How often do you use milk on cereal? B2MILK	①	②	③	④	⑤	⑥	⑦	⑧	⑨	Don't ask			
Cottage cheese B2COTT	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2COTTSZ ① A ② B ③ C ④ D			
Other cheese or cheese spread, including on sandwiches B2CHES	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many slices? B2CHESSZ ① 1 ② 2 ③ 3 ④ 4			
When you eat cheese is it...? B2FAT1	① Usually low-fat ② Sometimes ③ Rarely or never low-fat ④ N/A												
Yogurt or frozen yogurt B2YOGR	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2YOGRSZ ① A ② B ③ C ④ D			
When you eat yogurt is it...? B2FAT2	① Usually low-fat ② Sometimes ③ Rarely or never low-fat ④ N/A												



FOOD FREQUENCY QUESTIONNAIRE

How often do you eat the following vegetables, including fresh, frozen, canned or in stir-fry, at home or in a restaurant?

Interviewer Note: REQUIRED-Show Card B	How often?								How much each time?						
	Never	1-11 times per year	Once per mon.	2-3 times per mon.	Once per week	Twice per week	3-4 times per week	5-6 times per week	Every Day	Portion Size					
Type of Food															
How often do you eat...?															
French fries and fried potatoes B2FRYS	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
White potatoes not fried, including boiled, baked, mashed & potato salad B2POTA	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
*When you ate boiled or baked potatoes, how often did you eat them without butter, margarine, or sour cream?															
B2FAT3	①	Usually or Always	②	Often	③	Sometimes	④	Rarely or never							
Sweet potatoes, yams B2YAMS	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Rice, or dishes made with rice B2RICE	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Stuffing or dressing B2STUF	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Baked beans, chili with beans, blackeye peas, any other dried beans B2BEAN	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Corn B2CORN	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Green beans or green peas B2PEAS	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Broccoli B2BROC	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Carrots, or mixed vegetables containing carrots, or stews with carrots B2MVEG	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Spinach B2SPIN	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Collards, mustard greens, turnip greens B2GRNS	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Cole slaw, cabbage B2SLAW	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Green salad B2GSAL	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Raw tomatoes B2TOMA	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Salad dressing B2DRES	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many TSP?	①	②	③	④	
When you use salad dressing is it?: ① Always low-fat ② Sometimes ③ Rarely low-fat ④ N/A															
Any other vegetable, like okra, cooked green peppers, cooked onions B2OTHV	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much?	①	②	③	④	
Vegetable soup, vegetable beef, chicken vegetable, or tomato soup B2SOUP	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (bowl)	①	②	③	④	
Other soups, like chicken noodle, chowder B2OTHS	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (bowl)	①	②	③	④	

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FOOD FREQUENCY QUESTIONNAIRE

Interviewer Note: REQUIRED-Show Card C Type of Food	How often?									How much each time?					
	Never	1-11 times per year	Once per mon.	2-3 times per mon.	Once per week	Twice per week	3-4 times per week	5-6 times per week	Every Day	Portion Size					
Hamburgers, cheeseburgers, meat loaf, at home or in a restaurant B2BURG	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (model)	①	②	③	④	
Beef, including steaks, roasts, pot roast, or in sandwiches B2BEEF	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (model)	①	②	③	④	
Liver, including chicken livers or liverwurst B2LIVR	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (model)	①	②	③	④	
Pork, including chops, roasts, pigs feet, or dinner ham B2PORK	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (model)	①	②	③	④	
*When you cook red meat, how often do you trim all the fat before cooking?															
B2FAT5	①	Usually or Always	②	Often	③	Sometimes	④	Rarely or never	⑤	Don't know/Don't do					
When you eat beef or pork, how often do you eat the fat?	① Rarely or never ② Sometimes ③ Often eat the fat ④ N/A									B2FAT6					
Mixed dishes with meat, like corned beef hash, stuffed cabbage, pork chow mein, or frozen meals with meat B2MIXD	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (blocks or bowl)	①	②	③	④	
Fried chicken, at home or in a restaurant B2FRCH	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (model)	①	②	③	④	
Chicken or turkey, roasted or broiled, including on sandwiches B2CHIK	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (model)	①	②	③	④	
When you eat chicken, how often do you eat the skin?															
Chicken stew, chicken casserole, other mixed dishes like chicken & dumplings or frozen meals with chicken, or chicken pot pies B2STEW	① Rarely or never ② Sometimes ③ Often eat the skin ④ N/A									B2FAT7					
Shellfish like shrimp, scallops, crabs B2CRAB	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (blocks or bowl)	①	②	③	④	
Tuna, tuna salad, tuna casserole B2TUNA	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? of the tuna?	①	②	③	④	
Fried fish or fish sandwich, at home or in a restaurant B2FISH	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (model)	①	②	③	④	
Other fish, broiled or baked B2OTHF	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (model)	①	②	③	④	
Hot dogs B2HDOG	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many slices?	①	②	③	④	
Bologna, sliced ham, chicken salad, other lunch meats B2MEAT	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many slices?	①	②	③	④	
When you eat lunch meats, are they...?															
B2FAT8	①	Usually low-fat	②	Sometimes	③	Rarely low-fat	④	N/A							
Spaghetti or other pasta with tomato sauce, like lasagna B2PAST	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (bowl or blocks)	①	②	③	④	
Cheese dishes without tomato sauce, like macaroni and cheese, or cheese grits B2MACA	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? (bowl or blocks)	①	②	③	④	
Pizza, including carry out B2PIZZ	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many slices?	①	②	③	④	

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Interviewer Note: REQUIRED - Show Card D Type of Food	How often? →								How much each time?	
	Never or less than once per month	Once per mon.	2-3 times per mon.	Once per week	Twice per week	3-4 times per week	5-6 times per week	Every Day	2+ times per day	Portion Size
Now I'm going to ask you about five different types of bread. How often do you eat...?										
Biscuits, muffins B2MUFF	①	②	③	④	⑤	⑥	⑦	⑧	⑨	What size? How many pieces each time? B2MUFFSZ A ① ② ③ ④ B C D
Rolls, hamburger buns, English muffins, bagels B2ROLL	①	②	③	④	⑤	⑥	⑦	⑧	⑨	B2ROLLSZ A ① ② ③ ④ B C D
White bread, including French, Italian, or in sandwiches B2WBRD	①	②	③	④	⑤	⑥	⑦	⑧	⑨	B2WBRDSZ A ① ② ③ ④ B C D
Whole wheat, rye, other dark breads B2DBRD	①	②	③	④	⑤	⑥	⑦	⑧	⑨	B2DBRDSZ A ① ② ③ ④ B C D
Cornbread, corn muffins, hush puppies B2CBRD	①	②	③	④	⑤	⑥	⑦	⑧	⑨	B2CBRDSZ A ① ② ③ ④ B C D
Butter or margarine on bread or on potatoes, vegetables, etc. B2MARG	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many pats? B2MARGSZ A ① ② ③ ④ B C D
Mayonnaise, sandwich spreads B2MAYO	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many TBSP? B2MAYOSZ A ① ② ③ ④ B C D
Peanut butter B2PNUT	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many TBSP? B2PNUTSZ A ① ② ③ ④ B C D
Ketchup or salsa B2KTCH	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many TBSP? B2KTCHSZ A ① ② ③ ④ B C D
Gravy B2GRAV	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many TBSP? B2GRAVSZ A ① ② ③ ④ B C D
Snacks, like potato chips, corn chips, popcorn (not pretzels) B2SNCK	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2SNCKSZ A ① ② ③ ④ B C D
Peanuts, pecans, other nuts or seeds B2NUTS	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2NUTSSZ A ① ② ③ ④ B C D
Crackers B2CRCK	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2CRCKSZ A ① ② ③ ④ B C D

Type of Food	How often? →								How much each time?	
	Never or less than once per month	Once per mon.	2-3 times per mon.	Once per week	Twice per week	3-4 times per week	5-6 times per week	Every Day	2+ times per day	Portion Size
Doughnuts, Danish pastry B2DONU	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2DONUSZ A ① ② ③ ④ B C D
Cake, sweet rolls, coffee cake B2CAKE	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2CAKESZ A ① ② ③ ④ B C D
When you eat cake or coffee cake, is it...? B2FAT9	① Usually low-fat ② Sometimes ③ Rarely low-fat ④ N/A									
Cookies B2COOK	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2COOKSZ A ① ② ③ ④ B C D
When you eat cookies, are they...? B2FAT10	① Usually low-fat ② Sometimes ③ Rarely low-fat ④ N/A									
Ice cream, ice milk, ice cream bars B2ICEC	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How much? B2ICECSZ A ① ② ③ ④ B C D

When you eat ice cream, is it...? B2FAT11	① Usually low-fat	② Sometimes	③ Rarely low-fat	④ N/A		
Pumpkin pie, sweet potato pie B2PIES	①	②	③	④	⑤ ⑥ ⑦ ⑧ ⑨	How much? B2PIESSZ A ① ② ③ ④ B C D
Any other pies or cobbler B2OTHP	①	②	③	④	⑤ ⑥ ⑦ ⑧ ⑨	How much? B2OTHPs2 A ① ② ③ ④ B C D
Pudding B2PUDD	①	②	③	④	⑤ ⑥ ⑦ ⑧ ⑨	How much? B2PUDDSZ A ① ② ③ ④ B C D
Chocolate candy, candy bars B2CHOC	①	②	③	④	⑤ ⑥ ⑦ ⑧ ⑨	How much? B2CHOCs2 A ① ② ③ ④ B C D

Interviewer Note: REQUIRED - Show Card E Type of Food	How many? →								Which glass, can, or cup?	
	Never or 1-11 per year	1-3 per mon.	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4 per day	5+ per day	Portion Size
How many glasses of the following beverages do you drink per day or per week?										
How many glasses of orange juice or grapefruit juice? B2OJ	①	②	③	④	⑤	⑥	⑦			Which glass? B2OJSZ A ① ② ③ ④ B C D
When you drink orange juice, how often do you drink a calcium fortified brand? B2OJC	① Usually calcium-fortified ② Sometimes ③ Rarely/never calcium-fortified ④ N/A									
How many glasses of Hi-C, Kool-Aid, or other drinks with added vitamin C? B2HIC	①	②	③	④	⑤	⑥	⑦			Which glass? B2HICSZ A ① ② ③ ④ B C D
How many glasses of tomato juice or V-8 juice? B2V8	①	②	③	④	⑤	⑥	⑦			Which glass? B2V8SZ A ① ② ③ ④ B C D
How many glasses of other fruit juices like apple juice, prune juice, lemonade? B2FRUT	①	②	③	④	⑤	⑥	⑦			Which glass? B2FRUTSZ A ① ② ③ ④ B C D
How many glasses of instant breakfast milkshakes like Carnation, diet shakes like SlimFast, or liquid supplements like Ensure? B2SUPL	①	②	③	④	⑤	⑥	⑦	⑧		Standard serving will be assumed B2MLK2SZ A ① ② ③ ④ B C D
How many glasses of milk, chocolate milk or cocoa? B2MLK2	①	②	③	④	⑤	⑥	⑦	⑧		Which glass? B2MLK3 A ① ② ③ ④ B C D
When you drink glasses of milk is it usually...? B2MLK3	① Whole milk ② 2% milk ③ 1% milk ④ Skim milk ⑤ Soy milk ⑥ N/A									
How many regular soft drinks, or bottled sweetened teas (not diet)? B2SOFT	①	②	③	④	⑤	⑥	⑦	⑧	⑨	What size? B2SOFTSZ A ① ② ③ ④ B C D
How many bottles or cans of beer? B2BEER	①	②	③	④	⑤	⑥	⑦	⑧	⑨	What size? B2BEERSZ A ① ② ③ ④ B C D
How many glasses of wine or wine coolers? B2WINE	①	②	③	④	⑤	⑥	⑦	⑧	⑨	Which glass? B2WINESZ A ① ② ③ ④ B C D
How many glasses or shots of liquor or mixed drinks? B2SHOT	①	②	③	④	⑤	⑥	⑦	⑧	⑨	Standard serving will be assumed B2COFFSZ A ① ② ③ ④ B C D
How many cups of coffee, regular or decaf? B2COFF	①	②	③	④	⑤	⑥	⑦	⑧	⑨	Which glass? B2COFFSZ A ① ② ③ ④ B C D

How many cups of tea or iced tea, but not herbal teas? B2TEA	①	②	③	④	⑤	⑥	⑦	⑧	⑨	Which glass? B2TEASZ	① A	② B	③ C	④ D
How often do you have cream, half and half or nondairy creamer in coffee or tea? B2CRM	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many TSP in each cup? B2CRMSZ	① 1	② 2	③ 3	④ 4
How often do you have milk in coffee or tea? B2MLK4	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many TSP in each cup? B2MLK4SZ	① 1	② 2	③ 3	④ 4
How often do you have sugar or honey in coffee or tea or on cereal? B2SUGR	①	②	③	④	⑤	⑥	⑦	⑧	⑨	How many TSP in each cup? B2SUGRSZ	① 1	② 2	③ 3	④ 4
	Never or 1-11 per year	1-3 per mo	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4 per day	5+ per day					

Average use in the past year									
Interviewer Note: REQUIRED - Show Card F	Less than once per week	1-2 per week	3-4 per week	5-6 per week	1 per day	1 1/2 per day	2 per day	3 per day	4+ per day
About how many servings of vegetables do you eat per day or per week, not counting salad or potatoes? B2VEG	①	②	③	④	⑤	⑥	⑦	⑧	⑨
*How often did you add butter, margarine, salt pork, or bacon fat? B2FAT12	① Usually or Always	② Often	③ Sometimes	④ Rarely or never	⑧ Don't know				
*How often were they fried? B2FRIED	① Usually or Always	② Often	③ Sometimes	④ Rarely or never	⑧ Don't know				

About how many servings of fruit do you eat, not counting juices? B2FRUIT	①	②	③	④	⑤	⑥	⑦	⑧	⑨
How often do you use fat or oil to fry or stir fry, or to simmer or season your food? B2FAT13	①	②	③	④	⑤	⑥	⑦	⑧	⑨

IF FAT OR OIL ONCE PER WEEK OR MORE:

What kinds of fat or oil do you usually use to fry or stir-fry, or to simmer or season your food?
(Interviewer Note: Do not read response options. Mark only one or two answers.)

① Stick margarine B2MARGST	① Butter/Margarine blend B2BLEND	① Olive oil or canola oil B2OLVOIL	① PAM B2PAM
① Soft tub margarine B2MARGTB	① Low-fat margarine B2LOWFAT	① Lard, fatback, baconfat B2LARD	① Don't know B2DK
① Butter B2BUTTER	① Corn oil, vegetable oil B2VEGOIL	① Crisco shortening B2CRISCO	

*How often do you use Pam or other non-stick spray instead of oil, margarine, or butter to saute or pan fry foods? **B2SPRAY**

① Usually or Always ② Often ③ Sometimes ④ Rarely or never ⑧ Don't know/Don't do

*When you ate bread, rolls, muffins, or crackers, how often did you eat them with butter or margarine? **B2WBUTTR**

① Usually or Always ② Often ③ Sometimes ④ Rarely or never ⑧ Don't know

GRIP STRENGTH B3ID B3ACROS B3STFID

Hand-Held Dynamometry

Exclusion Criteria:

① Has any pain or arthritis in your hands gotten worse recently? **B3ARWRS**

① Yes ② No

Which hand? **B3HANDRL**

① Right ② Left ③ Both right and left

Do not test right. Do not test left. Do not test either hand.

② Have you had any surgery on your hands or wrists in the past three months? **B3WRST1**

① Yes ② No

Which hand? **B3WRTRL**

① Right ② Left ③ Both right and left

Do not test right. Do not test left. Do not test either hand.

Script: "I'd like you to take your right/left arm, rest it on the table, and bend your elbow. Grip the two bars in your hand, like this. You need to slowly squeeze the bars as hard as you can."

Hand the dynamometer to the participant. Adjust if needed.

Script: "Now try it once just to get the feel of it. For this practice, just squeeze gently. It won't feel like the bars are moving, but your strength will be recorded. Are the bars the right distance apart for a comfortable grip?"

Show dial to participant.

Script: "We'll do this two times. This time it counts, so when I say squeeze, squeeze as hard as you can. Ready. Squeeze! Squeeze! Squeeze! Now, STOP."

Right **B3NOTST**

① Unable to test/exclusion

B3RTR1 Trial 1 kg **B3RF1** Refused (Examiner Note: Wait 15-20 seconds before second trial.)

"Now, one more time. Squeeze as hard as you can. Ready. Squeeze! Squeeze! Squeeze! Now, STOP."

B3RTR2 Trial 2 kg **B3RF2** Refused

Repeat the procedure on the left side.

Script: "Now we'll test your left side. When I say squeeze, squeeze as hard as you can. Ready. Squeeze! Squeeze! Squeeze! Now, STOP."

Left **B3LNTST**

① Unable to test/exclusion

B3LTR1 Trial 1 kg **B3LRF1** Refused (Examiner Note: Wait 15-20 seconds before second trial.)

"Now, one more time. Squeeze as hard as you can. Ready. Squeeze! Squeeze! Squeeze!"

B3LTR2 Trial 2 kg **B3LRF2** Refused

LONG-DISTANCE CORRIDOR WALK ELIGIBILITY ASSESSMENT

- 1** Before Testing:
Are there abnormal Marquette ECG hardcopy references from baseline that would preclude testing?
(Examiner Note: Refer to Data from Baseline Visit Form.)

☐ 1 Yes

☐ 0 No

B3MARQ

☐ 3	Wolff-Parkinson-White (WPW) or ventricular pre-excitation
☐ 4	Idioventricular rhythm
☐ 5	Ventricular tachycardia
☐ 6	Third degree or complete A-V block
☐ 7	Any statement including reference to acute injury or ischemia, or marked T-wave abnormality

B3HRT

Do not test.

- 2** a. Radial pulse (from page 7):

bpm

B3PULSE1

Is radial pulse > 110 or < 40 bpm?

☐ 1 Yes

☐ 0 No

B3PULSE2

Do not test.

- b. Initial standing blood pressure (from page 8):

B3SYSB2

Systolic blood pressure

mmHg

Is systolic > 199 mmHg?

☐ 1 Yes

☐ 0 No

B3SYSYN

Do not test.

B3DIAB2

Diastolic blood pressure

mmHg

Is diastolic > 109 mmHg?

☐ 1 Yes

☐ 0 No

B3SYDIYN

Do not test.

- 3** Does the participant use a walking aid, such as a cane?

☐ 1 Yes

☐ 0 No

B3WKAID2

Do not test.

- 4** Inform Participant About Tests:

Script: "The next tests assess your physical fitness by having you walk rapidly for 2 minutes and after that, having you walk about 1/4 mile at a steady pace."

Exclusion Questions:

Script: "First I need to ask you a few questions to see if you should try the test."

1. Within the past 3 months, have you had a heart attack?	☐ 1 Yes	→	Do not test.	☐ 0 No	B3HA
2. Within the past 3 months, have you had angioplasty?	☐ 1 Yes	→	Do not test.	☐ 0 No	B3ANG
3. Within the past 3 months, have you had heart surgery?	☐ 1 Yes	→	Do not test.	☐ 0 No	B3HS
4. Within the past 3 months, have you seen a health professional or thought about seeing a health professional for new or worsening symptoms of...?					
a. Chest pain	☐ 1 Yes	→	Do not test.	☐ 0 No	B3CP
b. Shortness of breath	☐ 1 Yes	→	Do not test.	☐ 0 No	B3SB
c. Fainting	☐ 1 Yes	→	Do not test.	☐ 0 No	B3FA
d. Angina	☐ 1 Yes	→	Do not test.	☐ 0 No	B3ANGI



LONG-DISTANCE CORRIDOR WALK INSTRUCTIONS & SCRIPT

Attachment of Heart Rate Monitor:

Script: "This device measures your pulse, or how often your heart beats."

Attach the monitor.

Explain Borg Perceived Exertion Scale:

Script: "During this exercise test, we want you to pay attention to how you are feeling."

Show the participant the Borg exertion scale which will be posted on the wall where they can see it as they walk the course.

Script: "After you walk, I want you to tell me the number that best matches how you were feeling. For example, the number '0' would be like doing nothing at all, '5' means putting forth a strong effort, and the number '10' would be working as hard as you can. Do you understand?"

Demonstrate and Introduce Both Walks:

Demonstrate how to walk around the cone and describe the 2 minute walk.

Script: "This is a two-part walking test. **For the first part I would like you to walk for 2 minutes, trying to cover as much ground as possible at a pace you can maintain.** Starting at this cone, walk to the cone at the other end of the hall, go around it and return, go around this cone and keep walking in the same fashion, until 2 minutes are up."

"When the 2 minutes are up I will tell you to stop. Please stay where you are so that I can record the distance you covered."

Stopping Criteria for 2-Minute Walk: If the participant's heart rate exceeds 135 bpm twice or falls below 40 bpm or if they report chest pain, tightness or pressure in the chest, shortness of breath, feeling faint, lightheaded or dizzy, or report leg pain, stop the test.

Record which test was stopped and record the reason on the "Stop Values" section of the Long-Distance Corridor Walk Data Collection Form (page 23 of the Year 2 Clinic Visit Workbook).

LONG-DISTANCE CORRIDOR WALK DATA COLLECTION FORM B3STFID4

2-Minute Walk

1

a. Cross off as each lap is completed:

1	2	3	4	5	6	7	8

Trial 1

b. Is heart rate > 135 bpm? ☐ Yes ☐ No
B3B2PL

Examiner Note: Wait 5 minutes and begin the walk again. Cross off the laps on the 'Trial 2' lap chart below.

c. Cross off as each lap is completed:

1	2	3	4	5	6	7	8

Trial 2

d. Is heart rate > 135 bpm? ☐ Yes ☐ No
B3PLS2
Do not do 400m walk.

e. Number of laps completed: laps **B32LAP**

f. Meter mark: meters **B32MTR**

g. Heart rate at end of 2-minute walk: bpm **B32BPM**

h. Is heart rate > 135 bpm? ☐ Yes ☐ No
B32PLS
Do not do 400m walk.

i. Perceived exertion at end of 2-minute walk:

Borg Exertion #: **B32BORG**

400m Walk

1

a. Cross off as each lap is completed:

0	1	2	3	4	5	6	7	8	9	10

B34LAP

b. Number of laps completed: laps

c. (If walk is stopped before 400m): **B34MTR** meters

2

Record time at 400 m or at stop:

	:		.	
Min		Seconds		Hundredths/sec

B34TIME

Restart stopwatch

3

B34BPM

Heart rate at 400m or at stop: bpm

4

Perceived exertion at 400m or at stop:

B34BORG

Borg Exertion #:

5

Blood pressure at 400m or at stop:

a. Systolic blood pressure: mm Hg **B34SYS**

b. Diastolic blood pressure: mm Hg **B34DIA**

6

Heart rate 2 minutes after completion of 400 m walk:

B34HR bpm

Stop Values:

i. If stop values are exceeded or symptoms are reported, check appropriate box and STOP TEST. Check only one.

B3STOPV

- ☐ Heart rate > 135 bpm
- ☐ Heart rate < 40 bpm
- ☐ Reports chest pain
- ☐ Reports shortness of breath
- ☐ Reports feeling faint
- ☐ Reports leg pain
- ☐ Other (Please specify:)

ii. Which test was stopped?

- ☐ 2-minute walk ☐ 400-meter walk
- B3STPTST**

PERIODONTAL EXAM ELIGIBILITY ASSESSMENT

1

Do you have any of your natural teeth? **B3NTEETH**

☐ Yes ☐ No ☐ Don't know ☐ Refused

a. How many years ago did you lose your last tooth?
If you are unsure, please make your best guess.

B3LSTTH years ☐ Less than 1 year ago **B3LTOOTH**

b. Do you have any dental implants? **B3IMPLNT**

☐ Yes ☐ No ☐ Don't know ☐ Refused

Not eligible for assessment. Go to Question #11.

2

Has a dentist or a doctor ever told you that you need to take antibiotics before every dental visit? **B3ANTIBI**

☐ Yes ☐ No ☐ Don't know ☐ Refused

Please explain why:

Go to Question #3.

Not eligible for assessment. Go to Question #11.

3

Has a doctor ever told you that you have any of the following...? **B3MURMUR**

a. A heart murmur? ☐ Yes ☐ No ☐ Don't know ☐ Refused

Not eligible for assessment. Go to Question #11.

b. Congenital heart disease? (a heart problem you were born with) ☐ Yes ☐ No ☐ Don't know ☐ Refused

Not eligible for assessment. Go to Question #11.

B3CHSRD

c. Rheumatic heart disease? ☐ Yes ☐ No ☐ Don't know ☐ Refused

Not eligible for assessment. Go to Question #11.

B3RHD

Draft

d. An infection of the lining of the heart called endocarditis?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused **B3ENDO**

↓

Not eligible for assessment. Go to Question #11.

e. Mitral valve prolapse?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused **B3MVP**

↓

Not eligible for assessment. Go to Question #11.

4 Are you taking prednisone or any immunosuppressive medication?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused **B3PRED**

↓

Not eligible for assessment. Go to Question #11.

5 Do you have a cardiac pacemaker?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused **B3PACEM**

↓

Not eligible for assessment. Go to Question #11.

6 Do you have a surgically implanted heart valve, shunt, or artificial joint?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused **B3VALVE**

↓

Not eligible for assessment. Go to Question #11.

7 Have you had major surgery, radiation, or chemotherapy for cancer within the last 2 months?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused **B3CANCER**

↓

Not eligible for assessment. Go to Question #11.

8 Are you on kidney dialysis?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused **B3KIDNEY**

↓

Not eligible for assessment. Go to Question #11.

9 Have you had a heart, kidney, or other organ transplant?

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused **B3TRNPLT**

↓

Not eligible for assessment. Go to Question #11.

10 Did you ever take FenPhen to lose weight?
(Examiner Note: If participant says they used another diet pill but they do not remember the name of the pill, check "X" yes.)

☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused **B3FENPHN**

↓

Not eligible for assessment. Go to Question #11.

11 Is the participant eligible for the periodontal assessment? **B3ELIG**

☐ 1 Yes, eligible for the periodontal exam

↓

Eligible for the periodontal exam.
(Examiner Note: Read the following statement.)

This next measurement includes a simple examination of your mouth to see if there are any cavities, gum disease, or spaces between your teeth and gums. We will also collect a little plaque and pick up some fluid from around your teeth. Most people find these procedures quite comfortable.

Do you have any questions?

If you would like us to send your dentist a copy of your dental exam report, please provide us with their name and address.

Dentist's Name: _____

Address: _____

☐ 0 No, not eligible for the periodontal exam

↓

Not eligible for the complete periodontal exam.
(Examiner Note: Read the statement below.)

Thank you for your responses. This next measurement includes a simple examination of your mouth.

DENTAL EXAMINATION

1 SOFT TISSUES EXAM *(Examiner Note: Check all positive findings and comment.)*

☐ Lips B3LIPS ☐ Labial mucosa B3LABMUC ☐ Buccal mucosa B3BUCMUC	☐ Cheeks B3CHEEKS ☐ Palate B3PALATE ☐ Uvula B3UVULA	☐ Dorsal tongue B3DORTON ☐ Vent. tongue B3VENTON ☐ Floor of mouth B3FLOORM

Comment: _____

2 DENTURES

☐ Full Upper ☐ Full Lower ☐ Partial Upper ☐ Partial Lower	B3FUPPER B3FLOWER B3PUPPER B3PLOWER

3 Is participant eligible for the periodontal exam? *(Examiner Note: Refer to Periodontal Exam Eligibility Assessment Form, in the Year 2 Clinic Visit Workbook, pgs. 28-30.)*

☐ Yes ☐ No **B3ELIGPR**

STOP. Do not perform periodontal exam;
 do assess missing teeth and plaque score.

Appendix I. Questionnaire in 1997-1998 at Year 1

(only those which apply to this thesis)

RSID



RECRUITMENT STATUS FORM

Interviewer ID #: RSINTID

RSBMAIL

Is the screenee part of a batch mailing? 1 Yes 0 No

Does the screenee live with someone contacted in a batch mailing?

RSLIVE 1 Yes 0 No

HCFA ID # of batch mailing contact:RSBMCON

STATUS

(Interviewer Note: Please check only one)

1 Unable to contact (No phone # or unlisted #)

2 Unable to contact (No answer or No forwarding address)

3 Out of Area

4 Institutionalized

5 Deceased

6 Refused telephone screen or No telephone screen conducted

7 Ineligible on telephone screen

8 Refused home visit

9 Ineligible at home visit

10 Refused clinic visit

RSTDATE
Date telephone screen conducted
Month / Day / Year

RSHVDATE
Date home visit conducted
Month / Day / Year

RSCVDATE
Date clinic visit conducted
Month / Day / Year

RSSTATUS Go to RSF Addendum

Interviewer Note: Please check the MAIN reason the telephone screening interview was NOT conducted.

Refused Telephone Screen or No Telephone Screen Conducted

- 0 Not English-speaking
- 1 Cognitively impaired
- RAFAR 2 Self-reported ineligible
- 3 Proxy-reported ineligible
- 7 Not interested / Refused telephone screen

Date Status Established

/ / RADATEST

Month Day Year

Health ABC **PHYSICAL ACTIVITY and EXERCISE**

Now I am going to ask some questions about the type and amount of physical activity that you did in the past 12 months and what you usually do in a typical week.

- 16.** In the past 12 months, since last (*current month*), did you do gardening or yardwork, like mowing or raking the lawn, or weeding (or shoveling snow), at least 10 times?

FPPA12MO ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

Go to Question #17

- a.** In the past 7 days, since last (*current day*), did you do any gardening or yardwork?

☐ 1 Yes

☐ 0 No **FPPA7DAY**

Go to Question #17

- b.** About how much time did you spend gardening or doing yardwork in the past 7 days (not counting rest periods)?
(*Interviewer Note: If less than one hour, record number of minutes.*)

FPPAHR **FPPAMIN**
Hours Minutes

- 17.** In the past 12 months, did you do heavy or major chores like scrubbing windows or walls, vacuuming, mopping floors, or cleaning gutters; home maintenance activities like painting, scraping, hanging wall paper, or anything like these activities at least 10 times?

FPHC12MO ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

Go to Question #18

- a.** In the past 7 days, did you do heavy chores or home maintenance activities?

☐ 1 Yes

☐ 0 No **FPHC7DAY**

Go to Question #18

- b.** About how much time did you spend doing heavy chores or home maintenance activities in the past 7 days (not counting rest periods)?
(*Interviewer Note: If less than one hour, record number of minutes.*)

FPHCHRS **FPHCMIN**
Hours Minutes

- 18.** In the past 12 months, did you do light work around the house like cooking meals, baking, washing dishes, making beds, straightening up, dusting or light cleaning, at least 10 times?

FPLW12MO ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

Go to Question #19

- a.** In the past 7 days, did you do any light work around the house?

☐ 1 Yes

☐ 0 No **FPLW7DAY**

Go to Question #19

- b.** About how much time did you spend doing light housework, in the past 7 days?
(*Interviewer Note: If less than one hour, record number of minutes.*)

FPLWHR **FPLWMIN**
Hours Minutes

- 19.** In the past 12 months, did you go or help with grocery shopping at least 10 times?
(*Interviewer Note: "Help with grocery shopping" includes help buying, carrying or unpacking groceries.*)

FPGS12MO ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

Go to Question #20

- a.** In the past 7 days, did you go or help with grocery shopping?

☐ 1 Yes

☐ 0 No **FPGS7DAY**

Go to Question #20

- b.** About how many bags of groceries did you buy or help with in the past 7 days (for yourself and others)?

bags **FPGSNBAG**

- c.** About how many of these bags did you carry yourself?

bags **FPGSBAGC**

- d.** About how many of these bags did you unpack yourself?

bags **FPGSBAGU**

23. In the past 12 months, did you do any other type of walking, such as walking to work, the store, to church, or walking the dog, at least 10 times?

FPOW12MO Yes No Don't know Refused

Go to Question #24

In the past 7 days, did you do other walking?

Yes **FPOW7DAY** No

a. FPOWTIME How many times did you do other walking in the past 7 days?

FPOWTIME times

b. About how much time, on average, did you spend doing other walking each time you walked (excluding rest periods)?
(Interviewer Note: If less than 1 hour, record number of minutes.)

FPOWHR **FPOWMINS**

Hours Minutes

c. When you do other walking, do you usually walk at a brisk pace (as fast as you can), a moderate pace, or at a leisurely stroll?

brisk
 moderate **FPOWPACE**
 stroll

d. About how many blocks, on average, did you walk each time?

blocks **FPOWBLUK** Number of blocks unknown

FPOWBLOX

Do you know how far you usually walk in something other than blocks, e.g., mail lengths, miles, laps around a track?

Yes No **FPOWDIST**

What is the unit of measure? **FPOWUNIT**

How many do you walk, on average?

units **FPOWNUMU**

24. In the past 12 months, did you do aerobics, calisthenics, slimnastics, at least 10 times?

FPAC12MO Yes No Don't know Refused

Go to Question #25

a. In the past 7 days, did you do aerobics, calisthenics, slimnastics?

Yes **FPAC7DAY** No

Go to Question #25

b. In the past 7 days, about how much time did you spend doing aerobics, calisthenics, slimnastics? (Interviewer Note: If less than 1 hour, record number of minutes.)

FPACHRS **FPACMINS**

Hours Minutes

25. In the past 12 months, did you do any weight or circuit training, at least 10 times?

FPTR12MO Yes No Don't know Refused

Go to Question #26

a. In the past 7 days, did you do weight or circuit training?

Yes **FPTR7DAY** No

Go to Question #26

b. In the past 7 days, about how much time did you spend doing weight or circuit training? (Interviewer Note: If less than 1 hour, record number of minutes.)

FPTRHRS **FPTRMINS**

Hours Minutes

26. In the past 12 months, did you do any high intensity exercise activities such as bicycling, swimming, jogging, racquet sports or using a stair-stepping, rowing or cross country ski machine or exercycle, at least 10 times?

FPHI12MO ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

Go to Question #27

In the past 7 days, did you do high intensity exercise activities?

☐ 1 Yes **FPHI7DAY** ☐ 0 No

a. What activity(ies) did you do?
(Interviewer Note: *OPTIONAL - Show card #3. Check all that apply.*)

☐ -1 bicycling/exercycle **FPHIABE**
☐ -1 swimming **FPHIASWM**
☐ -1 jogging **FPHIAJOG**
☐ -1 aerobics **FPHIAAER**
☐ -1 stair-stepping **FPHIASS**
☐ -1 racquet sports **FPHIARS**
☐ -1 rowing machine **FPHIAROW**
☐ -1 cross country ski machine **FPHIASKI**
☐ -1 other (Please specify): **FPHIAOTH**

b. In the past 7 days, about how much time did you spend doing (first named activity)?
(Interviewer Note: *If less than 1 hour, record number of minutes.*)

IA1HR **FPHIA1MN**
Hours Minutes

Go to Question #26c

What is the main reason you have not done any high intensity exercise activities in the past 7 days?
(Interviewer Note: *OPTIONAL - Show card #4.*) **FPHINDEX**

☐ 1 bad weather
☐ 2 not enough time
☐ 3 injury
☐ 4 health problems
☐ 5 lost interest
☐ 6 felt unsafe
☐ 7 not necessary
☐ 8 other

Go to Question #27

26c. Did you do (first named activity) with a light, moderate, or vigorous effort?

- ☐ 1 light
☐ 2 moderate **FPHIA1EF**
☐ 3 vigorous

d. In the past 7 days, about how much time did you spend doing (second named activity)? (Interviewer Note: *If less than 1 hour, record number of minutes.*)

FPHIA2HR **FPHIA2MN**
Hours Minutes

e. Did you do (second named activity) with a light, moderate, or vigorous effort?

- ☐ 1 light
☐ 2 moderate **FPHIA2EF**
☐ 3 vigorous

f. In the past 7 days, about how much time did you spend doing (third named activity)? (Interviewer Note: *If less than 1 hour, record number of minutes.*)

FPHIA3HR **FPHIA3MN**
Hours Minutes

g. Did you do (third named activity) with a light, moderate, or vigorous effort?

- ☐ 1 light
☐ 2 moderate **FPHIA3EF**
☐ 3 vigorous

h. In the past 7 days, about how much time did you spend doing (fourth named activity)? (Interviewer Note: *If less than 1 hour, record number of minutes.*)

FPHIA4HR **FPHIA4MN**
Hours Minutes

i. Did you do (fourth named activity) with a light, moderate or vigorous effort?

- ☐ 1 light
☐ 2 moderate **FPHIA4EF**
☐ 3 vigorous

27. In the past 12 months, did you do any moderate intensity exercise activities such as golf, bowling, dancing, skating, bocce, table tennis, hunting, sailing or fishing, at least 10 times?

FPMI12MO ☐ 1 Yes ☐ 0 No ☐ 8 Don't know ☐ 7 Refused

Go to Question #28

In the past 7 days, did you do moderate intensity exercise activities?

☐ 1 Yes ☐ 0 No FPMI7DAY

- a. What activity(ies) did you do?
(Interviewer Note: *OPTIONAL - Show card #5. Check all that apply.*)

- ☐ -1 golf FPMIGOLF
☐ -1 bowling FPMIBOWL
☐ -1 dancing FPMIDANC
☐ -1 skating FPMISKAT
☐ -1 bocce FPMIBOCC
☐ -1 table tennis FPMITENN
☐ -1 billiards/pool FPMIPOOL
☐ -1 hunting FPMIHUNT
☐ -1 sailing/boating FPMIBOAT
☐ -1 fishing FPMIFISH
☐ -1 other (Please specify): FPMIOT1

- b. In the past 7 days, about how much time did you spend doing (first named activity)?
(Interviewer Note: *If less than 1 hour, record number of minutes.*)

FPMIA1HR FPMIA1MN
Hours Minutes

Go to Question #27c

- What is the main reason you have not done any moderate intensity exercise activities in the past 7 days?
(Interviewer Note: *OPTIONAL - Show card #6.*)

- FPMINDEX
☐ 1 bad weather
☐ 2 not enough time
☐ 3 injury
☐ 4 health problems
☐ 5 lost interest
☐ 6 felt unsafe
☐ 7 not necessary
☐ 8 other

Go to Question #28

- 27c. Did you do (first named activity) with a light, moderate, or vigorous effort?

☐ 1 light
☐ 2 moderate FPMIA1EF
☐ 3 vigorous

- d. In the past 7 days, about how much time did you spend doing (second named activity)? (Interviewer Note: *If less than 1 hour, record number of minutes.*)

FPMIA2HR FPMIA2MIN
Hours Minutes

- e. Did you do (second named activity) with a light, moderate, or vigorous effort?

☐ 1 light
☐ 2 moderate FPMIA2EF
☐ 3 vigorous

- f. In the past 7 days, about how much time did you spend doing (third named activity)? (Interviewer Note: *If less than 1 hour, record number of minutes.*)

FPMIA3HR FPMIA3MN
Hours Minutes

- g. Did you do (third named activity) with a light, moderate, or vigorous effort?

☐ 1 light
☐ 2 moderate FPMIA3EF
☐ 3 vigorous

- h. In the past 7 days, about how much time did you spend doing (fourth named activity)? (Interviewer Note: *If less than 1 hour, record number of minutes.*)

FPMIA4HR FPMIA4MN
Hours Minutes

- i. Did you do (fourth named activity) with a light, moderate or vigorous effort?

☐ 1 light
☐ 2 moderate FPMIA4EF
☐ 3 vigorous

**WORK, VOLUNTEER,
&
CAREGIVING ACTIVITIES**

The next set of questions concern any work, volunteer, caregiving and social activities that you do.

28. Do you currently work for pay, either at a regular job, consulting, or doing odd jobs?

1 Yes **0** No **8** Don't know **7** Refused **FPVWCURJ**

Go to question #29

a. On average, how many hours do you work per week?

hours

FPVWAHWR

b. How many months of the year do you work?

months

FPVWMOW

c. Which of the following categories best describes the type of activity you do in your job? Would you say...

(Interviewer Note: **REQUIRED** - Show card #7.)

1 Mainly sitting

2 Sitting, some standing and/or walking

3 Mostly standing and/or walking

4 Mostly walking and lifting and/or carrying;
heavy manual work

FPVWWACT

29. Do you currently do any volunteer work?

1 Yes **0** No **8** Don't know **7** Refused **FPVWCURV**

Go to question #30

a. On average, how many hours do you volunteer per week?

hours

FPVWAHVW

29b. How many months of the year do you do this?

months

FPVWMOV

c. Which of the following categories best describes the type of activity you do?
(Interviewer Note: **REQUIRED** - Show card #7.)

1 Mainly sitting

2 Sitting, some standing and/or walking

3 Mostly standing and/or walking

4 Mostly walking and lifting and/or carrying;
heavy manual work

FPVWVACT

30. Do you currently provide any regular care or assistance to a child or a disabled or sick adult?

1 Yes **0** No **8** Don't know **7** Refused **FPVWCURA**

Go to question #31

About how many hours per week do you provide care to another person?

hours

FPVWAHAW

31. About how many hours per week do you spend watching television?
(Interviewer Note: **REQUIRED** - Show card #8.)

0 Zero

1 More than 0 but less than 7 hours/week

2 At least 7, but less than 14 hours/week

3 At least 14, but less than 21 hours/week **FPVWTV**

4 21 or more hours/week

8 Don't know

7 Refused

32. About how many hours per week do you spend reading, including books, newspapers, and magazines?

FPVWREAD

hours

8 Don't know

7 Refused

FPVWRDRF

SMOKING HABITS

61. Have you smoked at least 100 cigarettes in your entire life?
(Interviewer Note: 100 cigarettes is equal to 5 packs.)

1 Yes **0** No **8** Don't know **7** Refused **BQSC100**

Please go to Question #62

a. How old were you when you first started smoking cigarettes fairly regularly?

BQSCAGEB

BQSCNSM

I was years old

-1 I never smoked regularly

b. On the average of the entire time you have smoked, how many cigarettes did you usually smoke per day?

BQSCCGAV

cigarettes per day

c. Do you smoke cigarettes now?

1 Yes

0 No **BQSCSNOW**

How old were you when you stopped smoking?

I was years old

BQSCAGES

On the average, about how many cigarettes a day do you smoke now?

BQSCCGNO
cigarettes per day

62. Have you ever smoked a pipe or cigars?

1 Yes **0** No **8** Don't know **7** Refused **BQSCPOC**

Please go to Question #63

a. How old were you when you first started smoking a pipe or cigars fairly regularly?

I was years old.

-1 I never smoked regularly **BQSCPCNS**

BQSCPCAG

b. Do you smoke a pipe or cigar now?

1 Yes

0 No **BQSCPCY**

How old were you when you stopped smoking a pipe or cigars?

I was years old.

BQSCPCSM

63. During the past 12 months, how many drinks did you have in a typical week? If you are unsure, please make your best guess. (Interviewer Note: Do NOT read response categories.)

- 1** None – do not drink alcohol at all
- 2** An occasional drink, but less than once a week
- 3** 1-3 drinks per week
- 4** 4-7 drinks per week
- 5** 8-14 drinks per week
- 6** 15-21 drinks per week
- 9** 22-27 drinks per week
- 10** 28 or more drinks per week
- 8** Don't know
- 7** Refused

BQDA12MO

What is your primary reason for not drinking very much?
(Interviewer Note: Do NOT read response options. Please check only one answer.)

- 1** No need/not necessary
- 2** Don't care for it/dislike it
- 3** Medical/health reasons
- 4** Religious/moral reasons
- 5** Recovering alcoholic
- 6** Family member an alcoholic or problem drinker
- 7** Costs too much
- 8** Other reasons (Please specify:)

BQDARND

HEART CONDITIONS

93. Has a doctor ever told you that you had...?
(Interviewer Note: Repeat "Has a doctor ever told you that you had..." after every three questions.)

	Yes	No	Don't Know	Refused
a. Heart attack or myocardial infarction? MHHCHAMI	1	0	8	7
b. Angina pectoris or chest pain due to heart disease? MHHCAPCP	1	0	8	7
c. Congestive heart failure? MHHCCHF	1	0	8	7
d. Intermittent claudication or pain in your legs from a blockage of the arteries? MHHICPL	1	0	8	7
e. TIA, transient ischemic attack, or mini-stroke? MHHCTIA	1	0	8	7
f. Stroke, CVA, or cerebrovascular accident? MHHCCVA	1	0	8	7
g. Rheumatic heart disease or valvular heart disease? MHHCHBP	1	0	8	7
h. Hypertension or high blood pressure? MHHCHBP	1	0	8	7

1 Has a doctor ever told you that you have diabetes or sugar diabetes?

1 Yes **0** No **8** Don't know **P1DIAB**

Do you take insulin or oral hypoglycemic medications to control your diabetes? (Refer to the list to the right) **P1INOH**

1 Yes, insulin **2** Yes, oral hypoglycemics **0** No **8** Don't know

Check N/A box next to cryovial #26 on Laboratory Processing Form.

Do NOT administer OGTT.

Verify from Baseline Health Questionnaire Q#116 or Medication Inventory Form

Oral Hypoglycemics

Generic Name	Trade Name
Tolbutamide	Orinase
Acetohexamide	Dymelor
Tolazamide	Tolinase
Chloropropamide	Diabinese
Glipizide	Glucotrol
Glyburide	Diabeta, Micronase
Metformin	Glucophage
Acarbose	Precose
Glicazide	Diamicron
Glimepride	Amaryl
Troglitazone	Rezulin

193. How would you describe your primary racial or ethnic group?
(Interviewer Note: Please check only one box.)

- 1** Asian/Pacific Islander
- 2** Black/African-American
- 3** White/Caucasian
- 4** Latino/Hispanic **LPRACE**
- 8** Don't know
- 6** Other (Please specify:)
- 7** Refused

194. What is the highest grade or year of school that you completed?
(Interviewer Note: Please check only one box.)

LPSCHOOL

- 0** No formal education **10** Grade 10
- 1** Grade 1 **11** Grade 11
- 2** Grade 2 **12** Grade 12
- 3** Grade 3 **13** Vocational/tradeschool **WITHOUT** high school or the GED
- 4** Grade 4 **14** Vocational/trade school **AFTER** high school
- 5** Grade 5 **15** Some college/Associate degree
- 6** Grade 6 **16** College graduate (4 or 5 year program)
- 7** Grade 7 **17** Master's degree (or other post-graduate training)
- 8** Grade 8 **18** Doctoral degree (PhD, MD, EdD, DVM, DDS, JD, etc.)
- 9** Grade 9 **77** Refused

Appendix J. Further Adjustment for Self-Rated General Health (Chapter 4)

Table J1. Odds ratios (95%CI) for the associations of oral health problems with mobility limitations and Activities of Daily Living (ADL) difficulties in older British men aged 71-92 years in the BRHS, further adjusted for self-rated general health.

Oral Health Problems	Mobility limitations (n=564; 27%)			ADL difficulties (n=412; 20%)		
	N (%)	Fully adjusted ^a OR (95% CI)	Adjusted for general health OR (95% CI)	N (%)	Fully adjusted ^a OR (95% CI)	Adjusted for general health OR (95% CI)
Tooth loss						
≥21 teeth	106 (18%)	1.00	1.00	70 (12%)	1.00	
15-20 teeth	68 (20%)	0.93 (0.62, 1.38)	0.98 (0.64, 1.51)	44 (13%)	0.97 (0.62, 1.53)	1.15 (0.70, 1.86)
8-14 teeth	79 (30%)	1.48 (0.98, 2.22)	1.28 (0.81, 2.00)	57 (22%)	1.65 (1.05, 2.57)	1.42 (0.87, 2.32)
1-7 teeth	38 (32%)	1.23 (0.73, 2.07)	1.41 (0.80, 2.47)	22 (18%)	1.02 (0.56, 1.86)	1.19 (0.62, 2.26)
0 teeth	103 (31%)	1.14 (0.76, 1.69)	0.84 (0.54, 1.31)	76 (23%)	1.28 (0.82, 1.99)	0.97 (0.59, 1.58)
Complete tooth loss						
≥1 teeth	291 (22%)	1.00	1.00	193 (15%)	1.00	1.00
0 teeth	103 (31%)	1.01 (0.72, 1.42)	0.75 (0.51, 1.10)	76 (23%)	1.12 (0.78, 1.62)	0.83 (0.55, 1.26)
Periodontal disease (% of sites with loss of attachment >5.5 mm)						
≤20%	190 (21%)	1.00	1.00	103 (11%)	1.00	1.00
>20%	69 (23%)	0.91 (0.63, 1.32)	0.94 (0.63, 1.41)	38 (13%)	1.14 (0.76, 1.71)	1.20 (0.77, 1.86)
Self-rated oral health						
Good or excellent	290 (22%)	1.00	1.00	217 (17%)	1.00	1.00
Fair or poor	241 (34%)	1.44 (1.12, 1.85)	1.06 (0.80, 1.40)	170 (24%)	1.23 (0.94, 1.60)	0.87 (0.64, 1.17)
Dry mouth symptoms						
0	135 (18%)	1.00	1.00	92 (12%)	1.00	1.00
1-2	153 (23%)	1.26 (0.92, 1.72)	1.14 (0.81, 1.61)	108 (16%)	1.24 (0.88, 1.75)	1.11 (0.76, 1.61)
≥3	245 (41%)	2.89 (2.14, 3.91)	2.13 (1.53, 2.96)	188 (31%)	2.68 (1.94, 3.69)	1.91 (1.35, 2.71)

^aadjusted for age, social class, smoking, physical activity, history of CVD and diabetes

Table J1 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with mobility limitations and Activities of Daily Living (ADL) difficulties in older British men aged 71-92 years in the BRHS, further adjusted for self-rated general health.

	Mobility limitations (n=564; 27%)			ADL difficulties (n=412; 20%)		
		Fully adjusted ^a	Adjusted for general health		Fully adjusted ^a	Adjusted for general health
	N (%)	OR (95% CI)	OR (95% CI)	N (%)	OR (95% CI)	OR (95% CI)
Cumulative oral health problems^b						
0	43 (13%)	1.00	1.00	24 (7%)	1.00	1.00
1	232 (23%)	1.27 (0.83, 1.93)	1.11 (0.70, 1.76)	161 (16%)	1.64 (0.98, 2.72)	1.54 (0.89, 2.66)
2	191 (36%)	2.25 (1.45, 3.48)	1.65 (1.02, 2.66)	146 (27%)	3.29 (1.96, 5.52)	2.62 (1.50, 4.59)
≥3	98 (44%)	2.83 (1.71, 4.67)	1.74 (1.01, 3.02)	81 (36%)	4.19 (2.36, 7.43)	2.73 (1.47, 5.07)

^aadjusted for age, social class, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table J2. Odds ratios (95%CI) for the associations of oral health problems with Instrumental Activities of Daily Living (IADL) difficulties in older British men aged 71-92 years in the BRHS, further adjusted for self-rated general health.

Oral Health Problems	IADL difficulties (n=367; 17%)		
		Fully adjusted ^a	Adjusted for general health
	N (%)	OR (95% CI)	OR (95% CI)
Tooth loss			
≥21 teeth	56 (10%)	1.00	1.00
15-20 teeth	45 (14%)	1.31 (1.12, 2.95)	1.56 (0.92, 2.66)
8-14 teeth	44 (17%)	1.54 (0.92, 2.58)	1.14 (0.65, 2.02)
1-7 teeth	20 (17%)	1.00 (0.51, 1.95)	1.15 (0.56, 2.35)
0 teeth	74 (22%)	1.82 (1.12, 2.95)	1.46 (0.86, 2.47)
Complete tooth loss			
≥1 teeth	165 (13%)	1.00	1.00
0 teeth	74 (22%)	1.51 (1.03, 2.22)	1.22 (0.80, 1.87)
Periodontal disease (% of sites with loss of attachment >5.5 mm)			
≤20%	124 (13%)	1.00	1.00
>20%	48 (16%)	0.94 (0.59, 1.50)	0.96 (0.57, 1.61)
Self-rated oral health			
Good or excellent	182 (14%)	1.00	1.00
Fair or poor	171 (24%)	1.66 (1.24, 2.22)	1.17 (0.84, 1.61)
Dry mouth symptoms			
0	77 (10%)	1.00	1.00
1-2	109 (17%)	1.67 (1.15, 2.47)	1.59 (1.05, 2.40)
≥3	164 (27%)	2.90 (2.01, 4.18)	2.18 (1.46, 3.25)
Cumulative oral health problems^b			
0	20 (6%)	1.00	1.00
1	146 (14%)	1.77 (0.98, 3.19)	1.66 (0.88, 3.14)
2	128 (24%)	3.01 (1.65, 5.49)	2.19 (1.14, 4.19)
≥3	82 (36%)	5.94 (3.10, 11.37)	4.22 (2.09, 8.48)

^aadjusted for age, social class, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table J3. Odds ratios (95%CI) for the associations of oral health problems with mobility limitations, and Activities of Daily Living (ADL) difficulties in American men and women aged 71-80 years in the HABC Study, after further adjustment for self-rated general health.

Oral Health Problems	Mobility limitations (n=882; 29%)			ADL difficulties (n=467; 17%)		
	N (%)	Fully-adjusted ^a OR (95% CI)	Adjusted for general health OR (95% CI)	N (%)	Fully-adjusted ^a OR (95% CI)	Adjusted for general health OR (95% CI)
Tooth loss						
≥21 teeth	212 (23%)	1.00	1.00	138 (15%)	1.00	1.00
15-20 teeth	90 (25%)	0.95 (0.70, 1.29)	0.93 (0.68, 1.27)	61 (17%)	1.15 (0.82, 1.62)	1.15 (0.81, 1.62)
8-14 teeth	96 (34%)	1.44 (1.06, 1.98)	1.43 (1.04, 1.98)	68 (25%)	1.74 (1.23, 2.47)	1.76 (1.23, 2.52)
1-7 teeth	55 (30%)	1.12 (0.77, 1.65)	1.09 (0.73, 1.63)	33 (18%)	1.24 (0.79, 1.93)	1.21 (0.76, 1.91)
0 teeth	70 (34%)	1.02 (0.70, 1.49)	0.92 (0.62, 1.36)	30 (15%)	0.91 (0.57, 1.44)	0.82 (0.51, 1.31)
Complete tooth loss						
≥1 teeth	453 (26%)	1.00	1.00	300 (17%)	1.00	1.00
0 teeth	70 (34%)	0.94 (0.66, 1.33)	0.86 (0.60, 1.24)	30 (15%)	0.74 (0.48, 1.15)	0.68 (0.44, 1.06)
Periodontal disease (% of sites with pocket depth ≥3 mm)						
≤20%	103 (20%)	1.00	1.00	83 (16%)	1.00	1.00
>20%	165 (26%)	1.18 (0.87, 1.60)	1.21 (0.88, 1.66)	96 (15%)	0.97 (0.69, 1.36)	0.97 (0.69, 1.37)
Self-rated oral health						
Good or excellent	435 (23%)	1.00	1.00	278 (15%)	1.00	1.00
Fair or poor	300 (36%)	1.19 (1.10, 1.30)	1.08 (0.99, 1.18)	185 (22%)	1.27 (1.15, 1.41)	1.16 (1.05, 1.29)
Dry mouth						
No	689 (26%)	1.00	1.00	428 (16%)	1.00	1.00
Yes	52 (49%)	2.26 (1.50, 3.39)	1.86 (1.22, 2.85)	35 (33%)	2.23 (1.46, 3.41)	1.83 (1.17, 2.85)

^aadjusted for age, gender, race, education, smoking, physical activity, history of CVD and diabetes

Table J3 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with mobility limitations, and Activities of Daily Living (ADL) difficulties in American men and women aged 71-80 years in the HABC Study, after further adjustment for self-rated general health.

		Mobility limitations (n=882; 29%)			ADL difficulties (n=467; 17%)	
		Fully adjusted ^a	Adjusted for general health		Fully adjusted ^a	Adjusted for general health
	N (%)	OR (95% CI)	OR (95% CI)	N (%)	OR (95% CI)	OR (95% CI)
Cumulative oral health problems^b						
0	173 (22%)	1.00	1.00	108 (14%)	1.00	1.00
1	355 (26%)	0.98 (0.78, 1.22)	0.86 (0.68, 1.08)	202 (15%)	1.07 (0.82, 1.39)	0.95 (0.73, 1.25)
2	120 (31%)	1.14 (0.85, 1.53)	0.90 (0.66, 1.22)	86 (22%)	1.61 (1.16, 2.24)	1.30 (0.93, 1.83)
≥3	107 (48%)	2.19 (1.56, 3.07)	1.88 (1.32, 2.68)	71 (32%)	2.63 (1.81, 3.81)	2.25 (1.53, 3.29)

^aadjusted for age, gender, race, education, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table J4. Odds ratios (95%CI) for the associations of oral health problems with handgrip strength and walking speed in older British men aged 71-92 years in the BRHS, further adjusted for self-rated general health.

Oral Health Problems	Bottom quintile of handgrip strength (n=347; 21%)			Top quintile of walking speed (n=337; 21%)		
	N (%)	Fully-adjusted ^a OR (95% CI)	Adjusted for general health OR (95% CI)	N (%)	Fully-adjusted ^a OR (95% CI)	Adjusted for general health OR (95% CI)
Tooth loss						
≥21 teeth	111 (19%)	1.00	1.00	91 (16%)	1.00	1.00
15-20 teeth	59 (18%)	0.89 (0.61, 1.29)	0.88 (0.60, 1.28)	49 (15%)	0.63 (0.41, 0.98)	0.61 (0.39, 0.97)
8-14 teeth	58 (23%)	1.11 (0.74, 1.66)	1.06 (0.70, 1.60)	60 (25%)	1.00 (0.64, 1.56)	0.84 (0.53, 1.33)
1-7 teeth	26 (22%)	1.00 (0.59, 1.72)	0.98 (0.57, 1.69)	29 (26%)	0.93 (0.53, 1.62)	0.98 (0.55, 1.73)
0 teeth	79 (24%)	1.20 (0.82, 1.76)	1.22 (0.83, 1.80)	96 (31%)	1.16 (0.77, 1.74)	0.95 (0.62, 1.47)
Complete tooth loss						
≥1 teeth	254 (20%)	1.00	1.00	229 (18%)	1.00	1.00
0 teeth	79 (24%)	1.21 (0.87, 1.68)	1.25 (0.89, 1.75)	96 (31%)	1.30 (0.92, 1.84)	1.12 (0.77, 1.62)
Periodontal disease (% of sites with pocket depth >3.5 mm)						
≤20%	153 (18%)	1.00	1.00	158 (18%)	1.00	1.00
>20%	86 (25%)	1.59 (1.14, 2.20)	1.57 (1.13, 2.18)	70 (20%)	1.18 (0.82, 1.68)	1.21 (0.85, 1.76)
Self-rated oral health						
Good or excellent	224 (21%)	1.00	1.00	185 (18%)	1.00	1.00
Fair or poor	105 (19%)	0.83 (0.62, 1.10)	0.79 (0.58, 1.06)	128 (25%)	1.00 (0.73, 1.35)	0.74 (0.53, 1.03)
Dry mouth symptoms						
0	107 (18%)	1.00	1.00	91 (15%)	1.00	1.00
1-2	118 (22%)	1.25 (0.91, 1.72)	1.27 (0.94, 1.75)	106 (21%)	1.34 (0.93, 1.91)	1.16 (0.80, 1.69)
≥3	102 (22%)	1.15 (0.83, 1.61)	1.14 (0.81, 1.61)	120 (28%)	1.75 (1.22, 2.50)	1.33 (0.91, 1.94)
Cumulative oral health problems^b						
0	63 (19%)	1.00	1.00	51 (16%)	1.00	1.00
1	169 (22%)	1.16 (0.81, 1.66)	1.11 (0.77, 1.59)	146 (19%)	0.84 (0.56, 1.26)	0.75 (0.49, 1.15)
2	81 (21%)	1.03 (0.68, 1.56)	0.94 (0.62, 1.43)	85 (23%)	0.92 (0.58, 1.44)	0.71 (0.44, 1.14)
≥3	34 (20%)	1.03 (0.61, 1.74)	0.98 (0.58, 1.66)	55 (35%)	1.52 (0.90, 2.57)	1.10 (0.63, 1.91)

^aadjusted for age, social class, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table J5. Odds ratios (95%CI) for the associations of oral health problems with chair stand speed in older British men aged 71-92 years in the BRHS, further adjusted for self-rated general health.

Oral Health Problems	Top quintile of chair-stand speed (n=390; 24%)		
	N (%)	Fully-adjusted ^a OR (95% CI)	Adjusted for general health OR (95% CI)
Tooth loss			
≥21 teeth	112 (20%)	1.00	1.00
15-20 teeth	62 (20%)	1.19 (0.81, 1.75)	0.81 (0.54, 1.21)
8-14 teeth	71 (29%)	1.23 (0.73, 2.06)	1.07 (0.71, 1.62)
1-7 teeth	34 (31%)	1.22 (0.82, 1.83)	1.32 (0.78, 2.23)
0 teeth	99 (32%)	0.83 (0.56, 1.22)	1.01 (0.68, 1.51)
Complete tooth loss			
≥1 teeth	279 (23%)	1.00	1.00
0 teeth	99 (32%)	1.15 (0.83, 1.61)	1.01 (0.71, 1.43)
Periodontal disease (% of sites with pocket depth >3.5 mm)			
≤20%	194 (22%)	1.00	1.00
>20%	82 (23%)	0.96 (0.69, 1.35)	0.97 (0.68, 1.37)
Self-rated oral health			
Good or excellent	226 (22%)	1.00	1.00
Fair or poor	141 (27%)	1.01 (0.76, 1.35)	0.83 (0.62, 1.12)
Dry mouth symptoms			
0	123 (21%)	1.00	1.00
1-2	116 (23%)	0.96 (0.70, 1.33)	0.85 (0.61, 1.19)
≥3	131 (30%)	1.33 (0.96, 1.84)	1.05 (0.75, 1.47)
Cumulative oral health problems^b			
0	53 (16%)	1.00	1.00
1	184 (24%)	1.23 (0.84, 1.81)	1.15 (0.78, 1.71)
2	101 (27%)	1.38 (0.90, 2.10)	1.12 (0.73, 1.74)
≥3	52 (33%)	1.58 (0.95, 2.63)	1.18 (0.69, 2.01)

^aadjusted for age, social class, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table J6. Odds ratios (95%CI) for the associations of oral health problems with handgrip strength and walking speed in American men and women aged 71-80 years in the HABC Study, after further adjustment for self-rated general health.

Oral Health Problems		Bottom quintile of grip strength (n=469; 20%)		Top quintile of walking speed (n=375; 20%)		
		Fully-adjusted ^a	Adjusted for general health OR (95% CI)	Fully-adjusted ^a	Adjusted for general health OR (95% CI)	
	N (%)	OR (95% CI)		N (%)	OR (95% CI)	
Tooth loss						
≥21 teeth	159 (20%)	1.00	1.00	49 (7%)	1.00	1.00
15-20 teeth	59 (19%)	0.85 (0.59, 1.24)	0.85 (0.58, 1.24)	20 (8%)	1.08 (0.73, 1.62)	1.07 (0.72, 1.60)
8-14 teeth	36 (16%)	0.66 (0.42, 1.03)	0.65 (0.41, 1.02)	19 (12%)	1.08 (0.68, 1.71)	1.05 (0.66, 1.67)
1-7 teeth	24 (15%)	0.71 (0.42, 1.21)	0.70 (0.41, 1.19)	11 (10%)	1.08 (0.63, 1.85)	1.08 (0.62, 1.87)
0 teeth	30 (18%)	0.72 (0.43, 1.21)	0.71 (0.42, 1.20)	15 (11%)	1.15 (0.70, 1.89)	1.08 (0.65, 1.79)
Complete tooth loss						
≥1 teeth	278 (18%)	1.00	1.00	99 (8%)	1.00	1.00
0 teeth	30 (18%)	0.86 (0.53, 1.40)	0.86 (0.53, 1.40)	15 (11%)	1.06 (0.67, 1.68)	1.01 (0.63, 1.61)
Periodontal disease (% of sites with loss of attachment ≥3 mm)						
≤20%	55 (15%)	1.00	1.00	18 (6%)	1.00	1.00
>20%	114 (18%)	1.46 (0.98, 2.17)	1.44 (0.97, 2.14)	39 (8%)	0.92 (0.61, 1.40)	0.90 (0.60, 1.37)
Self-rated oral health						
Good or excellent	317 (19%)	1.00	1.00	101 (7%)	1.00	1.00
Fair or poor	148 (21%)	1.06 (0.96, 1.18)	1.03 (0.92, 1.14)	74 (15%)	1.16 (1.03, 1.30)	1.10 (0.97, 1.23)
Dry mouth						
No	430 (19%)	1.00	1.00	167 (9%)	1.00	1.00
Yes	33 (37%)	2.43 (1.47, 4.01)	2.29 (1.38, 3.79)	8 (14%)	1.54 (0.82, 2.89)	1.43 (0.76, 2.69)
Cumulative oral health problems^b						
0	130 (19%)	1.00	1.00	35 (6%)	1.00	1.00
1	235 (20%)	1.01 (0.77, 1.32)	0.97 (0.74, 1.28)	91 (10%)	1.40 (1.03, 1.91)	1.34 (0.98, 1.82)
2	63 (19%)	0.92 (0.63, 1.34)	0.85 (0.58, 1.24)	28 (11%)	1.31 (0.88, 1.97)	1.18 (0.78, 1.78)
≥3	41 (22%)	1.06 (0.67, 1.67)	1.00 (0.63, 1.59)	22 (18%)	1.40 (0.84, 2.33)	1.24 (0.74, 2.08)

^aadjusted for age, gender, race, education, smoking, physical activity, history of CVD and diabetes

^b<21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Appendix K. Further Adjustment for CRP (Chapter 5)

Table K1. Odds ratios (95%CI) for the associations of oral health problems with top tertiles of IL-6 in British men aged 71-92 years in the BRHS and American men and women aged 71-80 years in the HABC Study, after further adjustment for CRP.

	BRHS			HABC Study	
	Top tertile of IL-6 ^a (n=539, 33%)			Top tertile of IL-6 ^c (n=912, 33%)	
Oral Health Problems	Fully adjusted ^b	Further adjusted for CRP	Oral Health Problems	Fully adjusted ^d	Further adjusted for CRP
	OR (95% CI)	OR (95% CI)		OR (95% CI)	OR (95% CI)
Tooth loss			Tooth loss		
≥21 teeth	1.00	1.00	≥21 teeth	1.00	1.00
15-20 teeth	1.29 (0.94, 1.77)	1.23 (0.88, 1.72)	15-20 teeth	1.05 (0.79, 1.39)	0.94 (0.70, 1.27)
8-14 teeth	1.20 (0.85, 1.70)	1.18 (0.81, 1.71)	8-14 teeth	1.45 (1.07, 1.96)	1.40 (1.02, 1.93)
1-7 teeth	1.18 (0.75, 1.88)	1.16 (0.71, 1.91)	1-7 teeth	1.27 (0.89, 1.82)	1.14 (0.78, 1.66)
0 teeth	1.22 (0.87, 1.71)	1.05 (0.73, 1.51)	0 teeth	1.24 (0.87, 1.78)	1.09 (0.74, 1.59)
Complete tooth loss			Complete tooth loss		
≥1 teeth	1.00	1.00	≥1 teeth	1.00	1.00
0 teeth	1.06 (0.79, 1.43)	0.94 (0.68, 1.29)	0 teeth	1.10 (0.79, 1.53)	1.02 (0.72, 1.45)
Partial tooth loss			Partial tooth loss		
≥21 teeth	1.00	1.00	≥21 teeth	1.00	1.00
<21 teeth	1.23 (0.96, 1.59)	1.16 (0.89, 1.52)	<21 teeth	1.22 (0.98, 1.51)	1.11 (0.89, 1.44)
Periodontal disease (% of sites with loss of attachment >5.5 mm)			Periodontal disease (% of sites with loss of attachment ≥3 mm)		
≤20%	1.00	1.00	≤20%	1.00	1.00
>20%	1.32 (0.97, 1.78)	1.18 (0.85, 1.64)	>20%	1.11 (0.83, 1.48)	1.08 (0.79, 1.46)
Self-rated oral health			Self-rated oral health		
Good or excellent	1.00	1.00	Good or excellent	1.00	1.00
Fair or poor	1.24 (0.98, 1.58)	1.20 (0.93, 1.55)	Fair or poor	1.17 (0.97, 1.41)	1.18 (0.97, 1.43)

^a values for top tertile of IL-6 = 3.90-30 pg/ml, reference group= <3.90 pg/ml

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

^c values for top tertile of IL-6= 3.29-32.87 pg/ml, reference group= <3.29 pg/ml

^d adjusted for age, gender, race, education, smoking, history of CVD and diabetes, BMI

Table K1 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with top tertiles of IL-6 in British men aged 71-92 years in the BRHS and American men and women aged 71-80 years in the HABC Study, after further adjustment for CRP.

	BRHS			HABC Study	
	Top tertile of IL-6 ^a (n=539, 33%)			Top tertile of IL-6 ^d	
Oral Health Problems	Fully adjusted ^b	Further adjusted for CRP	Oral Health Problems	Fully adjusted ^e	Further adjusted for CRP
	OR (95% CI)	OR (95% CI)		OR (95% CI)	OR (95% CI)
Dry mouth symptoms			Dry mouth		
0	1.00	1.00	No	1.00	1.00
1-2	0.84 (0.65, 1.11)	0.83 (0.62, 1.10)	Yes	1.29 (0.85, 1.95)	1.27 (0.82, 1.96)
≥3	0.96 (0.73, 1.27)	0.83 (0.62, 1.13)			
Cumulative oral health problems^c			Cumulative oral health problems^f		
0	1.00	1.00	0	1.00	1.00
1	1.23 (0.90, 1.68)	1.21 (0.87, 1.68)	1	1.18 (0.96, 1.46)	1.13 (0.91, 1.41)
2	1.21 (0.85, 1.72)	1.11 (0.76, 1.62)	2	1.05 (0.79, 1.39)	0.95 (0.71, 1.28)
≥3	1.07 (0.68, 1.68)	0.94 (0.58, 1.53)	≥3	1.65 (1.19, 2.31)	1.58 (1.12, 2.25)

^a values for top tertile of IL-6 = 3.90-30 pg/ml, reference group= <3.90 pg/ml

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

^c <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

^d values for top tertile of IL-6= 3.29-32.87 pg/ml, reference group= <3.29 pg/ml

^e adjusted for age, gender, race, education, smoking, history of CVD and diabetes, BMI

^f <21 teeth, dry mouth when eating, difficulty eating or chewing, limitation of food due to gum problems

Table K2. Odds ratios (95%CI) for the associations of oral health problems with top tertiles of fibrin d-dimer, and vWF in British men aged 71-92 years in the BRHS, further adjusted for CRP.

Oral Health Problems	Top tertile of fibrin d-dimer ^a (n=537, 33%)			Top tertile of vWF ^a (n=537, 33%)		
	N (%)	Fully adjusted ^b OR (95% CI)	Further adjusted for CRP OR (95% CI)	N (%)	Fully adjusted ^b OR (95% CI)	Further adjusted for CRP OR (95% CI)
Tooth loss						
≥21 teeth	145 (26)	1.00	1.00	175 (31)	1.00	1.00
15-20 teeth	96 (30)	1.17 (0.84, 1.62)	1.14 (0.81, 1.62)	95 (30)	0.88 (0.64, 1.21)	0.84 (0.61, 1.16)
8-14 teeth	80 (33)	1.19 (0.83, 1.72)	1.19 (0.81, 1.74)	84 (34)	1.02 (0.72, 1.44)	1.02 (0.72, 1.44)
1-7 teeth	52 (46)	1.93 (1.22, 3.05)	2.09 (1.30, 3.37)	48 (42)	1.44 (0.93, 2.23)	1.37 (0.87, 2.14)
0 teeth	141 (45)	1.64 (1.16, 2.30)	1.60 (1.12, 2.28)	109 (35)	0.91 (0.65, 1.28)	0.87 (0.62, 1.23)
Complete tooth loss						
≥1 teeth	373 (30)	1.00	1.00	402 (32)	1.00	1.00
0 teeth	141 (45)	1.38 (1.03, 1.85)	1.34 (0.99, 1.82)	109 (35)	0.89 (0.66, 1.19)	0.87 (0.64, 1.17)
Partial tooth loss						
≥21 teeth	145 (26)	1.00	1.00	175 (31)	1.00	1.00
<21 teeth	369 (37)	1.37 (1.05, 1.77)	1.36 (1.04, 1.78)	336 (34)	0.98 (0.77, 1.25)	0.94 (0.74, 1.21)
Periodontal disease (% of sites with loss of attachment >5.5 mm)						
≤20%	258 (29)	1.00	1.00	283 (32)	1.00	1.00
>20%	86 (32)	0.98 (0.71, 1.36)	0.90 (0.64, 1.25)	105 (39)	1.17 (0.87, 1.58)	1.13 (0.83, 1.53)
Self-rated oral health						
Good or excellent	325 (32)	1.00	1.00	314 (31)	1.00	1.00
Fair or poor	185 (35)	1.06 (0.83, 1.36)	1.05 (0.81, 1.36)	197 (38)	1.24 (0.98, 1.57)	1.25 (0.98, 1.59)
Dry mouth symptoms						
0	178 (31)	1.00	1.00	192 (33)	1.00	1.00
1-2	163 (32)	1.11 (0.84, 1.46)	1.08 (0.81, 1.45)	157 (31)	0.90 (0.69, 1.18)	0.89 (0.68, 1.17)
≥3	167 (38)	1.24 (0.93, 1.66)	1.22 (0.90, 1.64)	168 (38)	1.27 (0.97, 1.67)	1.23 (0.93, 1.62)

^a values for top tertile of fibrin d-dimer= 277.27-2000 ng/ml, reference group= <277.27 ng/ml; values for top tertile of vWF= 132.69-433.17 IU/dl, reference group= <132.69 IU/dl

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

Table K2 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with top tertiles of fibrin d-dimer, and vWF in British men aged 71-92 years in the BRHS, further adjusted for CRP.

Oral Health Problems	Top tertile of fibrin d-dimer ^a (n=537, 33%)			Top tertile of vWF ^a (n=537, 33%)		
	N (%)	Fully adjusted ^b OR (95% CI)	Further adjusted for CRP OR (95% CI)	N (%)	Fully adjusted ^b OR (95% CI)	Further adjusted for CRP OR (95% CI)
Cumulative oral health problems^c						
0	87 (27)	1.00	1.00	90 (28)	1.00	1.00
1	244 (32)	1.09 (0.79, 1.50)	1.09 (0.78, 1.52)	244 (32)	1.16 (0.85, 1.58)	1.15 (0.84, 1.57)
2	145 (39)	1.38 (0.97, 1.98)	1.39 (0.96, 2.02)	142 (38)	1.49 (1.05, 2.09)	1.47 (1.04, 2.09)
≥3	61 (38)	1.23 (0.78, 1.94)	1.26 (0.79, 2.02)	61 (38)	1.49 (0.97, 2.30)	1.49 (0.96, 2.32)

^a values for top tertile of fibrin d-dimer= 277.27-2000 ng/ml, reference group= <277.27 ng/ml; values for top tertile of vWF= 132.69-433.17 IU/dl, reference group= <132.69 IU/dl

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

^c <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table K3. Odds ratios (95%CI) for the associations of oral health problems with top tertile of t-PA in British men aged 71-92 years in the BRHS, further adjusted for CRP.

Oral Health Problems	Top tertile of t-PA ^a (n=537, 33%)		
	N (%)	Fully adjusted ^b OR (95% CI)	Further adjusted for CRP OR (95% CI)
Tooth loss			
≥21 teeth	180 (32)	1.00	1.00
15-20 teeth	95 (30)	0.93 (0.67, 1.28)	0.85 (0.61, 1.18)
8-14 teeth	87 (35)	1.13 (0.80, 1.60)	1.11 (0.78, 1.58)
1-7 teeth	41 (36)	1.08 (0.68, 1.71)	1.10 (0.69, 1.76)
0 teeth	114 (37)	1.08 (0.76, 1.52)	1.03 (0.72, 1.46)
Complete tooth loss			
≥1 teeth	403 (32)	1.00	1.00
0 teeth	114 (37)	1.06 (0.78, 1.43)	1.03 (0.76, 1.40)
Partial tooth loss			
≥21 teeth	180 (32)	1.00	1.00
<21 teeth	337 (34)	1.03 (0.80, 1.33)	0.98 (0.76, 1.27)
Periodontal disease (% of sites with loss of attachment >5.5 mm)			
≤20%	276 (31)	1.00	1.00
>20%	93 (34)	1.12 (0.82, 1.52)	1.05 (0.77, 1.44)
Self-rated oral health			
Good or excellent	317 (31)	1.00	1.00
Fair or poor	196 (37)	1.27 (1.00, 1.61)	1.23 (0.96, 1.57)
Dry mouth symptoms			
0	189 (33)	1.00	1.00
1-2	176 (34)	1.06 (0.81, 1.39)	1.09 (0.83, 1.43)
≥3	149 (34)	0.95 (0.71, 1.27)	0.91 (0.68, 1.22)
Cumulative oral health problems^c			
0	102 (32)	1.00	1.00
1	238 (32)	0.97 (0.71, 1.32)	0.94 (0.69, 1.28)
2	140 (37)	1.11 (0.78, 1.56)	1.09 (0.76, 1.55)
3	57 (36)	1.16 (0.74, 1.80)	1.09 (0.69, 1.72)

^avalues for top tertile t-PA= 10.63-50 ng/ml, reference group= <10.63 ng/ml

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

^c<21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Table K4. Odds ratios (95%CI) for the associations of oral health problems with top tertiles of hsTnT, and NT-proBNP in British men aged 71-92 years in the BRHS, further adjusted for CRP.

Oral Health Problems	Top tertile of hsTnT ^a (n=534, 33%)			Top tertile of NT-proBNP ^a (n=534, 33%)		
	N (%)	Fully adjusted ^b OR (95% CI)	Further adjusted for CRP OR (95% CI)	N (%)	Fully adjusted ^b OR (95% CI)	Further adjusted for CRP OR (95% CI)
Tooth loss						
≥21 teeth	148 (26)	1.00	1.00	166 (29)	1.00	1.00
15-20 teeth	101 (32)	1.33 (0.94, 1.87)	1.31 (0.93, 1.85)	114 (36)	1.40 (1.01, 1.94)	1.38 (1.00, 1.91)
8-14 teeth	85 (34)	1.24 (0.85, 1.81)	1.26 (0.86, 1.84)	80 (32)	1.08 (0.75, 1.56)	1.07 (0.74, 1.54)
1-7 teeth	48 (42)	1.31 (0.81, 2.12)	1.29 (0.80, 2.10)	40 (35)	0.95 (0.59, 1.53)	0.97 (0.60, 1.57)
0 teeth	129 (42)	1.40 (0.98, 2.02)	1.38 (0.96, 1.98)	121 (40)	1.09 (0.76, 1.55)	1.07 (0.75, 1.52)
Complete tooth loss						
≥1 teeth	382 (31)	1.00	1.00	400 (32)	1.00	1.00
0 teeth	129 (42)	1.19 (0.87, 1.63)	1.17 (0.86, 1.61)	121 (40)	0.99 (0.73, 1.34)	0.97 (0.71, 1.32)
Partial tooth loss						
≥21 teeth	148 (26)	1.00	1.00	166 (29)	1.00	1.00
<21 teeth	363 (37)	1.32 (1.01, 1.74)	1.31 (1.00, 1.72)	355 (36)	1.17 (0.91, 1.52)	1.16 (0.90, 1.51)
Periodontal disease (% of sites with loss of attachment >5.5 mm)						
≤20%	240 (27)	1.00	1.00	273 (30)	1.00	1.00
>20%	107 (39)	1.49 (1.08, 2.07)	1.46 (1.06, 2.03)	98 (36)	1.12 (0.81, 1.54)	1.09 (0.79, 1.51)
Self-rated oral health						
Good or excellent	310 (31)	1.00	1.00	323 (32)	1.00	1.00
Fair or poor	191 (37)	1.20 (0.93, 1.56)	1.20 (0.93, 1.56)	178 (34)	1.07 (0.83, 1.38)	1.06 (0.82, 1.37)
Dry mouth symptoms						
0	184 (32)	1.00	1.00	168 (29)	1.00	1.00
1-2	157 (31)	0.87 (0.65, 1.16)	0.87 (0.65, 1.17)	173 (34)	1.20 (0.90, 1.59)	1.18 (0.89, 1.57)
≥3	162 (37)	1.00 (0.74, 1.35)	1.00 (0.74, 1.35)	165 (38)	1.25 (0.93, 1.68)	1.21 (0.90, 1.63)

^a values for top tertile of hsTnT= 14.34-407.10 ng/l, reference group= <14.34 ng/l; for NT-proBNP= 226-15899 ng/l, reference group= <226 ng/l

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

Table K4 (*continued*). Odds ratios (95%CI) for the associations of oral health problems with top tertiles of hsTnT, and NT-proBNP in British men aged 71-92 years in the BRHS, further adjusted for CRP.

Oral Health Problems	Top tertile of hsTnT ^a (n=534, 33%)			Top tertile of NT-proBNP ^a (n=534, 33%)		
	N (%)	Fully-adjusted ^b OR (95% CI)	Further adjusted for CRP OR (95% CI)	N (%)	Fully-adjusted ^b OR (95% CI)	Further adjusted for CRP OR (95% CI)
Cumulative oral health problems^c						
0	86 (27)	1.00	1.00	101 (31)	1.00	1.00
1	248 (33)	1.17 (0.84, 1.63)	1.17 (0.84, 1.64)	229 (30)	0.81 (0.59, 1.12)	0.81 (0.59, 1.12)
2	140 (38)	1.33 (0.91, 1.93)	1.32 (0.91, 1.92)	147 (40)	1.16 (0.81, 1.66)	1.15 (0.80, 1.64)
≥3	60 (38)	1.31 (0.82, 2.10)	1.29 (0.81, 2.07)	57 (37)	1.03 (0.65, 1.62)	1.02 (0.64, 1.60)

^a values for top tertile of hsTnT= 14.34-407.10 ng/l, reference group= <14.34 ng/l; for NT-proBNP= 226-15899 ng/l, reference group= <226 ng/l

^b adjusted for age, social class, smoking, history of CVD and diabetes, BMI

^c <21 teeth, ≥3 dry mouth symptoms, difficulty eating, sensitivity to hot/cold/sweets

Appendix L. Simple Longitudinal Analysis for the Association of Oral Health Problems with Incident Disability as Part of Causal Mediation.

Table L1. Population characteristics for British men aged 60-79 years (20-year re-examination) in the BRHS and US men and women aged 70-80 years in the HABC Study.

BRHS (n=4252)		HABC Study (n=3075)	
Age (years) , mean $\pm$ sd	68.7 $\pm$ 5.5	Age (years) , mean $\pm$ sd	73.6 $\pm$ 2.9
Smoking (n=4245), n (%)		Smoking (n=3070), n (%)	
Never smoker	548 (13)	Never smoker	1348 (44)
Current smoker	1233 (29)	Current smoker	318 (10)
Former smoker	2464 (58)	Former smoker	1404 (46)
Physical Activity (n=4097), n (%)		Physical Activity (n=3075), mean $\pm$ sd	82.9 $\pm$ 69.3
Inactive	471 (12)		
Occasional	957 (23)		
Light	767 (19)		
Moderate	591 (14)		
Moderate-vigorous	690 (17)		
Vigorous	621 (15)		
Alcohol (4185), n (%)		Alcohol (n=3063), n (%)	
None	431 (10)	No consumption past year	1546 (50)
Occasional (<1 drink/week)	1124 (27)	Less than once per week	635 (21)
Light (1-15/week)	1825 (44)	1-7 times per week	655 (21)
Moderate (16-42/week)	654 (16)	More than 1 per day	227 (7)
Heavy (>42/week)	125 (3)		
History of CVD (n=2093), n (%)	500 (24%)	History of CVD (n=3075), n (%)	410 (13)
History of diabetes (n=2090), n (%)	321 (16%)	History of diabetes (n=3074), n (%)	460 (15)
BMI (4232), n (%)		BMI (n=3075), n (%)	
Normal	1285 (30)	Normal	991 (32)
Overweight	2209 (52)	Overweight	1300 (42)
Obese	735 (17)	Obese	784 (26)

Table L2. Odds ratios (95% CI) for the associations of oral health problems with risk of incident mobility limitations in older British men in the BRHS and older US men and women in the HABC Study (adjusted for confounders measured prior to exposure, restricted for CRP, IL-6, and fibrin d-dimer causal analysis sample size).

BRHS							
Oral Health Problems	Incident Mobility Limitations (n=175, 15%)						
	CRP	IL-6		Fibrin d-dimer			
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)	Age adjusted OR (95% CI)	Fully adjusted ^a OR (95% CI)
Partial tooth loss							
≥21 teeth	34 (9%)	1.00	1.00	1.00	1.00	1.00	1.00
<21 teeth	111 (19%)	2.03 (1.29, 3.21)	1.88 (1.15, 3.08)	2.19 (1.40, 3.43)	1.79 (1.08, 2.94)	2.19 (1.40, 3.43)	1.79 (1.08, 2.94)
Periodontal disease (% of sites with loss of attachment >5.5 mm)							
<20%	71 (12%)	1.00	1.00	1.00	1.00	1.00	1.00
≥20%	38 (21%)	1.74 (1.04, 2.89)	1.77 (1.03, 3.04)	1.79 (1.06, 3.01)	1.80 (1.04, 3.13)	1.79 (1.06, 3.01)	1.80 (1.04, 3.13)
Dry mouth symptoms							
0	49 (11%)	1.00	1.00	1.00	1.00	1.00	1.00
1-2	62 (16%)	1.58 (0.97, 2.56)	1.51 (0.92, 2.47)	1.65 (1.01, 2.70)	1.57 (0.95, 2.59)	1.65 (1.01, 2.70)	1.57 (0.95, 2.59)
≥3	59 (22%)	2.22 (1.34, 3.68)	2.29 (1.34, 3.89)	2.20 (1.30, 3.71)	2.25 (1.30, 3.89)	2.20 (1.30, 3.71)	2.25 (1.30, 3.89)
HABC Study							
	Incident Mobility Limitations (n=380, 20%)						
	CRP	IL-6					
	N (%)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	Age adjusted OR (95% CI)	Fully adjusted ^b OR (95% CI)	-	-
Complete tooth loss							
≥1 teeth	210 (17%)	1.00	1.00	1.00	1.00	-	-
0 teeth	38 (31%)	2.16 (1.41, 3.29)	1.91 (1.19, 3.07)	2.17 (1.42, 3.31)	1.88 (1.16, 3.02)	-	-

^aadjusted for age, social class, smoking, alcohol, physical activity, history of CVD and diabetes, and BMI

^badjusted for age, gender, race, education, smoking, alcohol, physical activity, history of CVD and diabetes, and BM

