

Association between oral health and dementia

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ASSOCIATION BETWEEN ORAL HEALTH AND DEMENTIA

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ABSTRACT

Introduction: Dementia and oral diseases are two major public health problems in the world. There has been growing interest in examining their associations for disease prevention and health care. A few studies suggested that the association could be bidirectional, but the evidence is still inconclusive. This PhD study aimed to comprehensively assess whether poor oral health increased the risk of dementia while people with dementia had increased oral diseases regardless of other factors.

Methods: A mixed method of quantitative and qualitative approaches was employed, including meta-analysis from literature, analysing the data of a hospital-based case-control study and a population-based cohort study (i.e., English longitudinal study of ageing [ELSA]) and running three focus groups. The case-control study was carried out in Guangzhou, China, interviewing 233 patients with dementia and 233 controls without dementia. ELSA dataset included the participants from wave 3 (2006-07) to wave 9 (2018-19), each wave having around 9,800 participants and recording dementia and oral health problems. In standard methods of interview, the participants in the case-control study and ELSA had documented the data of demographics, lifestyles, cardiovascular risk factors, oral health and other disease risk factors. The associations between dementia and oral health problems were analysed in multivariate-adjusted logistic regression models. The three focus groups included 17 caregivers of people with dementia in Wolverhampton, UK, and their data were examined using thematic analysis.

Findings: Both the case-control study and ELSA cohort study showed a significant association of poor oral health with dementia; multiple adjusted odds ratio (OR) of dementia in poor self-rated oral health (SROH) was 1.97 (95%CI 1.01-3.85) and 1.93 (1.00-3.72) respectively. The case-control study also demonstrated increased ORs of dementia in periodontal disease (PD) (OR 1.92, 95%CI 1.17-3.17) in no teeth (6.51, 2.47-17.15) and in other indicators of poor oral

health. ELSA further found a non-significant increased OR of incident dementia in those oral impact variables. In examining the association of dementia with poor oral health, the case-control study, where 17.6% of participants reported poor SROH, 55.6% fair, and 26.8% good, showed a non-significantly increased OR of poor SROH in patients with dementia, but significantly increased ORs of moderate/severe PD, the number of teeth and less oral care. The ELSA study showed that dementia was not significantly associated with incident poor SROH; however, combined data of dementia and severe cognitive impairment (SCI) suggested a significant OR of incident poor SROH (1.90, 1.22-2.98) although increased ORs of the total score of oral impacts and edentulism were not significant. The overall quality of identified studies was good. In the meta-analysis, pooled data from ten studies showed an overall significant association of PD with dementia [relative risk (RR) 1.43, 95% CI 1.15-1.79] and the pooled RR from six studies for dementia and cognitive impairment was 1.54 (1.18-2.01). The data from the focus group supported the findings of quantitative studies by their theme relation, care and external factors.

Conclusions: This PhD research has suggested that poor oral health may increase the risk of dementia, and people with dementia or SCI could increase the risk of poor oral health. Maintaining oral hygiene and care in people with dementia or SCI is needed to ensure a better quality of life in older people, while keeping good oral health in the general population would help reduce the incidence of dementia worldwide.

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LIST OF ABBREVIATIONS

AAP: clinical criteria of American Academy of Periodontology
ABL: Alveolar bone loss
AD: Alzheimer Disease
ADJ: Adjusted
ADHS: Adult Dental Health survey
AGES: Aichi Gerontological Evaluation Study
ANOVA: Analysis of variance
BDT: block design test
BI: Bleeding index
BMI: Body mass index
BOP: Bleeding on probing
CAL: Clinical Attachment loss
CHD: Coronary heart disease
CI: Confidence interval
CKD: Chronic Kidney Disease
COPD: Chronic Obstructive pulmonary disease
CP: chronic periodontitis
CPITN: Community Periodontal Index for Treatment Needs
CPI: Community Periodontal Index
CVD: Cardiovascular Disease
CVDRFs: Cardiovascular Disease Risk Factors
DLB: Dementia of Lewy Body
DM: Diabetes Mellitus
DMFT/ DMFS: Decayed, missing and filled teeth/ surfaces
DMS: Dementia Management System
DSM-III R: Diagnostic and Statistical, Manual of Mental Disorders, Third Edition, Revised
DSM IV: Diagnostic and Statistical Manual of Mental Disorders criteria, fourth edition
DSM-5: Diagnostic and Statistical Manual of Mental Disorders
DSST: Digital symbol substitution test
DWR: Delayed word recall
ETS: Environmental Tobacco Smoke
FTD: Frontotemporal Dementia
GBD: Global burden of disease
GBI: Gingival bleeding index
GI: Gingival index
HR: Hazard ratio
ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification
ICD-9/10: International Statistical Classification of Diseases and Related Health Problems
9/10th revision diagnostic criteria
ICD-10: International Statistical Classification of Diseases and Related Health Problems 10th
revision diagnostic criteria
LHID: Longitudinal Health Insurance Database
LMICs: Low-income and middle-income countries
LOA: Loss of attachment

MABL: Marginal alveolar bone loss
MCI: Mild cognitive impairment
MMSE: Mini Mental State Examination
NCDs: Non-Communicable Diseases
NHANES: National Health and Nutrition Examination Survey
NIA-AA: National Institute on Aging and Alzheimer's Association guidelines
NIDR: National Institute of Dental Research criteria
NINCDS-ADRDA: National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association
NINDS-AIREN : National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences
NHIRD: National Health Insurance Research Database
OR: Odds ratio
PD: Periodontal Disease
PES: Physical Examination Service System
PI: Plaque Index
PIs: Periodontal Inflammations
PPD: Periodontal probing depth/ Probing Pocket depth
POH: Poor oral health
RA: Rheumatoid Arthritis
RR: Relative risk
SCD: Subjective cognitive decline
SCT: Spatial copy task
SES: Socio-economic status
SD: Standard Deviation
SROH: Self-rated oral health
SRP: Scaling and Root Planning
T2DM: Type 2 Diabetes Mellitus
UN: United Nations
UK: United Kingdom
US: United States of America
VaD: Vascular Dementia
WAIS: Wechsler Adult Intelligence Scale,
WF: Word Fluency
WHO: World Health Organization
YLD: Years Lived with Disability

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CHAPTER ONE: INTRODUCTION

1.1 Introduction

The chapter presents an overview and background of the thesis. It includes an overview of oral health and dementia as public health issues and their association. This chapter also presents a brief outline of the thesis structure.

1.2 Overview of the research topic

Population ageing is a global phenomenon affecting all facets of life. Recent studies have indicated a shift in the world population age where we now have more grandparents than grandchildren (Duarte, 2019). A better understanding of the changing relationship between health and ageing is crucial if we are to create a sustainable global society in the future.

1.2.1 Ageing population is increasing worldwide

In recent years, an increase in the ageing population has emerged as one of the most significant problems challenging world health systems and the global economy. United Nation's "World Population Aging 2020" report states that globally, there were 727 million persons aged 65 years or over in 2020. By 2050, this number will reach over 1.5 billion (UN, 2020). The findings by Age UK are consistent with these claims, reporting that approximately 12 million people are aged 65 years and above in the UK. In the next 50 years, this number is expected to increase by an additional 8.6 million people, and with the over 85 years age group rising at the fastest rate, their number will double to 3.2 million by 2041 and treble by 2066 (AgeUK, 2019). One of the fastest-growing ageing populations in the world is China; the population of people over 60 years old in China is projected to reach 28% by 2040 (WHO, 2021a).

A dramatic rise in life expectancy has been seen in the last century, which may be due to various contributing factors, especially reduction in infant mortality rates and improved standard of living (Eurostat, 2021). In high-income countries (HICs), the phenomenon started a few

decades ago, while in low-middle income countries (LMICs), the process of population ageing started later, giving them less time to adjust (Sudharsanan *et al.*, 2018). The rise in life expectancy in recent years is significant because it will have an impact on the formulation of important policies and decision making. The ageing process will especially reflect on the policies determining the age of retirement and decisions regarding the provision of health care services to older populations so that the quality of life and overall well-being is maintained. (Kyu *et al.*, 2018; He *et al.*, 2016).

1.2.2 Non-communicable diseases including oral health diseases present a public health challenge

In the last decade, there has been a change in the profile of the dominant cause of death in the world population, with Non-Communicable Diseases (NCDs) emerging as a major killer, causing nearly 41 million deaths per year, contributing to almost 71% of all global deaths. Additionally, a 40.1% (36.8%-43.0%) increase was seen in global age-standardised Disability-Adjusted Life-Years (DALY) rates for NCDs (Kyu *et al.*, 2018). Although NCDs are prevalent in LMICs and HICs, existing research has indicated that NCDs tend to occur at an older age in HICs, thus contributing to more people living longer and fewer early deaths compared to LMICs, which account for nearly 77% of all NCDs related deaths. The delayed age of onset of NCDs in HICs might be explained by better health care facilities and public health policies (WHO, 2015). However, this reduction in mortality leads to an increase in the prevalence of chronic NCDs such as neurodegenerative conditions including dementia (Prince *et al.*, 2015).

Oral health problems such as dental caries, periodontitis, and even oral cancer are common and preventable NCDs (Wolf *et al.*, 2021). Therefore, WHO highlights the needs for oral health problems to be considered among the major NCDs by Public Health authorities especially when developing policies and strategies for disease prevention and health promotion (Wolf *et al.*, 2021). Emerging data (Wolf *et al.*, 2021) has shown that oral diseases significantly contributed

to healthcare burdens, and a country cannot overcome the NCDs related challenges unless it establishes a dedicated service to meet oral health care needs (Wolf *et al.*, 2021). Oral health conditions share a variety of risk factors with other NCDs. These risk factors include smoking and poor diet, and it is thought that the underlying biochemical pathways that may be shared amongst oral health and NCDs. Hence, poor oral conditions can worsen many systematic conditions (Dörfer *et al.*, 2017).

1.2.3 Oral health problems increase with ageing

Currently, oral diseases account for one of the most prevalent global health conditions worldwide, affecting nearly 3.58 billion people in the world (WHO, 2022). The prevalence of oral health problems like dental caries, tooth loss and periodontitis increases with age (Murray Thomson, 2014), which can adversely impact the quality of life (Griffin *et al.*, 2012). Also, a two-way relationship has been reported between oral health conditions and other NCDs, such as cerebrovascular diseases, including dementia (Daly *et al.*, 2018; Noble *et al.*, 2013). The older population is more susceptible to these oral problems because they experience a number of physiological and psychological changes as they approach later life, affecting their functionality, including self-care and performing oral hygiene routines. Therefore, more intensive preventative and interventional methods are required to rehabilitate their oral care (Velasco-Ortega *et al.*, 2013; Chen *et al.*, 2013c).

Tooth loss is common with ageing, and many studies showed that the number of teeth can be a significant marker when predicting life expectancy and longevity (Jansson *et al.*, 2002; Abnet *et al.*, 2005; Friedman and Lamster, 2016). Through improving oral health with change in behaviour and lifestyle, the rate of 5-year survival can be increased by 4% for every retained tooth after reaching 70 years of age (Hirotsu *et al.*, 2015).

1.2.4 Dementia in relation to ageing

Dementia is a neurodegenerative condition associated with impairment of cognitive skills and memory loss (Ogawa, 2014). In recent years dementia has become a significant concern for public health, especially with the expected increase in the ageing population. Worldwide around 50 million people live with dementia, and this number is projected to increase to 139 million by 2050, particularly rising in LMICs, where around 60% of people with dementia live (WHO, 2021b). A recent study has estimated that by the year 2040, there will be more than 1.9 million dementia patients in England and Wales alone (Ahmadi-Abhari *et al.*, 2017). Consequently, it is predicted that dementia related complications might contribute to the death of one-third of the UK's population (Livingston and Frankish, 2015).

At present, nearly 850,000 people in the UK are affected by dementia (AlzheimersSociety, 2021b). Moreover, this is a condition which not only affects the patient in a fundamental way but also places an enormous burden on relatives and people who have to look after a patient with dementia. This aspect is discussed in detail in the section on the caregivers' perceptions (see chapter 8).

1.3 Background

The following sections cover the global overview of oral health and dementia as public health problems and the association between oral health and dementia.

1.3.1 Dementia as a public health issue

Dementia is the clinical syndrome of progressive loss of cognitive abilities such as thinking, language, and behaviour. Dementia is now the 7th leading cause of death worldwide and one of the most important causes of dependency and disability (WHO, 2021b), making it one of the world's biggest public health challenges (WHO, 2021b), especially in LMICs, including China,

where the availability of social services, care and support is deficient (Prince, 2015; WHO, 2021b).

A rise in dementia cases is a serious matter of concern. According to a study conducted in 2016 on the global burden of disease, the number of individuals living with dementia was 43.8 million (95% uncertainty interval [UI] 37.8–51.0) in 2016, increased from 20.2 million (17.4–23.5) in 1990 (Launer, 2019). In the USA, in 2000-2018, the deaths to Alzheimer's Disease (AD) increased by 146.2%, while mortality concerning other diseases decreased (Zhao, 2020). Furthermore, nearly one-third of the UK population might die of dementia or its complications (Livingston and Frankish, 2015; Livingston *et al.*, 2017).

In the UK, it is estimated that dementia costs around £26 billion annually. The NHS picks up £4.3 billion of the costs and social care £10.3 billion (publicly and privately funded). Caregivers (usually family) who are not paid for their time and effort contributes £11.6 billion (Prince *et al.*, 2014b). Therefore, without its control or intervention, dementia could create a considerable economic and social burden in terms of treatments, health care use, professional care, informal care provided by family and others in primary care settings, the community and residential care, social care, and costs of lost productivity (Shah *et al.*, 2016; WHO, 2021b). In addition, surveys conducted by the 10/66 Dementia Research Group (DRG) in Latin America and China reported that the cost of dementia exceeded the individual costs of other conditions such as depression, hypertension, diabetes, ischemic heart disease and stroke (Prince *et al.*, 2012; Jia *et al.*, 2020).

There are different types of dementia, with AD being the most common, accounting for nearly 60-70% of all dementia cases (Alzheimer's Society, 2021a). Other common types of dementia include vascular dementia (VaD) and Lewy Body Dementia (LBD), which account for up to 20% and 10-15%, respectively. Also, frontotemporal dementia (FTD) accounts for another 2%

in addition to mixed dementia (AlzheimersSociety, 2021a). These types and their aetiology are discussed further in the literature review (Chapter 2, section 2.5).

1.3.2 Oral health as a public health issue

According to WHO (WHO, 2021b), oral health is a “determinant factor” for quality of life. Poor oral health (POH) is characterised by tooth loss, dental caries experience, high prevalence rates of periodontal disease (PD), xerostomia and oral pre-cancer (Petersen and Yamamoto, 2005). In recent decades, the diseases of oral pathology have become quite prevalent, and several studies have indicated that oral diseases are a huge economic burden globally (Jin *et al.*, 2016; Peres *et al.*, 2019). The global burden of oral disease evaluated in 2010 by Murray *et al.* (Murray *et al.*, 2012) reported an increase in oral conditions including PD, oral cancer and dental caries in last 20 years (from 1990 to 2010) by approximately 45.6%. A similar study performed in 2016 (The Global Burden of Disease Study, 2016) estimated that approximately 3.5 billion people worldwide were affected by oral diseases, with caries of the permanent teeth being the most prevalent of all conditions assessed (Vos *et al.*, 2017; Peres *et al.*, 2019), which increased considerably from 2010 to 2017 due to population ageing (Kyu *et al.*, 2018).

Although a variety of oral health conditions including caries, tooth loss, edentulism, loss of mastication and congenital defects are prevalent among all age groups (Tonetti *et al.*, 2017), for the purpose of this study PD has been discussed as an indicator for poor oral health and is discussed in detail in chapters 2 and 4 (Systematic reviews and Meta-analyses).

1.3.3 Association between oral health and dementia

Epidemiological studies have noted a bi-directional association between oral health and dementia (Noble *et al.*, 2013). While oral hygiene routines can be negatively affected by decreased cognition and dementia, oral health changes can also lead to dementia (Tada and Miura, 2017). Poor oral hygiene leading to the development of dental caries and PD, which

induces soft-tissue inflammation and ultimately tooth loss, has been associated with an increased risk of dementia in several longitudinal studies (Gatz *et al.*, 2006; Stewart *et al.*, 2013).

In the last decade, several systematic reviews and meta-analyses were published presenting the associations between oral health and cognition (Cerutti-Kopplin *et al.*, 2016; Tonsekar *et al.*, 2017; Wu *et al.*, 2016; Zeng *et al.*, 2021; Tada and Miura, 2017) which are discussed in detail in the literature review chapter.

One of the earliest reviews related to poor oral health and dementia conducted by Noble *et al.* in 2013 showed links between the two due to dietary changes, malnutrition, and systemic inflammatory response associated with increased risk of stroke and AD (Noble *et al.*, 2013). Another systematic review conducted by Wu *et al.* (2016) on 16 longitudinal studies discussed the possible bidirectional relationship, but the strength of evidence was weak, and findings were often inconsistent (Wu *et al.*, 2016). Similar evidence was reported by rapid review having 16 papers (11 cohort and 5 case-control studies) and sample size ranged from 59-11,140 participants, which showed the bidirectional relationship between poor oral health and dementia. However, they found tooth loss could be a risk factor for dementia but found weak evidence related to tooth brushing, gingivitis and denture related problems (Daly *et al.*, 2018).

1.4 Significance of the research

The findings from this thesis would help clarify whether oral health and dementia have a bidirectional relationship. In addition, the evidence of the impact of poor oral health, especially PD, on increased risk of dementia would be helpful in public health interventions for the prevention of dementia.

This thesis highlights that dementia patients have impaired cognitive, communication, and physical skill that make their daily activities, including oral care, challenging, and they can be aggressive towards caregivers. Hence many dementia patients have poor oral health. The findings from this thesis will be essential in helping to design public health strategies to improve oral health in people with dementia. Furthermore, by investigating the impacts of poor oral health on dementia, we can develop strategies to reduce modifiable risk factors such as PD, thereby reducing dementia and improving quality of life.

Overall, the thesis will help to better understand the risk factors and health effects of the association between oral health and dementia and will provide evidence to assist in development of policies and practices.

1.5 Outline of the thesis

This thesis examines the association between oral health and dementia using a mixed-method approach that is based on two existing secondary datasets (quantitative studies) from the United Kingdom (UK) and China. In addition, a focus group study (qualitative study) was also conducted in the UK. This thesis presents nine chapters as follows:

Chapter 1 sets the context and provides an overview of the research topic, the background on oral health and dementia as a public health issue and the association between oral health and dementia.

Chapter 2 presents a critical review of the literature. It explains the oral health and general common risk factors, oral health epidemiology and conditions, especially PD and its types, PD in relation to systemic conditions. This is followed by dementia epidemiology and a detailed explanation of the bidirectional association between oral and dementia which includes the systematic literature review and a meta-analysis on the association of cognitive impairment

and dementia with PD risk. At the end research questions and objectives, as well as the conceptual model for the research are given.

Chapter 3 provides an account of the methodology; it includes justifications for the research approach, study design for the project and procedures involved in data collection for the quantitative and qualitative studies, including the rationale for the choices made.

Chapter 4 shows a systematic literature review and meta-analysis is done on the impacts of PD on dementia risk.

Chapter 5 investigates the association of oral health problems with the risk of dementia in a case-control study. This study used self-reported oral health measures: self-rated oral health, number of teeth, self-rated oral health questions on quality of life, oral hygiene habits and PD indicators.

Chapter 6 examines the impact of oral health on the increased risk of dementia in a cohort study. The aims are to examine self-rated oral health, tooth conditions and oral health impact on quality of life in people with dementia.

Chapter 7 evaluates the association of dementia/cognitive impairment with oral health in data analysed from the case-control and cohort studies. It investigated if there is a relation of dementia with self-reported oral health status, the number of teeth, oral impact, oral hygiene indicators, and PD indicators.

Chapter 8 presents the qualitative findings of this thesis that involves three focus group discussions to explore caregivers' perception of the association between oral health and dementia and discusses the research findings in the light of evidence from the literature.

Chapter 9 presents the overall discussion by summarizing key findings and integrating all the results findings of previous chapters. It also gives the strengths, limitations and suggestions for future research, the implications of findings and recommendations. Finally, the contribution to knowledge, and conclusions of the thesis. This is followed by the references and appendices.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter presents a detailed review of literature on the association between oral health and dementia. The chapter commences with the common risk factors for oral health (with a especial focus on PD) and dementia. In addition, this chapter presents an overview of the epidemiology of oral health and dementia. This chapter also reviews the bidirectional association between oral health and dementia, including performing a systematic literature review and meta-analysis to investigate the association of dementia and cognitive impairment with poor oral health. The research questions and objectives and the conceptual model for the research are also discussed.

2.2 Oral health

According to the World Health Organization:

“Oral health is essential to general health and well-being and greatly influences quality of life. It is defined as a state of being free from mouth and facial pain, oral diseases and disorders that limit an individual’s capacity in biting, chewing, smiling, speaking and psychosocial well-being.” (WHO, 2021c)

Oral health as an integral part of general health

Oral health has been recognised as an essential part of general health. The interrelationship between general health and oral health is especially noticeable among older people, as compromised oral health reduces overall health and quality of life (Gift and Atchison, 1995). In addition, poor oral health, poor general health, and quality of life are interrelated because of common risk factors (Watt and Sheiham, 2012).

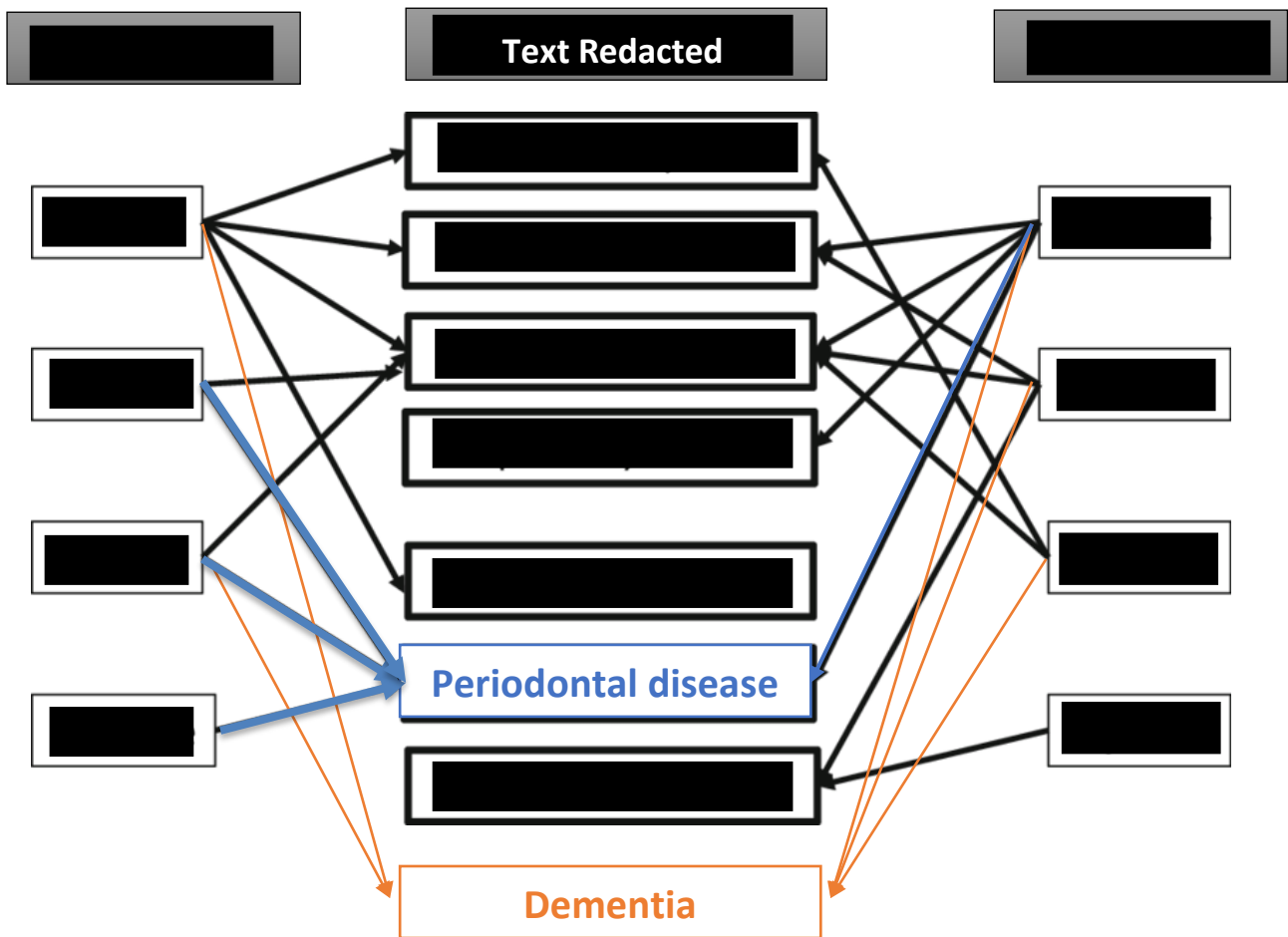


Figure 2.1: Common risk factor approach adapted from Sheiham and Watt (2000).

The risk factors implicated in poor oral health (periodontal disease and caries) are also associated with a wide range of diseases (such as cardiovascular disease, cancer, diabetes, dementia and other diseases) (Sheiham and Watt, 2000). Tobacco (smoking), alcohol, diet and socioeconomic status are known as common or shared risk factors (Sheiham and Watt, 2000). Therefore, adopting a shared approach is more rational than a disease-specific approach (Sheiham and Watt, 2000). The common risk factor approach is an important element to be considered in preventing poor oral health (periodontal disease) and has been presented in Figure 2.1. This is discussed later in the section on PD association with general health.

2.2.1 Oral health epidemiology

There is a high prevalence of oral diseases in marginalised older populations in developed and developing countries (Petersen, 2003). Poor oral health is characterised by tooth loss, dental caries experience, high prevalence rates of periodontal, xerostomia and oral pre-cancer and oral cancer. (De Visschere and Vanobbergen, 2006; Petersen and Yamamoto, 2005).

2.2.1.1 Dental Caries

Dental caries is multifactorial caused by the host, agent, and environmental factors. When exposed to organic acids, the acid-soluble minerals are lost from enamel and dentine in a process termed “demineralization”. However, the body has a natural repair mechanism, mainly supported by calcium and phosphate in the saliva, which can remineralise and thus repair the damage. Where demineralisation exceeds remineralisation over prolonged periods, the dental tissue is effectively lost the resulting disease is dental caries (decay) (Fejerskov *et al.*, 2015).

Dental caries is a significant public health problem globally and is the most widespread non-communicable disease (NCD). However, recent studies showed an increase of primary coronal caries (caries at chewing surfaces) (Murray Thomson, 2014). It could be due to the increased retention of natural teeth among the older population in the last decades (Tonetti *et al.*, 2017). Untreated dental caries (tooth decay) in permanent teeth is the most common health condition according to the Global Burden of Disease (GBD) 2017, affecting 2.5 billion people worldwide (Kassebaum *et al.*, 2017).

2.2.1.2 Tooth loss

Tooth loss is a complex outcome that reflects an individual’s history of dental disease and its treatment by dental services over the life course (Baelum *et al.*, 2007). Severe tooth loss and edentulism were among the leading ten causes of Years Lived with Disability (YLD) in some high-income countries due to ageing populations (Vos *et al.*, 2017). In the GBD 2017,

edentulism and severe tooth loss were the primary cause of more than 7 million DALY globally as the most effective oral disorder (Kyu *et al.*, 2018). The prevalence of edentulism (complete tooth loss status) among older adults has declined in the last decades but is still relatively common. In the Adult Dental Health Survey (ADHS), the prevalence of edentulism ranged from 15% of adults aged 65 to 74 and 30% of adults aged 75 to 84 and reached up to 47% of adults aged 85 and older (ADHS, 2009). Two leading causes of tooth loss are dental caries and periodontal disease.

2.2.1.3 Oral cancer

Oral cancer is one of the widely prevalent cancer types emerging as a growing problem in various world regions. In worldwide reports, cancers of all areas of the oral cavity and pharynx are grouped and collectively represent the sixth most common cancer in the world (Warnakulasuriya, 2009). There are an estimated 657,000 new cases of cancers of the oral cavity and pharynx each year, and more than 330,000 deaths (Montero and Patel, 2015). The main causes of oral cancer are tobacco and alcohol use, accounting for about 90 per cent of oral cancers (WHO, 2021c). Chewing tobacco, often with other carcinogenic substances, e.g., betel quid, is a common cause in Asia. At the same time, human papillomavirus (HPV) infection is an emerging risk factor, mainly in HICs (WHO, 2021c).

2.2.1.4 Periodontal disease

Periodontitis is a progressive, destructive, and inflammatory condition affecting the oral cavity, eventually leading to tooth loss if left untreated (Van Dyke and van Winkelhoff, 2013). Periodontal disease (PD) is characterised by inflammation of the gingiva, periodontal ligaments and alveolar bones. It is believed that there are over 800 different bacterial species in the oral cavity (Ashby *et al.*, 2009). The host-response mechanism resulting from bacterial infection leads to inflammatory changes that result in periodontal pockets, resorption of alveolar bone

and clinical attachment loss (CAL) (Newman, 2012). PD has been used as one of the main indicators for oral health for this study and is discussed further in detail in section 2.3.

2.2.2 Risk factors for oral health

Many modifiable risk factors can lead to oral diseases, for example tobacco use, alcohol consumption and unhealthy diets high in free sugars.

2.2.2.1 Tobacco smoking

The use of tobacco is positively correlated to higher PD and oral cancer rates (WHO, 2021c). Smoking is one of the most important risk factors for periodontitis, and the reduction in PD prevalence is related to the drop-in smoking rates (Bergstrom, 2014). Smokers are three times more likely to have a severe PD than non-smokers (Johnson and Hill, 2004).

Smokers also tend to have greater numbers of deep periodontal pockets and higher averages of periodontal probing depth leading to more severe disease (Paul *et al.*, 2014). The smokers present significantly increased loss of alveolar bone and a higher prevalence of tooth loss and other periodontal inflammatory conditions than non-smokers. They have poor outcomes of all forms of periodontal treatments (Underner *et al.*, 2009). Not only does smoking cause PD, but also second-hand smoke is associated with PD (Javed *et al.*, 2014).

Similarly, cigarette smoking is a contributing factor to the development of oral cancer (WHO, 2021c). Evidence has shown nicotine causes vasoconstriction and a decrease in oxygen tension and can suppress osteoblast proliferation, causing the neutrophils and chemotaxis to be suppressed (Arbes *et al.*, 2001). According to Warnakulasuriya *et al.* tobacco use constitutes more than 80% of the risk associated with oral cancer and more significant loss of teeth and implant failure (Warnakulasuriya *et al.*, 2010).

2.2.2.2 Alcohol

There is a large body of evidence that alcohol is a significant risk factor for oral cancer. It has been estimated that 3.6% of all cancers worldwide, and over 30% of all cases of oral pharyngeal cancer, are attributable to alcohol consumption (Boffetta *et al.*, 2006). Previous meta-analyses strongly support the association between alcohol drinking and head and neck cancer (HNC) risk (Bagnardi *et al.*, 2015; Turati *et al.*, 2013) and oral malodour (Suzuki *et al.*, 2009).

Overall, 22% of all facial trauma was related to alcohol consumption (Hutchison *et al.*, 1998). Additionally, the prevalence of dental trauma is significantly higher in those that binge drink (Paiva *et al.*, 2015). Tezal *et al.* found an odds ratio of 1.65 of having higher gingival bleeding and 1.36 of having more severe clinical attachment loss in those consuming five or more drinks per week, compared to those consuming fewer than five, after adjusting for confounders. “One drink” was defined as 12 ounces of beer, 4 ounces of wine, or 1 ounce of hard liquor which all contain the same amount of pure alcohol (one unit) (Tezal *et al.*, 2001). A review by Amaral *et al.* has provided evidence that alcohol consumption is a risk indicator for periodontitis (Amaral Cda *et al.*, 2009). There was a linear dose-response relationship between alcohol consumption and PD risk, with increased risk of periodontitis by 0.4% [95% CI (1.002–1.007) (p = 0.002)] for each one g/day increment in alcohol consumption (Wang *et al.*, 2016). Enberg *et al.* also found significantly more caries and fewer teeth present in an alcohol-dependent group than a control group of social drinkers (Enberg *et al.*, 2001).

2.2.2.3 Poor Oral hygiene

Oji *et al.* reported in a case-control study that poor oral hygiene due to infrequent tooth brushing was associated with primary oral cancer (Oji and Chukwuneke, 2012). Poor oral hygiene score was associated with a significant risk of oral cancer (adjusted OR=6.98; 95%CI 3.72-13.05) (Gupta *et al.*, 2017). A meta-analysis of 15 studies reported the pooled effect of fair oral health (OH) *versus* good OH, and poor OH *versus* good OH on periodontitis, with pooled odds ratios

(ORs) of 2.04 (1.65–2.53) and 5.01 (3.40–7.39), respectively (Lertpimonchai *et al.*, 2017).

There is a pronounced relationship between poor oral hygiene and increased accumulation of dental plaque, high prevalence and increased severity of PD (Albandar, 2002).

2.2.2.4 Diet

Diet influences the health of the oral cavity, conditioning the onset of caries, the development of the enamel, the onset of dental erosion, the state of periodontal health, and the oral mucous in general (Scardina and Messina, 2012). Poor diet is a diet with nutritional imbalance due to a lack of important vitamins and minerals. This poor diet has been found to be significantly associated with an increased risk of oral diseases (Scardina and Messina, 2012), while high sugar diets can lead to demineralization of enamel and dentine (Bang and Kristoffersen, 1972). The anaerobic metabolism of sugar by bacteria in the oral cavity results in organic acid production in dental plaque. In contrast, communities with a low sugar diet have very low dental caries (Scheinin and Mäkinen, 1976). Similarly, fluoride prevents sugar metabolism by bacteria and facilitates remineralisation of damaged enamel with resistant fluorapatite. Studies (Belcastro *et al.*, 2007) have also reported that along with oral hygiene and professional oral care, fluoride prophylaxis and a healthy diet are very important for oral diseases prevention.

2.2.2.4.1 Vitamins

Vitamins (Vit) are important for oral and general health because they play a significant role in metabolism of proteins, fats and carbohydrates for energy, growth and cell maintenance. (Cagetti *et al.*, 2020). There are three main sources of vitamins: sunlight, foods and supplements (Millen and Pavlesen, 2020).

Vitamin D 25-hydroxyvitamin D [25 (OH) D] is mainly synthesized by human body from sunlight exposure but can also be taken through diet and dietary supplements. Vitamin D deficiency (VDD) affects odontogenesis, resulting in a reduced mineralization increasing the

risk of dentition fracture and caries lesions (Schroth *et al.*, 2013). VDD also affects immune mechanisms and might increase periodontal infection leading to poor oral health (White, 2012).

The *protective role of Vitamin D* in oral health is indicated by the presence of CYP27A1 gene, which encode 25-hydroxylase, in human gingival fibroblasts and periodontal ligament cells as extra-hepatic sites of 25(OH)D synthesis (Liu *et al.*, 2012). In a randomized control trial of calcium and vitamin D supplementation in 145 participants (≥ 65 years), Krall *et al.* (Krall *et al.*, 2001) found that tooth loss was significant, fewer in those on supplements compared to placebo after three years (13% versus 27%, $p < 0.05$). While the diet and dietary supplements account for almost $< 10\%$ of the variation in circulating 25(OH)D concentrations between people, the rest can be explained by differences in sunlight exposure, metabolism, or genetics (Millen *et al.*, 2010). Two more studies used radiographic evidence to evaluate alveolar bone loss after periodontal surgery (Bashutski *et al.*, 2011) and tooth extraction (Wical and Brussee, 1979), and they found that calcium and vitamin D helped reduce bone loss after tooth extraction and facilitate bone gain following after periodontal surgery.

Vitamin A deficiency also increases the risk of PD reported in the nutritional survey in over 21,000 people in Alaska, Ethiopia, Ecuador, South Vietnam, Chile, Colombia, Thailand and Lebanon (Russell *et al.*, 1963). In addition, the survey found that the population deficient in Vitamin A had higher scores for PD (Dommisch *et al.*, 2018).

Vitamin B 12 deficiency can cause PD (Zong *et al.*, 2016) and low levels of vitamin B1, B2 and B3 also increase the risk of gingivitis. Vitamin B3 deficiency showed 1.25 times higher odds of periodontitis (OR 1.25, 95%CI 1.07-1.46) (Lee *et al.*, 2020). Similarly, Vitamin B2, B3, B6 and B12 deficiencies were associated with haemorrhagic gingivitis and periodontitis (Hatipoglu *et al.*, 2012; Sheetal *et al.*, 2013). Vitamin B6 (folic acid) deficiency results in loss of gingiva keratinisation, decreased cell regeneration turnover rate, reduced resistance to

infections, and destruction of gingival and periodontal tissues (George *et al.*, 2013). Therefore, *Vitamin B complex intake can help protect* against PD and promote periodontal wound healing in people with chronic PD who have undergone periodontal surgery (Neiva *et al.*, 2005). Folate (Vit B6) containing mouthwash also reduces BOP and gingival redness, as reported in a double-blinded placebo-controlled trial (Pack, 1984). Also, fluoridated toothpastes containing Vitamin B3 and B5 significantly reduce calculus build-up when compared to fluoridated toothpaste which did not contain vitamins ($p = 0.01$) (Llena *et al.*, 2009).

Epidemiological studies have reported an inverse association between *Vitamin C deficiency* and PD (Chapple *et al.*, 2007; Park *et al.*, 2017). People with low Vitamin C levels have greater LOA when compared to those with normal levels of Vitamin C (Amaliya *et al.*, 2015). Local Vitamin C injection reduced inflammation and improved healing by increasing collagen and gingival circulation (Yussif *et al.*, 2016; Yussif *et al.*, 2019), decreased sulcus bleeding scores (Staudte *et al.*, 2005) and was used in surgical and non-surgical treatment for PD (Raghavendra *et al.*, 2018).

2.2.2.5 Socioeconomic factors

Peres *et al.* in 2019 reported that oral diseases disproportionately affect the poor and socially disadvantaged members of society. Furthermore, they found a robust and consistent association between poor socioeconomic status (income, occupation, and educational level) and the prevalence and severity of oral diseases (Peres *et al.*, 2019).

2.3 Periodontal disease

For this thesis, PD has been discussed as an indicator for poor oral health and is explored in detail below. The two most prevalent PD are gingivitis, which causes no permanent damage to the periodontal support, and periodontitis, which results in bone loss and loss of attachment (LOA). Clinical features of gingivitis include the classical signs of inflammation (redness and

oedema), loss of mucosal stippling, increased flow of gingival crevicular fluid (GCF), BOP and increased pocket depths but no LOA or bone loss (Løe *et al.*, 1978; Trombelli *et al.*, 2018)

Periodontitis can cause varying degrees of permanent damage to the periodontal support (bone loss and LOA), resulting in gingival recession, increased tooth mobility, furcation involvement, migration (drifting) and in severe cases, tooth loss (Tonetti *et al.*, 2018; Papapanou *et al.*, 2018). This damage can result in significant aesthetic and functional issues, leading to impaired quality of life and expensive dental care (Ferreira *et al.*, 2017).

2.3.1 Diagnosis of periodontal disease

Differences in the methodology adopted for diagnosing PD have led to difficulty defining its global prevalence. The diagnosis of PD is almost entirely based on clinical examination, which provides a practical qualitative and quantitative evaluation of the subgingival microflora and gingival crevicular fluid, which is used in conjunction with the patient's signs and symptoms and radiological evidence (Rahnama *et al.*, 2014). Furthermore, the PD may also be asymptomatic and painless.

Periodontitis is diagnosed based on clinical findings such as the presence of periodontal pockets, bleeding, attachment loss and loss of alveolar bone, which are then evaluated and adjusted, together with radiological evidence, to estimate the degree of PD (Highfield, 2009). Based on these values, diagnostic criteria can be established, such as those mentioned in the International Statistical Classification of Diseases and Related Health Problems (ICD) (World Health, 2015). On the other hand, gingivitis can be confirmed if gingival tissues show reduced resistance to periodontal probing and by the presence of a deep gingival pocket or sulcus indicating loss of periodontal attachment (Gomes-Filho *et al.*, 2018).

A variety of indices are available for evaluating periodontal health and screening for PD, which vary in type of measures including Community Periodontal Index for Treatment Needs

(CPITN), PD Index (PDI) and Community Periodontal Index (CPI) (Beltrán-Aguilar *et al.*, 2012). Besides measuring periodontal tissue health, these measures also guide treatment (Dhingra and Vandana, 2011).

2.3.2 Epidemiology of periodontal disease

Periodontal conditions are considered the primary cause of tooth loss and (have been) were reported as a significant threat to oral health (Nazir, 2017). According to the WHO, PD is significantly prevalent in developed and developing countries, affecting nearly half of the world's population (WHO, 2021c). Globally 1 in 10 adults suffer from severe PD making it a concern for public health (WHO, 2021c) and it is the 11th most prevalent condition in the world (GBD, 2017).

The prevalence of PD was reported to range from 20% to 50% globally (Sanz, 2010). Still more recently, in 2020, a variation of 25.0% to 90.2% was reported by Conceicao *et al.* (Conceição *et al.*, 2020) which was attributed to variation in the diagnosing criteria chosen. In the past, WHO has also highlighted that the number of people suffering from PD might be underestimated, with middle-aged individuals alone accounting for nearly 15-20% worldwide (WHO, 2021c).

Studies (Kassebaum *et al.*, 2017; Nazir, 2017b) indicate that the prevalence of PD increases with age and the older population is at higher risk of developing more severe periodontitis. It might be due to age-related increased susceptibility to other systemic conditions and poor oral health and hygiene of older aged individuals. Another factor thought to be contributing is increased population ageing, with more people living into old age and retaining more teeth (Kassebaum *et al.*, 2017). Furthermore, periodontal pockets with a depth of 6 mm or more are exhibited in more considerable magnitude by older individuals (65-74 years) in developing and developed countries (Nazir, 2017). Considering the statistics in the UK alone, about 60% of

the population between the ages 65-84 years and approximately 47% of those aged 85 years and above have at least one deep periodontal pocket, while loss of attachment (LOA) of 4mm and 6mm or more, was reported to be 65 % and 20 %, respectively, in population aged > 55 years (ADHS, 2009; Steele *et al.*, 2012).

However, its impact on oral function, pain, and the individual's health, and the socioeconomic effect on populations, not many authorities support the opinion that PD is a problem of public health (Kinane *et al.*, 2017), indicating an increased need for further research to understand its significance and global burden of disease (section 2.3.6).

2.3.3 Aetiology and risk factors of periodontal disease

Aetiology

The primary etiological factor in PD is dental plaque (Socransky and Haffajee, 1994). Most patients who experience an accumulation of plaque will develop gingivitis (Löe *et al.*, 1978). Dental plaque is classified as supra-gingival and subgingival. The sub-gingival plaque holds key importance in the pathogenesis of periodontitis. There are several reasons for an increase in susceptibility to periodontitis. The differences in patients' susceptibility are attributed to the amount of plaque, the microbial composition of the plaque, and the host response to the presence of dental plaque (Socransky and Haffajee, 1994). Dental plaque is a poly-microbial biofilm containing up to 500 species of bacteria. Up to half of these species are yet to be cultured (Paster *et al.*, 2001). Dental plaque begins to form as soon as the teeth erupt. After prophylaxis, the teeth are initially colonised by *Streptococci* and *Actinomyces* species. As the biofilm matures, the type of bacteria contained within the plaque changes, from one composed primarily of Gram-positive aerobic bacteria to one composed of primarily Gram-negative motile rods (Kolenbrander *et al.*, 2006).

Risk factors for PD

2.3.3.1 Non -Modifiable risk factors

Studies have shown an increased risk of loss of periodontal connective tissue attachment with *age*. This may be due to increased exposure to other internal and external risk factors alongside the ageing process (Petersen *et al.*, 2005; Sheiham and Netuveli, 2002), such as the presence of systemic diseases, decreased dexterity and decreased frequency of regular dental visits (Persson, 2017). Women have better periodontal health when compared to men, but this may be due to their increased use of health services (Christensen *et al.*, 2003). Specific *genotypes* are significantly associated with the severity of PD (Loos *et al.*, 2015). Studies investigating familial aggregation report that aggressive PD is an inherited trait, with up to 50% of siblings being affected (Meng *et al.*, 2011).

2.3.3.2 Modifiable risk factors

There is an inverse relationship between the percentage of individuals who report problems with their teeth and of the *country's income level* in which they live (Petersen, 2008). Data collected in the 2009 ADHS, UK showed that low *education* status was significantly linked to decreased frequencies of tooth brushing and dental attendance (Chadwick *et al.*, 2011). In a study conducted in Brazil, authors found that poor periodontal health was significantly associated with years of formal education and low income (Bonfim Mde *et al.*, 2013). Evidence also suggests a dose-dependent related relationship between *smoking* and periodontitis (Grossi *et al.*, 1995; Tomar and Asma, 2000). In a study conducted in 2012 (Lages *et al.*, 2012), authors found a decreased prevalence of PD in groups of patients who did not drink *alcohol* or were occasional users, compared to patients who were moderate alcohol users or intense alcohol users (Lages *et al.*, 2012). Lack of adequate *oral hygiene* measures facilitates deposition and maturation of plaque that triggers chronic inflammatory pathology of periodontitis (Socransky and Haffajee, 1994). Local retentive factors such as mal-aligned teeth and ill-fitting restorations

further contribute to increased risk of periodontitis by facilitating plaque retention and making oral hygiene measures ineffective (Javali *et al.*, 2020).

Systematic conditions and diseases

This is explained in detail later in this chapter (section 2.4).

2.3.4 Treatment of periodontal disease

The treatment modalities employed are divided into non-surgical and surgical types supplemented with antimicrobials where needed and supportive periodontal therapy (SPT). Mechanical *non-surgical* periodontal treatment, which includes oral hygiene instruction, supragingival scaling, and root surface debridement, is considered highly effective for treating periodontitis (Badersten *et al.*, 1985; Hill *et al.*, 1981). *Antibiotics* can be used in some cases to help destroy bacteria beneath the gum line and help preserve the tooth's attachment and prevent loosening and eventual loss (Guerrero *et al.*, 2005). *Surgical therapy*, such as gingivectomy, is indicated in the specific clinical situation in which there is a persistence of the periodontal lesion to (adequately) debride the root surface, root concavities and furcation and recreate more favourable anatomy for gingival tissues (Heitz-Mayfield and Lang, 2013, Drisko, 2014). *SPT* is employed to reduce the probability of re-infection and progression of the disease, maintain teeth without pain, excessive mobility or persistent infection in the long term, and prevent related oral diseases (Manresa *et al.*, 2018).

2.3.5 Prognosis of periodontal disease

There is no established universal set of criteria for the assignment of periodontal prognosis. Dental practitioners usually rely on the clinical parameters to predict the long-term outcome of the provided periodontal therapy. The most used measures are Probing Pocket Depth (PPD) Gingival Recession and Attachment Level (AL). Other clinical parameters have also been used to assess the prognosis, such as bleeding on probing (BOP), presence of plaque, furcation

involvements, and the lesion site (Persson, 2005). One study made a comparison between prognosis and actual outcome to determine if clinical parameters are effective in assigning an accurate tooth prognosis (McGuire and Nunn, 1996). The results indicate that teeth with a good prognosis generally remained good. In teeth with less than good prognosis, the overall accuracy in assigning prognosis was only 43% at five years and 35% at eight years. Both clinical and specific immunological and microbiological parameters have also been evaluated for predicting change in clinical status and tooth loss (Machtei *et al.*, 1997).

2.3.6 Global burden of periodontal disease

Studies indicate that PD seems to become more aggressive with age, and this increase in its occurrence has been seen mainly in adults aged 30 to 40 years. According to existing studies (Tonetti *et al.*, 2017; Jepsen *et al.*, 2018), the global periodontitis burden tends to increase with the increasing global tooth retention and the growing ageing population. In 2016, the Global Burden of the Disease study reported PD as the 11th most prevalent condition globally (GBD, 2017). Consequently, PD was responsible for 3.5 million years lived with disability (YLD) globally (GBD, 2017). Moreover, there has been a further increase of 57.3% in disease burden globally in the two decades 1990-2010, with an overall prevalence of 11.2% and around 743 million affected people (Jin *et al.*, 2016). Furthermore, PD was estimated to be responsible for nearly \$ 54 billion worth of loss of productivity globally in 2010, while the total economic impact of PD was approximately \$442 billion (Listl *et al.*, 2015).

PD also shares a variety of risk factors, both medical and socioeconomic components, with numerous other systemic conditions (discussed in section 2.4). It also increases social inequality and has affected the exposed, vulnerable segments of the population (Jepsen *et al.*, 2018). Unfortunately, the prevalence of PD and its global burden have been predicted to rise further in

future, mainly due to an increase in the ageing population with less tooth loss and more retained teeth (Tonetti *et al.*, 2017).

2.4 Association of periodontal disease with other diseases

Studies have shown poor oral health, especially PD, is an independent risk factor for many systemic conditions, such as coronary heart diseases (CHD) (Humphrey *et al.*, 2008) and stroke (Syrjänen *et al.*, 1986). Sfyroeras *et al.* (2012) carried out a meta-analysis to investigate whether PD was an independent risk factor for stroke and found that OR of stroke in subjects with periodontitis was 1.47 (1.13-1.92) in prospective studies and 2.63 (1.59-4.33) in retrospective studies (Sfyroeras *et al.*, 2012). Evidence from the latest review of multiple studies by Zardani *et al.* (2021) also establishes a link between PD and Atherosclerotic Cardiovascular Disease (ACVD) by highlighting several mutual systemic inflammatory mechanisms, including increases in levels of inflammatory mediators, lipids and hemostatic and thrombotic factors in addition to common risk factors such as smoking and genetics (Zardawi *et al.*, 2020). In addition, recent evidence has indicated that poor oral health, especially PD, can lead to significant respiratory conditions, including bacterial pneumonia and chronic obstructive pulmonary disease (COPD) (Bansal *et al.*, 2013). This association can be explained by the role of oral and periodontal microorganisms in causing respiratory diseases (Paju and Scannapieco, 2007).

Mental health conditions like depression can lead to poor oral health through negligence towards self-care and other mechanisms involving disturbance of the immune system via hypothalamic-pituitary axis (HPA) system (Kurer *et al.*, 1995). Stress stimulates HPA resulting in a rise in cortisol levels in blood, saliva, and other body fluids (Deinzer *et al.*, 2004). The cortisol hormone suppresses several host response mechanisms such as T-helper cell function, which might increase the risk for periodontitis (Genco *et al.*, 1998). Previous studies have

reported that psychological stress also causes an increase in serum interleukin (IL)-1b and IL-6 (Maes *et al.*, 1997; Owen *et al.*, 2001) in patients with early-onset periodontitis (Kamma *et al.*, 2004).

Since the 1990s, several epidemiological studies have indicated a bidirectional relationship between diabetes mellitus (DM) and PD (Wu *et al.*, 2020; Zhang *et al.*, 2021). Additionally, the recurrence of PD is more common and hard to manage if the diabetes is not adequately controlled (Llambés *et al.*, 2005).

Several meta-analyses reported that PD could increase the risk of cancers of the oral cavity, upper GI tract, pancreas, and lungs (Javed and Warnakulasuriya, 2016; Zhang *et al.*, 2020). The findings from these studies can help establish strategies for prevention and managing cancer risk through better oral health care. A recent systematic review and meta-analysis conducted on association between PD and chronic kidney disease (CKD) was significant after adjustment for major CKD risk factors for severe PD OR was 2.26 (1.69–3.01) (Deschamps-Lenhardt *et al.*, 2019).

Overweight and obesity have also been associated with periodontitis. Nascimento *et al.* reported obesity increases the odds of tooth loss and edentulism by OR 1.49 and 1.25. On the other hand, tooth loss increased OR for obesity by 1.41, and edentates had even higher odds (OR 1.60) (Nascimento *et al.*, 2016).

2.5 Epidemiology of dementia

2.5.1 Definition of dementia

The term “dementia” is used to describe irreversible and progressive degenerative changes in the brain, causing loss of memory and impaired behaviour and thinking, thus resulting in loss of ability to perform activities of daily living (WHO, 2021b). It is associated with a decline in

cognitive skills from a previous level of functioning, both at a personal level as well as socially and can also lead to disturbance in behaviour (DementiaUK, 2021). Although it is more prevalent in older adults, dementia is not a standard part of growing old (WHO, 2021b). A variety of conditions can contribute to the early development of dementia, for example, stroke, smoking, substance use (discussed further in the section on risk factors) (WHO, 2021b).

Dementia presents diverse clinical symptoms, which vary from mild to severe (WHO, 2021b). Depending on the part of the brain involved, it can present with a variety of cognitive impairments such as amnesia (memory decline), apraxia (tasks), aphasia (language), agnosia (pattern recognition) or impaired executive functioning (Beydoun *et al.*, 2014). It can also cause an array of psychological symptoms ranging from depression and aggressive behaviour to wandering and psychosis, thus creating a challenge for dementia patients and those providing care to dementia patients (DOH, 2009). Since dementia can impair every aspect of life, including work and social engagements, WHO has declared it as one of the major challenges facing public health today, requiring urgent attention (Shah *et al.*, 2016).

2.5.2 Types of dementia and their aetiology

Although the underlying aetiology of dementia is not fully understood, it has been classified into different subtypes. These include Alzheimer's disease (AD), Vascular dementia (VaD), dementia with Lewy body (DLB), Frontotemporal dementia, Young-onset dementia, Mixed dementia and Parkinson's disease dementia. The neuropathological pathways for different subtypes of dementia vary considerably. AD is marked by brain atrophy due to the accumulation of B-amyloid plaques (extracellular), intracellular NFTs (neurofibrillary tangles) and degeneration of neurons (nerve cells) (Hugo and Ganguli, 2014). Changes related to the brain's blood supply, for example, blood clots or haemorrhage causing stroke, can lead to Vascular Dementia (VaD) (Rizzi *et al.*, 2014). DLB results from the intracellular collection of

alpha-synuclein called Lewy bodies. In contrast, frontotemporal dementia is called so because it is associated with degenerative changes in frontal and temporal lobes of the brain, due to the accumulation of proteins, for example, tau proteins or TDP-43 protein (Gomperts, 2016). The term ‘mixed dementia’ is used when underlying pathology shows the feature of more than one type. Although a dominant type of pathology can be identified in such cases, there is a significant overlapping of the clinical picture. This type of dementia is usually seen in a combination of AD and VaD or AD and DLB (Bhagal *et al.*, 2013). Other less common types of dementia include Parkinson’s disease dementia and Young-onset dementia.

Dementia Diagnosis

The diagnosis of dementia is complex, involving careful but detailed assessment by a physician and neurologist, including detailed medical and family history especially exploring any change to psychology (changes in emotional response, for example agitation, anxiety, aggression, etc.), cognition or behaviour (AlzheimerSociety, 2021). Other investigative tests, including blood tests and MRI scans, also play a role in diagnosing dementia and its types.

2.5.3 Prevalence and incidence of dementia

Dementia has emerged as a significant problem for public health. In 2020, WHO (WHO, 2021b) reported that nearly 55 million individuals suffer from dementia globally, a figure much higher than reported in 2015 by Prince *et al.* (Prince *et al.*, 2015), i.e., prevalence of 46.8 million. An annual incidence of over 9.9 million was reported in 2015 (Prince *et al.*, 2015), indicating a new dementia case is being diagnosed every 3.2 seconds (Prince *et al.*, 2015) with low and middle-income countries (LMICs) being affected the most. These LMICs already account for nearly 61% of global dementia cases, and according to reports, the number will rise to 71% by the year 2050 (ADI, 2021). According to recent report by Jia *et al.* 2020, (Jia *et al.*, 2020; GDB, 2019), China alone accounts for 25 % of all dementia cases. On the other hand, in

the UK, 954,099 people over the age of 65 years have dementia and it is expected that this number will rise to 2,092,945 by the year 2051 (Prince *et al.*, 2014b). Recently it is estimated that by 2040, the UK may have over 1.5 million people suffering from dementia (AlzheimersSociety, 2021a). More recently, WHO reported that by 2050 there would be 139 million dementia cases globally an expected increase of nearly 10 million new cases per year (WHO, 2021b).

2.5.4 Risk factors for dementia

Several epidemiological studies have confirmed that dementia or cognitive decline can be influenced by several risk factors, modifiable or non-modifiable (Baumgart *et al.*, 2015). Among the non-modifiable risk factors, *age* is the single most dominant risk factor for dementia (Kukull *et al.*, 2002). Similarly, *gender* is also significant in dementia patients, with females at higher risk. It is believed that hormonal changes associated with menopause and increased longevity might be responsible for this (Rocca *et al.*, 2014). The risk of dementia increases by 25-50 % if *family history* is positive for dementia (Milne *et al.*, 2008). Different genes are involved in dementia pathology, especially the $\epsilon 4$ allele of Apolipoprotein E (ApoE $\epsilon 4$) plays a significant role in AD (Teruel *et al.*, 2011). The AD risk is dose-dependent, as those carrying one APOE $\epsilon 4$ allele have a 2–3-fold increased risk, while those carrying two $\epsilon 4$ alleles have a 10–15-fold increased risk (Corder *et al.*, 1993; Troutwine *et al.*, 2021). The presence of the APOE $\epsilon 4$ allele is also associated with increased risk for cerebral amyloid angiopathy by binding to hydrophobic amyloid- β (A β) peptide and cell surface receptors and age-related cognitive decline during normal ageing. (Liu *et al.*, 2013).

In addition to these unchangeable factors, the development of dementia can be influenced by a variety of modifiable risk factors (Livingston *et al.*, 2020; Livingston *et al.*, 2017). In particular systemic diseases such as *cardiovascular diseases* can significantly increase

dementia risk and mortality (Prince *et al.*, 2014a). Although the underlying mechanism for this is not fully understood, several studies have reported that managing these systemic conditions can remarkably reduce the risk of cognitive impairment (Baumgart *et al.*, 2015).

The systemic diseases that increase the progression of cognitive impairment and dementia include *diabetes*; in particular it is strongly associated with vascular dementia and diabetic patients at 60 % increased risk of vascular dementia (Chatterjee *et al.*, 2016). Hence, it is no surprise that *obesity* and associated metabolic syndrome can also increase the risk of cognitive decline and dementia (Ylilauri *et al.*, 2017).

Besides systemic conditions, several *psychological* and *lifestyle factors* can have a significant bearing on cognition. Studies show that adversities such as *poverty*, *poor education* and related *factors*, such as lack of medical awareness or difficult access to health care, can lead to dementia. This may be due to an increased susceptibility to other pathologies and systemic conditions, which then contribute to dementia risk (Xu *et al.*, 2014; McDowell *et al.*, 2007). *Smoking* is one such lifestyle factor that adversely affects cognition. Although the details of the casual mechanism remain unclear, long-term quitters and never smokers had decreased risk of dementia compared to smokers (Choi *et al.*, 2018).

Similarly, the *impairment* of the central nervous system due to neurotoxicity caused by heavy *alcohol intake* can harm cognition (Wilhelm *et al.*, 2015). Furthermore, a history of repeated *minor head injuries*, especially those involving loss of consciousness, can lead to anatomical changes in the brain, thus elevating the risk of developing dementia (Hugo and Ganguli, 2014). On the other hand, from a *psychology* point of view, mood disturbances such as *depression* can not only be a risk factor of dementia but may also be the presenting complaint (Mohd Zulkifly *et al.*, 2016). *Midlife hearing*, *hypertension*, *air pollutants*, *social contact* and *physical inactivity* are other modifiable risk factors for dementia (Livingston *et al.*, 2020).

Diet is another modifiable risk factor for dementia and AD. For example, a Mediterranean diet rich in unsaturated fats and antioxidants offers protection against AD compared to diets rich in trans fats and low levels of antioxidants (de Wilde *et al.*, 2017).

Antioxidants prevent damage caused by reactive oxygen species by stabilizing the neuronal membranes; docosahexaenoic acid (DHA) helps clear the A β peptide and, together with choline and uridine, aids in the synthesis of the neuronal membrane (Scarmeas *et al.*, 2009; de Wilde *et al.*, 2017). Similarly, fatty acids (including fish oil), antioxidants such as vitamins E and C, fruits and vegetables, vitamins B6, B12 (cobalamine) and folate also offer neurocognition protection (Smith and Blumenthal, 2010). Phospholipid composition is essential in neuronal membrane function. Thus, adequate intake of DHA, eicosapentaenoic acid (EPA), uridine monophosphate, choline, folate, vitamins B6, B12, C, and E, and selenium contribute to a better synthesis of phospholipids and, consequently, to synaptic function preservation and protects against neurodegeneration (de Wilde *et al.*, 2017).

Vitamin D, especially 25-hydroxyvitamin D, is an important steroid hormone that could reduce the risk of dementia and AD (Knekt *et al.*, 2014; Shen and Ji, 2015). Besides regulating calcium metabolism and bone density, vitamin D has some functions in the central nervous system, such as regulation of neurotrophic factors, calcium homeostasis, acts on oxidative stress mechanisms, immune system modulation and inflammation (Landel *et al.*, 2016). Therefore, VDD can lead to vascular dysfunction and ischemic stroke risk (Brøndum-Jacobsen *et al.*, 2013) as well as brain atrophy (Annweiler *et al.*, 2013b). Previous prospective studies indicated that the elderly population with VDD had an increased risk of cognitive decline (Slinin *et al.*, 2012; Annweiler *et al.*, 2013a.). Furthermore, it has been hypothesized that the risk of cognitive decline markedly increases when Vitamin D levels fall below a threshold between 25 and 50 nmol/L (Dickens *et al.*, 2011). Interestingly, reverse causation is also possible, as the onset of

dementia may lead to dietary changes and reduced outdoor activity, resulting in lower vitamin D concentrations (Dickens *et al.*, 2011).

2.5.5 Prognosis and global burden of dementia

Dementia is an irreversible condition with a poor prognosis and an estimated mortality risk twice than people without dementia (Van de Vorst *et al.*, 2015; Dewey and Saz, 2001). A prospective cohort study performed in 2005 by Guehne *et al.* on 1670 participants aged more than 65 years reported an increased risk of mortality with dementia irrespective of subtype, especially a 40% increased mortality in patients with AD compared to those without (Guehne *et al.*, 2005). Studies show that in the future, dementia might emerge above cardiovascular conditions as a major cause of death worldwide (James *et al.*, 2014; Weuve *et al.*, 2014).

In 2020 WHO described dementia as one of the most significant causes of disability in the older population, impacting the psychical and psychological well-being of the dementia patient and their families, carers, and general society (WHO, 2021b). Consequently, the costs associated with dementia represent a substantial economic burden globally. In 2010, worldwide dementia costs were estimated to be US \$ 604 billion, with western Europe and North America accounting for 70% of these costs (Wimo *et al.*, 2013). The costs rose to 818 billion in 2015, and it was predicted that they will increase to 1 trillion and then to 2 trillion by the years 2018 and 2030, respectively (Prince *et al.*, 2015; Prince *et al.*, 2014b). Due to the increasing population of older people worldwide, there is a significant risk of a further increase in these costs, especially in LMIC, where informal care accounts for most of the expenses (Wimo *et al.*, 2013). Therefore, dementia cases will soon become an overwhelming burden for world public health and the world economy.

2.6 Association between oral health and dementia

2.6.1 Oral health associated with dementia risk

Multiple studies have examined the association between dementia and oral diseases, such as tooth loss, dental caries and PD. This association is briefly elaborated below.

2.6.1.1 Tooth loss associated with dementia risk

Since the early 1990s, studies have evaluated dental status as a risk factor for AD, and results suggested that having a small number of teeth may be a risk factor for AD (Kondo *et al.*, 1994). Similarly, the Nun Study, a longitudinal study of ageing and AD findings, reported relative risk (RR) of developing dementia in people with < 10 teeth (1–9 teeth) was 2.2 times higher than in those who have > 10 teeth (10–28 teeth) (Stein *et al.*, 2007).

Syrjala *et al.* did not find that edentulous individuals had an increased risk of dementia (Syrjala *et al.*, 2012); however, a prospective longitudinal study conducted in France by Arrive *et al.* (2012) reported a significant interaction ($p = 0.002$) between education level and the number of missing teeth. The Hazard ratio (HR) for dementia was 1.27 (95% CI = 0.70 to 2.31) in persons with >10 missing teeth and with higher levels of education and 0.40 (95% CI = 0.17 to 0.94) in those edentates with lower levels of education (Arrivé *et al.*, 2012).

In an earlier meta-analysis conducted by Shen *et al.* (2016), including 11 studies and 20,858 participants, it was concluded that tooth loss was a risk factor for dementia. However, due to its inclusion of cross-sectional designed studies, the temporality of the associations is questionable. Furthermore, neither the process for the literature search (PRISMA guidelines) nor for assessing the quality of evidence used standardised tools and publication bias was given in the review and meta-analysis (Shen *et al.*, 2016).

Cerutti-Kopplin *et al.* (2016) in their meta-analysis of 8 studies of low heterogeneity found individuals with suboptimal dentition (<20 teeth) were at a 20% higher risk for developing

cognitive decline (HR 1.26, 95% CI = 1.14 to 1.40) and dementia (HR 1.22, 1.04 to 1.43) than those with optimal dentition (≥ 20 teeth). But the follow-up periods of the studies included in the meta-analysis varied from 4 to 32 years, which might explain the differences in the findings, and the information of the publication bias was missed for testing in the meta-analysis. Moreover, the four studies included were self-administered questionnaire which might not be as accurate as clinical studies (Cerutti-Kopplin *et al.*, 2016). Tonsekar *et al.* reported similar results in 2017, highlighting that tooth loss can lead to reduced masticatory function, which can diminish cerebral blood flow and proprioception to the brain. However, the results showed an inconclusive association (Tonsekar *et al.*, 2017) in the eight studies they reviewed.

Two years later, Oh *et al.* published a meta-analysis including 11 cohort studies, reporting that people with high residual teeth had decreased risk of dementia by approximately 50% compared to those low residual teeth (Oh *et al.*, 2018). But in their research, the observation period varied from 3-32 years, had different dementia definitions, and high/low number group might have led to over-generalisation of the findings, which may affect the quality of study for evidence.

A similar analysis conducted by Fang and colleagues found that the adjusted OR of 21 studies was 2.62 (1.90–3.61), and when adjusted results were pooled from 18 studies OR was 1.55 (1.41–1.70) (Fang *et al.*, 2018). The results should be viewed with caution as cross-sectional studies were included in the overall findings reported and they had missed an important cohort study by Arrive *et al.* (2012) which showed an inverse association of tooth loss with dementia risk.

Furthermore, a meta-analysis by Chen *et al.* (2018) indicated that patients with tooth loss faced a 1.34 times greater risk of developing dementia RR 1.34 (1.19-1.51). The result from this

dose-response meta-analysis, in a linear model, suggested that every missed tooth might increase the risk of dementia by 1.01 times RR 1.01(1.00-1.02) (Chen *et al.*, 2018).

Previous meta-analyses (Shen *et al.*, 2016; Cerutti-Kopplin *et al.*, 2016; Chen *et al.*, 2018; Fang *et al.*, 2018; Oh *et al.*, 2018) investigated the association of tooth loss with dementia and cognitive impairment. However, the findings from some systematic reviews were unclear about the association between tooth loss and dementia risk (Chen *et al.*, 2018; Tonsekar *et al.*, 2017), which could be due to issue related to the methodological quality from their synthesized evidence. In two meta-analyses (Shen *et al.*, 2016; Fang *et al.*, 2018) the findings of incident dementia were inaccurate as they included cross-sectional studies. Another issue was that two meta-analyses (Chen *et al.*, 2018, Shen *et al.*, 2016) did not show the quality appraisal of evidence using structured tools which lead to bias in the synthesized result reported. Four meta-analysis studies (Shen *et al.*, 2016; Chen *et al.*, 2018, Fang *et al.*, 2018, Oh *et al.*, 2018) failed to analyze cognitive impairment and dementia separately. The level of cognitive and functional impairment differs in people with dementia and MCI or other forms of mild impairment. Longitudinal design allows us to comment on the direction of the association between tooth loss and cognitive decline, heterogeneity across different studies still exists, such as the different methodological approaches and range of indicators used for dementia and oral health (PD). Furthermore, tooth loss could be due to PD, which could be the cause for tooth loss leading to increase of dementia as mentioned in next section.

2.6.1.2 Caries associated with dementia risk

Caries is another oral health condition with a strong association with dementia. In an early study, Chalmer *et al.* (2002) reported that coronal and root caries incidence and increments were significantly higher in the community-living older adults with dementia over the one-year follow-up period (Chalmers *et al.*, 2002).

Similar results were reported in a cross-sectional study conducted in nursing homes in the UK. It was found that decayed, missing and filled teeth (DMFT) scores were similar when compared between severe/moderate dementia versus no/mild dementia (Adam and Preston, 2006). In a Finnish cohort of older adults, similar patterns of increased caries rates were associated with cognitive impairment (Syrjälä *et al.*, 2007).

A 32-year follow-up cohort study of male veterans showed that the development of new caries or need for new restorations was associated with a greater risk of poor performance in MMSE and was more significant in men over 45.5 years of age at baseline (Kaye *et al.*, 2010).

In short summary, few studies have been conducted on especially caries relation with dementia risk, and the results are inconsistent. There are urgent needs of carrying out well-designed cohort studies to investigate the impact of caries on dementia.

2.6.1.3 Oral health factors associated with dementia risk

Denture

In 18-year follow-up cohort study in a retirement community in the US suggests that for denture wearers, adequate masticatory function involving ten or more upper and six or more lower teeth was associated with a lower risk of dementia (Paganini-Hill *et al.*, 2011). In contrast, a four-year cohort study in Japan showed that people with fewer teeth and no dentures were at greater risk for dementia (Yamamoto *et al.*, 2012). Compared with people having 20 or more teeth, those with fewer teeth and no dentures were at almost twice the risk of dementia (1.85, 95%CI 1.04 – 3.31, $p=0.04$); however, general health status, health behaviour and forgetfulness attenuated the association (Paganini-Hill *et al.*, 2011; Yamamoto *et al.*, 2012). In a meta-analysis of 8 cohort studies, it was reported that tooth loss patients without dentures might have a higher risk of dementia RR 1.53 (1.19-1.97) than those with dentures RR 0.98 (0.87-1.10) (Chen *et al.*, 2018).

Few studies of tooth loss associated with dementia included denture information. Future studies are required to include denture wearing information so that the readers can find its impact on dementia risk.

Mastication

Okamoto and collaborators reviewed the literature on the interaction between dental occlusion and human brain function. They concluded that ‘mastication and other movements stimulate the activity in the cerebral cortex and may help prevent degradation of brain function’ (Okamoto *et al.*, 2010). The proposed reasoning is that blood flow in the brain is increased, and parts of the cortex are activated during rhythmic chewing movements (Onozuka *et al.*, 2002). This was further supported by a study by Tada and colleagues in 2017, which found that masticatory disorders are risk factors for dementia or mild memory impairment (Tada and Miura, 2017).

Dry mouth

Dry mouth is the most prominent oral health problem among seriously ill patients and affects more than 90% of hospice cancer patients. This condition arises in advanced age not only due to somatic pathology but also due to a large number of medications taken (for example, non-selective β -adrenoceptor blockers, selective β (1)-adrenoceptor blockers, anticholinergic drugs, etc.) (Johanson *et al.*, 2015). In addition, reduction in salivary flow may be a fundamental factor of oral diseases such as dental caries and mucosal lesions (Chen and Kistler, 2015). Moreover, hyposalivation is also associated with dysphagia, halitosis and affects social activities (Chen and Kistler, 2015; Takeuchi *et al.*, 2015). In 2018, Sorensen *et al.* (Sørensen *et al.*, 2018) conducted a study on Danish men that reported poor salivary flow rates, hyposalivation, dry mouth, and poor oral health are risk factors for the decline in cognition in later years.

2.6.1.4 PD associated with dementia risk

As mentioned earlier PD was taken as a main indicator for poor oral health in this thesis. The findings of previous studies investigating PD associated with impact on increased risk of dementia risk were inconclusive. The results from seven studies (Nadim *et al.*, 2020) showed that pooled RR of dementia in relation to PD from all high-quality studies was 1.38 (95%CI 1.01–1.90). Further details are given in chapter 4.

2.6.2 Dementia associated with poor oral health

The poor oral health in people with dementia could be attributed to several reasons. First, it is difficult for dementia patients to maintain good oral health and personal hygiene (Hugo and Ganguli, 2014; Elsig *et al.*, 2015). Second, a patient's motor impairment, behavioural, and psychological disturbances can also make it difficult for caregivers to provide adequate care, resulting in more dental plaque accumulation, thus, increasing their risk of developing PD and dental caries (Zenthöfer *et al.*, 2017). Third, since behavioural and psychological aspects of dementia are dealt with as priorities, oral health care is often neglected by caregivers (Ettinger, 2000; Yi Mohammadi *et al.*, 2015).

One of the earliest systematic reviews was restricted to nursing homes residents with dementia and included seven controlled studies published until 2002 (Rejnefelt *et al.*, 2006). It reported the oral health status of people with dementia was poorer compared to those without dementia.

Another review (Delwel *et al.*, 2017), including 37 studies, found that older people with dementia have worse overall oral health than those without dementia. However, its results overlooked that number of teeth cannot represent the actual oral tooth condition, and there was unclear differentiation between people with and without dementia (Delwel *et al.*, 2017). Similar results were seen in other systematic review and meta-analysis studies (Foley *et al.*, 2017). However, the quality assessment for the review and publication bias for meta-analysis was not

given, which showed that it did not follow PRISMA guidelines, so the result should be viewed with caution as they also included cross-sectional study in findings (Foley *et al.*, 2017).

Recent systematic review and meta-analysis of nine case-control studies revealed that AD patients had an increased risk of missing teeth HR 1.52 (1.00–2.30) and edentulous condition HR 2.26 (1.70–3.01) (Dioguardi *et al.*, 2019). However, as all were case-control studies, the evidence might not be strong and did not show that tooth loss was only due to AD. On the contrary, a review by Lauritano *et al.* (Lauritano *et al.*, 2019) did not find any significant difference in the number of teeth between dementia and non-dementia groups (Lauritano *et al.*, 2019).

Three systematic reviews mentioned above (Delwel *et al.*, 2017; Lauritano *et al.*, 2019; Dioguardi *et al.*, 2019) showed that overall poor quality of evidence was emerging from the studies. Furthermore, in the recent systematic review found no significant differences between dementia and non-dementia group in increased risk of tooth loss or poor oral health (Lauritano *et al.*, 2019). These above reviews demonstrated the lack of high-quality studies present and gap in the knowledge in current literature.

2.6.2.1 Dementia associated with tooth loss risk

Nordenum (1996) examined differences in nutritional, dental status and oral function between institutionalised patients with Alzheimer's disease and cognitively healthy older adults living in the community. The study reported that having some natural teeth without dentures was the most common dental status and almost equal in the groups, 57%, 64%, 55% for controls, moderate and severe Alzheimer's groups respectively (Nordenram *et al.*, 1996).

Similar results were reported in a retrospective longitudinal study based on existing dental records. The mean numbers of teeth lost in 5 years were 1.21 for participants with dementia and 1.01 for participants without dementia (P=0.89) (Chen *et al.*, 2010).

Klotz (2020) reported that more advanced age and extended nursing home stay were significantly associated with a more significant number of missing teeth. In contrast, a shorter nursing-home stay was associated with a greater number of filled teeth (Klotz *et al.*, 2020). A recent case-control study conducted in Spain by Jornet *et al.* (2021), found that the patients with more severe disease were more likely to have fewer natural teeth (OR 11.00, 95% CI 1.28–23.22; $p = 0.001$), a higher plaque index ($p = 0.001$), and a greater bleeding index ($p = 0.001$) than the control group (Lopez-Jornet *et al.*, 2021).

2.6.2.2 Dementia associated with caries risk

In 1994, a longitudinal study conducted in the USA on age and gender-matched case-control followed up for 2-3 years reviewed the total number of remaining teeth and surfaces with coronal and cervical caries; revealed no statistical differences between dementia and non-dementia groups (Ship and Puckett, 1994). However, in 1997, Warren *et al.* reported that those with severe dementia had poorer gingival health and oral hygiene but better self-perceived mouth health. (Warren *et al.*, 1997).

Similar results were reported by Ellefson *et al.* in a cohort study (Ellefsen *et al.*, 2008). These results were also supported by a review (Lauritano *et al.*, 2019) showing that coronal caries and root caries were more common in people with dementia (than in those without dementia).

A recent meta-analysis (Zeng *et al.*, 2021) performed with twenty-four studies examined oral health in patients with and without dementia. Compared to controls, people with dementia had a significantly higher DMFT Index total score (MD 3.80, 95% CI: 2.21, 5.39) and a significantly lower number of remaining teeth (RT) (MD -3.15, 95% CI: -4.23, 2.06). Moreover, the pooled score for each component was 2.38 (1.56, 3.20) in decayed teeth (DT), 18.39 (15.92, 20.87) in missing teeth (MT), 2.29 (0.62, 3.95) in filled teeth (FT), and 11.59 (9.14, 14.05) in RT. (Zeng *et al.*, 2021). In this meta-analysis, cross-sectional studies were used, quality of the

studies were of poor quality, and most of the studies included did not report the type and severity of dementia and cognitive test results. There are few cohort studies on dementia association with caries.

2.6.2.3 Dementia associated with oral health factors

Denture

The findings are equivocal but highlight various issues relating to wearing and caring for dentures. In edentulous individuals, Adam and Preston (2006) conducted a care homes study. They showed that 60% of those with moderate to severe dementia wore no dentures at all compared with only 10% of those with no or mild dementia ($p=0.04$) (Adam and Preston, 2006). Hatipoglu *et al.* suggested that community-living people with moderate or severe dementia were less likely to remove their denture at night and were more likely to have denture-related stomatitis in both the maxilla and mandible ($p=0.001$ for all) (Hatipoglu *et al.*, 2011).

Dry mouth

A study conducted in Spain by Gil Montoya *et al.* (2016) reported that more than 70% of participants diagnosed with cognitive impairment or dementia had xerostomia compared to 36.5 % of those without (Gil-Montoya *et al.*, 2016). In an earlier study Ship *et al.* found that the submandibular gland salivary flow rate was significantly reduced in people with early AD. However, parotid gland salivary flow rates were the same as the control group (Ship and Puckett, 1994).

2.6.2.4 Dementia and cognitive impairment associated with PD risk

This section performed a systematic review and meta-analysis to examine the association of dementia and cognitive impairment with PD risk.

Background: People with dementia and cognitive impairment find it difficult to perform neuromuscular actions such as swallowing, walking, performing oral hygiene procedures to

remove plaque and stop the progression of PD (Chu *et al.*, 2015; Plassman *et al.*, 2007; Sanz *et al.*, 2017). It is unclear whether dementia or cognitive impairment also are associated with increased risk of PD. The findings of the current literature on this topic have been inconsistent; some studies have suggested that dementia (or cognitive impairment) is associated with an increased risk of PD (Zenthöfer *et al.*, 2016; Kaye *et al.*, 2010), while others did not (Ship and Puckett, 1994). This systemic review and meta-analysis aims to comprehensively examine the effects of dementia and cognitive impairment on PD risk and add new knowledge on this topic.

2.6.2.4.1 Methods

I followed the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (Liberati *et al.*, 2009) to run this systematic literature as I did in previous publication.

Search strategy

Relevant studies were identified through systematic search of the MEDLINE, PubMed, CINAHL, PsychINFO and SocINDEX databases from their inception to 25th October 2021. The strategy for the database search was developed using the Population, Exposure/intervention, Comparison and Outcome framework (PECO) (Liberati *et al.*, 2009). This strategy aimed to answer the following question: *Is there an association of dementia and cognitive impairment with PD in adults?* For all databases, I used the same terms for literature search: (oral health or oral hygiene or dental health or tooth loss or periodontal disease or periodontitis or gingivitis or periodontal infection or caries) AND (dementia or Alzheimer's disease or vascular dementia or cognitive decline or cognitive impairment). In addition, the bibliographies of relevant original articles and reviews were screened. The search for relevant articles included all studies with no language restriction. To ensure all searches were performed according to the planned protocol, another researcher (Dr JT) also used the same key terms to search all databases.

Inclusion and exclusion criteria

The selection of articles for the systematic review was based on the following inclusion criteria: (1) the study investigates an association of dementia and cognitive impairment with PD; (2) a cohort study or case-control study (in which cases were PD patients and controls were non-PD participants); (3) the study elaborates on dementia or cognitive impairment (or cognitive decline) diagnosis criteria; (4) the study's outcome of interest was PD and it reports any of the following periodontal parameters or indices: PPD, CAL, modified community periodontal index (MCPI), community periodontal index treatment need (CPITN), BOP, GBI, AAP and ICD codes and studies reporting periodontal indexes. Studies were excluded if they were: (1) a cross-sectional study; (2) a case report, commentaries, editorial, review, animal studies or clinical trial; and (3) the outcome of interest was not PD. The titles and abstracts of all articles identified by the search were screened and assessed according to the criteria. If risk estimates were reported in several multivariate-adjusted models in the original studies, the one reported in the fully adjusted model was extracted. If two studies (Zenthöfer *et al.*, 2016; Zenthöfer *et al.*, 2014) were published using the same cohort data but with different follow-up periods, the study with longer follow-up period and greater sample size was used (Zenthöfer *et al.*, 2016). Grey literature was searched, and e-mails were sent to authors of potentially relevant articles for more information to judge their eligibilities.

Data extraction

Each of the articles was reviewed by two reviewers and assessed independently. A predesigned data extraction form was used to extract the necessary information from the chosen studies. Differences in reviewing literature and extracting data between the two reviewers were resolved through face-to-face discussion; if differences remained, a third reviewer (RC) discussed with them to reach an agreement. Data extraction included first author's name, publication year, study location, participants' recruitment strategy, sample size and follow up

period, baseline dementia (including any type of dementia, e.g., AD and VaD) and cognitive impairment diagnosis criteria, endpoint outcomes for PD cases and diagnosis criteria, data analysis and adjustment for confounders, and the findings.

Quality assessment

Quality assessment of each article was conducted by employing the Newcastle-Ottawa Scale (NOS) (Stang, 2010) (full details on the quality assessment procedure seen in chapter 4).

Meta-analysis

The available data from the selected studies, including HR or OR and their 95% confidence intervals (CIs), were pooled together as a relative risk (RR) of PD in dementia/cognitive impairment, with the assumption of achieving a common unit of comparison. The data were pooled from each studied population, for all types of dementia first (if the studied population did not provide data of all dementia, subtypes data was used), and then for cognitive impairment separately. In the studies where RR of PD in relation to dementia (or cognitive impairment) was not presented but the study provided basic data, the crude RR was calculated and 95% CIs. Random effect model was used to estimate RR provided there was a statistically significant heterogeneity test, indicative of differences amongst included studies; otherwise, a fixed-effect model was employed. A funnel plot was used to assess small-study effects, and the possibility of publication bias was evaluated using Egger's regression asymmetry test (Egger *et al.*, 1997).

All the studies which provided adjusted RR or crude RR were used for the main analyses to assess association of dementia and cognitive impairment with PD. If the study gave dementia and CI values, both were used, and if there were more than one dementia/ cognitive impairment measures all were taken for the analyses. Further analysis was also performed to calculate the

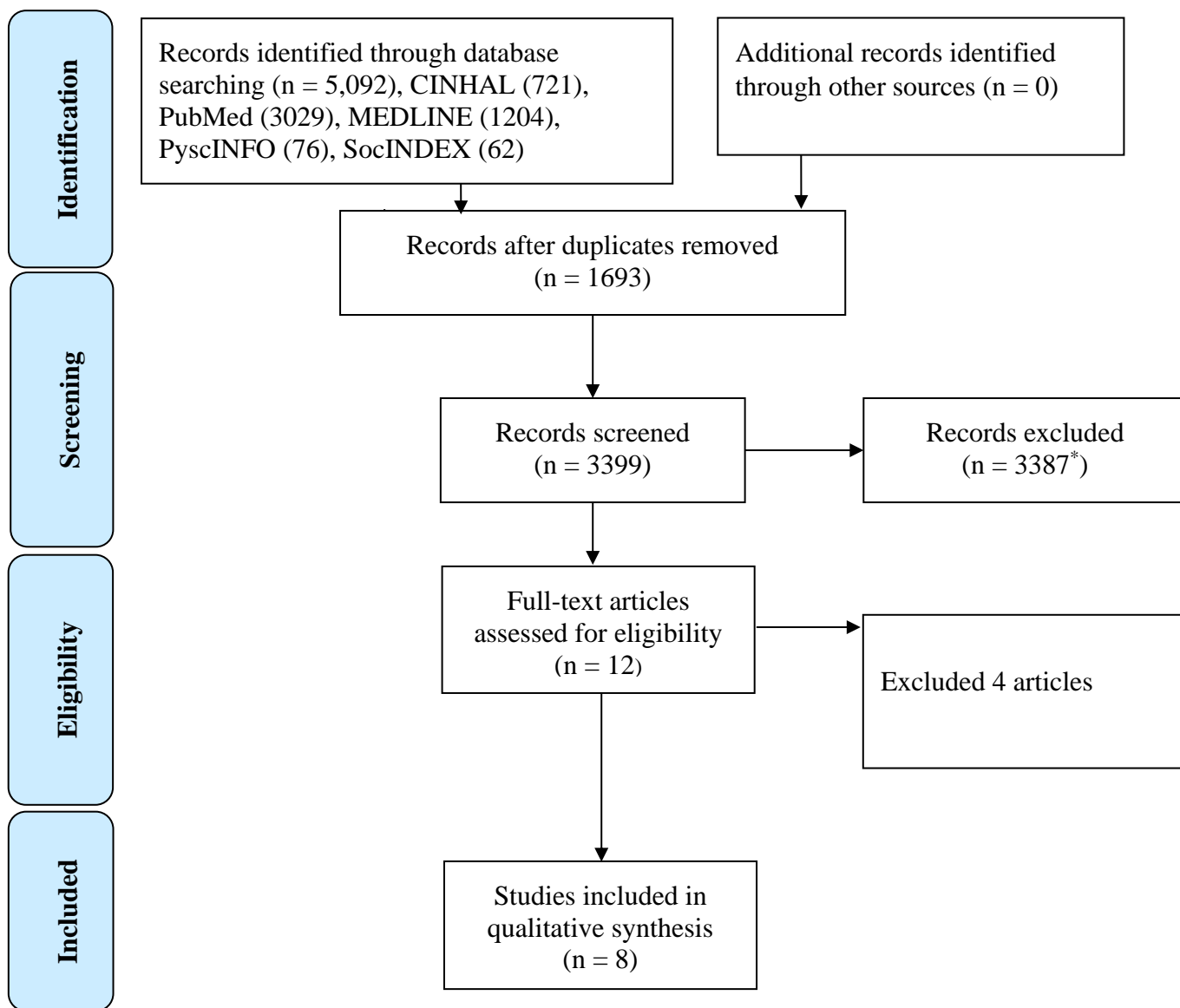
pooled RR of different study designs (case-control and cohort studies) and using only adjusted RR studies.

2.6.2.4.2 Results

Findings of the systematic literature review

The searches retrieved 5092 hits from five databases. After removing duplicates, 3399 papers were screened on basis of their titles and abstracts. Once those which did not meet the inclusion criteria were removed, 12 papers remained. After reviewing the abstracts and main text of papers, eight papers (Ship and Puckett, 1994; Chen *et al.*, 2010; Naorungroj *et al.*, 2013; Kamer *et al.*, 2012; Zenthöfer *et al.*, 2017; Ma *et al.*, 2021; Gil-Montoya *et al.*, 2017; Aragon *et al.*, 2018) were included in the review (figure 2.2).

Figure 2.2: Flow chart for literature search, selection and inclusion of studies for systematic review on association of dementia and cognitive impairment with periodontal disease



* Reasons for exclusions: Appropriate outcome not reported, Randomized control trial; Assessed another exposure other than dementia (or any specific type of dementia), Assessed another outcome other than PD, Articles on association between tooth loss and dementia or cognitive impairment, News briefs, Articles on caries, mastication and denture, Literature review/meta-analysis, Presentation, Cross-sectional study design

Of the eight articles included in the review, four were prospective cohort studies, two retrospective cohort studies, and two case-control studies. Five studies (Aragon *et al.*, 2018; Ship and Puckett, 1994; Chen *et al.*, 2010; Zenthöfer *et al.*, 2017; Ma *et al.*, 2021) examined dementia only, two studies assessed (Kamer *et al.*, 2012; Naorungroj *et al.*, 2013) cognitive impairment only, and one study examined both dementia and cognitive impairment (Gil-Montoya *et al.*, 2017). The identified studies were published between 1994 and 2021. All eight studies were conducted in high-income countries (HICs) or regions; three were from the USA (Ship and Puckett, 1994; Chen *et al.*, 2010; Naorungroj *et al.*, 2013), two were from Spain (Aragon *et al.*, 2018; Gil-Montoya *et al.*, 2017) and one each were from Germany (Zenthöfer *et al.*, 2017), Denmark (Kamer *et al.*, 2012) and Taiwan (Ma *et al.*, 2021). Of the eight studies, six were cohort studies (Ship and Puckett, 1994; Chen *et al.*, 2010; Naorungroj *et al.*, 2013; Kamer *et al.*, 2012; Zenthöfer *et al.*, 2017; Ma *et al.*, 2021), with sample sizes which varied from 42 to 17280 participants and follow-up periods between 2 to 20 years. Two were case-control studies (Aragon *et al.*, 2018; Gil-Montoya *et al.*, 2017), which included 670 participants (two case-control studies had 310 cases and 360 controls).

Quality of the eligible studies

The overall quality of these studies was good, with a mean score of 6.63 (as summarised in Tables 2.1 and 2.2).

2.6.2.4.3 Review and synthesis of the eight studies

The descriptive account and the findings of each of the included studies are as follows. Appendix 12 and 13 document the details of the characteristics and outcomes for the six cohort studies and the two case-control studies, respectively.

Table 2.1: Quality evaluation of the cohort studies using Newcastle-Ottawa Scales (NOS)

Cohort studies	<i>Chen et al.</i>	<i>Zenthofar et al.</i>	<i>Kamer et al.</i>	<i>Naorungroj et al.</i>	<i>Ship et al.</i>	<i>Ma et al.</i>
Selection of cohort						
1 Representativeness of the exposed cohort	★		★	★	★	★
2 Selection of the non-exposed cohort	★	★	★	★	★	★
3 Ascertainment of exposure	★	★	★	★	★	★
4 Demonstration that outcome of interest was not present at start of study		★		★		★
Comparability of cohorts						
1 Comparability of cohorts on the basis of the design or analysis	★	★	★	★ ★		★ ★
Outcome						
1 Assessment of outcome	★	★	★	★		★
2 Was follow-up long enough for outcomes to occur		★	★	★		★
3 Complete follow up- all subjects accounted for	★					★
Total score:	6/9	6/9	6/9	8/9	3/9	9/9

Table 2.2: Quality evaluation of the case-control study using Newcastle-Ottawa Scales (NOS)

Case-control studies	Aragon <i>et al.</i>	Gil Montoya <i>et al.</i>
Selection		
1 Is the case definition adequate?	★	★
2 Representativeness of the cases	★	★
3 Selection of Controls	★	
4 Definition of Controls		★
Comparability		
1 Comparability of cases and controls on the basis of the design or analysis	★ ★	★ ★
Exposure		
1 Ascertainment of exposure		
2 Same method of ascertainment for cases and controls	★	★
3 Non-Response rate	★	★
Total score:	7/9	7/9

2.6.2.4.4 Meta-analysis of eligible studies

The pooled data of all the eligible articles from described above indicate the influence of dementia/cognitive impairment with PD. Two studies (Ship and Puckett, 1994; Aragon *et al.*, 2018) had data that could not be used for the calculation of risk (Aragon *et al.*, 2018). Thus, data from six studies (Chen *et al.*, 2010; Naorungroj *et al.*, 2013; Zenthöfer *et al.*, 2017; Kamer *et al.*, 2012; Gil-Montoya *et al.*, 2017; Ma *et al.*, 2021) (including nine studied population) were used for meta-analysis (Figure 2.3). Of them, four studies (Naorungroj *et al.*, 2013; Kamer *et al.*, 2012; Zenthöfer *et al.*, 2017; Ma *et al.*, 2021) (which studied six populations) provided data of multiple adjusted RR and 95% CIs of PD and two studies (Chen *et al.*, 2010; Gil-Montoya *et al.*, 2017) (which studied three populations) provided crude data for calculating OR only. One study provided data for both dementia and cognitive impairment in findings (Gil-Montoya *et al.*, 2017).

Overall, among nine studied populations, the RR of PD in dementia or cognitive impairment was 1.54 (95% CI 1.18-2.01) (Figure 2.3). The funnel plot did not suggest any publication bias (Eggers' method, $p=0.372$) (Figure 2.4). Data from three studies of dementia patient populations (Chen *et al.*, 2010; Gil-Montoya *et al.*, 2017; Ma *et al.*, 2021) demonstrated a significant positive association of dementia with PD (RR 1.92, 1.78-2.08). Pooled data from six studied populations examining cognitive impairment (Kamer *et al.*, 2012; Naorungroj *et al.*, 2013; Gil-Montoya *et al.*, 2017; Zenthöfer *et al.*, 2017) showed a non-significant positive association (RR 1.09, 0.95-1.24) (Figure 2.3).

Figure 2.3: Forest plot of case-control and cohort studies for the pooled (RR) of cognitive impairment and dementia with PD

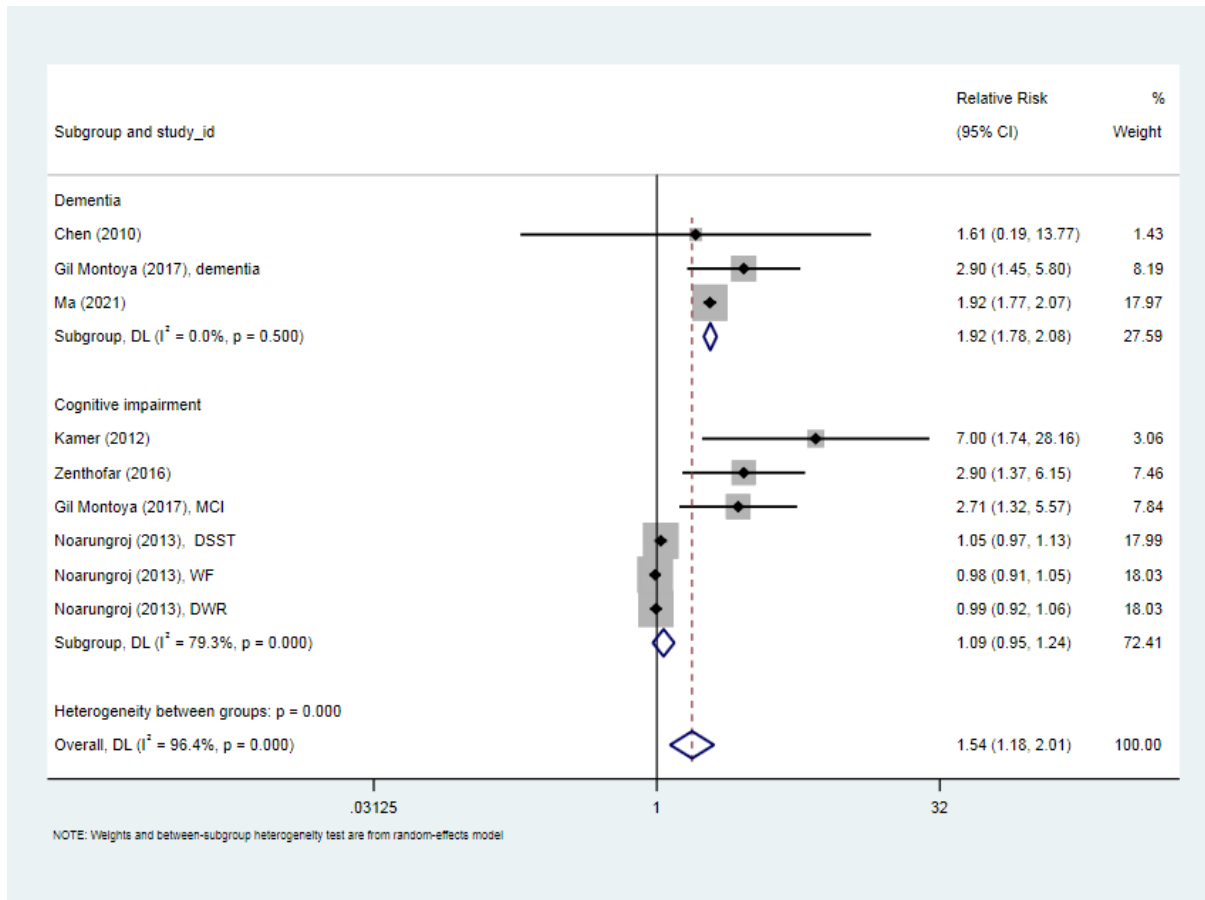


Figure 2.4: Funnel plot assessing publication bias of case-control and cohort studies

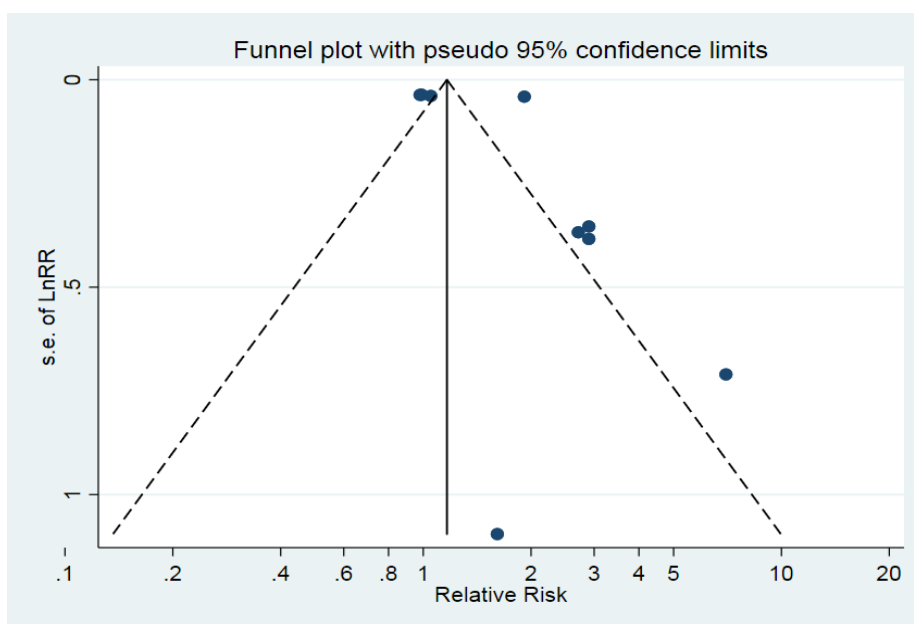
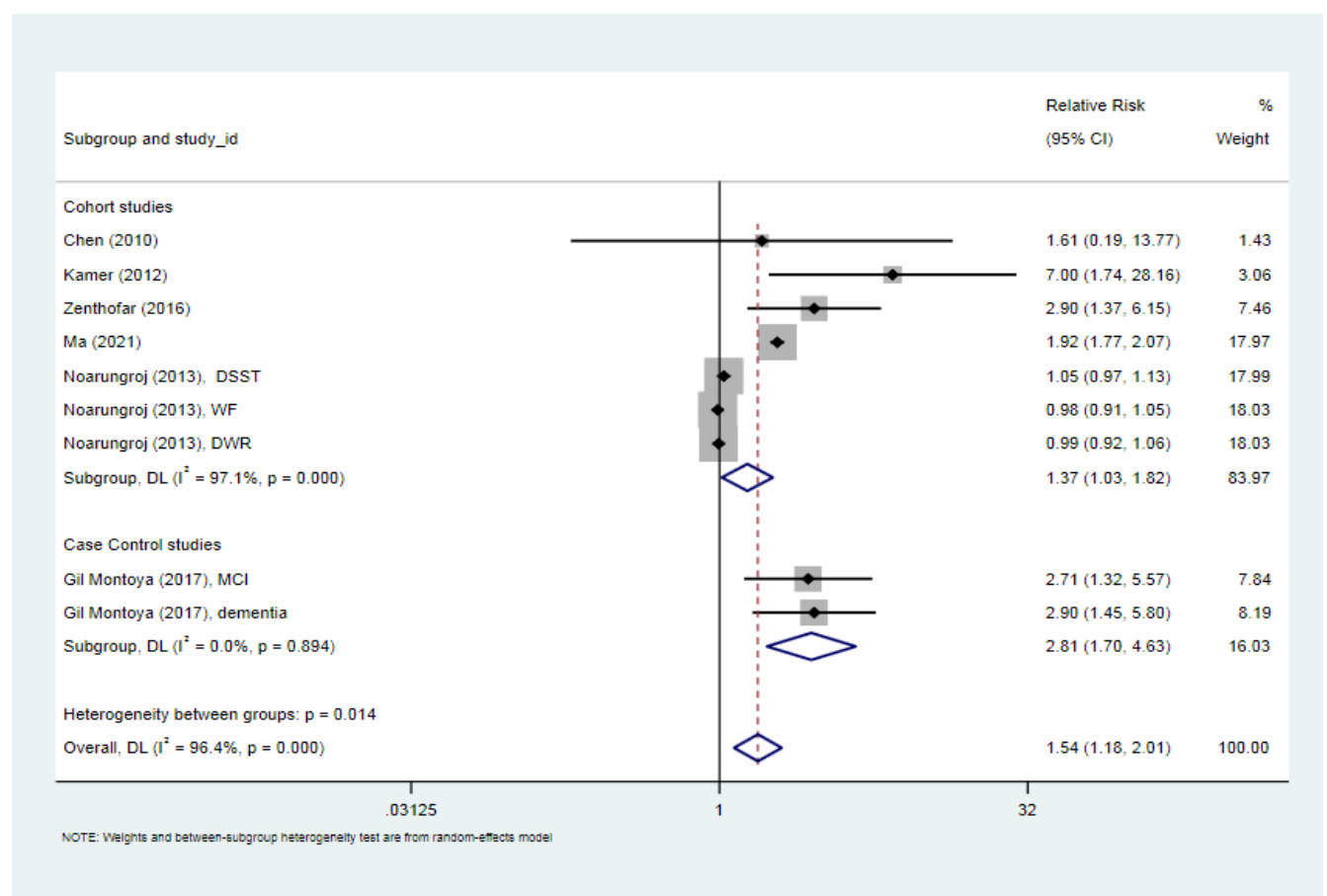


Figure 2.5 shows further analyses by study design (nine studied populations). The pooled data of seven studied populations from the cohort studies showed a RR of 1.37 (1.03-1.82) of PD, and the pooled data of two studied populations from the case-control studies revealed a higher RR (2.81,1.70-4.63).

Figure 2.5: Forest plot showing pooled relative risk (RR) of PD in the cohort and case-control studies respectively



In the five cohort studies of dementia and cognitive impairment, the overall pooled RR of PD was 1.37 (1.03-1.82), as shown in Figure 2.6. After excluding two studies (Chen *et al.*, 2010; Gil-Montoya *et al.*, 2017) which only provided the crude OR data, the pooled RR from four adjusted RR studies (Naorungroj *et al.*, 2013; Zenthöfer *et al.*, 2017; Kamer *et al.*, 2012; Ma *et al.*, 2021) was 1.36 (1.02-1.82) (Figure 2.7).

Figure 2.6: Forest plot showing pooled relative risk (RR) of all cohort studies

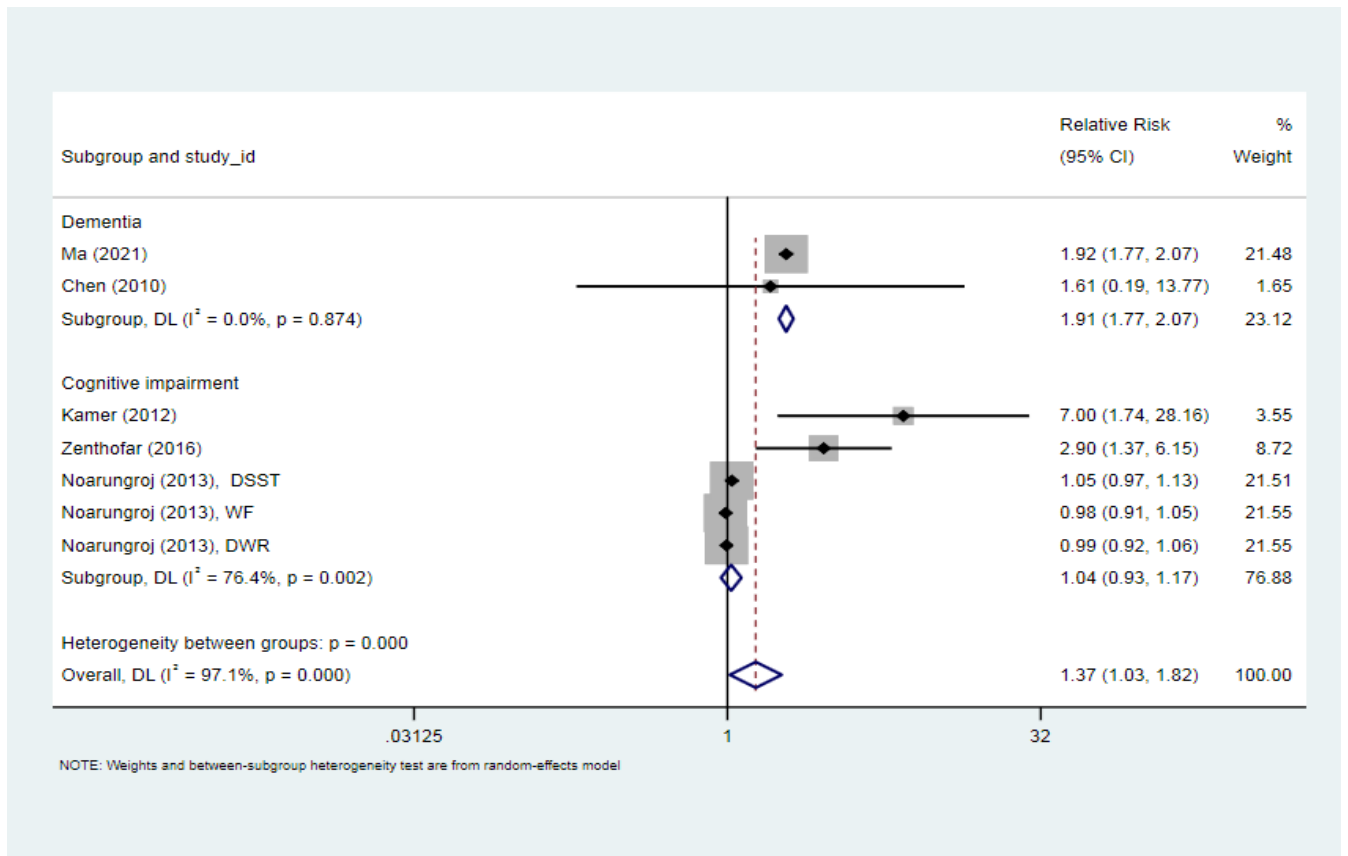
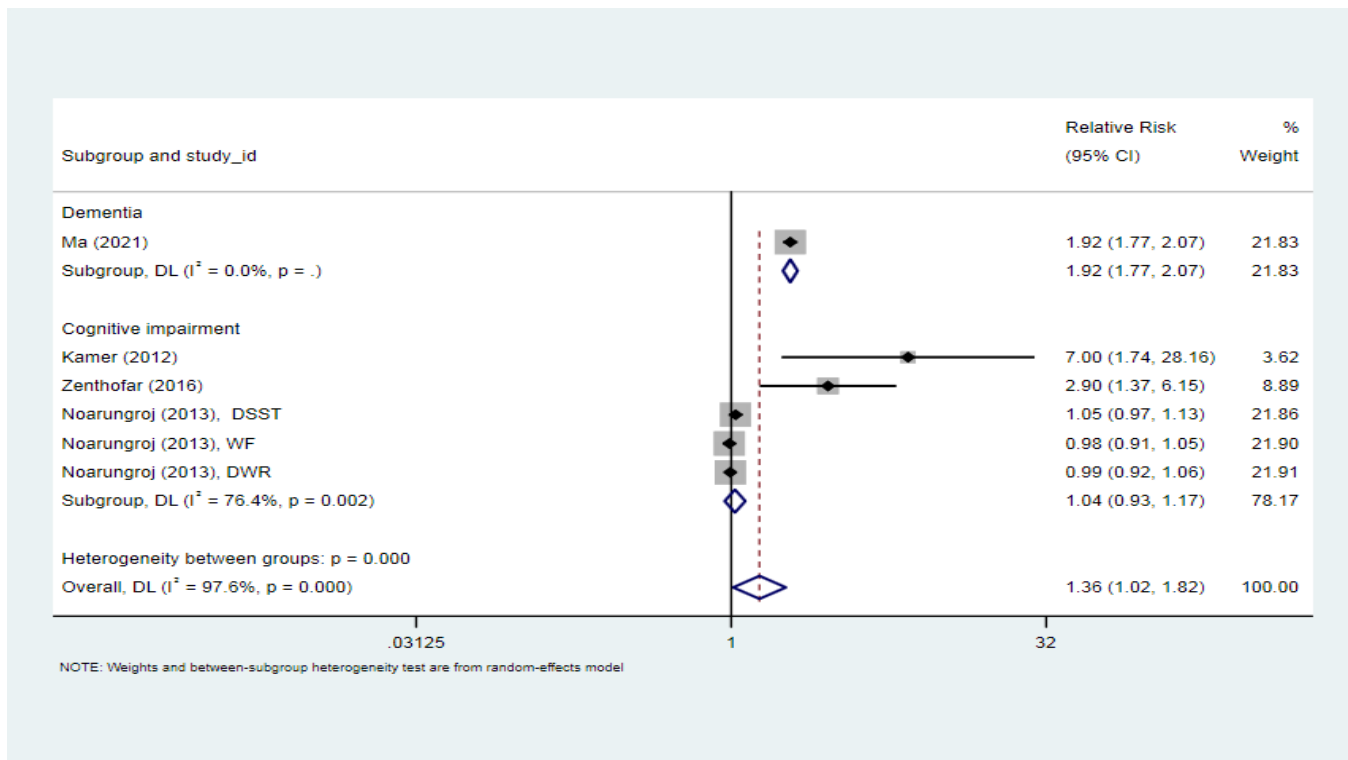


Figure 2.7: Forest plot showing pooled relative risk (RR) of adjusted cohort studies only.



2.6.2.4.5 Discussion

Strength and limitations

To the best of my knowledge, this study is the first systematic review and meta-analysis that comprehensively explored dementia and cognitive impairment relation with risk of PD in the general population. In this systematic review, case-control and cohort studies were selected and data was further analysed using only cohort studies in meta-analysis to measure the association of dementia/cognitive impairment with PD; the results remained similar. Furthermore, the quality of the included studies was evaluated and shows the overall quality is good for the evidence of dementia/cognitive impairment association with PD.

There are a few limitations to this study. First, there is considerable variation in the selected studies concerning the criteria used to define PD and diagnosis for dementia or cognitive impairment. The variation in the methods used to assess dementia/cognitive impairment and PD in the studies may influence the pooled data findings, but they could not be analysed separately due to the small number of studies in each of those methods. However, as the measures used in each study were validated, the influence on the results of this study should be minimal. Second, all the studies included in this systematic literature review were from high-income countries/regions (HICs), and no study was from low income or middle-income countries (LMICs) where the risks of dementia are higher than HICs. Thus, the findings may have a generalisation issue globally. Third, two studies with crude RR data were included in the meta-analysis, which might influence the result due to residual confounding. Moreover, the majority of studies did not include adequate control for known confounders (for example, age, gender, smoking, alcohol, education, income and co-morbidities as mentioned in Appendix 12 and 13), and only four studies (Naorungroj *et al.*, 2013; Zenthöfer *et al.*, 2017; Kamer *et al.*, 2012; Ma *et al.*, 2021) adjusted for covariates. Also, the small number of primary studies present in the literature may limit the application of the findings, and further studies are

warranted to validate these findings. Future original studies should be encouraged to analyse the data for dementia and cognitive impairment separately, which would contribute to identifying their differences in their association with PD.

Biological mechanism

A possible *biological* mechanism through which dementia may independently contribute to declining oral health (PD) can be because of saliva (Ship and Puckett, 1994). Salivary gland function is controlled by the autonomic and central nervous system. Parasympathetic nerve stimulation increases secretion of saliva from the salivary glands (Pedersen *et al.*, 2012). Salivary gland hypofunction can be due to medication intake, trauma or behavioural factors of neurogenic origin (Sørensen *et al.*, 2018). Saliva is essential for the maintenance of a healthy oral flora, and diminished output may cause loss of buffering capacity and creating a potential for plaque build-up, gingivitis and PD (Mandel, 1989). Another plausible mechanism is the loss of cognitive and motor skills as dementia progresses reduces sufferer's the ability to care for themselves. This includes carrying out oral hygiene procedures can thus lead to PD (Warren *et al.*, 1997). Existing research also shows that oral health problems become even more prevalent in older people with dementia; as the disorder progresses, cognition, motor skills, and self-care decline increasing the risk of oral health problems (Noble *et al.*, 2013; Elsig *et al.*, 2015). Another biologic plausibility includes shared genetic risk factors for PD and dementia. AD related genes from Genome Wide Association Studies (GWAS) overlap with the PD genes, including bacteria (*Porphyromonas gingivalis*), which is main pathogen in causing PD suggesting that susceptibility genes and pathogen, and this may promote pathogens and genes condition each other (Carter *et al.*, 2017).

2.6.2.4.6 Implications and conclusions

This section of the systematic literature review and meta-analysis study demonstrated that people with dementia/ cognitive impairment had an increased risk of PD. As the world's ageing population is growing, more people have dementia and cognitive impairment. This implies that an increased number of older adults would be susceptible to dental diseases. Specified policy and individual changes should be introduced to delay the onset of PD in patients with cognitive impairment and dementia.

In conclusion, this meta-analysis study has provided the evidence for a positive association of dementia/cognitive impairment with PD risk. Improving oral health for people with dementia can reverse most of the PD complications. More research using prospective cohort study designs is now required to better understand potential direction of causality between dementia and PD.

2.6.3 Summary of association between oral health and dementia for the knowledge gap

In summary, in the past two decades, bidirectional association between oral health and dementia has been investigated. However, the findings of the studies are inconsistent (Wu *et al.*, 2016; Kapellas Kostas 2019; Liccardo *et al.*, 2020), which could be due different in methodologies and measures used for assessing both oral health and dementia. Also, most of the existing studies are from HICs, and few studies have been done in middle-income countries (MICs) and LMICs. Furthermore, the current knowledge from quantitative studies cannot reflect caregivers' perceptions and views on the association between oral health and dementia, and no focus group study has been done on this topic. Hence there is a gap in knowledge indicating a need for further study.

2.7 Rationale of the study

Very few studies have explored the bidirectional association between oral health and dementia. However, in the last decade, there has been growing interest in investigating whether poor oral health causes dementia and vice versa.

Although studies have been carried out to examine this association, their findings are inconsistent, predominantly those from the HIC countries, while data from LMIC information is limited. Also, there is no consistency as exposure and outcome measures are varied, making conclusions difficult. Therefore, exploring the bidirectional relationship between oral health and dementia is paramount.

Moreover, previous studies on oral health and dementia are predominantly of quantitative design (Lee, 2000; Choi *et al.*, 2019; Demmer *et al.*, 2020; Lee *et al.*, 2017a), which could not reflect people's views and perceptions. Therefore, it is expected that discussing with caregivers and getting their personal experience and perception, the public's views on the oral health association with dementia and the determinants that can affect them will be better understood.

2.8 Research questions and objectives

2.8.1 Research questions

Does poor oral health increase the risk of dementia? If yes, which oral health measures significantly predict the risk of dementia?

Do people with dementia or severe cognitive impairment have worse oral health than people without dementia? If yes, what are the reasons for it?

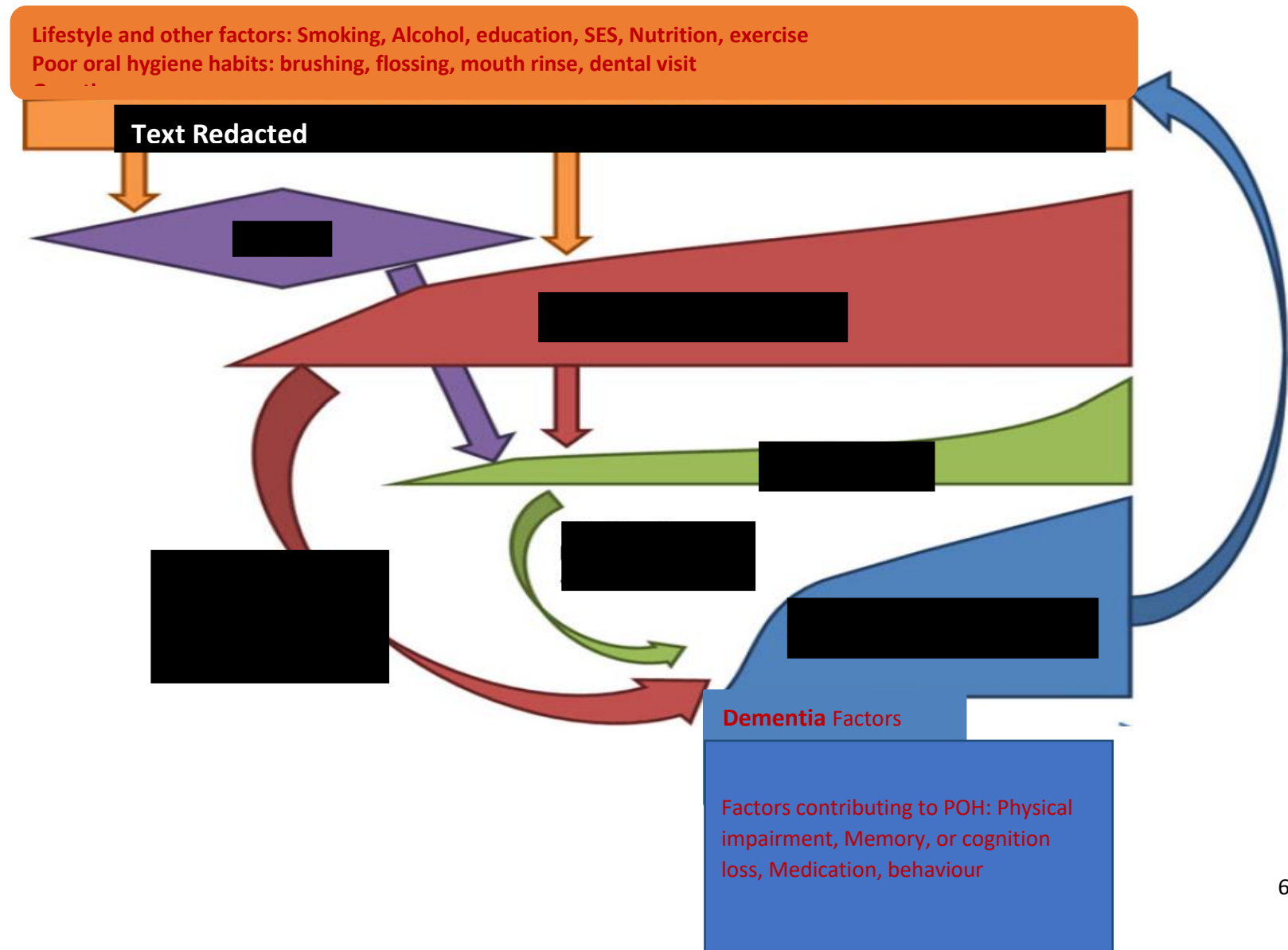
2.8.2 Specific objectives

- To investigate the influence of periodontal disease and oral hygiene conditions on the increased risk of dementia.

- To examine the impact of oral health on incident dementia.
- To investigate whether people with dementia or cognitive impairment had an increased risk of incident oral health problems.
- To examine the influence of dementia on periodontal disease and oral hygiene conditions.
- To explore caregivers' perception of the bidirectional association between oral health and dementia.

2.9 Conceptual framework

Figure 2.8 Modified proposed pathway associating poor oral health with cognitive impairment and dementia (Noble *et al.*, 2013).



The conceptual model and research design for the study

The thesis used a conceptual pathway model of the association between poor oral health and cognitive impairment proposed by Noble *et al.* (2013), which was slightly modified for my PhD research work (Figure 2.8) (Noble *et al.*, 2013). It has been used as a testing framework for the project and to reflect the assumed causal thinking by the researcher. The thesis uses a mixed-method design based on convergent parallel databases. It includes quantitative research based on data from a cohort study conducted in the UK, a case-control study in China and a qualitative study of data generated from focus group discussions in the UK to understand the bidirectional association between oral health and dementia.

The original model by Nobel *et al.* (2013) considered the association between poor oral health and cognitive impairment. Two pathways were considered as the potential responsible mechanisms of how poor oral health could be associated with cognitive impairment and vice versa: inflammatory and nutritional. These two pathways, inflammatory and nutritional, were cited by different reviews (Wu *et al.*, 2016; Noble *et al.*, 2013).

In terms of the modified model, I used red font to highlight changes. I added “dementia” in the outcome in addition to cognitive impairment, resulting from poor oral health. Hence, dementia also becomes a factor contributing to poor oral health (PD and caries). The shared risk factors for this bidirectional relationship have been explained in detail, including environmental and lifestyle factors such as smoking, alcohol, education, SES, nutrition, exercise, poor oral hygiene habits: brushing, flossing, mouth rinse, dental visit and genetics to give a clearer picture of the association. These pathways are mentioned in chapters 2 and 4.

2.10 Summary

The current literature review has given an insight into the association between oral health and dementia. However, the lack of standardisation and homogeneity among variables in most of

the available literature highlights the need for further investigation and high-quality studies to determine the bidirectional relationship between oral health and dementia and explore which factors influence oral health and dementia.

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter describes and justifies the methodology of the current study, which explored and examined the association between oral health and dementia utilizing a mixed methodology combining quantitative and qualitative approaches. It also provides the background and an explanation of the rationale for using the mix-method design followed by an evaluation of its strengths and limitations. The quantitative and qualitative components of the overall design in terms of the case-control, prospective cohort, and focus group studies employed as well as the rationales for the choices made are explained. This chapter also describes the study design, participants, data collection method (e.g., interview materials and instruments), data analysis methods, trustworthiness, and ethical considerations of this study.

3.2 Mixed methodology

The thesis used a mixed methods approach to investigate the association between oral health and dementia. The overall goal of mixed methods research is to expand and strengthen a study's conclusions. Creswell and Clark (2007) defined mixed methods research as a research design with philosophical assumptions and methods of inquiry (Creswell and Clark, 2007).

“As a methodology, it involves philosophical assumptions that guide the direction of the collection and analysis of data and the mixture of qualitative and quantitative approaches in many phases in the research process. As a method, it focuses on collecting, analyzing, and mixing both quantitative and qualitative data in a single or series of studies. Its central premise is that the use of quantitative and qualitative approaches in combination provides a better understanding of research problems than either approach alone.”

This was later approved by a different researcher who suggested that mixed methods approach increases the strengths and reduces the weaknesses of using only a quantitative or qualitative research method because both research approaches are valuable and significant (Johnson and Onwuegbuzie, 2004, Kelle, 2006). This definition helps us understand that a careful combination of different study approaches can address various problems that arise from using one methodology. Furthermore, it has helped to answer research questions outlined in the thesis, thus making the results more robust.

3.3 Research paradigms

A paradigm is defined by Kuhn (1970) as a world view about a phenomena under investigation, referring to the beliefs shared by members of a specific scientific society that lead to the establishment and development of scientific knowledge (Kuhn, 2012). Paradigms are said to “*[establish] the parameters and [set] the boundaries for scientific research and, in the ordinary course of events, scientific enquiry is carried out strictly in line with it*” (Crotty, 1998).

3.3.1 Pragmatism

The philosophy of pragmatism appraises this thesis's study approach, which examines the association between oral health and dementia. It is not dedicated to a particular philosophical paradigm (Mackenzie and Knipe, 2006); instead, it emphasises the “what” and “how” of a research problem (Creswell, 2003) and is outcome-orientated (Biesta, 2010). The pragmatist approach is a theoretical stance that has been widely regarded as the “third paradigm” (Johnson *et al.*, 2007; Creswell, 2003). Therefore, pragmatism is a paradigm that provides the fundamental theoretical framework for the mixed-methods approach, where two traditional perspectives (positivist and interpretivist) are combined to achieve a better understanding (Tashakkori and Teddlie, 2003; Somekh and Lewin, 2005). Pragmatism is not committed to

any one system of philosophy and reality (Creswell, 2007). According to Tashakkori and Teddlie (1998), a pragmatic approach allows researchers to “*study what interests and is of value to [them], study it in the different ways that [they] deem appropriate and use the results in ways that can bring about positive consequences within [their] value system*”. The pragmatism paradigm aims not to replace either of the aforementioned paradigms but rather to draw from their strengths and minimise their weaknesses in single research studies and across multiple studies (Johnson and Onwuegbuzie, 2004). It is closely associated with quantitative and qualitative research methods (Tashakkori and Teddlie, 2010). Therefore, pragmatics utilises both the qualitative and quantitative modes of data collection to achieve the research objectives, concentrating on the outcomes and applications of research (Feilzer, 2010).

The current thesis has adopted a pragmatic approach as a mixed-methods design can strengthen the interpretations of research findings (Tashakkori and Teddlie, 2003). This pragmatic framework remains the most suitable theoretical framework for this study because the other available frameworks are not enough to answer the research questions. Pragmatism covers obvious limitations inherent in the quantitative and qualitative strategies of inquiry while leveraging their strengths and underpinning philosophies.

3.3.2 Positivism

Positivism can be described as one objective reality that is singular and unrelated to consciousness (Quinlan *et al.*, 2015). Moreover, Saunders *et al.* (2016) portray positivism as typically deductive and mainly used in quantitative research (Saunders *et al.*, 2016). The quantitative methodological approach mostly aligns with the positivist paradigm, which includes collecting facts, exploring the associations between them, and determining how they agree or disagree with the findings of previous studies (Mackenzie and Knipe, 2006). This philosophical paradigm assumes that the social and the natural world can be studied using a

similar approach, thereby providing explanations of a causal nature (Mertens, 2005). At the ontological level, through observation and experimentation, positivists focus on exploring social reality (Cohen and Manion, 2013). From the epistemological view, positivists attempt to keep their personal beliefs and insights detached from the investigated phenomena to avoid bias (Antwi and Hamza, 2015). The objectivist ontology and empiricist epistemology, confined in the positivist paradigm, require a quantitative research method that is objective or detached. Here the emphasis is on measuring variables and testing hypotheses linked to general causal explanations (Antwi and Hamza, 2015). Fadhel *et al.* (2002) describe it being “*chosen as the preferred worldview for research, which tries to interpret observations in terms of facts or measurable entities*” (Fadhel, 2002).

3.3.3 Interpretivism

Interpretivism dictates that all knowledge is about interpretation (Quinlan *et al.*, 2015). Also known as constructivism or subjectivism, is an approach to research that intends to understand peoples’ life experiences (Cohen and Manion, 2013). Constructivists differ from positivists in their assumptions about the nature of reality. In particular, they argue that truth and knowledge are subjective and culturally and historically situated based on people’s experiences and interpretations of reality (Ryan, 2018). Interpretivists use an inductive approach to generate theory through sensitive data gathering methods within a context, such as an interview, focus group (FG) discussion, or naturalistic observation that encourages participants to speak freely and understand the investigator’s quest for insight into a phenomenon that the respondent has experienced (Green, 2014). The “interpretivists” paradigm, although applicable to the quantitative approach, mostly aligns with the qualitative methodological approach or the mixed methodological approach to complement and support their findings (Mackenzie and Knipe, 2006).

3.4 Quantitative and qualitative research designs

3.4.1 Quantitative research

Quantitative research methods use numerical data or coded numerically to investigate relationships between variables (Quinlan *et al.*, 2015). One of the significant strengths of the quantitative research approach is the generation of highly consistent, precise, and reliable data (Apuke, 2017). Another major benefit is that scientific data collection and analysis methods make generalization possible with this type of approach (Queirós *et al.*, 2017). Due to applying well-established standards, quantitative research can be replicated, analysed, and compared with similar studies (Choy, 2014). In addition, another advantage of the approach is that data analysis can be conducted by a computer using statistical software packages, making it easier and more time efficient and requiring less effort when describing data results compared to the alternative approach, i.e., qualitative research (Gorard, 2001). Further, researcher detachment reduces personal bias, such bias can be avoided or minimised by keeping a “distance” from participating subjects and using accepted computational techniques. This helps to guarantee respondent anonymity and ensure that the objectivity of the researcher is not compromised (Eyisi, 2016). However, the quantitative research method has some limitations; for instance, its inability to independently generate in-depth knowledge about a particular topic under investigation as human behaviour or experience is not included (Crossan, 2003). Another limitation is the lack of resources for large-scale research and the need for a large sample size (Choy, 2014). I tried to overcome the limitation of quantitative study by using mixed methods approach so that qualitative data provided the information about carers’ beliefs and perceptions. The details of these limitations are mentioned in Chapter 9 section 9.4.2.

3.4.2 Qualitative research

Qualitative research, broadly defined, means “*any kind of research that produces findings not arrived at by means of statistical procedures or other means of quantification*” (Strauss and Corbin, 1990). The data collected through qualitative research are obtained through studying the experiences of individuals or groups, analysing interactions and communications of participants, and collecting and interpreting different types of documents, such as texts and images (Flick, 2007). Studies involving qualitative approaches are regarded as being subjective, where the researcher interpretation of the recorded events is paramount to address “*research questions that require explanation or understanding of social phenomena and their contexts*” (Snape D, 2003).

One of the strengths of qualitative research is the use of open-ended interview questions, which allow the researcher to learn and understand the underlying values and perceptions of participants (Choy, 2014). It is less structured than quantitative methods as it allows for flexibility, including probe and follow-up questions, during the interview process (Creswell, 2003). Qualitative research also uses an inductive analytical approach to explore and understand participants' perspectives on a research problem by identifying themes from the answers to the research questions (Creswell, 2012). This approach achieves research outcomes from a real-world situation by gradually unfolding a natural phenomenon. Furthermore, unlike quantitative research, which demands greater resources with limited options, data collection in qualitative research is more cost-effective with multiple sources available to the researcher (Choy, 2014).

The qualitative research approach also has some limitations, the most significant being that the process is time-consuming and there could be a lack of rigour in the findings, which could be due to the researcher's high involvement in the interview and other research aspects (Saunders *et al.*, 2016). Qualitative research is also fundamentally interpretative as the data can be

subjective to participants' views (Creswell, 1994) and is not concerned about the causal association, prediction, and generalisability of findings (Hoepfl, 1997). Finally, the qualitative research process demands that interviewers (researchers) be highly skilled to ensure that truthfulness, worthiness, rigour, and reliability is maintained throughout the process (Choy, 2014). However qualitative data was used as a part of mixed method approach and it helped in bridging the gap in knowledge from the quantitative data. The limitations of my study have been further discussed in detail in Chapter 9 section 9.4.2.

3.5 Rationale for mixed methods approaches

Mixed methods approaches vary and may incorporate various aspects of research such as methods, processes, and philosophy or a combination of these (Creswell and Clark, 2017). However, as seen in this thesis, the combined use of quantitative (cohort study and case-control) and qualitative (focus group) data in the research project will help to maximise the strengths of the study and limit the weakness associated with either approach.

The principal rationale for integrating quantitative and qualitative methods in the same study concerns the context of the research problem and the study's questions or aims (Creswell and Clark, 2017). In terms of this study, the quantitative phase of the research seeks to obtain numerical data that is generalisable to the entire population while the qualitative phase aims to use words to describe and understand the perceptions of caregivers on the association between dementia and oral health of people with dementia.

While mixing methods may pose challenges, it is deemed the most appropriate approach to meet the objectives of this thesis. Given the limited research on poor oral health influence on dementia and vice versa (as highlighted within the literature and systematic review), a mixed methods investigation is desirable to gain a broader and deeper understanding of the phenomena. Neither quantitative nor qualitative data in isolation could fully answer all the research questions (see Section 2.8). For example, quantitative data could be used to investigate

oral health status for people with dementia by examining the number of teeth present or the presence/absence of PD. However, this data cannot explore various perspectives such as why or how oral hygiene related factors could lead to good or poor oral health or increased risk of dementia. Therefore, this thesis includes quantitative data to objectively investigate cause and effect relationships and qualitative data from focus groups to examine the research questions through participants' perceptions. This data will support the thesis' findings and produce valuable recommendations for people with dementia that may assist policymakers in proposing appropriate policies and strategies.

3.5.1 Strengths and limitations of a mixed methods approach

Mixed methods are utilised when either the quantitative or qualitative method cannot by itself answer the research objectives in sufficient depth or breadth (Johnson *et al.*, 2007; Tashakkori and Teddlie, 2010); that is, it counterbalances the limitations of using quantitative or qualitative research alone (Johnson and Onwuegbuzie, 2004). Therefore, using mixed methods helps maximise strengths while minimising weaknesses. Furthermore, it strengthens the research by providing in-depth information, resulting in a better understanding of the research problem (Feilzer, 2010, Johnson and Onwuegbuzie, 2004). The use of mixed methods creates more differing results, increasing the robustness of the findings and strengthening the interpretations of a given result. Additionally, it provides an opportunity to obtain a more comprehensive and clearer picture of the study under investigation and mutual validation of results (Kelle, 2006). A mixed methods approach also presents a significant opportunity to enhance research skills and helps several publications from the work (Creswell and Clark, 2017).

Despite the strengths of mixed methods research, this methodology does have a few limitations, namely the requirement for knowledge of both quantitative and qualitative methods and the time-intensive nature of extensive data collection and analysis (Creswell, 2009). In addition to needing to understand more than one method, one must have technical knowledge of how to

integrate quantitative and qualitative studies and how to resolve any disagreement in terms of findings from various mixed methods research approaches, which poses a significant challenge (Johnson and Onwuegbuzie, 2004, Creswell and Clark, 2017).

3.5.2 Mixed methods design of this study: the convergent design by parallel databases

Creswell and Plano Clark (2017) have three core mixed method designs, including convergent, explanatory sequential, and exploratory. These design aspects include the timing, weighting, and mixing of quantitative and qualitative elements of a research project.

The *explanatory sequential design* (also referred to as the explanatory design) occurs in two distinct interactive phases. This design starts with the collection and analysis of quantitative data. The first phase is followed by the collection and analysis of qualitative data to explain or expand on the first phase's quantitative results (Creswell and Clark, 2017).

The *exploratory sequential design* (also referred to as the exploratory design) uses sequential timing and occurs in three phases. The first phase begins with the collection and analysis of qualitative data. The researcher conducts a development phase by designing a quantitative feature (e.g., new variable, instrument, intervention etc.) based on the qualitative results. Finally, in the last phase, the investigator quantitatively tests the new feature (Creswell and Clark, 2017).

The *convergent design* occurs when results of quantitative and qualitative data are collected and analysed independently, and their results are compared and combined during interpretation to find whether they support or contradict each other (Creswell and Clark, 2017).

The mixed methods design chosen for this research was the convergent mixed methods design (sometimes called a parallel study, convergence model, or simultaneous triangulation) (Creswell and Clark, 2017). A convergent mixed methods design was chosen for this thesis to obtain “different but complementary data on the same topic” (Morse, 1991). This design was important for this thesis as the quantitative and qualitative research questions (thus different

data) were mapped to an overarching, complementary research objective to develop a “complete” understanding of the phenomena (Creswell and Clark, 2017).

The parallel database variant of the convergent design adopted in this thesis is a newer type of convergent design. Creswell and Clark (Creswell and Clark, 2017) explained the convergent design with parallel databases is a “common approach in which two parallel strands of data are collected and analysed independently and are only brought together during the interpretation. The researcher uses the two types of data to examine facets of the same phenomenon, and the two sets of independent results are then synthesised or compared during the discussion”.

This thesis involves the use of three parallel databases or independent studies based on the data from case-control, prospective cohort, and focus group studies to examine the association between oral health and dementia. Figure 3.1 illustrates the convergent design using parallel databases for data collection and analysis in this thesis and shows the procedures for the quantitative and qualitative research approaches as components of the overall design. It also includes the point of integration of the findings at the interpretation stage (Chapter 9). Other variants of convergent design such as Questionnaire variant were not used as it gives one questionnaire with both quantitative and qualitative questions. Data-transformation variant was not used as qualitative data was not needed to be transformed into quantitative data. Fully integrated variant would not be appropriate for the research project data because it would not be able to capture the intended information needed for research questions of this project (Creswell and Clark, 2017). Also, it was already planned that three studies would be conducted, one of which had big dataset from ELSA and focus group for in-depth information which was necessary to answer research questions. Furthermore, there was not enough time or resources available to consider a cohort study design for this research work.

As mentioned above, three crucial aspects help decide choosing convergent mixed method. Timing could be sequential or concurrent. In this research, concurrent timing was adopted

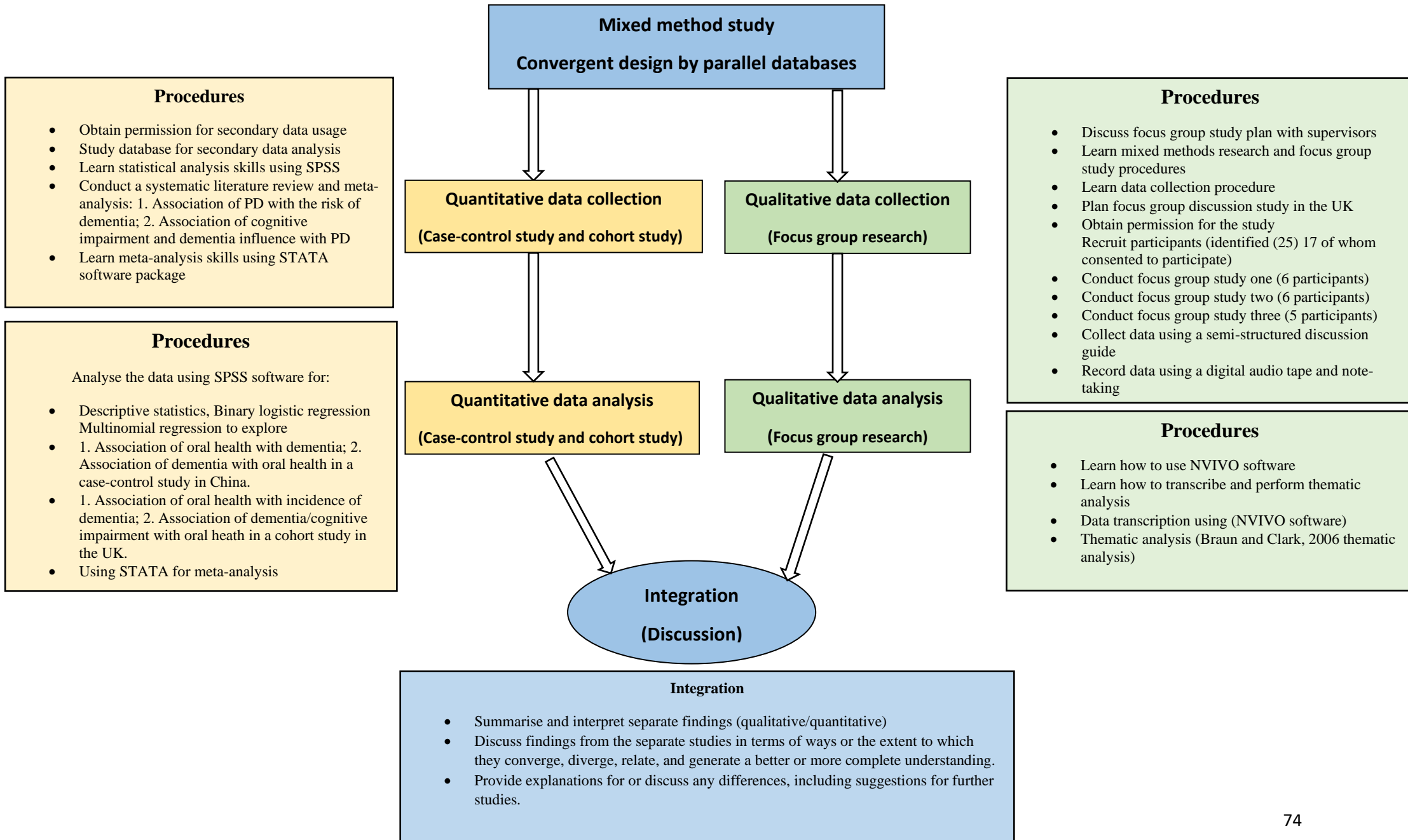
where quantitative and qualitative data were collected in parallel and both processed the data collection concurrently. Another compelling reason to use convergent design was due to limited time for collecting data to gather both types of data and ethical permissions needed for this research project. Which is the reason sequential mixed methods (exploratory or explanatory sequential method) conduct was not adopted.

Weighting shows degree of priority assigned to the two data collection phases in a mixed method research (Creswell, 2009). It is possible for the two parts to be unequal (i.e., putting emphasis on one method than the other). Both qualitative and quantitative strands had equal emphasis in this research, and the results of the separate strands were converged therefore playing complementary role to each other.

Integration type of mixing was chosen in this study. This involves integrating two parallel databases i.e., both quantitative and qualitative data together for comparison to know where they converge or diverge (Fetters, Curry and Creswell, 2013). In this study, both the quantitative and qualitative data are collected and analysed separately and mixed at the interpretation phase (discussion), with both the quantitative and the qualitative data complementing each other through provision of additional information.

In the diagram (Figure 3.1), the quantitative research involves examining the data of a large-scale cohort study (UK) and a case-control study from China to determine oral health association with dementia. The diagram (Figure 3.1) also showed that cohort and case-control studies were used to assess the association of dementia with oral health. The systematic review and meta-analysis, part of the quantitative research work, are also identified in the design. The qualitative aspect involves data from three focus group studies, the details of which are later explained, including the analysis strategy. The methodological framework for the selected mixed methods design is presented in Figure 3.1 below.

Figure 3.1: Methodological Framework: Convergent Parallel Database Mixed Method Design [modified from Creswell and Clark (2017)].



3.6 Quantitative research design

3.6.1 Case-control study

A case-control study is a type of observational study that retrospectively looks at factors associated with diseases or outcomes (Song and Chung, 2010). The researcher first identifies the cases (a group known to have the outcome) and the controls (a group known to be free of the outcome). The cases selected should have defined inclusion and exclusion criteria prior to case selection. Moreover, they should represent cases in the target population to strengthen the study's external validity (Song and Chung, 2010). The control group should have the same distribution of exposure as the case group (Song and Chung, 2010), be easily identifiable, and all controls need to be explained (e.g., population or hospital controls) (Mann, 2003, Song and Chung, 2010). Finally, the case-control study looks back to assess whether there is a statistically significant difference in exposure rates to a defined risk factor between the case and control groups (Lewallen and Courtright, 1998).

3.6.1.1 Strengths and limitations of the case-control study

Case-control studies are well suited to evaluate rare outcomes or outcomes with a long latency period because subjects are selected from the outset by their outcome status (Song and Chung, 2010). Thus, in comparison to cohort studies, case-control studies are quick, relatively inexpensive to implement, require comparatively fewer subjects, can utilise existing records, and allow for multiple exposures or risk factors to be assessed for one outcome (Song and Chung, 2010). Due to their efficiency, case-control studies may also be ideal for preliminary investigation of a suspected risk factor for a common condition; its conclusions may then be used to justify a more costly and time-consuming longitudinal study (Song and Chung, 2010). However, case-control studies are prone to selection or recall bias. These biases decrease the internal validity of the investigation and thus should be carefully addressed and reduced as much as possible in the study design (Mann, 2003). In addition, a case-control study can

investigate only one disease outcome at a time and no time sequence can be established; therefore, the results cannot be used to demonstrate causality (Hulley, 2007).

3.6.1.2 Rationale for using case-control study data in the thesis

A comparatively small number of participants are required for case-control studies, so more resources are available for studying each group. Consequently, more variables can be included for data collection. As aforementioned, this type of study is useful for generating hypotheses that can then be tested using other types of studies (Mann, 2003). Because of its efficiency, the case-control study may also be ideal for preliminary investigation of a suspected risk factor for a common condition (Rothman *et al.*, 2008). Given the multifactorial nature of dementia and PD, a case-control design also allows multiple risk factors or exposures for one outcome to be assessed (Song and Chung, 2010). In this study, the case-control design was primarily chosen because it allows for efficient use of the currently available data. If there is a confounder in the source population, the process of matching will superimpose a selection bias over the initial confounder, generally leading to biasing the results toward the null value of effect (Rothman *et al.*, 2008). If controls are selected to match the cases on a factor that is correlated with the exposure, controls who are more similar to cases with respect to exposure will be selected compared to when controls are randomly selected (Rothman *et al.*, 2008). As a result, the crude exposure frequency among controls will become similar to that of cases.

I have designed a case-control study to examine the association between oral health and dementia. The questionnaire for the case-control study is available in Appendix 11. Initially, I proposed collecting the data for the case-control study in Wolverhampton, UK, having received ethical approval from the National Health Service (NHS) [IRAS Project ID. 257823]. However, in March 2020, the data collection of the case-control study in Wolverhampton was suspended due to the COVID-19 pandemic. Fortunately, my supervisor, Dr James J Tang, had returned to Guangzhou, China for his research project (a case-control study of “air pollution and

dementia”) and completed his data collection, which included necessary variables for oral health measurements. Therefore, the research work in this thesis is based on the analysis of secondary data from a completed case-control study in Guangzhou, China. The reason for selecting this secondary dataset was that it had the same questionnaire and methodology as the case-control study in the UK. Approval for use and access to case-control data had already been granted for the research project, thereby reducing the burden on the researcher in terms of cost and time spent collecting new data.

3.6.1.3 Hospital-based case-control study

A hospital-based case-control study was chosen instead of a population-based study for three main reasons. First, after much consideration, hospital controls were preferred to community controls because they provide more similar information and have a similar usage of hospital services as the cases; dementia patients of this age group were likely to be hospitalised for multiple reasons. Second, the hospital-based case-control study could be more easily implemented and would enable interviewers to expediently contact cases and controls, thus facilitating data monitoring and quality assurance within a given time and budget. Third, extensive training for interviewers and close monitoring of data were required. This could be better accomplished by organising an interviewer team consisting of the co-investigators and focal points at each study site (hospital departments) rather than sending an individual interviewer to conduct interviews at different locations.

3.6.2 Guangzhou case-control study

The quantitative research for this thesis involves data from the Guangzhou case-control study in China. The method for the case-control study is described in the following sections.

3.6.2.1 Study location

Guangzhou is the capital of Guangdong Province (also known as Canton in China) and a thriving commercial centre. Located on the Pearl River, it is the third most populous city in China with 13.6 million people (see Figure 3.2).



Figure 3.2 Location of Guangzhou, China

3.6.2.2 Study design and setting

The case-control study was conducted at Guangzhou Hui'ai Hospital (Guangzhou Brain Hospital), which is the first psychiatric hospital to be operated in China. The case-control study employed a quantitative health survey as this method is typically used in epidemiological

research. The data collection of the case-control study took place from July 2020 to October 2020.

3.6.2.3 Study Population

Participant's recruitment and sample selection

Cases and controls were identified through the community health service clinics in Guangzhou city, which then transferred patient information to the dementia management system (DMS) and the physical examination service system (PES).

Cases were subsequently enrolled from the Community Neurology Management Department, Huihai Hospital (HuiH) through DMS, a system used to manage patients with dementia in Guangzhou. Annual follow-ups must be conducted on all patients in the system who have been diagnosed as having dementia by a neurologist using ICD-10 codes. The medical examination was provided by the Physical Examination Department, HuiH.

The control group was selected through the community health service clinics during an annual health check that included a cognitive function test. The data was then sent to the PES, which is managed by the Health Committee of Guangzhou for management and storage. With the support of four neurologists in HuiH, a local research team in Guangzhou (comprised of six graduate students and 18 community health staff), which was led by my co-supervisor (Prof Jie Tang) randomly recruited 233 cases and 233 controls from DMS and PES, respectively.

The inclusion and exclusion criteria are as follows:

Inclusion criteria for cases: (1) adults above the age of 50 years; (2) diagnosed with dementia.

All dementia cases were confirmed by a neurologist using the International Statistical Classification of Diseases and Related Health Problems (ICD) 10th revision diagnostic criteria (World Health Organization, 1992). *Inclusion criteria for controls:* (1) adults above the age of 50 years, (2) not dementia.

Exclusion criteria for cases and controls: The exclusion criteria for both case and control groups were as follows: (1) diagnosis of epilepsy; (2) diagnosis of meningioma or any other tumour; (3) diagnosis of psychiatric diseases (e.g., depression, schizophrenia, affective disorder and paranoid psychosis).

All participants and family members were informed about the study and the caregivers or legal representatives were required to sign an informed consent form prior to participation. Eligible participants were approached initially by two staff members at Huihai Hospital to protect patient privacy. Informed consent was obtained from each participant. If an individual was unable to provide informed consent due to disability or limited educational level, their next of kin or caregivers were invited to provide assent for participation. Then his or her details were handed to the investigator to make further contact. After contacting the individual and arranging a meeting, a face-to-face interview was conducted in a separate and safe place (their home, a hospital, or another place), which was determined in advance by the research team. The face-to-face interview for each participant lasted approximately 45 minutes. Participants were encouraged to have a family member or caregiver present during the interview for support. After completing the questionnaire, its integrity was reviewed, and the data encoded. Finally, the investigators signed the questionnaire interview completion form.

3.6.2.4 Data collection and tool development for the case-control study

3.6.2.4.1 Data collection measurement

In this research, validated standardised interviewed-administered questionnaires were used to collect information about the participants, which are described in more detail below.

3.6.2.4.2 General health and risk factor questionnaire

During the investigations, the main interview material employed was a validated Chinese version of the General Health and Risk Factor Questionnaire that was previously used in a case-

control study of elderly in China (Chen *et al.*, 2013b). The General Health and Risk Factors Questionnaire collects information on the following:

1. Socio-demographics, including age, gender, marital status, education, occupation, employment, accommodation, and social-economic status;
2. Air pollution (estimated by participants' residential home address and past movement);
3. Doctor diagnosed medical conditions and diseases and self-assessment of physical health and dental history;
4. Active and passive smoking;
5. Diet intake;
6. Social networking; and
7. Self-reported oral health.

3.6.2.4.3 Oral health measures

Oral health measures were documented from self-reports during interviews. Self-reported oral health was measured from questions on self-rated oral health status, oral hygiene, number of teeth present question and periodontal disease (as gum related problems and periodontal problems questions). The self-reported oral health is a broad multidimensional subjective assessment of oral health, which reflects current oral health status, but it also gives an indication about the mood and emotional state of the respondent (Locker *et al.*, 2005).

Self-rated oral health status question: Each participant was asked “*How do you perceive your dental health?*” (very good, good, fair, poor and very poor).

Self-reported oral health conditions question: Each participant was asked “*did you ever had: Teeth problems limit foods, Difficulties swallowing food, Sip liquid to aid swallowing food, Mouth feel dry when eating food*” (always, frequently, often, occasionally, never).

Oral hygiene questions: Each participant was asked “*Do you use dental floss and dental rinse/mouthwash* (always, frequently, often, occasionally, never). Each participant was asked about *brushing habits* (do not brush, less than once a day, once a day, twice a day, more than twice a day) and *dental visit habits*” (every six months, once a year, every two years, more than two years, try to avoid, have never been to the dentist).

Number of teeth present question: Each participant was asked “*How many natural teeth do you have in your mouth?*”.

Gum disease questions: Participants were asked about their gum condition with the following question: “*Have you ever had bleeding gums, swollen gums, painful gums, oral ulcers, and bad breath/taste?*” (always, often, sometimes, rarely, never).

Self-reported periodontal problems: Periodontitis-related questions were asked to each participant about “*Have you noticed that your front teeth have moved forward (toward the lips) or that gaps have developed between your front teeth?*”; “*Have any teeth become loose on their own, without any injury?*”; “*Have you ever received treatment for gum disease, such as scaling and root planning, sometimes called deep cleaning?*”; and “*Have you ever been told by a dental professional that you have lost bone tissue around your teeth?*” (yes, no, do not know/unknown).

3.6.2.4.3 Measures for dementia

Dementia was diagnosed by doctors using ICD-10 codes, which is the diagnostic classification standard for all clinical and research purposes.

3.6.2.5 Data entry

To establish a database, Epidata 3.1 software was used and to ensure the accuracy of the data entered; two investigators separately entered the same questionnaire responses. The final

electronic data were saved on the researcher's computer in an Excel file. The data was encrypted during the transfer process and could only be accessed by the research team.

3.6.3 ELSA Cohort study

3.6.3.1 The prospective cohort study design

Cohort studies are marked by the terms “follow-up”, “longitudinal”, and “prospective” to emphasise the following or tracking of a group of people with a defined characteristic (cohort) over time (Bhopal, 2016). The prospective cohort study design is a type of observational study that involves assessing exposure at baseline and conducting follow-ups to determine the outcome over a period of time. It involves measuring exposures as they occur in real time (Mann, 2003).

3.6.3.2 Strength and limitations of a cohort study

The prospective cohort study design is used for investigating cause and effect relationships (Caruana *et al.*, 2015). Cohort studies more clearly indicate the temporal sequence between exposure and outcome. As cohort studies measure potential causes before the outcome has occurred, the study can demonstrate that these “causes” precede the outcome, thereby avoiding the debate about cause and effect (Mann, 2003). It is a perfect fit for hypothesis testing and generation and makes it possible to determine and describe the incidents that occur throughout the natural disease history (Bhopal, 2016).

Limitations of cohort studies are that they require significant funds and are often time-consuming since cases take a long period of follow-up visits (Caruana *et al.*, 2015). The loss of some cohort members during follow-up is due to challenges of attrition (Caruana *et al.*, 2015). Another problem with cohort studies is that they are unsuitable for rare diseases or rare health events. The number of subjects studied in cohort studies is often large (since the majority might not show symptoms of the disease), making cohort studies impractical or unfeasible

(Mann, 2003). There is also the challenge of confounding variables, which demands a robust design that anticipates the limitations and uses sound statistical methods to address them (Caruana *et al.*, 2015).

3.6.3.4 Rationale for using a cohort study

Given the longitudinal nature of the research questions, a secondary dataset that asks questions on oral health and dementia at repeated time points was used. There was neither the capacity nor time to set up a new cohort study as part of this PhD. The English Longitudinal Study of Ageing (ELSA) was identified as the best available survey because it contained the data on oral health measures and dementia/cognitive impairment required to answer the research questions and has a large sample of adults aged 50 years and older. Furthermore, the prospective cohort study data for the thesis is based on over 8 years of follow-up. Potential confounders were assessed at baseline assessment and rigorous statistical methods were selected in the analysis to adequately limit bias in the study.

3.6.3.4 English Longitudinal Study of Aging (ELSA)

ELSA is a nationally representative multidisciplinary biennial longitudinal study of adults living in England aged 50 or above. ELSA was set up to capture the experience of growing old amongst the English population. It offers high-quality panel data that can be used to explore changes in economic circumstances, social status, physical and mental health, social relationships, cognitive function, and biology as people prepare for and move into retirement and old age (Steptoe *et al.*, 2012). The original sample was drawn from individuals who previously participated in the Health Survey for England (HSE) in the years 1998, 1999, and 2001 in an annual cross-sectional household survey, and wave 1 started in 2002–2003 (ELSA, 2019). Figure 3.3 for an overview of the original participants in ELSA below.

Figure 3.3: Summary of data collection in ELSA cohort (waves 1–9). (Source ELSA website)



3.6.3.5 Data collection

At each wave, data was collected from all participants, who were interviewed face to face (a computer-assisted personal interview [CAPI] followed by a self-completion questionnaire) every two years and subject to a nurse assessment every four years. Hence, nurse visits were carried out at waves 2, 4, 6, 8, and 9, during which various physical examination and performance data were obtained and blood samples collected for analysis. The study was replenished at waves 3, 4, 6, 7, and 9 with new HSE participants to maintain sample size and representativeness. Oral health data was reported at waves 3, 5, 7, 8, and 9. However, most of the questions remained the same through all the waves.

In this cohort study, all the variables analysed in this thesis are covered in the CAPI interview and the self-completion questionnaire, except for BMI data from the wave 4 nurse visit dataset. Participants in all cohorts gave full informed consent for participation. Ethical consent was obtained for all waves and components of ELSA, according to the ethical approval system in operation at the time.

Computer-assisted personal interviewing (CAPI)

The CAPI interview takes the form of a face-to-face interview. It contains various modules, each covering a different area of enquiry, such as household demographics, individual demographics, health, oral health, and financial and cognitive functions (CF).

Self-completed questionnaire

The self-completed questionnaire asks participants about their quality of life, social participation, control at work, life satisfaction, social network, diet and alcohol consumption, among others.

3.6.3.6 Data selection: Waves of ELSA used in this thesis

The analysis for this cohort study took data from wave 3 survey to wave 9 over a 14-year follow-up ELSA cohort. In the data analysis, data at wave 5 was taken as a baseline as this survey had a diagnosis for oral health and dementia, while necessary information from waves 3 and 4 would be used.

The first cohort data analysis sample was for studying *poor oral health association with incident dementia* (Chapter 6). In the cohort, the dataset *exposure* variables were three oral health measures, and the *outcome* variable was dementia. The oral health questionnaire was added to the survey from the third wave onwards. Therefore, the sample was drawn from those with early data in wave 3 and wave 5, preserving an adequate latency period for dementia diagnosis to the most recent available wave 9. The diagnosed dementia participants at waves 3-5 were excluded in order to obtain incident cases of dementia in the follow-up waves. Additionally, to minimise a potential bias from participants lost at follow-up, the participants for analysis would need to be interviewed at waves 3 to 5. The total number of participants 7,349 who were interviewed at wave 5 and also at wave 4 and wave 3. After excluding 112 participants aged below 50 years at wave 5, 163 participants were diagnosed with dementia at wave 5, wave 4 and wave 3; 610 participants were lost to the follow-up at waves 6-9; and 6,464 participants were left for analysis. I could not control selection bias in both the wave 3 and wave 5 of the study, but they were random samples so they could be similar to those in other waves, and the selective bias will be minimised.

The second cohort data analysis sample was used to examine *dementia/cognitive impairment association with poor oral health* (Chapter 7). Cognitive impairment was included as it could increase the number of participants as those “exposure”. In this cohort dataset, the *exposure* variables were dementia or cognitive impairment while the *outcome* variables were incident cases of three oral health measures. I selected participants from the wave 5 interviews as a

baseline since this survey had oral health questionnaire measures. The participants could have a diagnosis of dementia from waves 3 and 4, which helped identify those with dementia. Also, to minimise a potential bias from lost to follow-up, the participants for analysis were required to have interviews at waves 3, 4, 6 and 7. Thus the total number of participants for this cohort data analysis was 5,412, after excluding those who were below 50 years of age and had “poor SROH” at wave 5 (n=80). The number of participants analysed for different OH measures in the cohort follow-up (SROH, no teeth and oral impact) varied (see chapter 7 tables 7.12 -7.19 footnotes for detail). I could not control selection bias in waves 3, 4, 5, 6 and 7 of the study, but they were random samples so they could be similar to those in the other waves, and the selective bias will be minimised.

3.6.3.7 Variables of interest

3.6.3.7.1 Oral health variables

Oral health status was measured in this study using three self-reported oral health outcomes: edentulousness (the presence of natural teeth), self-rated oral health, and the Oral Impacts on Daily Performance (OIDP) questionnaire.

Self-rated oral health: In the ELSA dataset, self-rated oral health was assessed by a single question, “*Would you say dental health (mouth, teeth and/or dentures) is...?*”, with five responses categories: excellent, very good, good, fair and poor.

Oral impact: Oral health-related quality of life (OHRQoL) was measured in ELSA as the prevalence of oral impacts assessed through the simplified version of the Oral Impacts on Daily Performance (OIDP) questionnaire for elderly populations (Tsakos *et al.*, 2001). Self-rated oral health-related quality of life (OHRQoL) can be collected easily and inexpensively. Therefore, it could be used to quantify the impact of oral health on an individual’s daily functioning, well-being, or overall quality of life, (Lee *et al.*, 2013). This variable was assessed using five

commonly reported indicators included in the Oral Impacts on Daily Performance (OIDP) questionnaire via the following questions: “*In the past six months, have any problems with mouth, teeth, or dentures caused any of the following conditions?*”. There were six possible answers: Q1. *Difficulty eating food*; Q2. *Difficulty speaking clearly*; Q3. *Problems with smiling, laughing and showing teeth without embarrassment*; Q4. *Problems with emotional stability; e.g., becoming more easily upset than usual*; Q5. *Problems with enjoying the company of other people such as family, friends, and neighbours*; Q6. *None of these (total summed options 1–5)* with two possibilities: mentioned and not mentioned.

Tooth conditions: ELSA participants were asked, “*In relation to dental health, which of the following applies to you?*” with four categories to choose from: 1. *No natural teeth and wear dentures*; 2. *Both natural teeth and dentures*; 3. *Only natural teeth*; and 4. *Neither natural teeth nor dentures*.

Edentulism: A dichotomised variable was derived: dentate (having natural teeth) versus edentate (not having any natural teeth).

3.6.3.7.2 Dementia and cognitive impairment variables

Dementia: This was derived from ELSA participant’s questionnaire, which was combined self-reported doctor-diagnosed dementia and AD from each wave (waves 3-9). The question used was “*diagnosed dementia fed forward and diagnosed Alzheimer’s Disease (AD) fed forward*”.

Other related questions present in ELSA were “*Whether confirms dementia /AD diagnosis; Reason disputed dementia / AD diagnosis fed forward; Whether still has dementia /AD diagnosis and dementia/AD diagnosis newly reported*”.

Cognitive impairment: A memory index was taken from the ELSA dataset at wave 5. This variable combines results from three memory tests: 1. Asks respondents today's date, 2. Asks

respondents to carry out an instruction given to the respondent earlier in the interview, and 3. Asks respondents to remember a word list both immediately and after a delay.

Cut off point for cognitive impairment: The range of possible values for scores on the memory index spanned from 0 to 30 (Steel *et al.*, 2002). Mini mental state examination (MMSE) was used for cut-off points (<9 was severe cognitive impairment, 10–20 was moderate cognitive impairment, 21–26 was mild cognitive impairment, and ≥ 27 was normal) (Barrett and Burns, 2014) as it is commonly used for screening cognitive function and this memory index score was used to indicate the presence of cognitive impairment.

3.6.3.7.3 Covariates

Covariates taken at wave 5 were used for both cohort studies. The details of each variable category are presented in Chapter 6 (Tables 6.1 and 6.2) and Chapter 7 (Table 7.11).

Demographic variables: age (50 and above), gender, education level, employment status, marital status, and equivalised total income in quintiles.

Lifestyle factors: smoking status, alcohol consumption in the past 12 months, and BMI (Kg/m^2).

Cardiovascular disease conditions risk factors: the self-reported doctor-diagnosed cardiovascular conditions were hypertension, high blood cholesterol, diabetes mellitus, stroke, angina and heart attack.

Other systemic conditions including psychosocial variables: the self-reported doctor-diagnosed non-cardiovascular conditions were cancer, chronic lung disease, asthma osteoporosis, Parkinson's disease, and emotional, nervous, and psychiatric problems.

3.6.4 Data analysis

The data of the Guangzhou case-control study had already been cleaned by the research team in China and were ready for statistical analysis. The ELSA dataset was taken from the UK data service website. After data access was granted, I carefully managed it and explored the variables of interest using their data dictionaries. I cross-checked the dataset and recoded some variables for later use. I also merged some variable categories or modified variables for further analysis such as data transformation. This was accomplished by applying the transformation and recoding into different variable functions in SPSS on a computer. The variables merged are explained in Chapters 5, 6, and 7 in the sections on data analysis as well as in the table's footnotes.

In the Guangzhou case-control study and ELSA cohort study, there were a number of variables with missing data. Missing data (or missing values) is the data value that is not stored for a variable in the observation of interest (Graham, 2009). The problem of missing data is relatively common in almost all studies and may significantly affect the conclusions that can be drawn from the data (Graham, 2009). In the current thesis, the participants with missing data in covariates were treated as a special group for analysis. This is because those participants who did not provide information on a variable may have a special reason for not answering the survey question. All analyses were performed using SPSS version 26.0 (SPSS Inc., Chicago, USA).

Descriptive statistics

Descriptive statistics were used to examine the mean and standard deviation (SD) of continuous variables and percentage (%) and the corresponding P-value was presented. The differences in the proportions of controls and cases were tested using the Chi-squared test for categorical variables. Where the count was smaller than five, the Fisher's exact test or Likelihood ratio

was reported. The number of study participants in each category, percentages, and the corresponding P-value were presented.

Multivariate logistic regression

The analysis of case-control study data for the studies in the thesis involved multivariate regression analysis. It adjusts for confounding variables when measuring the association between exposures and an outcome. The thesis used two types of regression model analysis: binary logistic regression and multinomial logistic regression.

In Chapters 5 and 6, the *binary logistic regression* model was employed to calculate the odds ratio (OR) and 95% confidence intervals (CI) to examine different oral health measures with dementia.

In Chapter 7, the binary logistic regression model was employed in cohort studies to calculate the OR and 95% CIs to assess oral health measure association with dementia. *Binary or multinomial logistic regression models* were employed for data derived from case-control study to assess ORs, 95% CI, and overall P-values to a measure risk of self-reported oral health variables in participants with or without dementia.

3.7 Systematic literature review and meta-analysis

I included a systematic literature review and meta-analyses in the thesis method to assess the knowledge from literature and produce evidence on the association of oral health (PD) with dementia and vice versa. In the systematic review and meta-analysis, I took PD as the main indicator for poor oral health, as mentioned in Chapter 2. The details are presented in Chapters 2 and 4, and a summary of the approach used in the systematic literature review and meta-analyses is presented below.

3.7.1 Systematic literature review

A systematic review attempts to gather all available empirical research using clearly defined, systematic methods to obtain answers to a specific question (Ahn and Kang, 2018). It uses explicit, systematic methods that are selected to minimise bias; thus ensuring reliable findings from which conclusions can be drawn and decisions can be made (Liberati *et al.*, 2009). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Liberati *et al.*, 2009) was used, which has been shown to greatly help standardise and improve the quality of systematic reviews and meta-analyses (Willis and Quigley, 2011). This includes having a clear objective and rationale for the study and methods that involve a systematic search of the literature, as outlined in the PRISMA flow chart. The review developed a comprehensive database search strategy using PECO (population, exposure/intervention, comparison, and outcome) framework (Liberati *et al.*, 2009). The standard protocol followed involved using three independent reviewers and assessing the quality of included studies using the Newcastle Ottawa scale (Stang, 2010). The data from included studies were extracted and presented (Chapters 2 and 4).

3.7.2 Meta-analysis

Systematic reviews include a meta-analysis component utilising statistical techniques to synthesise the data from several studies into a single quantitative estimate or summary effect size. Meta-analysis involves combining or pooling all the reported numerical data from the identified studies in a systematic literature review (Liberati *et al.*, 2009). Meta-analysis results can improve the effect estimate of the risk factors of a particular disease and resolve differences that could arise from inconsistent study results (Cooper, 2015). The pooled estimate is the outcome of the meta-analysis and is typically explained using a forest plot. The black squares in the forest plot are the relative risk (RR) and 95% confidence intervals in each study. Meta-analysis involves the random effect model, which considers both within- and between- study

variability and the fixed effect model, which yields only within-study variability. The choice of statistical model depends on the outcome of the heterogeneity test performed in the analysis (Higgins *et al.*, 2003). The details of the meta-analysis are presented in Chapters 2 and 4.

3.8 Qualitative study: A focus group study

In this thesis, to give comprehensive answers to research questions alongside quantitative study results, qualitative research was also undertaken. Qualitative data are sometimes defined as being ‘rich’ or ‘contextualised’, suggesting they are descriptive (White and Rayner, 2014). Therefore, the best methodological fit for this research was to also employ qualitative methods by conducting a focus group study. Focus group research is becoming increasingly popular and is commonly used in social, health, and medical research to study health problems (Onwuegbuzie *et al.*, 2009; Krueger and Casey, 2015). This focus group study employed a semi-structured discussion guide to collect data from the participants who consented to participate in one of the three focus group discussions. Data was analysed using a thematic analysis approach, as highlighted in Braun and Clark’s (2006) study.

3.8.1 Justification for the focus group study

This section explains why I used focus groups and highlights their advantages over other methods.

A focus group discussion is a technique in which a researcher assembles a group of individuals to discuss a specific topic, aiming to draw from participants’ complex personal experiences, beliefs, perceptions, and attitudes through a moderated interaction (Morgan, 1996; Kitzinger, 1994). This definition supports the researcher’s decision regarding focus groups being the best method to collect data in a group setting.

Focus group research provides an alternative qualitative study method. Unlike traditional one-to-one interviews or observations, focus groups permit more active and dynamic social

discussions, thus allowing a cumulative understanding of the research enquiry (Gillis and Jackson, 2002). A well-conducted focus group can encourage the participation of those who would be reluctant to participate in a one-on-one interview or those who feel their views are not relevant (Stewart and Shamdasani, 2014). Many experts have discussed how and why focus groups are used instead of other research techniques (Lederman, 1990; Franklin and Knight, 1995). Along with this, Bertrand *et al.* (1992) pointed out that little training is required to conduct such a study, the data are easy to interpret, and focus groups create opportunities for participants to provide in-depth insights (Bertrand *et al.*, 1992). In these circumstances, participants can develop ideas that have already been proposed, challenge these ideas, suggest new ideas of their own, and share common experiences and feelings, thus generating deep and enriched data during the interactive session. Lederman (1990) summarised this benefit, explaining that focus groups allow the researcher to find the ‘why’ behind the numbers (Lederman, 1990).

3.8.2 Rationale for the focus group study

The focus group research was conducted as part of the larger doctoral research project to achieve the aims and objectives using descriptive data. Since the research work in this thesis adopts a mixed methods design employing a convergent parallel database, it comprises different datasets and the three focus groups were conducted to provide the qualitative data for this research study. The focus groups study helps to answer the research questions by exploring the dementia patients’ carers’ knowledge and perceptions about association between oral health and dementia. The research questions are given in section 2.8.1. Both are answered through focus group discussions. The researcher explored if carers’ think poor oral health increases dementia risk and if so what are the mechanisms/pathways for it. The carers also express the reasons why they believe that dementia or severe cognitive impairment worsens the oral health. To the best of my knowledge, no qualitative research is available on the subject; thus, the

findings can contribute to new knowledge and understanding. It will also highlight the need for similar studies in other settings to guide future policymakers and researchers.

3.8.3 Focus group study design

The focus group discussion (FGD), a qualitative design method, was employed in this part of the research. The qualitative research for the project focused on a group of caregivers from the community and care homes representing the population segment of interest to the researcher. This study intended to understand the caregivers' perceptions of the association between oral health and dementia. Three focus groups (with different participants) were conducted to explore the same topic, emphasising group interaction and bearing in mind the earlier selected analysis plan (Braun and Clarke, 2006). Data generated from the different focus groups can then be combined into one large dataset for thematic analysis.

The budget and time available for the research project were fully maximised by carefully planning and executing the three focus groups in the most efficient way to optimise the generation of quality data that could help address the projects' research aims. Moreover, focus groups are deemed to be reasonably quick and easy to set up and can be used to simultaneously educate the group and gather opinions on service improvement (Krueger and Casey, 2015). Bertrand *et al.* (1992) highlighted focus groups' effectiveness due to the fact that the results are relatively easy to comprehend (Bertrand *et al.*, 1992). The steps taken to conduct the focus group study, including data analysis, the proposed approach to interpretation, and the presentation of findings, are explained below.

3.8.4 Data collection procedure

3.8.4.1 Study population

The participants for the focus group were recruited from the population of caregivers in the Wolverhampton area of Black Country in the West Midlands, UK. Caregivers included both

family caregivers and professional carers from care homes, provided they were primary carers for a patient with dementia. Wolverhampton is a diverse city located in the West Midlands with a heterogeneous mix of nationalities, religions, and ethnic groups above the average English city and has a population of 256,600. As of December 2018, 4.81% of residents were over 65, and a total of 2,171 individuals had been diagnosed with dementia in Wolverhampton. This is higher than both the national (4.33%) and West Midlands (4.14%) averages (Wolverhampton Council, 2019).

3.8.4.2 Sampling design

Purposive sampling was used to recruit caregivers of people with dementia. Purposive sampling is a sampling method in which the researcher hand-picks participants that had contributed to the study's information needs (Polit and Beck, 2004). According to Denzin and Lincoln (1994, p.229), Patton (1990) provides clear guidelines for sampling and suggests that the logic and power behind purposeful selection of informants is that the sample should be information rich. The same logic was applied in this study caregivers who were well versed with the subject area were invited to participate in a focus group discussion.

3.8.4.3 Recruitment procedure

The researchers approached local care homes and face-to-face meetings were arranged with care home managers to explain the research procedure. Once participants were identified with the help of the care home manager, they were approached in person at care homes and handed an information sheet and an invitation letter (see Appendix 7 and 3) with the researchers' contact details. Interested participants contacted the researcher. After checking that each individual met the eligibility criteria, all participants signed an informed consent form (see Appendix 6) before participating in the focus group discussions. The date, time, and place for conducting focus groups was decided in advance. However, due to difficulties finding a time

and place suitable for all participants when conducting the first group, the remaining two focus groups were held at care homes with the permission of the care home management (see Appendix 2).

3.8.4.4 Data collection tools and procedure

The data was collected from the focus group discussion with the help of a short questionnaire and a focus group topic guide (see Appendix 5 and 4), which was pre-approved by the research ethics committee of the University of Wolverhampton (UoW). Open-ended questions were used to encourage the free flow of ideas (Krueger and Casey, 2015) and were formulated after consulting an experienced researcher in the field. Pattons (1990) stated that the advantage of using an interview guide is that it increases the comprehensiveness of the data and creates a more systematic data collection process for respondents. The researcher (moderator) facilitated the discussion with the help of probe questions while a co-moderator helped manage notes and organise the venue. The focus groups were audio recorded and the researcher also took brief field notes throughout the session. The data was recorded and stored according to general data protection regulations (GDPR). The details of the study population, sampling design, recruitment procedure, and data collection tools and procedure are explained in Chapter 8, *“Caregivers perception on the association between oral health and dementia: focus group research”*.

3.8.5 Data analysis

Data analysis is the process of converting raw data into meaningful and useful information. First, the audio recorded in the three focus groups discussions was uploaded onto a computer and transcribed verbatim in Microsoft Word. The Nvivo version 12 Pro qualitative software program was used to organise, store, and manage the data during transcription before manually embarking on thematic analysis. The thematic analysis strategy employed by Braun and Clarke

(2006) was used, which facilitates the generation of a rich and complex account of the data that can be used to answer the research question, was applied in this study. Braun and Clarke's (2006) thematic analysis consist of six phases: familiarising oneself with the data, generating initial codes, searching for themes, reviewing themes, defining and naming themes, and producing the analysis report. These are outlined in Chapter 8 (Section 8.3). The emerging themes were checked and compared with the transcript to ensure reliability. Any doubts or differences were resolved through discussions with the supervisors. In Chapter 8 (Section 8.4), a thematic map was created for all three focus group discussions to illustrate the main themes.

3.8.6 Trustworthiness in research

Trustworthiness in research involves using a rigorous approach to accomplish the specific research objectives, specifically by applying appropriate research instruments (Mays and Pope, 2000). Qualitative research has four dimensions that must be considered to enhance data trustworthiness: credibility, transferability, dependability, and confirmability (Lincoln and Guba, 1985). These criteria measure the character of the data and assess interpretations and conclusions (Polit and Beck, 2004). In the focus group, the thematic analysis method provided by Braun and Clark (2006) was strictly followed (Braun and Clarke, 2006). Thematic analysis was also recommended by Nowell *et al.* (2017) for meeting trustworthiness criteria (Nowell *et al.*, 2017). Trustworthiness is briefly discussed below.

3.8.6.1 Credibility

The first aspect of trustworthiness is credibility, which presents the extent to which the data and its interpretation reflect the truth (Polit and Beck, 2004). There are several techniques that can be used to enhance a study's credibility. As it implies confidence in the truth and findings of the qualitative study, it is one of the most important criteria (Lincoln and Guba, 1985). Lincoln and Guba (1985) highlighted some of the credibility strategies used in focus groups,

including prolonged engagement, debriefing, triangulation, and audit trail, which are discussed below.

Prolonged engagement refers to being engaged with the research for an extended period of time. It is important to have sufficient time to collect data to gain an in-depth understanding of the study subjects (Polit and Beck, 2004). In our study, this was achieved by personally going to care homes and talking to care home managers and interested participants. Information about the focus group study was provided in advance, along with clarifications in the case that individuals had any queries. Participants who were contacted through word of mouth (e.g., volunteer organisations) also received a full, face-to-face explanation of various aspects of the focus group after they decided to take part in the study.

Triangulation is a technique that refers to applying multiple sources of data. It allows for a comprehensive understanding and conceptualisation of a phenomenon (Polit and Beck, 2004). In our research, this was accomplished using a tape recorder and note-taking.

Peer debriefing is another technique used to enhance study credibility that requires the researcher to participate in sessions with peers regarding various aspects of the enquiry (Tashakkori and Teddlie, 2010). In this study, I had continuous discussions with colleagues in the department, research assistants, and other PhD students to discuss the research enquiries.

Audit trail of the research was achieved by keeping notes that contain the interpretations of the findings during the data analysis.

3.8.6.2 Transferability

Transferability is equivalent to generalisability in quantitative data; it describes the extent to which the findings can be transferred to other contexts or settings (Polit and Beck, 2004). In considering the transferability aspect, this study ensured detail, reflection, justification, and clarification as underpinning the philosophy involved in the development of this research.

Therefore, this study provided a detailed rationale for the research and justifications for the choice of method, instrument adopted, as well as the data collection and recruitment procedures. At the analysis stage, the details of the framework that enabled the presentation of the findings were given. The presentation of data involved the exact words used and interpretations of the findings took into account the context. For instance, the transcribed data coding included surrounding texts from participants' expressions of their views and experiences to better clarify and understand the context.

3.8.6.3 Dependability

Dependability is the equivalent of reliability in quantitative studies; it is defined as the stability of the data over time and under various conditions. It produces similar results when conducted in a similar setting with similar participants under the same condition (Polit and Beck, 2004). In a focus group, it has been suggested that dependability can be achieved by having other researchers reuse the audit trail retained for the research process to arrive at similar findings ((Plummer-D'Amato, 2008). This is required to ascertain if the findings and their interpretation is in accordance with the data (Lincoln and Guba, 1985). In this study, there was also external auditing of the entire research process and an audit trail of the difficulties faced during the process. This included raw data, note-taking, transcripts, data analysis, and reporting through close and constant observation from the supervisory team, which ensured consistency in the interpretations and presentation of the findings.

3.8.6.4 Conformability

Confirmability seeks to verify that other researchers can validate or corroborate the research findings to ensure they are a true representation of the participants' viewpoints without researcher interference, free from the researcher's motivations, interests, and biases (Polit and Beck, 2004). According to Guba and Lincoln (1989), confirmability is established when

credibility, transferability, and dependability are achieved (Guba, 1989). In this study, the researcher documented the data analysis process in various documents, including the focus group transcript, field notes, and data analysis records, all of which were provided to both supervisors. Furthermore, the study methodologies, including the study design, sampling, settings, data collection methods and data analysis, were described in detail. This means that there is a written record of all the data collected in the study, thereby allowing for confirmation and validation of the analysis results.

3.8.6.5 Reflexivity

The reflexive journal allowed me to better understand the qualitative research process. The data collected in the journal greatly assisted me and supported the data collected in the focus group discussions. Each focus group setting was both comfortable and private, thus allowing the caregivers the opportunity to share their experiences safely. Observations written in the journal included the atmosphere of the setting (formal or informal), meetings with my supervisors, and discussions with colleagues and peers promoted reflexive questioning.

3.9 Data transcribing and data management

Data management is described as the operations needed for systematic, coherent data collection, storage, and retrieval (Denzin and Lincoln, 1998, p.180). The participants' information was collected and recorded with a notebook containing their appointment schedules and contact details. Confidentiality was maintained in line with GDPR guidance. Data were audio recorded during the focus group and later recordings were transcribed verbatim (see Appendix 8) by the researcher before data analysis was conducted with the help of NVivo 11 software to organise, store, and manage data. Only the researcher and study supervisors had access to the secondary datasets for Guangzhou case-control study, ELSA, and primary data from the focus groups. All data was stored on a password-protected computer in

accordance with GDPR. Both secondary datasets did not contain any personal details of the participants (names, addresses, and contact details). In the focus group study, all personal data were kept securely; identification numbers were given instead of participants names on study records and computer files to maintain anonymity and prevent any accidental breach of confidentiality.

3.10 Ethical considerations

The entire study was carried out in accordance with the approved research protocol. Focus group study approval was taken from the Research Ethics Committee of the Faculty of FEHW, UK (see Appendix 1). The care homes granted permission to recruit their members for the focus group study (see Appendix 2). An information sheet detailing the purpose of the study and the ethical issues (see Appendix 7) was prepared and given to participants. All participants provided written informed consent indicating that they understood the research's aim and what measures would be taken to ensure confidentiality and anonymity. Participants were given one week to decide whether to participate in the study. The participants confirmed their voluntary agreement to participate in writing by signing the consent form on the day of the focus group discussion after reading and confirming that they understood the participants' information sheet (see Appendix 6 and Appendix 7). The focus group questions were carefully designed not to offend or embarrass participants, were clearly related to the topic in question, and were approved by the ethics committee of the UoW. All the participants were informed that they could freely withdraw if they wanted at any time. Confidentiality was maintained and no information was shared with other personnel except those directly involved in this study, such as research supervisors, as per GDPR guidance. By using codes on focus group transcripts,

other personnel could not link data to participants, thus ensuring anonymity. The data is securely stored in a locked location, according to the UoW regulations on data storage.

I ran the secondary data analysis for the Guangzhou case-control study (the data was already translated in English language when I received it) and the ELSA cohort study. The data collection for the Guangzhou case-control study was granted by the Research Ethics Committee of Guangzhou Medical University in China and also the Research Ethics Committee of Faculty of Education, Health, and Well-being (FEHW), University of Wolverhampton (UoW) through an EU MSCA funded research project of “air pollution and dementia” (DEMAIRPO-799247) which was led by Professors Ruoling Chen and Jie Tang. Access and permission to use the case-control study data for the doctoral study were granted after submitting an official request through the principal investigator (Professor Jie Tang) in the Guangzhou case-control study. ELSA dataset permission is an open access UK data service website: <https://ukdataservice.ac.uk/>, and ELSA data is free downloaded for use for all UK researchers. Both datasets are anonymous and there are no personal identifications of any participants in the dataset.

All electronic data above were kept safely in a password-protected computer that could only be accessed by the researcher and supervisors.

3.11 Summary

This chapter provided an overview of the quantitative and qualitative research methodologies and their applications in the research thesis. It provides justifications for the chosen research design to examine the association between oral health and dementia. The main study design selected to answer the research questions was a convergent parallel mixed methods design. The data analysis for the quantitative phase employed descriptive and inferential statistics while thematic analysis was used for the qualitative phase of this study. One crucial aspect is the

integration of the findings. As illustrated in Figure 3.1, the data from the quantitative and qualitative research will be analysed separately and the findings will be merged in the discussion section (Chapter 9) of the thesis.

CHAPTER FOUR: ASSOCIATION OF PERIODONTAL DISEASE WITH RISK OF DEMENTIA: A SYSTEMATIC REVIEW AND A META-ANALYSIS

4.1 Introduction

Periodontal disease (PD) and caries are two major causes of tooth loss (Tonetti *et al.*, 2017). This chapter is focused on PD because the age of peak prevalence of caries is more in the younger age group (<30 years) (Kassebaum *et al.*, 2015) compared to peak prevalence of PD which occur at an older age than caries (Kassebaum *et al.*, 2014). Since participants from most quantitative studies were aged 50 or above, it was more appropriate to take PD as an indicator for oral health. PD includes gingivitis and periodontitis, which are highly prevalent inflammatory diseases initiated by dysbiotic sub-gingival biofilms resulting in alveolar bone loss and eventually tooth loss (Van Dyke and van Winkelhoff, 2013; Page and Kornman, 1997). Severe PD has been reported to be the 11th most prevalent condition worldwide and affect around 20-50% of the global population (Kassebaum *et al.*, 2014; GBD, 2017). Previous studies showed that the number of missing teeth among adults was associated with an increased incidence of dementia (Fang *et al.*, 2018; Oh *et al.*, 2018). However, it is unclear whether PD also predicted the risk of dementia. The current literature has shown inconsistent findings; some studies reported a significant increase in the risk of dementia in people with PD (Lee *et al.*, 2017a; Chen *et al.*, 2017), while others did not (Arrivé *et al.*, 2012). Previously Leira *et al.* stated that they carried out their systematic literature to investigate whether this link existed and suggested quite a high risk of Alzheimer's disease (AD) in relation to PD (OR 1.69, 95% CI 1.21–2.35) (Leira *et al.*, 2017). However, their study included cross-sectional studies (Syrjälä *et al.*, 2012; Martande *et al.*, 2014), which would not make any prediction of PD on dementia risk and ineligible study in the meta-analysis (Syrjälä *et al.*, 2012), but also missed one eligible study in the review (Stein *et al.*, 2012). In this chapter, a standard systematic

literature review with meta-analysis was carried out to investigate the impact of PD with risk of dementia and Alzheimer's disease (AD) in the population.

4.2 Methods

In this study, PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) was used when conducting this study (Liberati *et al.*, 2009).

4.2.1 Search strategy

Relevant studies were identified by a systematic search of the MEDLINE, PubMed, CINAHL, PsychINFO and SocINDEX databases from the earliest date to 25th October 2021. The strategy for the database search was developed using the Population, Exposure/Intervention, Comparison and Outcome framework (PECO) (Liberati *et al.*, 2009). This strategy aimed to answer the following question: *Is PD associated with an increased risk of dementia?* For all databases, I used the same terms for literature search: (oral health or oral hygiene or dental health or periodontal disease or periodontitis or gingivitis or periodontal infection or caries or tooth loss) AND (dementia or Alzheimer's disease or vascular dementia or cognitive impairment or cognitive decline). In addition, the articles in reference lists of the original article and review were also screened. No language restriction was applied for searching or study inclusion. To ensure all searches were done according to planned protocol, another researcher (Dr JT) used the same key terms to search all databases.

4.2.2 Inclusion and exclusion criteria

The studies were included in the systematic review if it was original research published in a peer-reviewed journal that met the following criteria: (1) the study investigated an association of PD with dementia (any type of dementia); (2) designed as cohort study or case-control study; and (3) to report any of the following periodontal parameters: periodontal pocket depth (PPD), clinical attachment loss (CAL), community periodontal Index (CPI), bleeding on probing

(BOP), American Academy of Periodontology classification (AAP), Periodontal profile class (PPC) and International Classification of Diseases, Ninth Revision, Clinical Modification codes 523.0-523.5 (ICD-9-CM) or ICD-10 codes F00, F01 and G30, for PD (4) to have dementia diagnosis criteria and procedure elaborated. Studies were excluded if: (1) cross-sectional study; (2) case-report, commentaries, editorial, review, animal studies or clinical trial; and (3) the outcome of interest was not dementia or AD. The grey literature was explored, including contact with the authors of potential eligible articles, e.g., (Bramanti *et al.*, 2015). If risk estimates in the original study reported several multivariate-adjusted models, then the most fully adjusted model reported were extracted.

4.2.3 Data extraction

Each of the 15 studies was reviewed by two reviewers (RN and Dr JT) and assessed independently using a predesigned data extraction form to extract the necessary information from the chosen studies. The information extracted included the first author's name, year of publication, country of origin, participants' age range, sample size, baseline measurement of PD, endpoint outcome criteria of dementia diagnosis, and dementia cases, data analysis and adjustment for confounders, and the findings. Differences in reviewing literature and extracting data between the two reviewers were resolved through face-to-face discussion, and where differences remained, these were discussed with the third reviewer to reach an agreement.

4.2.4 Quality assessment

The quality of the selected studies was assessed using the Newcastle–Ottawa Scale (NOS) (Tables 4.1 and 4.2), which comprises of three domains: (1) sample selection, (2) comparability and (3) exposure/outcome. A star is assigned if a quality feature is scored one to nine (the comparability domain can score 1- 2 stars). Studies with NOS scores of 1 to 3, 4 to 6 and 7 to 9 were defined as poor, intermediate, and high [quality of studies] (Stang, 2010).

4.2.5 Meta-analysis

The available data of relative risk (RR), e.g., Hazard ratio (HR) or odds ratio (OR) and their 95% Confidence Intervals (CIs) of dementia in relation to PD, were pooled from each eligible study. Since the odds ratio (OR) in the case-control study may overestimate the RR of dementia in relation to PD, I used a formula proposed by Zhang and Yu to convert OR into the RR (Zhang and Yu, 1998) before being pooled. The data of each studied population from these articles were analysed. The pooled data, where available for all types of dementia first (if the studied population did not provide data of all dementia, its subtypes data would be used), and then for AD and vascular dementia (VaD) separately where given. If the study presented data of RRs for a different group of PD measured (Arrivé *et al.*, 2012; Lee *et al.*, 2017a; Gil-Montoya *et al.*, 2015) or severity level of PD, then each individual RR for pooling data was taken. In studies where RR of dementia in relation to PD was not presented, crude was calculated for RR and its 95% CIs if the study provided necessary data. All these measures and their 95% CI were pooled together as a RR with the assumption of attaining a common unit of comparison. The RR and 95% confidence intervals were pooled using a random-effects model, which includes the heterogeneity of within-study and between-study variation. I^2 metric (I^2 values of 25%, 50%, and 75% were considered as low, medium, and high heterogeneity, respectively) was used to assess heterogeneity across studies (Higgins *et al.*, 2003). Funnel plots were used to assess small-study effects, the possibility of publication bias was evaluated using Egger's regression asymmetry test (Egger *et al.*, 1997).

All the studies which provide adjusted RR were used for the main analyses. The subgroup analysis was also performed to calculate the pooled RR of different study designs (cohort and case-control studies), severity of PD, and for dementia subtypes (AD and VaD), where data was available in the studies. Sensitivity analyses were conducted to evaluate the influence of studies with extreme value RRs.

4.3 Results

4.3.1 Findings of systematic literature review

Based on five electronic dataset searches (Figure 4.1), 5,092 studies were initially identified. After eliminating duplicates, 3399 remained for reviewing titles and abstracts, of which 23 were potentially relevant for detailed examination. After carefully reviewing, I identified 15 published studies that met the inclusion criteria for this systematic review. They were conducted in Asia (n=7), Europe (n=4), North America (n=2), and South America (n=2) and were published between 1994 and 2021. Eight studies were cohort design (Arrivé *et al.*, 2012, Chen *et al.*, 2017; Lee *et al.*, 2017a; Lee *et al.*, 2017b; Tzeng *et al.*, 2016; Demmer *et al.*, 2020; Choi *et al.*, 2019; Lee *et al.*, 2020), with baseline ages of participants ranged from 18 to 102 years, sample size varied from 42 to 262,349, followed up between 3 and 20 years. Seven others were case-control studies (de Souza Rolim *et al.*, 2014; Gil-Montoya *et al.*, 2015; Holmer *et al.*, 2018; Stein *et al.*, 2012; Chu *et al.*, 2015; de Oliveira Araújo *et al.*, 2021), with sample size varied from 59 to 409 participant. The characteristics of 15 studies are shown in Appendix 14 and 15.

The overall quality of these studies was good, with a mean score of 7.13 (Tables 4.1 and 4.2). The characteristics of all 15 included studies are summarised in Appendix 14 (cohort studies) and 15 (case-control studies).

4.3.2 Meta-analysis

One study (Stein *et al.*, 2012) did not provide any data available for the meta-analysis, while three other studies (de Souza Rolim *et al.*, 2014; Bramanti *et al.*, 2015; Chu *et al.*, 2015), all of which were case-control studies, provided crude data enabling only calculation of unadjusted risk of dementia in relation to PD (see Appendix 15). One cohort study by Demmer *et al.* (Demmer *et al.*, 2020) with adjusted results presented combined findings of MCI and dementia, with more cases of MCI at the end of follow up; this was not included in main results Figure 4.2 but used when crude data was analysed with adjusted studies to see the association of PD with dementia risk. Thus, ten studies (Lee *et al.*, 2017a; Lee *et al.*, 2017b; Tzeng *et al.*, 2016; Arrivé *et al.*, 2012; Chen *et al.*, 2017; Gil-Montoya *et al.*, 2015; Holmer *et al.*, 2018; Choi *et al.*, 2019; Lee *et al.*, 2020; de Oliveira Araújo *et al.*, 2021), which provided multiple adjusted RR and 95% CIs of dementia, were used for meta-analysis. They included 17 studied populations for analysis (Figure 4.2), and the pooled data showed an overall significant association of PD with dementia (RR 1.43, 95% CI 1.15-1.79). There is no publication bias according to the Eggers' method ($p = 0.717$) (Figure 4.3).

Subgroup analysis

Among the 17 studied populations, analysis of the 13 studied populations of cohort studies showed a RR of 1.23 (1.07-1.41) for risk of dementia associated with PD, and the three case-control studies showed a RR of 2.45 (1.98-3.04) (Figure 4.2). In addition, analysis of all crude and adjusted studied populations showed similar results to Figure 4.2 with an overall dementia risk of RR 1.48 (1.24-1.77) (see Figure 4.4).

Figure 4.5 shows the PD influence on dementia (including AD and VaD) from adjusted studies was RR 1.24 (1.03-1.50) from the analyses (10 cohort studied populations) and for risk of AD was RR 1.90 (1.10-3.30) from 6 studied populations (two cohort and four case-control studied populations).

Figure 4.6 shows that three studies (de Souza Rolim *et al.*, 2014; Bramanti *et al.*, 2015; Chu *et al.*, 2015) provided crude data to calculate unadjusted OR (see Appendix 15). One above mentioned cohort study (Demmer *et al.*, 2020) was also added for analyses (see Appendix 14). After adding these studies (three crude and one cohort study), the results for the association of PD with risk of overall dementia was RR 1.48 (1.24-1.77). Furthermore, the analyses of dementia and its sub-types showed the risk of dementia was RR1.22 (1.06-1.40); AD was 1.88 (1.19-2.95), and VaD was 2.14 (0.57-8.01), respectively.

In the further analyses of AD by study design, in six studied populations (from adjusted studies), the cohort studies were non-significant (two studied population) RR of 1.29 (0.80-2.06) and case-control studies were significant RR of 2.45 (1.98-3.04) (four studied population) see Figure 4.7.

Sensitivity analysis

In Figure 4.2, one case-control study (Holmer *et al.*, 2021) had an extreme value of RR, and after excluding it, the overall RR was 1.35 (1.17-1.59) [in the case-control 2.16 (1.65-2.84)].

In further analyses six studies (Arrivé *et al.*, 2012; de Souza Rolim *et al.*, 2014; Chu *et al.*, 2015; Lee *et al.*, 2017a; Gil-Montoya *et al.*, 2015; Demmer *et al.*, 2020) provided “dose-response” data in terms of three levels of PD. Table 4.3 showed a dose-response relationship; compared to no/minor PD, risk of dementia in moderate PD was 1.17 (1.03-1.33), and severe PD was 1.29 (1.05-1.59).

4.4 Discussion

This chapter reported a comprehensive systematic review and a meta-analysis of data from population-based studies to evaluate the association of PD with the risk of dementia.

Identifying and reviewing 15 peer-reviewed articles found an overall significant and positive association of PD with increased dementia with a RR of 1.43 (1.15-1.79).

Kapellas *et al.* (Kapellas Kostas 2019) also carried out a systematic literature review and a meta-analysis using the four cohort studies (Iwasaki *et al.*, 2018; Lee *et al.*, 2017b; Chen *et al.*, 2017; Tzeng *et al.*, 2016). Their meta-analysis for the cohort studies of PD predicting dementia included one ineligible study which measured MCI rather than dementia (Iwasaki *et al.*, 2018) but missed two important cohort studies (Arrivé *et al.*, 2012; Lee *et al.*, 2017a) for reviewing and meta-analysis data. Hu *et al.* 2021 reported pooled risk of AD with RR of 1.78 (1.15–2.76), but they missed eligible study (Stein *et al.*, 2012) for review, including one cross-sectional study (Tiisanoja *et al.*, 2019) for their main analyses and had publication bias in analyses.

There are several potential biological reasons for explaining PD association with an increased risk of dementia. In older adults, PD and dementia are more prevalent. Recent studies have linked these two diseases as both have possible common pathophysiological mechanisms (systemic inflammation, bacterial infection and nutrition) (Watts *et al.*, 2008; Wahl *et al.*, 2018; Dominy *et al.*, 2019). PD increases the risks of cardiovascular disease (Hansen *et al.*, 2016), such as coronary heart disease (Janket *et al.*, 2003), stroke (Leira *et al.*, 2017b) and cerebrovascular diseases (Khader *et al.*, 2004). It is hypothesised that these cardiovascular diseases (Janket *et al.*, 2003; Hansen *et al.*, 2016) link with dementia and converge into a common pathway leading to neurodegeneration.

A plausible biologic mechanism has been found that periodontal infection leads to systemic inflammation (Watts *et al.*, 2008). High inflammatory immune responses (C-reactive protein, tumour necrosis factor, interleukin-1, interleukin-6, a-1-antichymotrypsin) can enter the blood-brain barrier and influence priming or activation of the microglial cells in the cerebral regions, which may contribute to the pathogenesis of dementia (Watts *et al.*, 2008).

A recent study showed that neuronal damage in AD pathogenesis is caused by porphyromonas gingivalis infection through the secretion of gingipains. Porphyromonas gingivalis enters the brain by direct infection, cranial nerves and infection of monocytes which also affect AD development (Dominy *et al.*, 2019).

Another plausible mechanism is that PD and dementia share genetic predisposition. The presence of Apolipoprotein E (ApoE ϵ 4) increases the risk of AD; the presence of one APOE ϵ 4 allele causes 2-3 times increased risk of AD (Teruel *et al.*, 2011; Troutwine *et al.*, 2001; Corder *et al.*, 1993). Porphyromonas gingivalis and host interactome related genes identified from genome-wide association studies (GWAS) overlap with susceptible genes involved in AD, suggesting that Porphyromonas gingivalis interactome were significantly enriched in genes deposited in GWAS genes related to cognitive disorders, AD and dementia (Carter *et al.*, 2017).

The pooled data in this study showed a dose-response relationship between PD and dementia was statistically significant. The risk of dementia significantly increased with moderate PD (1.17, 1.03-1.33) and severe PD (RR 1.29, 1.05-1.59), as shown in Table 4.3. Chen *et al.* also reported a significant dose-response association of tooth loss with dementia in their systematic literature review and meta-analysis study (Chen *et al.*, 2018). This also supports our finding of the dose-response association of PD with dementia. The association remained positive even after adjusted results; the data pooled from 18 studies showed an OR 1.55 (1.41–1.70) (Fang *et al.*, 2018).

Strengths and limitations

The current study of the systematic literature and meta-analysis included all eligible studies for review and meta-analysis to examine the association of PD with the risk of dementia, AD and VaD. The studies used for dementia and AD were adjusted for confounders. Moreover,

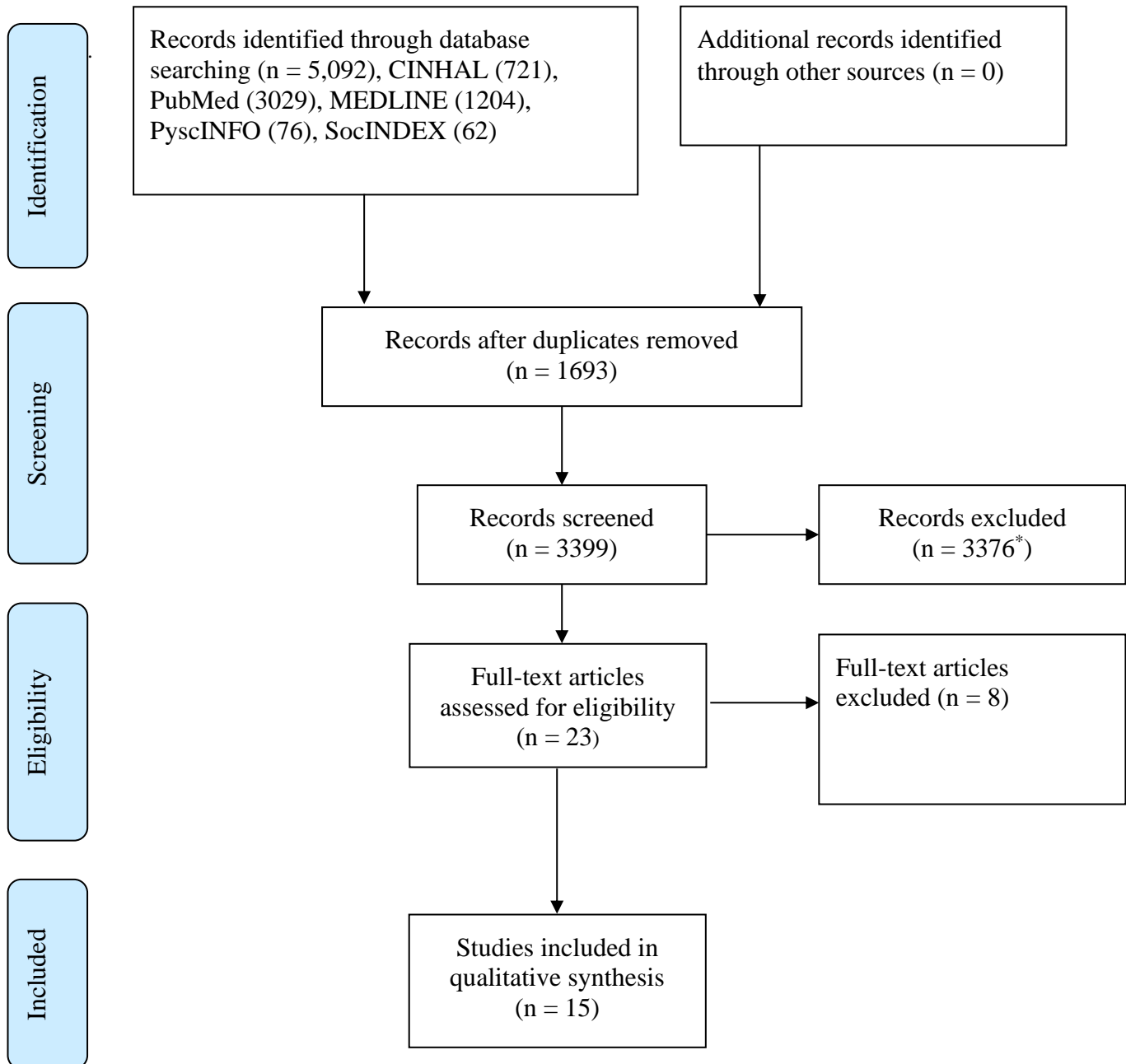
subgroup and sensitivity analyses were performed, and thus the findings from our study are robust. However, this study has several limitations. First, the studies which were identified for review used different measurements of PD, which could lead to inconsistent information on PD, including the severity of PD, attenuating the association of PD with dementia risk. Second, three studies (Chu *et al.*, 2015; Gil-Montoya *et al.*, 2015; Demmer *et al.*, 2020) included patients with minor PD in the reference group for analysis. This will attenuate the association of PD with an increased risk of dementia. The finding of the association of PD with dementia risk could be more conservative. Third, we found that most studies did not adjust for tobacco smoking. Since tobacco smoking is a common risk factor for dementia (Anstey *et al.*, 2007) and periodontitis (Ebersole *et al.*, 2014), the possibilities of residual confounding effects may not entirely be excluded from their studies. The current study has highlighted this methodological issue for future research on the impact of PD on dementia risk. Fourth, only two studies (Holmer *et al.*, 2018; Chen *et al.*, 2017) gave the results of the risk of VaD in relation to PD, and results were non-significant due to lack of studies. Moreover, only five studies (adjusted) gave data for meta-analysis for AD. Therefore, future studies on the topic should give the data of AD and VaD for meta-analysis, which will validate the findings.

4.5 Implications and conclusions

This chapter has shown that PD is significantly associated with increased risk of dementia. Population-based prevention of PD and improved strategies could reduce the burden of dementia and thereby decrease financial constraints in healthcare systems. It is imperative that all health and allied healthcare professionals, including dental teams, continue to promote and implement guidelines for the delivery of oral health that is bespoke at supporting the various stages of dementia prevention.

In *conclusion*, this chapter study provides evidence of a significant and positive association of PD with increased dementia risk. PD is a potential modifiable risk factor for dementia and AD. Therefore, globally reducing PD through timely interventions, enhanced screening services, efficient treatment, and dental care would lower the number of cases of dementia worldwide.

Figure 4.1: Flow chart for literature search, selection, and inclusion of studies for the systematic literature review examining the association of PD with dementia risk.



* Reasons for exclusions: Appropriate outcome not reported, Randomized control trial; Assessed another exposure other than periodontal disease, Assessed another outcome other than dementia (or any specific type of dementia), Articles on the importance of tooth loss to dementia and cognitive impairment, News briefs, Articles on caries, mastication and denture, Literature review/meta-analysis, Presentation, Cross-sectional study design

Figure 4.2: Forest plot for the pooled relative risk (RR) of all adjusted studies of PD and dementia and AD risk by study design in case-control and cohort studies.

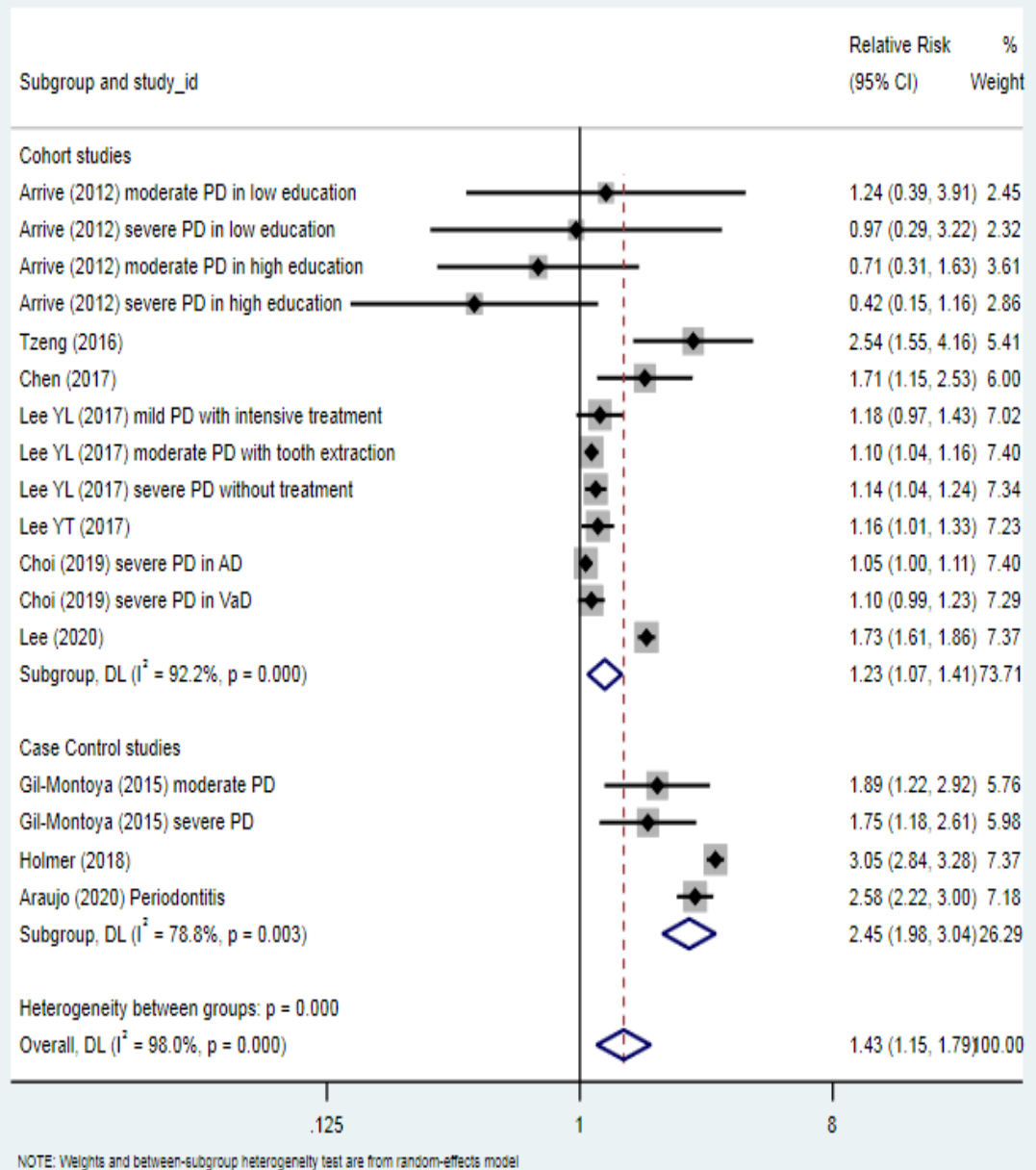


Figure 4.3: Funnel plot assessing publication bias of case-control and cohort studies

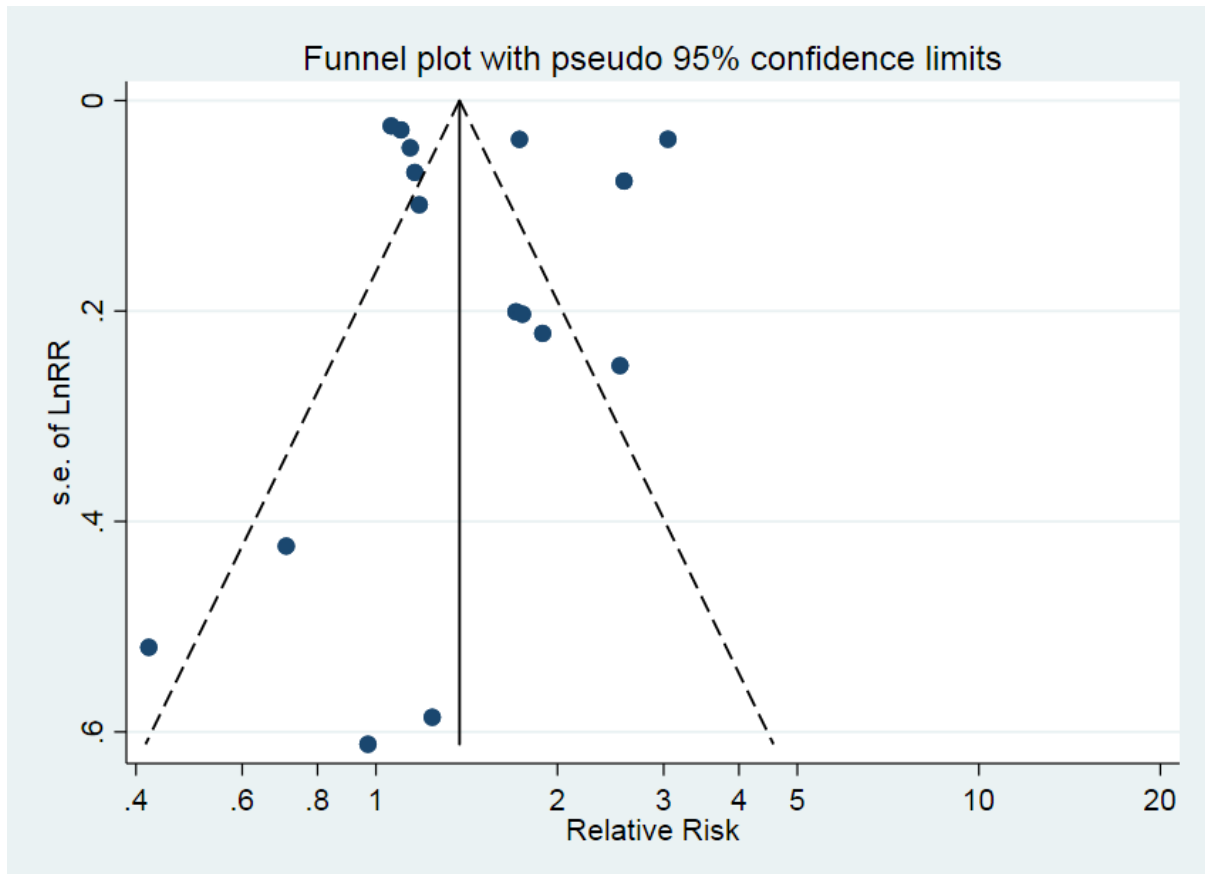


Table 4.1: Quality evaluation of the cohort studies using Newcastle-Ottawa Scales (NOS)

Selection of cohort studies		Chen <i>et al.</i>	Demmer <i>et al.</i>	Lee YL <i>et al.</i>	Lee YT <i>et al.</i>	Lee YC <i>et al.</i>	Tzeng <i>et al.</i>	Arrive <i>et al.</i>	Choi <i>et al.</i>
1	Representativeness of the exposed cohort	★	★	★	★	★	★	★	★
2	Selection of the non-exposed cohort	★	★	★	★	★	★	★	★
3	Ascertainment of exposure	★	★	★	★	★	★	★	★
4	Demonstration that outcome of interest was not present at the start of study	★	★	★	★	★	★		★
Comparability of cohorts									
1	Comparability of cohorts on the basis of the design or analysis	★ ★	★ ★	★ ★	★ ★	★ ★	★ ★	★ ★	★ ★
Outcome									
1	Assessment of outcome	★	★	★	★	★	★	★	★
2	Was follow-up long enough for outcomes to occur	★	★	★	★	★	★	★	★
3	Complete follow up- all subjects accounted for	★	★	★	★	★	★	★	★
Total score:		9/9	9/9	9/9	9/9	9/9	9/9	8/9	9/9

Table 4.2: Quality evaluation of the case-control studies using Newcastle-Ottawa Scales (NOS)

Selection of case-control studies		Holmer <i>et al.</i>	Brammati <i>et al.</i>	Gil Montoya <i>et al.</i>	Chu <i>et al.</i>	De Souza <i>et al.</i>	Stein <i>et al.</i>	Araujo <i>et al.</i>
1	Is the case definition adequate?	★	★	★		★		★
2	Representativeness of the cases	★	★	★	★	★	★	
3	Selection of Controls	★				★	★	★
4	Definition of Controls	★	★	★	★	★		
1	Comparability of cases and controls on the basis of the design or analysis	★ ★	★ ★	★ ★	★ ★	★	★	★
1	Ascertainment of exposure		★	★	★	★	★	
2	Same method of ascertainment for cases and controls	★	★	★		★	★	★
3	Non-Response rate			★		★	★	
Total score:		7/9	7/9	8/9	5/9	8/9	6/9	4/9

Table 4.3: Dose-response relationship between periodontal disease severity and dementia risk*

Periodontal disease (PD)	RR (95%CI)
Severity levels**	
0	REF
1	1.17 (1.03-1.33)
2	1.29 (1.05-1.59)

*Dose- response studies: (Chu *et al.*, 2015; Gil-Montoya *et al.*, 2015; Lee *et al.*, 2017a ; Arrivé *et al.*, 2012; de Souza Rolim *et al.*, 2014; Demmer *et al.*, 2020))

**PD severity levels:

0= Reference (REF): no PD (including minor PD (Chu *et al.*, 2015; Gil-Montoya *et al.*, 2015; Demmer *et al.*, 2020))

1= Moderate PD: bleeding, calculus, gingivitis, shallow pockets, PD with tooth extraction

2= Severe PD: deep pockets, PD without treatment, edentulous

Figure 4.4: Forest plot showing pooled relative risk (RR) of case-control and cohort studies including crude and adjusted studies for PD and dementia and AD risk by study design

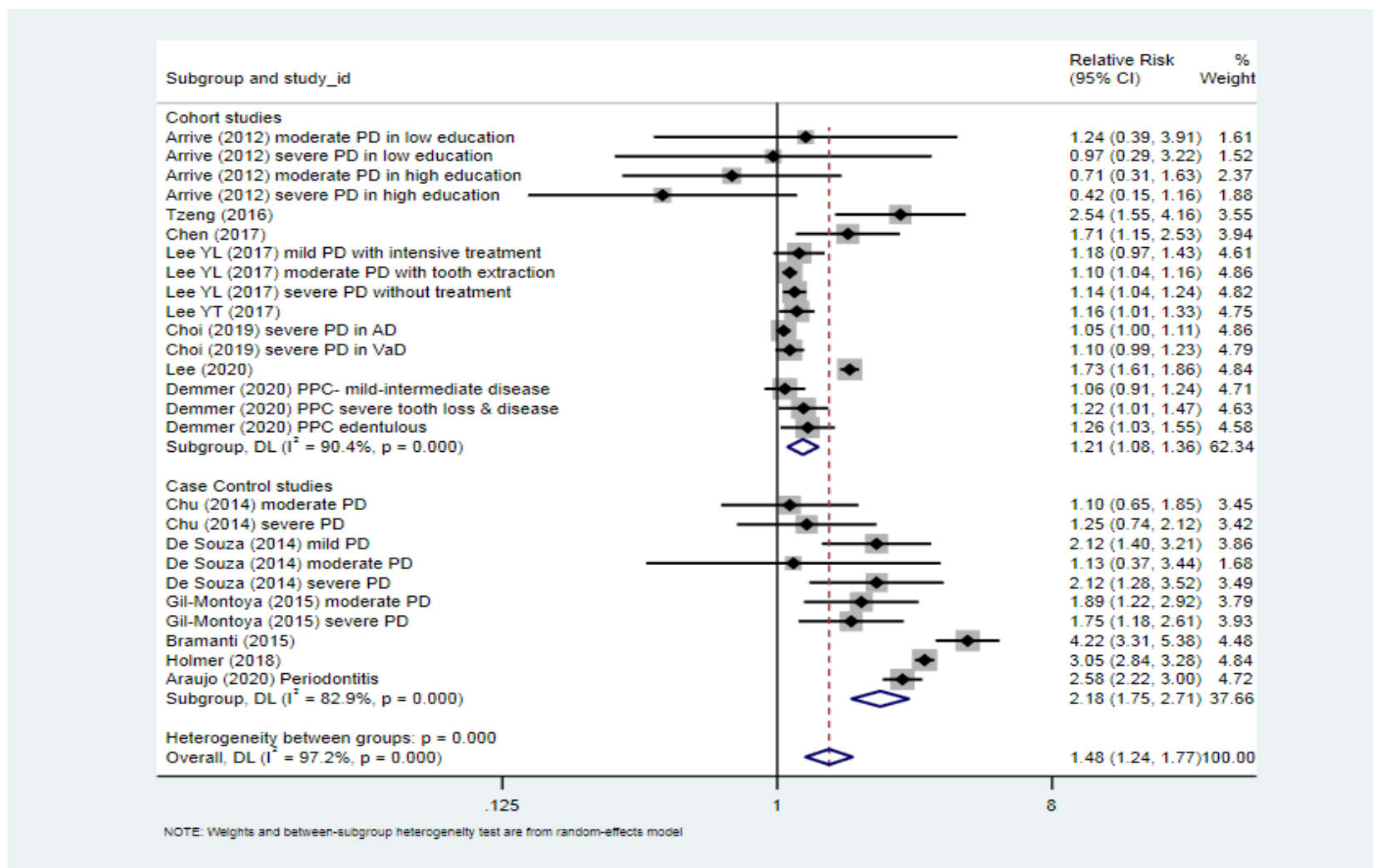
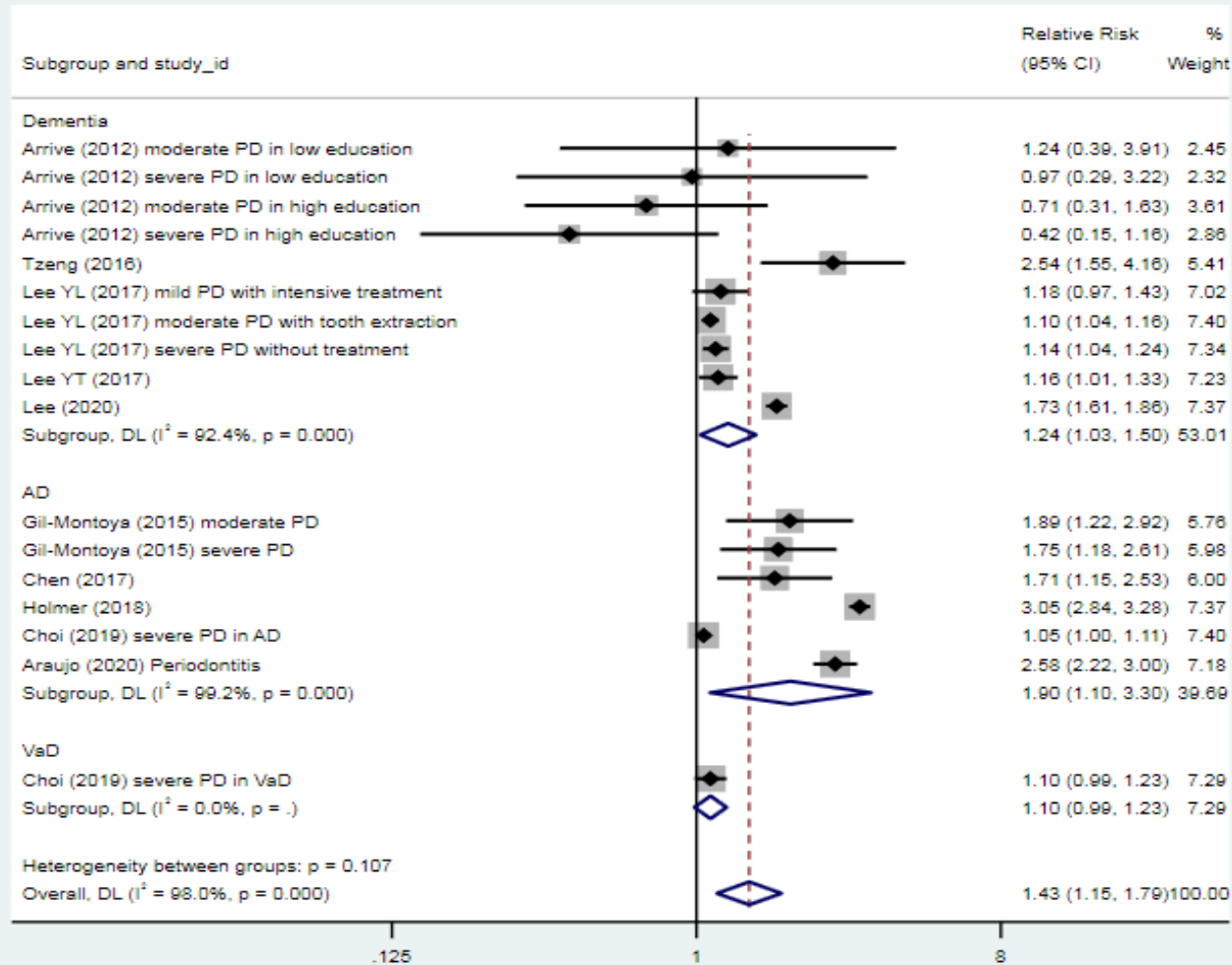


Figure 4.5: Forest plot showing pooled relative risk (RR) of adjusted case-control and cohort studies for PD and dementia and AD risk (by outcome)



NOTE: Weights and between-subgroup heterogeneity test are from random-effects model

Figure 4.6: Forest plot showing pooled relative risk (RR) of case-control and cohort studies including crude and adjusted for PD and dementia, AD and VaD risk (by outcome)

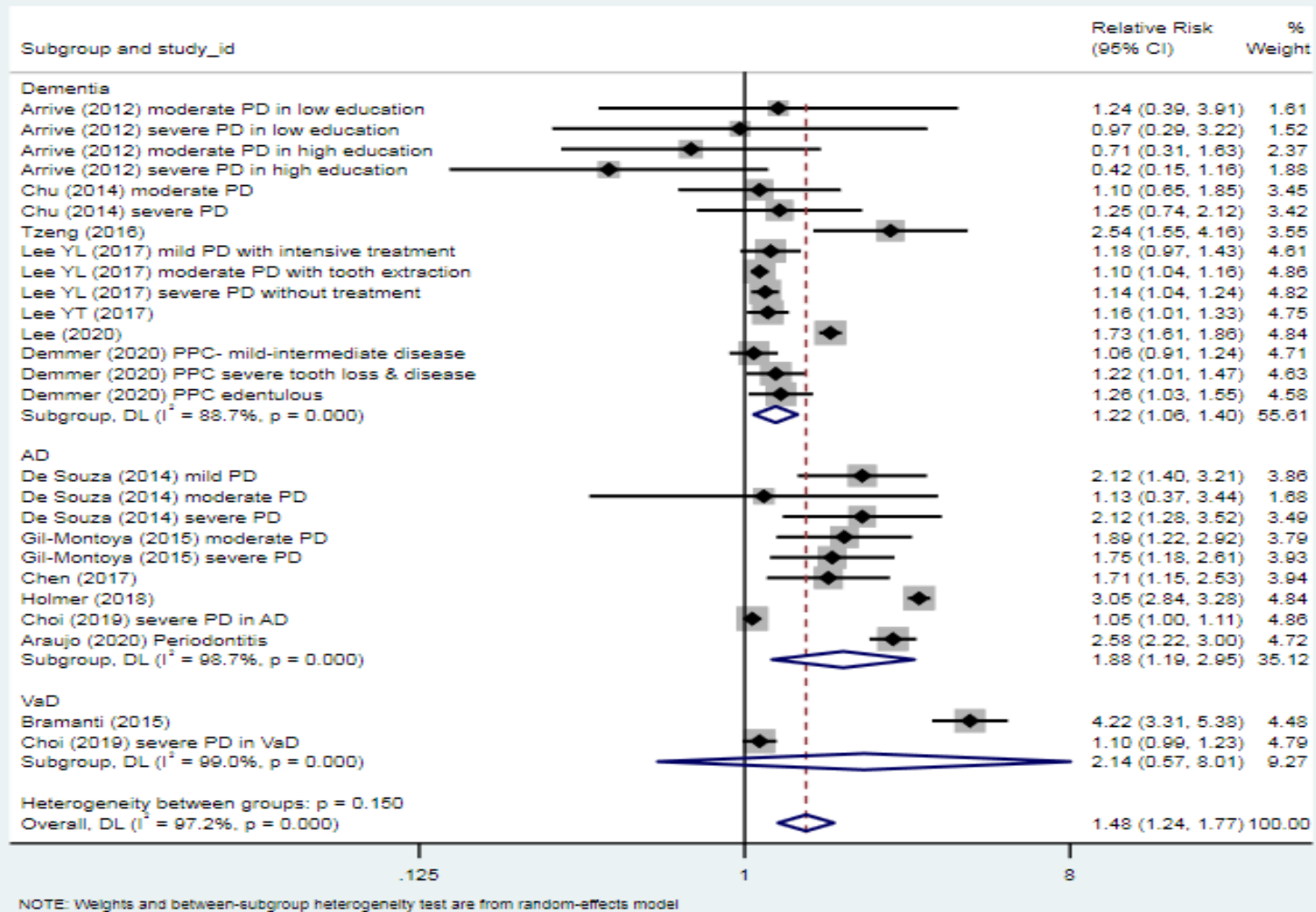
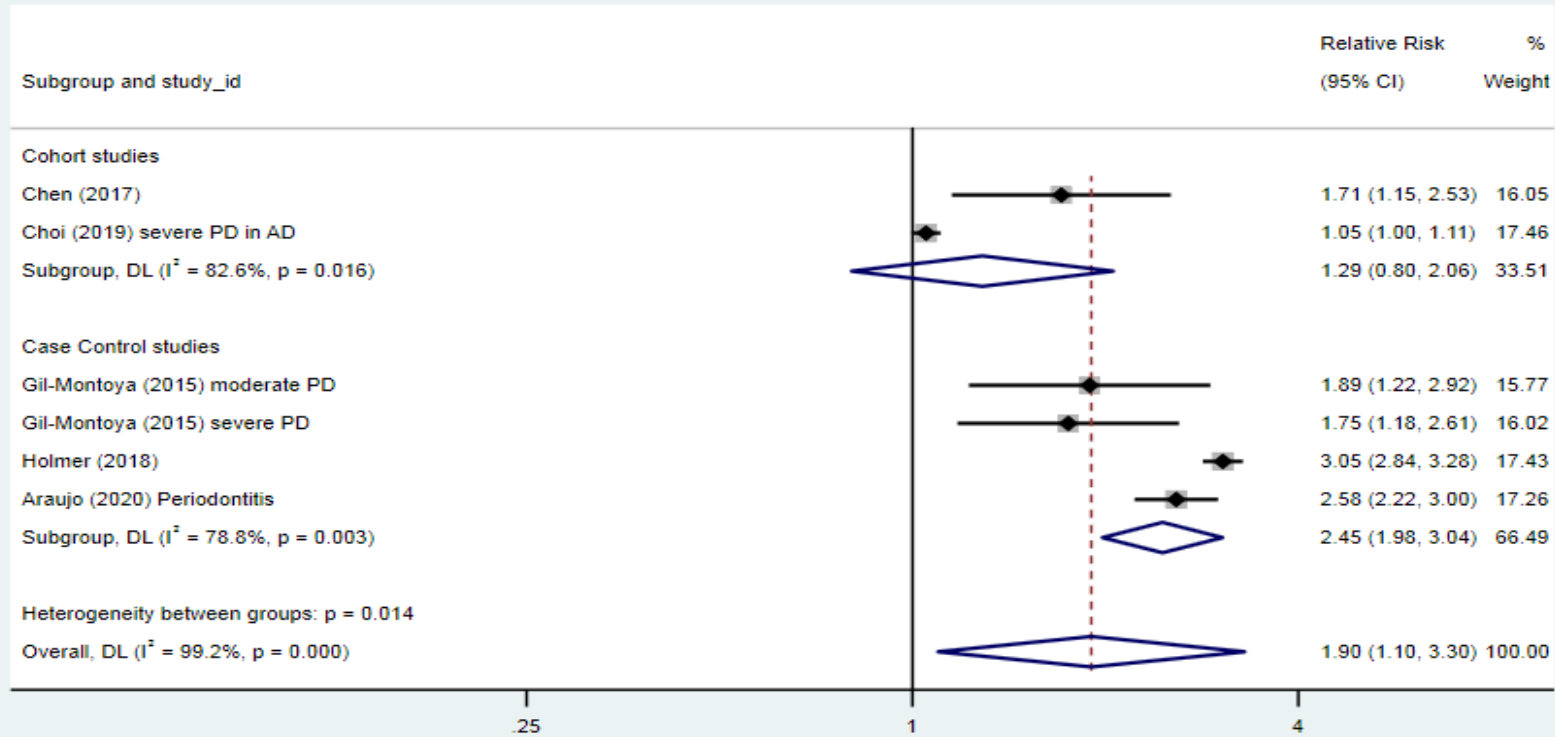


Figure 4.7: Forest plot showing pooled relative risk (RR) of adjusted case-control and cohort studies included for PD and AD risk by study design



NOTE: Weights and between-subgroup heterogeneity test are from random-effects model

CHAPTER FIVE: ASSOCIATION OF ORAL HEALTH WITH DEMENTIA: A CASE-CONTROL STUDY

5.1 Introduction

Previous literature showed inconsistent findings of the association of oral health with an increased risk of dementia. Some studies found a significant association between poor oral health and the risk of dementia (Tzeng *et al.*, 2016; Lee *et al.*, 2017a; Lee *et al.*, 2017b), while others did not (Arrivé *et al.*, 2012; Stein *et al.*, 2007). They used different measurements of oral health in the studies, and the findings varied. Also, almost all studies were undertaken in high income countries, and there was lack of data from LMICs, where oral diseases and dementia are more prevalent. China is the largest LMICs in terms of population and area. Despite the high prevalence of oral health problems, dental care service utilisation is low in China (Xu *et al.*, 2020). Additionally, dental care literacy among the Chinese population is still far behind developed countries (Zhu *et al.*, 2005). Most Chinese adults do not seek dental services unless they need dental treatment (Xu *et al.*, 2020). The prevalence of periodontitis among older adults ranging from 55-64 and 65-74 years of age is 69.3% and 64.6%, respectively (Jiao *et al.*, 2021).

In this chapter, a case-control study was carried out to examine the association of oral health (OH), oral hygiene habits, number of teeth present, SROH conditions and PD with dementia in China.

5.2 Methods

The studied population were derived from the Guangzhou case-control study in China. The methods of the study have been described in chapter 3, section 3.6.2.

5.2.1 Data Collection

Data was collected through face-to-face interviews conducted in a safe and quiet place in (e.g., clinic ward), Guangzhou, China. Before the interview, all participants were asked permission for interview along with written informed consent, or if this was not possible, from a consultee. The local interview team used a validated questionnaire, which I developed for oral health parts and other co-variables. The questionnaire includes socio-demographic, lifestyles, social networks and support, ETS exposure, dietary intakes, CVDRFs, and others (including oral health). In the interview, oral health questions were asked about SROH, SROH conditions (oral health-related quality of life), number of teeth present, oral hygiene and PD indicators. Each interview took around 45 minutes.

5.2.2 Data analysis

The distributions of the socio-demographic, dietary intake, oral health and clinical characteristics in participants were examined. The differences between case and control groups were tested using the Chi-squared test or Fisher exact test/Likelihood test for categorical variables and one way ANOVA for continuous variables. Binary logistic regression models were employed to calculate odd ratios (ORs) and 95% confidence interval (95%CI) to assess the risk of dementia with any level of oral health variables. Sensitivity analyses were done by excluding the participants who were older than 80 years of age. Unknown values in periodontitis indicators were changed into no values (see footnotes for details in table 5.9). In the regression models, different sets of confounding variables were adjusted (see footnotes in Tables 5.4-5.10).

5.3 Results

5.3.1 Descriptive statistics

Of 466 participants, the average age was 73.6 years ($SD_{\pm 9.5}$), 63.5% were females, and 50.9% were having the educational levels of primary school or illiteracy. Table 5.1 shows the characteristics of the participants in detail. Compared to the control, participants with dementia were more likely to be older, smokers (current or former), alcohol drinking (never or < once per month), illiterate, widowed, with a family income below 30,000 RMB and personal income below 10,000 RMB per annum, increased consumption of beef, lamb, pork, fruits and vegetable, and have coronary heart disease and stroke. There were no significant differences in gender, hypertension, diabetes and kidney disease between the cases and control groups (Table 5.1).

Table 5.2 shows the number and percentages of different levels of SROH and oral hygiene indicators in participants and their differences between the case and control groups. Most of the participants reported their SROH status as being good (23.4%) and average (56.0%). People with dementia are likely to have poorer SROH, SROH conditions, fewer teeth present and less brushing teeth and avoid seeing the dentist. There were no significant differences in the use of mouth wash and floss between participants with dementia and those without dementia.

Table 5.3 shows the number and percentages of different PD indicators (gingivitis/periodontitis) in participants with and without dementia. PD indicators showed that PD was likely to increase more in cases. Compared to the controls, participants with dementia were more likely to have bleeding gums, swollen gums, painful gums, oral ulcers, and bad breath. There were no differences in PD (periodontitis) indicators except for bone loss around the tooth variable.

5.3.2 Multivariate logistic regression analysis

Table 5.4 shows numbers, percentages and ORs of dementia in SROH, teeth number and edentulism. Compared to the control, participants with dementia were more likely to have increased “very good/good” and “very poor/poor” OH. After adjustment for age, gender and education in model 1, the ORs of having “very good/good” and “very poor/poor” OH in participants were 1.69 (95%CI 1.05-2.72) and 2.09 (1.19-3.65). Further adjustment for family income, marital status, lifestyles, and dietary intake did not substantially change the findings in model 2, the corresponding ORs were 1.74 (1.04-2.90) and 2.25 (1.22-4.16) respectively. In the fully adjusted model 3, the OR of “very good/good” in people with dementia was not statistically significant (1.61, 0.97-2.80). However, the OR of “very poor/poor” SROH remained significantly increased (1.97, 1.01-3.85). In the analysis for the number of teeth, adjusted ORs showed an inverse dose-response association of teeth number with the risk of dementia (Table 5.4). The results in the model 3 indicated such a dose-response relationship; compared to those with the number of teeth present ≥ 25 teeth, ORs of dementia in participants with 1-8 teeth present and with no tooth present/edentulous were 3.02 (1.37-6.67) and 6.51 (2.47-17.15). For “edentate and dentate”, the findings showed a significant association with dementia risk; the OR was 2.81 (1.30-6.08) in model 1, 2.64 (1.15-6.10) in model 2, and 3.16 (1.30-7.67) in model 3.

Table 5.5 shows numbers, percentages and ORs of dementia in different SROH conditions (OHRQoL). Significant results were found in all models when “always” was compared to “never” SROH condition. In the fully adjusted model 3, there was an increased risk of dementia; the OR of dementia was 3.20 (1.50-6.81) in “teeth problems limiting food intake”, 4.43 (1.63-12.05) in “slip liquid to aid in swallowing food”, and 4.48 (1.54-13.08) in “mouth feels dry when eating food”. However, data of “difficulties in swallowing food” showed a significant inverse association with dementia when “often/frequently/always” was compared

to “never” (OR 0.38, 0.19-0.75). A new variable (score of SROH conditions) was calculated based on the values of the above four variables (Table 5.4 see footnotes for detail). The SROH conditions of “always” (level four) when compared to “never” (level one) showed a significant risk of dementia; the ORs was 6.22 (2.56-15.08) in model 1, 5.44 (2.11-14.03) in model 2, and 5.09 (1.84-14.11) in model 3.

Table 5.6 shows numbers, percentages and ORs of dementia in oral hygiene habits. A non-significant association was found for flossing teeth when “frequently” was compared to “never”. Moreover, when the flossing teeth variable was examined, a decreased OR of dementia in “occasionally” versus “frequently” flossing teeth was observed, but the OR in “never” was not significant. Similarly, in the mouthwash, a non-significant association was found with “never” and with “occasionally”. However, “brushing teeth” and “visiting dentist” showed a significant and inverse association with the risk of dementia (see Table 5.6).

Table 5.7 shows the numbers, percentages and ORs of dementia in different PD indicators at three levels. The highest level (always) of bleeding gums, swollen gums and bad breath compared to their lowest level (never) was significantly associated with an increased risk of dementia. The increased OR at the middle level (sometimes) was not statistically significant. However, such an association was not found for oral ulcers and painful gums in the fully adjusted regression models. The pooled data for the above five variables (Table 5.7) showed that the fully adjusted ORs of dementia in the middle and highest levels of PD was 2.26 (1.34-3.84) and 3.72 (1.04-13.34), respectively (See details in footnotes of Table 5.7).

Table 5.8 shows the numbers, percentages and ORs of dementia in the self-reported PD indicators (*tooth moved forward, received any dental treatment, have been told of bone loss and the tooth has become loose*). There was a non-significant association in all of them, which could be due to the small numbers of participants in those periodontitis measurements. After recoding those “unknown” values as “no” values, four variables from above mentioned in

Table 5.8 were pooled to create two new variables “periodontitis” for analysis in Table 5.9 (comprising two and three levels, see footnotes in Table 5.9) and the results showed a non-significant inverse association of periodontitis indicators with dementia risk.

Table 5.10 shows the numbers, percentages and adjusted ORs of dementia in PD variables. The two PD variables were comprised of bleeding gums, swollen gums, bad breath, PD treatment and bone loss derived from Table 5.3. The PD variables were in three levels (normal, mild, and moderate/severe PD) and also in two levels (yes or no presence of PD) for analysis. The result of PD yes versus no showed that PD was significantly associated with an increased risk of dementia in all adjusted models. The findings in three levels of PD variable showed that when “moderate/severe PD” was compared with “normal” revealed that PD was significantly associated with an increased risk of dementia the ORs in model 1 was 2.83 (1.17-6.85), in model 2 was 3.12 (1.23-7.92), and in model 3 was 2.95 (1.06-8.19). There was a positive significant association of mild PD with an increase of dementia in all adjusted models (see table 5.10 footnotes).

Sensitivity analyses excluding 119 participants above 80 years of age were conducted to examine the associations, showing similar results to those in below analyses. The results changed from significant to non-significant with dementia risk for those cases who tried to avoid a dentist or have never been to a dentist (OR 2.04, 0.83-5.01).

Table 5.1: Characteristics of participants in Guangzhou case-control study

Variables	All participants		Dementia		Non-Dementia		P Value*
	n=466	(%)	n=233	(%)	n=233	(%)	
<u>Demographic factors</u>							
Age (years) Mean (SD)	73.60	9.46	77.2	10.51	70.00	6.55	<0.001
Age group (years)							
50-60	29	6.2	19	8.2	10	4.3	<0.001
61-70	169	36.3	43	18.5	126	54.1	
71-80	149	32.0	67	28.8	82	35.2	
81=>	119	25.5	104	44.6	15	6.4	
Gender							
Women	296	63.5	153	65.7	143	61.4	0.336
Men	170	36.5	80	34.3	90	38.6	
Smoking							
Never	380	81.5	183	78.5	197	84.5	0.002
Former	48	10.3	35	15.0	13	5.6	
Current	38	8.2	15	6.4	23	9.9	
^aDrinking any alcohol over the past two years							
Never or less than once per month	440	94.4	225	96.6	215	92.3	0.044
More than once month/ weekly/daily	26	5.6	8	3.4	18	7.7	
<u>Socioeconomic status</u>							
Educational level							
University and above	50	10.7	20	8.6	30	12.8	0.001
Senior high school	60	13.0	21	9.0	39	17.0	
Junior high school	118	25.4	55	23.6	63	27.2	
Primary school	151	32.3	79	33.9	72	30.6	
Illiteracy	87	18.6	58	24.9	29	12.3	

Personal/annual income (RMB)							
above 70000	47	10.1	33	14.2	14	6.0	0.001
50000-70000	62	13.3	18	7.7	44	18.9	
30000-50000	120	25.8	42	18.0	78	33.5	
10000-30000	136	29.2	65	27.9	71	30.5	
Below 10000	101	21.7	75	32.2	26	11.2	
Family income (RMB)							
70000 and above	70	15.0	42	18.0	28	12.0	0.004
50000-70000	72	15.5	29	12.4	43	18.5	
30000-50000	163	35.0	69	29.6	94	40.3	
30000 and below	161	34.5	93	39.9	68	29.2	
<u>Social network</u>							
Marriage							
Married or cohabiting	300	64.4	122	52.4	178	76.4	<0.001
Separated, divorced and never married	32	6.9	22	9.4	10	4.3	
Widowed	132	28.3	89	38.2	43	18.5	
*Missing	2	0.4	0	0	2	0.9	
<u>Dietary intake</u>							
<u>Meat consumption</u>							
Beef intake frequency in the past two years							
Never or less than once per month	281	60.3	130	55.8	151	64.8	<0.001
=< Once a week	95	20.4	37	15.9	58	24.9	
> Once a week and < daily	76	16.3	54	23.2	22	9.4	
Once a day/>= Twice a day	14	3.0	12	5.2	2	0.9	
Lamb intake frequency in the past two years							

Never or less than once per month	361	77.5	182	78.1	179	76.8	0.038
=< Once a week	57	12.2	22	9.4	35	15.0	
> Once a week and < daily	33	7.1	17	7.3	16	6.9	
Once a day/>= Twice a day	15	3.2	12	35.2	3	1.3	
Pork intake frequency in the past two years							
Never or less than once per month	32	6.9	13	5.6	19	8.2	<0.001
=< Once a week	41	8.8	28	12.0	13	5.6	
> Once a week and < daily	200	42.9	85	36.5	115	49.4	
Once a day	148	31.8	72	30.9	76	32.6	
>= Twice a day	45	9.7	35	15.0	10	4.3	
^bMeat consumption score							
0-3	24	5.2	12	5.2	12	5.2	0.031
4-5	147	31.5	68	29.2	79	33.9	
6-10	280	60.1	140	60.1	140	60.1	
11-15	15	3.2	13	5.6	2	0.9	
<u>Vegetable and fruit consumption</u>							
Vegetable frequency during past two years							
Never or less than once per month	11	2.4	8	3.4	3	1.3	<0.001
=< Once a week	17	3.6	15	6.4	2	0.9	
> Once a week and < daily	55	11.8	37	15.9	18	7.7	
Once a day	193	41.4	74	31.8	119	51.1	
>= Twice a day	190	40.8	99	42.5	91	39.1	

Fruit frequency during the past two years							
Never or less than once per month	24	5.2	21	9.0	3	1.3	<0.001
=< Once a week	46	9.9	32	13.7	14	6.0	
> Once a week and < daily	173	37.1	73	31.3	100	42.9	
Once a day	186	39.9	83	35.6	103	44.2	
>= Twice a day	37	7.9	24	10.3	13	5.6	
*Fruit and vegetable consumption scores							
0-3	10	2.1	8	3.4	2	0.9	0.006
4-5	26	5.6	20	8.6	6	2.6	
6-7	161	34.5	80	34.3	81	34.8	
8-10	269	57.7	125	53.6	144	61.8	
<u>Cardiovascular disease and risk factors</u>							
Hypertension status							
No	219	47.0	102	43.8	117	50.2	0.164
Yes	247	53.0	131	56.2	116	49.8	
Diabetes							
No	374	80.3	184	79.0	190	81.5	0.485
Yes	92	19.7	49	21.0	43	18.5	
Coronary heart disease							
No	423	90.8	205	88.0	218	93.6	0.037
Yes	43	9.2	28	12.0	15	6.4	
Stroke							
No	404	86.7	175	75.1	229	98.3	<0.001
Yes	59	12.7	55	23.6	4	1.7	
*Missing	3	0.6	3	1.3	0		
Kidney disease							

No	448	96.1	223	95.7	225	96.1	0.631
Yes	18	3.9	10	4.3	8	3.9	

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

^aDrinking any alcohol during the past two years: Variables pooled were average frequency use wine (glass), beer (bottle), other alcohol (red wine, rice wine, fruit wine, etc.) during the past two years [100ml]?

^bScores of Meat consumption: Variables pooled from pork, beef, and lamb. Scoring was 0-3- (Never); 4-5 (= < Once a week); 6-10 (> Once a week and < daily); 11-15- (once or more than once)

^cScores of fruits and vegetables consumption: Scoring was as 0-3 (Never); 4-5 (= < Once a week); 6-7- (> Once a week and < daily); 8-10 (once or more than once)

Table 5.2: Numbers and percentages of oral health measurements in people with and without dementia in Guangzhou case-control study

Oral health variables	All participants		Dementia		Non - Dementia		P Value*
	n=466	(%)	n=233	(%)	n=233	(%)	
Self-rated oral health							
Very good	14	3.0	11	4.7	3	1.3	0.003
Good	109	23.4	52	22.3	57	24.5	
Average	261	56.0	118	50.6	143	61.4	
Poor	61	13.1	36	15.5	25	10.7	
Very poor	20	4.3	16	6.9	4	1.7	
*Missing	1	0.2	0	0	1	0.4	
<u>Oral hygiene</u>							
Flossing							
Always	19	4.1	13	5.6	6	2.6	0.061
Frequently	13	2.8	6	2.6	7	3.0	
Often	19	4.1	7	3.0	12	5.2	
Occasionally	40	8.6	13	5.6	27	11.6	
Never	366	78.5	187	80.3	179	76.8	
*Missing	9	1.9	7	3.0	2	0.9	
Dental rinse or mouthwash							
Always	33	7.1	21	9.0	12	5.2	0.147
Frequently	23	4.9	15	6.4	8	3.4	
Often	30	6.4	17	7.3	13	5.6	
Occasionally	45	9.7	19	8.2	26	11.2	
Never	330	70.8	158	67.8	172	73.8	
*Missing	5	1.1	3	1.3	2	0.9	
Brushing teeth							

More than twice a day	21	4.5	7	3.0	14	6.0	<0.001
Twice	166	35.6	35	15.0	131	56.2	
Once a day	181	38.8	105	45.1	76	32.6	
Less than once a day	41	8.8	36	15.5	5	2.1	
Do not brush	57	12.2	50	21.5	7	3.0	

Dental visits

Every 6 months	24	5.2	6	2.6	18	7.7	<0.001
Once a year	34	7.3	15	6.4	19	8.2	
Every two year	34	7.3	3	1.3	31	13.3	
More than 2 years	153	32.8	81	34.8	72	30.9	
Try to avoid going to dentist	206	44.2	128	54.9	78	33.5	
*Missing	15	3.2	0	0	15	6.4	

Number of teeth present in the mouth

=>25 teeth	180	38.6	49	21.0	131	56.2	<0.001
17-24 teeth	99	21.2	55	23.6	44	18.9	
9-16 teeth	71	15.2	44	18.9	27	11.6	
1-8 teeth	67	14.4	46	19.7	21	9.0	
Edentulous	48	10.3	38	16.3	10	4.3	
*Missing	1	0.2	1	0.4	0	0	

^aSROH conditions

Do teeth problems limit foods?

Never	149	32.0	58	24.9	91	39.1	<0.001
Occasionally	114	24.5	42	18.0	72	30.9	
Often	114	24.5	63	27.0	51	21.9	
Always	89	19.1	70	30.0	19	8.2	

Difficulties swallowing foods?

Never	207	44.4	94	40.3	113	48.5	<0.001
Occasionally	125	26.8	49	21.0	76	32.6	
Often	88	18.9	48	20.6	40	17.2	
Always	43	9.2	39	16.7	4	1.7	
*Missing	3	0.6	3	1.3	0	0	

Slip liquid to aid in swallowing foods

Never	217	46.6	96	41.2	121	51.9	<0.001
Occasionally	117	25.1	44	18.9	73	31.3	
Often	75	16.1	44	18.9	31	13.3	
Always	52	11.2	44	18.9	8	3.4	
*Missing	5	1.1	5	2.1	0	3.4	

Mouth feels dry when eating foods?

Never	221	47.4	107	45.9	114	48.9	<0.001
Occasionally	119	25.5	43	18.5	76	32.6	
Often	85	18.2	50	21.5	35	15.0	
Always	35	7.5	28	12.0	7	3.0	
*Missing	6	1.3	5	2.1	1	0.4	

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

^aSROH conditions four level were used for analysis (always, often, occasionally, never)

Table 5.3: Numbers and percentages of periodontal disease in people with and without dementia: Guangzhou Case-Control Study

Oral health variables	All participants		Dementia		Non - Dementia		P Value*
	n=466	(%)	n=233	(%)	n=233	(%)	
<u><i>Periodontal Disease (gingivitis/periodontitis)</i></u>							
Bleeding gums							
Always	31	6.7	22	9.4	9	3.9	0.034
Sometimes	61	13.1	35	15.0	26	11.2	
Rarely	138	29.6	69	29.6	69	29.6	
Never	233	50.0	106	45.5	127	54.5	
*Missing	3	0.6	1	0.4	2	0.9	
Swollen gums							
Always	29	6.2	20	8.6	9	3.9	<0.001
Sometimes	67	14.4	42	18.0	25	10.7	
Rarely	123	26.4	72	30.9	51	21.9	
Never	245	52.6	98	42.1	147	63.1	
*Missing	2	0.4	1	0.4	1	0.4	
Painful gums							
Always	35	7.5	21	9.0	14	6.0	<0.001
Sometimes	69	14.8	46	19.7	23	9.9	
Rarely	129	27.7	75	32.2	54	23.2	
Never	232	49.8	90	38.6	142	60.9	
*Missing	1	0.2	1	0.4	0	0	
Oral ulcers							
Always	31	6.7	16	6.9	15	6.4	<0.001
Sometimes	57	12.2	37	15.9	20	8.6	
Rarely	146	31.3	87	37.3	59	25.3	

Never	229	49.1	92	39.5	137	58.8	
*Missing	3	0.6	1	0.4	2	0.9	
Bad breath							
Always	48	10.3	35	15.0	13	5.6	<0.001
Sometimes	73	15.7	47	20.2	26	11.2	
Rarely	149	32.0	72	30.9	77	33.0	
Never	190	40.8	76	32.6	114	48.9	
*Missing	6	1.3	3	1.3	3	1.3	
<u>PD (periodontitis)</u>							
Had treatment for gum disease, such as scaling and root planning, sometimes called ‘deep cleaning’?							
No	334	71.7	143	61.4	191	82.0	0.328**
Yes	37	7.9	19	8.2	18	7.7	
Unknown	95	20.4	71	30.5	24	10.3	
Have you been told by a dental professional that you lost bone around your teeth?							
No	325	69.7	130	55.8	195	83.7	0.032**
Yes	26	5.6	16	6.9	10	4.3	
Unknown	114	24.5	86	36.9	28	12.0	
*Missing	1	0.2	1	0.4	0	0	
Noticed that your front teeth moved forward or that gaps have developed between your front teeth?							
No	272	58.4	119	51.1	153	65.7	0.991**
Yes	87	18.7	38	16.3	49	21.0	
Unknown	107	23.0	76	32.6	31	13.3	

Have you had your teeth that became loose on their own, without any injury?							
No	235	50.4	102	43.8	133	57.1	<i>0.121**</i>
Yes	151	32.4	78	33.5	73	31.3	
Unknown	80	17.2	53	22.7	27	11.6	

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

**P-value in the Chi-square test was calculated based on available data, not including those “missing” and “unknown” data; if including those unknown for analysis, all p values in above variables were <0.001.

^aPD indicator (gingivitis/periodontitis) used four levels for analyses (always, sometimes, rarely, never).

Table 5.4: Association of oral health with dementia in Guangzhou case-control study

Self-reported oral health	Cases		Control		P*	Model 1			Model 2			Model 3					
	Dementia		Non-dementia			OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
	n=233	(%)	n=233	(%)													
^aSelf-rated oral health																	
Very Good/Good	63	27.0	60	25.8	0.011	1.69	1.05	2.72	0.032	1.74	1.04	2.90	0.036	1.61	0.97	2.80	0.090
Average	118	50.6	143	61.4		Ref				Ref				Ref			
Poor/very poor	52	22.3	29	12.4		2.09	1.19	3.65	0.010	2.25	1.22	4.16	0.010	1.97	1.01	3.85	0.047
*Missing	0	0	1	0.4													
Number of teeth present																	
=>25 teeth	49	21.0	131	56.2	<0.001	Ref				Ref				Ref			
17-24 teeth	55	23.6	44	18.9		2.79	1.60	4.87	<0.001	3.08	1.65	5.76	<0.001	2.84	1.45	5.55	0.002
9-16 teeth	44	18.9	27	11.6		3.46	1.84	6.49	<0.001	3.40	1.67	6.91	<0.001	2.87	1.32	6.21	0.008
1-8 teeth	46	19.7	21	9.0		3.46	1.78	6.74	<0.001	3.62	1.72	7.57	<0.001	3.02	1.37	6.67	0.006

0 edentulous	38	16.3	10	4.3		6.04	2.64	13.82	<0.001	5.92	2.37	14.71	<0.001	6.51	2.47	17.15	<0.001
*Missing	1	0.4	0	0													
<hr/>																	
^bEdentate- edentulous																	
Teeth present	194	83.3	223	95.7	<0.001	Ref				Ref				Ref			
Edentulous	38	16.3	10	4.3		2.81	1.30	6.08	0.009	2.64	1.15	6.10	0.023	3.16	1.30	7.67	0.011
*Missing	1	0.4	0	0													

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

^a Self-rated oral health (3 levels) derived from self-rated oral health (5 levels) variable in table 5.2

^bEdentulous (2 levels) variable was derived from the number of teeth present (5 levels) variable in table 5.2

Model 1: adjusted for age (cont.), gender and education

Model 2: adjusted for Model 1 plus family income, marital status, smoking, alcohol, fruit and vegetable consumption score, meat consumption score (lamb, beef, pork)

Model 3: adjusted for Model 2 plus hypertension, coronary heart disease, diabetes, stroke, kidney disease

Table 5.5 Association of self-reported oral health conditions with dementia in the Guangzhou case-control study.

SROH conditions	Cases- Dementia		Control- Non- dementia		P*	Model 1				Model 2			Model 3				
	n=233	(%)	n=233	(%)		OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
Teeth problems limit foods																	
Never	58	24.9	91	39.1	<0.001	Ref				Ref				Ref			
Occasionally	42	18.0	72	30.9		0.86	0.50	1.47	0.584	0.82	0.45	1.49	0.517	0.68	0.36	1.30	0.245
Often	63	27.0	51	21.9		1.57	0.92	2.68	0.097	1.45	0.81	2.60	0.207	1.16	0.62	2.15	0.647
Always	70	30.0	19	8.2		4.00	2.09	7.66	<0.001	3.78	1.87	7.64	0.001	3.20	1.50	6.81	0.003
Difficulties in swallowing foods?																	
Never	94	40.3	113	48.5	<0.001	Ref				Ref				Ref			
Occasionally	49	21.0	76	32.6		0.64	0.39	1.06	0.080	0.64	0.37	1.12	.116	0.75	0.41	1.36	0.337
Often/Frequently/Always	87	37.3	44	18.9		0.41	0.23	0.71	0.001	0.36	0.19	0.67	.001	0.38	0.19	0.75	0.005
*Missing	3	1.3	0														

Slip liquid to aid in swallowing foods																		
Never	96	41.2	121	51.9	<0.001	Ref					Ref							Ref
Occasionally	44	18.9	73	31.3		0.64	0.39	1.06	0.084	0.51	0.29	0.90	0.020	0.58	0.32	1.05	0.070	
Often	44	18.9	31	13.3		1.34	0.74	2.42	0.340	1.28	0.67	2.47	0.459	1.12	0.54	2.29	0.768	
Always	44	18.9	8	3.4		4.76	2.02	11.24	<0.001	4.12	1.64	10.43	0.003	4.43	1.63	12.05	0.004	
*Missing	5	2.1	0	3.4														
Mouth feels dry when eating foods?																		
Never	107	45.9	114	48.9	<0.001	Ref												
Occasionally	43	18.5	76	32.6		0.52	0.32	0.86	0.010	0.47	0.27	0.83	0.009	0.57	0.31	1.03	0.062	
Often	50	21.5	35	15.0		1.10	0.63	1.94	0.735	0.90	0.48	1.67	0.730	0.92	0.47	1.79	0.798	
Always	28	12.0	7	3.0		3.17	1.24	8.12	0.016	3.37	1.23	9.25	0.019	4.48	1.54	13.08	0.006	
*Missing	5	2.1	1	0.4														
^aPooled score of SROH conditions																		
0	45	19.3	81	34.8	<0.001	Ref				Ref				Ref				

1-4	69	29.6	80	34.3	1.37	0.82	2.29	0.234	1.33	0.76	2.34	0.322	1.05	0.57	1.92	0.883
5-8	68	29.2	63	27.0	1.37	0.79	2.36	0.259	1.18	0.65	2.15	0.583	1.03	0.54	1.95	0.929
9-12	46	19.7	8	3.4	6.22	2.56	15.08	<0.001	5.44	2.11	14.03	0.001	5.09	1.84	14.11	0.002
*Missing	5	2.1	1	0.4												

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

^aPooled score of SROH condition derived from Teeth problems limit foods, Difficulties in swallowing foods, Slip liquid to aid swallowing foods, mouth feels dry when eating foods; these variables are present in table 5.2. *Scores of SROH*: 0 (never); 1-4 (occasionally); 5-8 (often) and 9-12 (Always)

Model 1: adjusted for age (cont.), gender and education

Model 2: adjusted for Model 1 plus family income, marital status, smoking, alcohol, fruit and vegetable consumption score, meat consumption score (lamb, beef, pork)

Model 3: adjusted for Model 2 plus hypertension, coronary heart disease, diabetes, stroke, kidney disease

Table 5.6: Association of oral hygiene with dementia in Guangzhou case-control study.

Oral hygiene variables	Cases		Control		P*	Model 1			Model 2			Model 3					
	n=233	(%)	n=233	(%)		OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
^aFlossing																	
Frequently	19	8.2	13	5.6	0.025	Ref				Ref				Ref			
Occasionally	20	8.6	39	16.7		0.36	0.14	0.95	0.040	0.28	0.09	0.84	0.024	0.28	0.08	0.92	0.036
Never	187	80.3	179	76.8		0.73	0.33	1.62	0.437	0.66	0.27	1.56	0.340	0.69	0.26	1.79	0.440
*Missing	7	3.0	2	0.9													
^aMouthwash																	
Frequently	36	15.5	20	8.6	0.071	Ref				Ref				Ref			
Occasionally	36	15.5	39	16.7		0.68	0.32	1.48	0.336	0.45	0.19	1.10	0.079	0.40	0.16	1.03	0.058
Never	158	67.8	172	73.8		0.72	0.38	1.36	0.311	0.57	0.28	1.14	0.111	0.54	0.26	1.13	0.102
*Missing	3	1.3	2	0.9													
^aBrushing																	
More than once a day	42	18.0	145	62.2	<0.001	Ref				Ref				Ref			

Once a day	105	45.1	76	32.6		4.77	2.90	7.85	<0.001	5.19	2.99	9.00	<0.001	5.31	2.92	9.67	<0.001
Never or less than once a day	86	36.9	12	5.2		21.44	10.24	44.91	<0.001	19.80	9.11	43.05	<0.001	23.27	10.10	53.62	<0.001
^aDental visit																	
Every 6 months /Once a year	21	9.0	37	15.9	<0.001	Ref				Ref				Ref			
Every 2 years/> 2 years	84	36.1	103	44.2		1.46	0.76	2.82	0.260	1.28	0.62	2.63	0.508	1.23	0.56	2.71	0.602
Try to avoid dentist or never been to a dentist	128	54.9	78	33.5		2.94	15.2	5.67	0.001	2.59	1.25	5.35	0.010	2.43	1.11	5.35	0.027
*Missing	0	0	15	6.4													

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

^aClassification of Oral hygiene variables were changed into 3 levels for analyses: *Do you use a dental rinse or mouthwash to clean your mouth?* and *Do you use dental floss to clean your mouth??* (Always, frequently, sometimes, occasionally, and never) from table 5.2 were derived as frequently, sometimes, and never for analyses. *How often do you go to the dentist?* (Every 6 months, once a year, every two years, more than 2 years and try to avoid or never been to the dentist) from table 5.2 were derived as Every 6 months /Once a year, Every 2 years/> 2 years and Try to avoid the dentist or never been to a dentist. *How many times a day do brush your teeth* (Do not brush, less than once a day, once a day, twice a day and More than twice a day) were derived as More than once a day, Once a day and never or less than once a day.

Model 1: adjusted for age (cont.), gender and education

Model 2: adjusted for Model 1 plus family income, marital status, smoking, alcohol, fruit and vegetable consumption score, meat consumption score (lamb, beef, pork)

Model 3: adjusted for Model 2 plus hypertension, coronary heart disease, diabetes, stroke, kidney disease

Table 5.7: Association of periodontal disease indicators (gingivitis/periodontitis) with dementia

PD (gingivitis/ periodontitis)	Cases- Dementia		Control- Non- dementia		P*	Model 1			Model 2			Model 3					
	n=233	(%)	n=233	(%)		OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
*Bleeding gums																	
Never	175	75.1	196	84.1	0.019	Ref				Ref				Ref			
Sometimes	35	15.0	26	11.2		1.18	0.65	2.14	0.589	1.27	0.65	2.50	0.484	1.05	0.50	2.20	0.890
Always	22	9.4	9	3.9		2.81	1.16	6.84	0.023	3.29	1.27	8.54	0.015	4.07	1.47	11.28	0.007
*Missing	1	0.4	2	0.9													
*Swollen gums																	
Never	170	73.0	198	85.0	0.005	Ref				Ref				Ref			
Sometimes	42	18.0	25	10.7		1.69	0.94	3.05	0.080	1.80	0.93	3.45	0.079	1.43	0.70	2.96	0.329
Always	20	8.6	9	3.9		2.89	1.18	7.08	0.021	3.03	1.18	7.76	0.021	3.29	1.23	8.81	0.018
*Missing	1	0.4	1	0.4													
*Painful gums																	
Never	165	70.8	196	84.1	0.003	Ref				Ref				Ref			
Sometimes	46	19.7	23	9.9		2.13	1.18	3.86	0.012	2.01	1.04	3.88	0.037	1.65	0.80	3.42	0.176

Always	21	9.0	14	6.0		1.59	0.73	3.45	0.242	1.60	0.69	3.68	0.270	1.50	0.62	3.60	0.367
*Missing	1	0.4	0														

***Oral ulcers**

Never	179	76.8	196	84.1	0.053	Ref				Ref				Ref			
Sometimes	37	15.9	20	8.6		1.44	0.76	2.73	0.267	1.43	0.70	2.89	0.32	1.54	0.72	3.26	0.263
Always	16	6.9	15	6.4		1.09	0.50	2.40	0.823	1.32	0.55	3.20	0.54	1.26	0.49	3.21	0.630
*Missing	1	0.4	2	0.9													

***Bad breadth**

Never	148	63.5	191	82.0	<0.001	Ref				Ref				Ref			
Sometimes	47	20.2	26	11.2		1.63	0.91	2.89	0.099	1.77	0.94	3.33	0.079	1.56	0.79	3.09	0.199
Always	35	15.0	13	5.6		3.47	1.67	7.19	<0.001	3.44	1.57	7.50	0.002	3.17	1.35	7.44	0.008
*Missing	3	1.3	3	1.3													

^bPooled PD indicators score (gingivitis/periodontitis)

0	104	44.6	161	69.1	<0.001	Ref				Ref				Ref			
1-6	114	48.9	63	27.0		2.35	1.53	3.61	<0.001	2.42	1.49	3.92	0.001	2.26	1.34	3.84	0.002
7-10	12	5.2	5	2.1		3.46	1.08	11.02	0.036	3.44	1.03	11.53	0.045	3.72	1.04	13.34	0.044

*Missing 3 1.3 4 1.7

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

^aClassification always, sometimes, rarely, and never of PD indicators (gingivitis/periodontitis) from table 5.3 were derived as always, sometimes, and never for analyses

^bPooled PD problems (gingivitis/periodontitis) are aggregate of bleeding gums, painful gums, swollen gums, oral ulcer, and bad breath are taken from table 5.7. *Scores of pooled PD indicators score (gingivitis/ periodontitis):* 0 (never); 1-6 (mild/moderate); 7-10 (severe)

Model 1: adjusted for age (cont.), gender and education

Model 2: adjusted for Model 1 plus family income, marital status, smoking, alcohol, fruit and vegetable consumption score, meat consumption score (lamb, beef, pork)

Model 3: adjusted for Model 2 plus hypertension, coronary heart disease, diabetes, stroke, kidney disease

Table 5.8: Association of periodontal disease (periodontitis) with dementia in the Guangzhou case-control study.

Periodontal disease (periodontitis)	Cases		Control		P*	Model 1			Model 2			Model 3					
	Dementia		Non-dementia			OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
	n=233	(%)	n=233	(%)													
Tooth moved forward																	
No	119	51.1	153	65.7	<0.001	Ref				Ref				Ref			
Yes	38	16.3	49	21.0		0.87	0.52	1.48	0.614	0.80	0.45	1.42	0.437	0.770	0.42	1.42	0.402
Unknown	76	32.6	31	13.3		2.93	1.72	5.00	<0.001	3.98	2.18	7.29	<0.001	3.274	1.72	6.22	<0.001
Tooth loose																	
No	102	43.8	133	57.1	0.002	Ref				Ref				Ref			
Yes	78	33.5	73	31.3		1.21	0.77	1.89	0.412	1.12	0.68	1.83	0.663	1.08	0.64	1.84	0.777
Unknown	53	22.7	27	11.6		2.80	1.55	5.06	<0.001	3.37	1.75	6.52	0.001	3.18	1.55	6.51	0.002
PD Treatment																	
No	143	61.4	191	82	<0.001	Ref				Ref				Ref			
Yes	19	8.2	18	7.7		1.52	0.72	3.17	0.269	1.47	0.67	3.20	0.339	1.39	0.59	3.30	0.449
Unknown	71	30.5	24	10.3		4.02	2.29	7.06	<0.001	4.75	2.49	9.03	<0.001	4.42	2.24	8.73	<0.001
Bone loss																	

No	130	55.8	195	83.7	<0.001	Ref								Ref				
Yes	16	6.9	10	4.3		2.26	0.92	5.57	0.075	2.12	0.81	5.53	0.126	2.08	0.73	5.90	0.171	
Unknown	86	36.9	28	12.0		4.88	2.86	8.32	<0.001	5.03	2.77	9.16	<0.001	4.39	2.33	8.29	<0.001	

*Missing

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Model 1: adjusted for age (cont.), gender and education

Model 2: adjusted for Model 1 plus family income, marital status, smoking, alcohol, fruit and vegetable consumption score, meat consumption score (lamb, beef, pork)

Model 3: adjusted for Model 2 plus hypertension, coronary heart disease, diabetes, stroke, kidney disease

Table 5.9: Association of aggregated periodontal disease variable (periodontitis) with dementia.

PD variable	All		Cases		Control		Model 1				Model 2			Model 3					
	Participants		Dementia		Non-Dementia														
	n=466 (%)		n=233 (%)		n=233 (%)		P	OR	95% CI		P	OR	95% CI		P	OR	95% CI		P
^aPeriodontitis																			
Normal (no)	274	58.8	140	60.1	134	57.5	0.498	Ref				Ref				Ref			
Mild/moderate	168	36.1	79	33.9	89	38.2		0.75	0.49	1.15	0.192	0.68	0.43	1.08	0.104	0.67	0.41	1.10	0.116
Severe	24	5.2	14	6.0	10	4.3		1.21	0.49	3.01	0.685	1.05	0.40	2.79	0.919	0.94	0.32	2.74	0.912
^aPeriodontitis																			
No	274	58.8	140	60.1	134	57.5	0.572	Ref				Ref				Ref			
At least one periodontitis indicator reported (Yes)	192	41.2	93	39.9	99	42.5		0.80	0.53	1.20	0.283	0.72	0.46	1.13	0.148	0.70	0.43	1.13	0.143

Model 1: adjusted for age (cont.), gender and education

Model 2: adjusted for Model 1 plus family income, marital status, smoking, alcohol, fruit and vegetable consumption score, meat consumption score (lamb, beef, pork)

Model 3: adjusted for Model 2 plus hypertension, coronary heart disease, diabetes, stroke, kidney disease

^aFour variables from table 5.3 (noticed that your front teeth moved forward or that gaps have developed between your front teeth?; had your teeth that became loose on their own, without any injury?; had treatment for gum disease, such as scaling and root planning, sometimes called

'deep cleaning'; been told by a dental professional that you lost bone around your teeth?) where 'unknown' and 'missing' values were changed into 'no' values and were pooled together for PD problems (periodontitis). Scores of PD variable three level: normal (0); mild PD (1-2); moderate/severe PD (3-4)

Table 5.10: Association of periodontal disease with dementia in Guangzhou case-control study.

PD variable	All participants		Dementia		Non-Dementia		P	Model 1			Model 2			Model 3					
	n=466	(%)	n=233	(%)	n=233	(%)		OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
^aPeriodontal disease																			
Normal (no)	268	57.5	110	47.2	158	67.8	<0.001	Ref				Ref				Ref			
Mild PD	169	36.3	104	44.6	65	27.9		1.97	1.28	3.04	0.002	1.99	1.22	3.24	0.006	1.78	1.05	3.01	0.032
Moderate/ Severe PD	29	6.2	19	8.2	10	4.3		2.83	1.17	6.85	0.021	3.12	1.23	7.92	0.016	2.95	1.06	8.19	0.038
^aPeriodontal disease																			
No	268	57.5	110	47.2	158	67.8	<0.001	Ref				Ref				Ref			
At least one PD indicator reported (Yes)	198	42.5	123	52.8	75	32.2		2.08	1.38	3.14	<0.001	2.14	1.35	3.41	0.001	1.92	1.17	3.17	0.010

^aPeriodontal disease is comprised of bleeding gums, swollen gums, bad breath, PD treatment and bone loss derived from table 5.3. Scores of PD variable three level: normal (0); mild PD (1-5); moderate/severe PD (6-13)

Model 1: adjusted for age (cont.), gender and education

Model 2: adjusted for Model 1 plus family income, marital status, smoking, alcohol, fruit and vegetable consumption score, meat consumption score (lamb, beef, pork)

Model 3: adjusted for Model 2 plus hypertension, coronary heart disease, diabetes, stroke, kidney disease

5.4 Discussion

This case-control study examined the association of poor oral health indicated by different measurements with the risk of dementia. It showed that poor SROH, SROH conditions, number of teeth present, brushing teeth, dental visits, PD variable and PD indicators (bleeding gums, swollen gums and bad breath) were associated with increased risk of dementia. PD indicators (oral ulcers, painful gums and all periodontitis indicators) were not significantly associated.

In this study, the finding of very poor/poor SROH significantly associated with an increased risk of dementia was similar to those in previous studies (Paganini-Hill *et al.*, 2012; Yamamoto *et al.*, 2012). The current study demonstrated that *tooth loss* is a risk factor for dementia. Previously, several studies found a non-significant association between tooth loss and an increase in dementia risk (Gil-Montoya *et al.*, 2015; Holmer *et al.*, 2018; Arrivé *et al.*, 2012). However, a recent meta-analysis suggested that every missed tooth could increase the risk of dementia RR (1.01, 95% CI 1.00-1.02) (Chen *et al.*, 2018). Moreover, some investigators found that the loss of multiple teeth increased the risk of dementia by about 50% (Fang *et al.*, 2018; Oh *et al.*, 2018).

The prevalence of edentulous jaw (no teeth) remains high in older adults (Petersen and Yamamoto, 2005), although it has declined in recent years (Dye *et al.*, 2019). Our findings from this case-control study showed that edentulism was 16.3% in participants with dementia versus 4.3% in the participants without dementia. The result of the association of edentulism with dementia was significant even after adjustment for multiple cofounders (OR 3.16, 1.30-7.67). This is consistent with previous studies in the literature (Batty *et al.*, 2013; Demmer *et al.*, 2020; Takeuchi *et al.*, 2017).

In this study, *SROH conditions* and *pooled SROH conditions (food limiting eating, dry mouth, difficulties in swallowing food and drinking liquid in aid in swallowing)* were significantly

associated with increased risk of dementia (Tables 5.2 and 5.5). These contradicted the study by Yamamoto *et al.* (2012), which found that self-reported mastication difficulty was not associated with the incidence of dementia (Yamamoto *et al.*, 2012). Previous studies showed that more drug-induced (Anticholinergic drugs) xerostomia could increase the risk of dementia (Gil-Montoya *et al.*, 2016; Coupland *et al.*, 2019).

The data of this case-control study showed that more than 70% of the participants did not use both *mouth rinse* and *floss*, with no significant differences between the cases and the controls. Even after adjustment for multiple confounders, the differences between the two groups remained non-significant, which is similar to those in a previous study (Paganini-Hill *et al.*, 2012). Guangzhou case-control study demonstrated that brushing teeth never or less than once per day brushing teeth had a significant association with increased risk of dementia (adjusted OR 23.27, 10.10-53.62). In a cohort study of dentate individuals, participants who brushed their teeth daily had a 22% to 65% greater risk of dementia than those who brushed three times daily (Paganini-Hill *et al.*, 2012).

In the Guangzhou case-control study, 44.2% of the participants were found to have never experienced a *dental visit*, which is similar to the result of a previous study (Yamamoto *et al.*, 2012). According to the data from National Health and Nutrition Examination Survey (NHANES) conducted in the US from 2011 to 2014, 33.8% of adults aged over 30 reported not having a dental visit in the past 12 months (Adunola *et al.*, 2019). Furthermore, a study conducted in China using national data found the rates of not visiting a dentist in the past 12 months were relatively high; 78.6% for adults aged 35 to 44 years, and 79.3% for older adults aged 65 to 74 years (Xu *et al.*, 2020). The lower level of not having a dental visit in this study than the national data in China could be due to (1) its measurement duration of “never” vs “12 months”, and (2) the Guangzhou city area has much higher levels of economics and health care than other places in China. Nevertheless, our study showed a significant association of visiting

the dentist a few times with an increased risk of dementia. Reasons for not brushing teeth and not visiting a dentist are discussed in chapter 8.

In the Guangzhou case-control study, PD indicators had a positive association with an increased risk of dementia. *Bleeding gums* was significantly associated with dementia (adjusted OR 4.07, 1.47-11.28), similar to findings from previous studies (Batty *et al.*, 2013; Gil-Montoya *et al.*, 2015; de Souza Rolim *et al.*, 2014). Previous studies showed that oral hygiene habits and bleeding index were associated with the gradient of cognitive impairment and the worse values were observed with greater severity of cognitive impairment/dementia (Gil-Montoya *et al.*, 2015). The Guangzhou case-control study found that *halitosis* was significantly associated with an increased risk of dementia, which was similar to the findings of a previous study (Kazancioglu *et al.*, 2013).

The Guangzhou case-control study showed that *periodontitis indicators* (see Table 5.8) were non-significantly associated with dementia, but in a positive direction. The pooled data from four periodontitis indicators was an inverse non-significant association with an increased risk of dementia (Table 5.9). In a cohort study, Lee *et al.* (2017) found that PD was significantly associated with dementia in participants without PD treatment (HR 1.14, 1.04-1.24) but not significantly in those who received intensive treatment (1.08, 0.97-1.43) (Lee *et al.*, 2017a). In a cohort study conducted in South Korea, Yoo *et al.* found that the incidence of dementia decreased with periodontal treatment OR 0.96 (0.93–0.99) (Yoo *et al.*, 2019). In the Guangzhou case-control study, similar results were found where PD treatment was non-significant with an increased risk of dementia.

The periodontitis indicator *bone loss* variable (Table 5.8) was a non-significant factor associated with dementia. In contrast, a previous study showed that adjusted OR for generalised MABL (marginal alveolar bone loss) was 5.99 (1.02–35.13) for AD (Holmer *et al.*, 2018).

However, Stein and colleagues assessed periodontitis by measuring alveolar bone loss on dental radiographs. Although they found an association between a low number of remaining teeth and an increased risk of developing dementia, they failed to find a significant association between periodontitis and dementia (Stein *et al.*, 2007).

Although some indicators of periodontitis were not associated with an increased risk of dementia, *overall PD indicators* generated from original variables data demonstrated a significant link between PD and dementia risk (Table 5.10). Topic related studies examining the prediction of PD to dementia risk have been discussed in chapter 4.

Strengths and limitations

This case-control study has several key strengths and makes important contributions to the knowledge of the association of poor oral health with dementia. Firstly, this study is the first to use self-reported PD (indicators: gingivitis/periodontitis) as a risk factor for dementia in China. Secondly, this study included doctor-diagnosed confirmed dementia cases from the neurology department at Hai Hospital using ICD-10 criteria. Thirdly, the selection of an appropriate control is vital to prevent selection bias, and the controls should be comparable to cases in respect to the biases of hospitalisation and the choice of hospital. To ensure controls represented the distribution of exposure in the study population, the controls were selected from the same hospital as the cases, which produced more confidence in the validity of the study findings. Fourthly, different sets of confounders were used for the adjustment in the regression analysis, thus providing a higher validity of the study's findings to minimise the residual effects of confounding.

This study has several limitations. Firstly, due to the nature of the case-control study design, it is difficult to infer a causal relationship between poor oral health and the risk of dementia. Secondly, recruiting the participants from a hospital to explore the risk factors for dementia

may lead to selection bias for both cases and controls since many people with dementia in China were not detected (Chen *et al.*, 2013a). A large-scale community-based cohort study is required to examine further the association of poor OH with dementia risk in China. Thirdly, information was collected on OH using a self-reported questionnaire. Some degree of information bias might have occurred, as the participants were asked to recall, from memory, different kinds of prior. In this study, SROH as predictors for changes in dementia instead of using clinical parameters. However, we used different indicators to measure poor SROH, e.g., SROH, number of teeth present, oral hygiene habits and PD (gingivitis and periodontitis) to reduce the effect. Fourthly, there are certain levels of “unknown” or “missing” values in periodontitis variables, which may make it difficult in getting a “significant” association of periodontitis measurement with dementia risk and cause bias for the findings. To reduce the effects of these unknown values were changed into no values. This requires further validated in the analysis.

5.5 Implications and conclusions

This work provides new evidence of the oral health factors affecting the risk of dementia among older adults. In China, many traditional programs on oral health promotion are independent of general health promotion programs, which results in insufficient social, political, and economic attention on oral health. Hence, integrating oral health into overall health strategies and practices should be imperative for the promotion of OH and could even benefit the promotion of general health, particularly in the fight against NCDs (Zhou *et al.*, 2018). Despite the limitations mentioned above, this study has important policy and practice implications which can be used in both developed and developing countries.

In conclusion, this chapter explores the poor oral health as a modifiable risk factor for dementia. The findings point to the importance of assessing oral health issues in the general population.

Future studies should be cohort studies with a large sample size to determine the association of poor SROH with the incidence of dementia.

CHAPTER SIX: ASSOCIATION OF ORAL HEALTH WITH INCIDENT DEMENTIA: ENGLISH LONGITUDINAL STUDY OF AGING

6.1 Introduction

Oral diseases such as caries and periodontitis have become more prevalent among older people and if left untreated can lead to tooth loss, edentulism and loss of masticatory function (Griffin *et al.*, 2012; Noble *et al.*, 2013). According to the Global Burden of Disease Study 2017, around 3.5 billion people suffer from oral diseases (GBD, 2017). Caries is the most common condition of oral health, affecting nearly 2.3 billion people, while 796 million have severe periodontitis in the world (Bernabe *et al.*, 2020). The Adult Dental Health Survey [ADHS] (2009) reported that the older population in England and Wales has a high probability of tooth loss and poor dental function. The survey revealed 26% of older adults had untreated dental caries, and 45% suffered from at least one periodontal pocket > 4 mm (ADHS, 2009; White *et al.*, 2012). In recent years, emerging data have recognised poor oral health as a potential risk factor for dementia (Noble *et al.*, 2013; Yoo *et al.*, 2019; Lee *et al.*, 2020). However, some other studies did not show a significant association of poor oral health with an increased risk of dementia (Arrivé *et al.*, 2012; Matthews *et al.*, 2011). In chapter 5, the Guangzhou case-control study suggested the association of oral health measured in different indicators with dementia in China.

This chapter examines the association of oral health with dementia in England using the English Longitudinal Study of Ageing (ELSA). It aims to assess the associations of SROH, tooth conditions, and oral impact on oral health-related quality of life (OHRQoL) with incident dementia.

6.2 Method

The studied population is derived from the ELSA as described in the methodology (chapter three, section 3.6.3).

6.2.1 Participants selected for the study

The analytical sample used in this chapter was a subset of the ELSA data, designed for examining the association of oral health at a baseline with incident dementia. I selected participants who were interviewed at wave 5 as the baseline. This is because the survey documented both oral health measures and dementia. In addition, I excluded all the participants with dementia diagnosed from wave 3, wave 4 and wave 5 for analysis to minimise any potential bias from the reverse association of oral health with dementia. This fixed sub-cohort data would also help maintain a higher follow-up study in this analysis. The total number of participants 7,349 were interviewed at wave 5 (2010-2011), wave 4 (2008-2009) and wave 3 (2006-2007). After excluding 112 participants aged below 50 years at wave 5, 163 participants were diagnosed with dementia at wave 5, wave 4 and wave 3; 610 participants were lost to the follow-up at waves 6-9; and 6,464 participants were left for analysis.

6.2.2 Data collection

Data for the main ELSA questionnaire was collected by computer-aided personal interviewing (CAPI) and a self-completion questionnaire. Oral health data was reported at waves 3, 5, 7, 8 and 9. At waves 2, 4, 6, 8 and 9, a health examination was conducted by a nurse visit during which clinical, anthropometric information and blood samples were collected. BMI variable was taken from the nurse visit in wave 4 as no nurse data or BMI information is present in wave 5.

The *exposure variable* was oral health, which was measured in this study using three self-reported oral health variables. They included self-rated oral health (SROH), oral impacts, and

tooth conditions at wave 5 (2010-2011) as the baseline. In addition, a new variable, “edentate or dentate” was derived from tooth conditions. The *outcome variable* was dementia diagnosed by the doctor from wave 6 (2012-2013) to wave 9 (2018-2019).

6.3 Data analysis

Over 8 years of follow-up of the ELSA cohort, 274 participants developed dementia and 6,190 participants did not develop dementia. The distributions of the socio-demographics, lifestyles, risk factors, oral health measurements and comorbidities in participants were examined. Their differences between participants with and without incident dementia were tested using the Chi-squared test or Fisher exact test for categorical variables when appropriate, and one-way analysis of variance for continuous variables. Binary logistic regression models were employed to calculate the odds ratio (OR) and 95% confidence interval (95%CI) to assess the risk of incident dementia in relation to any level of oral health variables such as SROH, oral impacts (OHRQoL), tooth conditions (including dentate and edentate) at baseline. Stepwise logistic regression analyses were applied and three models including different sets of confounders for adjustment were computed to examine the association of OH variables with dementia for comparisons (see footnotes of Tables 6.2-6.5).

6.4 Results

6.4.1 Characteristics of ELSA participants

Table 6.1 shows the characteristics of the ELSA participants in the analysis. Of 6,464 participants, the average age was 67.4 years ($SD \pm 9.68$) and 57.0% were women. Compared to those without dementia, the participants with incident dementia were more likely to be older, employed/self-employed, separated, had no qualification and income, ex-smokers, did not drink alcohol over the past year and were overweight. A significant association and higher incident dementia were found in hypertension, high blood cholesterol, diabetes, stroke, angina,

heart attack, Parkinson's disease, and osteoporosis. However, there were no significant differences between participants with and without dementia in lung disease, asthma, psychiatric conditions, and cancer.

Table 6.2 demonstrates differences in incident dementia across different levels of SROH, tooth conditions and oral impact. There was a significant increase in having difficulty in eating, edentulism and tooth conditions in participants with incident dementia compared to those without dementia. However, differences in other oral health measures between the two groups were not significant.

6.4.2 Self-rated oral health with incident dementia

Table 6.3 shows adjusted ORs of incident dementia in participants across different levels of SROH. Compared to those with very good SROH, participants with poor SROH had a significantly increased risk of incident dementia. In model 1 with adjustment for age, sex, education, income and marital status, the OR of poor SROH in participants with incident dementia was 2.08 (95% CI 1.10-3.92), and in model 2 with additional adjustment for lifestyle factors (smoking, alcohol drinking, BMI) it was 1.99 (1.04-3.80). In model 3, which was further adjusted with comorbidities (high blood pressure, high cholesterol, diabetes, heart disease, stroke, Parkinson's disease, osteoporosis), there was a slight attenuation in the association between poor SROH and incident dementia, but the OR remained significant (1.93, 1.00-3.72).

Increased OR of fair SROH in a participant with incident dementia was not significant; its OR was 1.43 (0.95-2.15) in model 1, 1.41 (0.94-2.13) in model 2, and 1.38 (0.91-2.09) in model 3. All ORs of other levels of SROH (good and excellent) were not significant either, which showed similar trends to that in fair SROH (Table 6.3).

6.4.3 Oral impact with incident dementia

Table 6.4 illustrates the adjusted ORs of incident dementia in participants across different oral impact variables. The oral impact variables include five questions, and the sixth question is about the total sum of questions (Q) 1-5. Findings showed that there was no significant association of having difficulty in eating food (Q.1) with incident dementia in all models (the fully adjusted OR was 1.52, 0.99-2.34). The association of difficulty in speaking (Q.2) with incident dementia was not significant (fully adjusted OR 2.00, 0.89-4.52). Similar non-significant findings were found in “smiling, laughing and showing teeth without embarrassment” (Q.3), “emotional stability” (Q.4), “enjoying company of other people” (Q.5); their fully adjusted ORs were 1.75 (0.94-3.27), 2.72 (0.77-9.63) and 1.12 (0.14-8.88) respectively. These could be due to the small numbers of these “exposures”. The last question (Q.6), “difficulties caused by dental conditions none of these listed”, is a summed finding of all the above questions (Q1-Q5). Participants who reported at least one oral impact were likely to have incident dementia; increased OR was not significant in the fully adjusted model 3 OR 1.41 (0.95-2.09).

6.4.4 Tooth conditions with incident dementia

Table 6.5 shows the adjusted OR of incident dementia in participants with different tooth conditions. There were no significant adjusted ORs in participants who “had no natural teeth and wear dentures”, or “had both natural teeth and denture(s)” or “neither natural teeth nor dentures” in comparison to those with “only natural teeth”. Moreover, the association remained non-significant when combining these variables into ‘dentate and edentate’ [^aDentate codes 2 or 3 from Table 6.2, and ^aEdentate: codes 1 or 4 from Table 6.2]; and there was no significant risk of incident dementia in edentate participants compared with dentate in all models 1-2 and fully adjusted model 3 in Table 6.5.

Table 6.1: Basic characteristics of participants with and without dementia in ELSA cohort study

Variables	All participants		Non-dementia		Incident dementia		P Value
	n=6464	%	n=6190	%	n=274	%	
Basic characteristics							
Age (years)	67.36	9.68	66.93	9.47	77.08	9.08	<0.001
Mean (SD)							
Gender							
Men	2782	43.0	2682	43.3	100	36.5	0.025
Women	3682	57.0	3508	56.7	174	63.5	
Educational level							
Degree or equivalent	1110	17.2	1080	17.4	30	10.9	<0.001
Higher education	919	14.2	886	14.3	33	12.0	
Intermediate / low education	2779	43.0	2679	43.3	100	36.5	
No qualification	1597	24.7	1491	24.1	106	38.7	
*Missing	59	0.9	54	0.9	5	1.8	
Employment status							
Retired	3776	58.4	3552	81.8	224	57.4	<0.001
Employed +self employed	1970	30.5	1954	5.8	16	31.6	<0.001**
Unemployed	49	0.8	48	0.4	1	0.8	
Sick or disabled	246	3.8	230	5.8	16	3.7	
Looking after home or family	400	6.2	384	5.8	16	6.2	
Others	20	0.3	19	0.4	1	0.3	
*Missing	3	0.0	3		0		
Equivalent total income in quintiles							
Lowest	1073	16.6	1003	16.2	70	25.5	<0.001

2	1163	18.0	1101	17.8	62	22.6
3	1184	18.3	1117	18.0	67	24.5
4	1180	18.3	1147	18.5	33	12.0
Highest	1222	18.9	1194	19.3	28	10.2
*Missing	642	9.9	628	10.1	14	5.1

Marriage

Married or cohabiting or civil partners	4567	70.7	4411	71.3	156	56.9	<0.001
Unmarried/single	282	4.4	277	4.5	5	1.8	
Separated	1021	15.8	930	15.0	91	33.2	
Widowed	516	8.0	497	8.0	19	6.9	
Divorced	78	1.2	75	1.2	3	1.1	

Cardiovascular disease risk factors

Smoking

Never smoker	2370	36.7	2284	36.9	86	31.4	0.011
Ex-smoker	3259	50.4	3103	50.1	156	56.9	
Current smoker	773	12.0	752	12.1	21	7.7	
*Missing	62	1.0	51	0.8	11	4.0	

Drinking alcohol over the past 12 months

Daily or ≥ 5 times per week	1268	19.6	1233	19.9	35	12.8	<0.001
≤ 4 and ≥ 1 times per week	2200	34.0	2126	34.3	74	27.0	
Once or twice per month	675	10.4	655	10.6	20	7.3	
Occasionally (couple of months or once or twice a year)	965	14.9	928	15.0	37	13.5	
Never	718	11.1	669	10.8	49	17.9	

*Missing	638	9.9	579	9.4	59	21.5	
<hr/>							
^aBMI (Kg/m²)							
below 18.5	37	0.6	35	0.6	2	0.7	0.045
18.5-24.9	1307	20.2	1256	20.3	51	18.6	
25-29.9	2139	33.1	2029	32.8	110	40.1	
≥ 30	1620	25.1	1566	25.3	54	19.7	
*Missing	1361	21.1	1304	21.1	57	20.8	
<hr/>							
Hypertension							
No	4155	64.3	4001	64.6	154	56.2	0.004
Yes	2309	35.7	2189	35.4	120	43.8	
<hr/>							
High blood cholesterol							
No	4505	69.7	4332	70.0	173	63.1	0.016
Yes	1959	30.3	1858	30.0	101	36.9	
<hr/>							
<u>Co morbidities</u>							
Diabetes							
No	5873	90.9	5634	91.0	239	87.2	0.033
Yes	591	9.1	556	9.0	35	12.8	
<hr/>							
Stroke							
No	6227	96.3	5974	96.5	253	92.3	<0.001
Yes	237	3.7	216	3.5	21	7.7	
<hr/>							
Angina							
No	5659	87.5	5443	87.9	216	78.8	<0.001
Yes	805	12.5	747	12.1	58	21.2	
<hr/>							
Heart attack							
No	6110	94.5	5861	94.7	249	90.9	0.007
Yes	354	5.5	329	5.3	25	9.1	

Lung disease (Chronic bronchitis and emphysema)							
No	6229	96.4	5970	96.4	259	94.5	0.097
Yes	235	3.6	220	3.6	15	5.5	
Asthma							
No	5797	89.7	5560	89.8	237	86.5	0.077
Yes	667	10.3	630	10.2	37	13.5	
Parkinson's disease							
No	6438	99.6	6172	99.7	266	97.1	<0.001
Yes	26	0.4	18	0.3	8	2.9	<0.001***
^bPsychiatric condition							
No	5933	91.8	5682	91.8	5933	91.6	0.912
Yes	531	8.2	508	8.2	531	8.4	
Cancer							
No	6304	97.5	6038	97.5	266	97.1	0.628
Yes	160	2.5	152	2.5	8	2.9	
Osteoporosis							
No	6049	93.6	5801	93.7	248	90.5	0.034
Yes	415	6.4	389	6.3	26	9.5	

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

**Likelihood ratio was calculated based on available data, not including those “missing” data.

***Fischer Exact test was calculated based on available data, not including those “missing” data.

^a Body mass index (BMI) is taken from ELSA wave 4 as nurse data was not collected in ELSA wave 5. BMI grouped according to WHO definition as given in ELSA dataset < 18.5: underweight; 18.5-24.9: normal range; 25-29.9: overweight; ≥ 30: obese

^bPsychiatric problems include any psychiatric conditions such as depression, anxiety, hallucination etc.

Table 6.2: Differences in incident dementia across oral health groups in ELSA cohort study

Oral health measures at wave 5	All participants		Non-dementia		Incident dementia		P Value	
	n=6464	%	n=6190	%	n=274	%		
Self-rated oral health								
Excellent	913	14.1	871	14.1	42	15.3	0.312	
Very good	2046	31.7	1974	31.9	72	26.3		
Good	2405	37.2	2300	37.2	105	38.3		
Fair	859	13.3	817	13.2	42	15.3		
Poor	238	3.7	225	3.6	13	4.7		
*Missing	3	0.0	3	0.0	0	0		
<u>Oral impact</u>								
1. Difficulty in eating food								
Not mentioned	5849	90.5	5620	90.8	229	83.6	0.029	
Mentioned	467	7.2	439	7.1	28	10.2		
*Missing	148	2.3	131	2.1	17	6.2		
2. Difficulty in speaking								
Not mentioned	6215	96.1	5965	96.4	250	91.2	0.142	
Mentioned	101	1.6	94	1.5	7	2.6		0.194**
*Missing	148	2.3	131	2.1	17	6.2		
3. Problems in smiling without embarrassment								
Not mentioned	6103	94.4	5858	94.6	245	89.4	0.240	
Mentioned	213	3.3	201	3.2	12	4.4		0.218**
*Missing	148	2.3	131	2.1	17	6.2		

4. Problems with emotional stability							
Not mentioned	6281	97.2	6027	97.4	254	92.7	0.176
Mentioned	35	0.5	32	0.5	3	1.1	0.169**
*Missing	148	2.3	131	2.1	17	6.2	
5. Problems with enjoying company of others							
Not mentioned	6289	97.3	6033	97.5	256	93.4	0.923
Mentioned	27	0.4	26	0.4	1	0.4	1.000**
*Missing	148	2.3	131	2.1	17	6.2	
6. Difficulties caused by dental condition: None of the listed difficulties reported							
Not mentioned	639	9.9	605	9.8	34	12.4	0.091
Mentioned	5677	87.8	5454	88.1	223	81.4	
*Missing	148	2.3	131	2.1	17	6.2	
Tooth conditions							
Has no natural teeth and wear dentures	818	12.7	750	12.1	68	24.8	<0.001
Has both natural teeth and denture(s)	1877	29.0	1774	28.7	103	37.6	<0.001***
Has only natural teeth	3741	57.9	3639	58.8	102	37.2	
Has neither natural teeth nor dentures	25	0.4	24	0.4	1	0.4	
*Missing	3	0.0	3	0.0	0	0	
^aEdentulism							
^a Edentate	843	13.0	774	12.5	69	25.2	<0.001
^a Dentate	5618	86.9	5413	87.4	205	74.8	

*Missing 3 0 3 0.0 0 0

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

**Fisher exact test was calculated based on available data, not including those “missing” data.

***Likelihood ratio was calculated based on available data, not including those “missing” data.

^aEdentulism variable was derived from variable tooth conditions in table 6.2

^aDentate codes 2 or 3 from variable tooth conditions in table 6.2

^aEdentate codes 1 or 4 from variable tooth conditions in table 6.2

Table 6.3: Association of self-rated oral health with incident dementia in ELSA cohort study.

SROH at wave 5	Participants	Incident Dementia		Model 1			Model 2			Model 3		
	n=6464	n=274	%	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Excellent	913	42	4.60	1.47	0.98 2.20	0.061	1.46	0.97 2.20	0.079	1.48	0.98 2.22	0.061
Very good	2046	72	3.52	Ref			Ref			Ref		
Good	2405	105	4.37	1.21	0.88 1.66	0.232	1.19	0.86 1.64	0.310	1.19	0.86 1.64	0.289
Fair	859	42	4.89	1.43	0.95 2.15	0.083	1.41	0.94 2.13	0.105	1.38	0.91 2.09	0.129
Poor	238	13	5.46	2.08	1.10 3.92	0.024	1.99	1.04 3.80	0.042	1.93	1.00 3.72	0.049
Missing	3	0										

Stepwise logistic regression were run

Model 1: Adjusted for age, sex, education, income, marital status

Model 2: Adjusted for Model 1 plus smoking, alcohol drinking, BMI

Model 3: Adjusted for Model 2 plus high blood pressure, high cholesterol, diabetes, heart disease, stroke, Parkinson's disease, osteoporosis

Table 6.4: Association of oral impact with incident dementia in ELSA cohort study.

Oral impact at wave 5	All Participants	Incident dementia		Model 1			Model 2			Model 3					
	n=6464	n=274	%	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
1. Difficulty in eating food															
Not mentioned	5849	229	3.92	Ref			Ref			Ref					
Mentioned	467	28	6.00	1.49	0.98	2.28	0.063	1.52	0.99	2.32	0.057	1.52	0.99	2.34	0.056
Missing	148	17													
2. Difficulty in speaking															
Not mentioned	6215	250	4.02	Ref				Ref				Ref			
Mentioned	101	7	6.93	1.84	0.82	4.12	0.138	1.93	0.86	4.34	0.111	2.00	0.89	4.52	0.094
Missing	148	17													
3. Smiling, laughing, and showing teeth without embarrassment															
Not mentioned	6103	245	4.01	Ref				Ref				Ref			

Mentioned	213	12	5.63	1.72	0.93	3.18	0.087	1.74	0.93	3.25	0.082	1.75	0.94	3.27	0.080
Missing	148	17													
4. Emotional stability															
Not mentioned	6281	254	4.04	Ref				Ref				Ref			
Mentioned	35	3	8.57	2.74	0.78	9.62	0.117	2.67	0.75	9.54	0.130	2.72	0.77	9.63	0.121
Missing	148	17													
5. Problems enjoying company of other people															
Not mentioned	6289	256	4.07	Ref				Ref				Ref			
Mentioned	27	1	3.70	1.04	0.13	8.36	0.972	1.08	0.14	8.67	0.941	1.12	0.14	8.88	0.917
Missing	148	17													
6. Difficulties caused by dental condition: None of the listed difficulties reported															
Not mentioned	5677	223	3.93	Ref				Ref				Ref			
Mentioned	639	34	5.32	1.38	0.94	2.03	0.105	1.40	0.95	2.06	0.094	1.41	0.95	2.09	0.085
Missing	148	17													

Stepwise logistic regression were run

Model 1: Adjusted for age, sex, education, income, marital status

Model 2: Adjusted for Model 1 plus smoking, alcohol drinking, BMI

Model 3: Adjusted for Model 2 plus high blood pressure, high cholesterol, diabetes, heart disease, stroke, Parkinson's disease, osteoporosis

Table 6.5: Association of tooth condition with incident dementia in ELSA cohort study.

Tooth conditions at wave 5	All Participants	Incident dementia		Model 1			Model 2			Model 3					
	n=6464	n=274	%	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
Tooth conditions															
Has no natural teeth and wear dentures	818	68	8.31	1.08	0.76	1.56	0.658	1.04	0.72	1.51	0.830	1.01	0.70	1.48	0.941
Has both natural teeth and denture(s)	1877	103	5.49	1.18	0.88	1.59	0.278	1.20	0.89	1.62	0.234	1.21	0.89	1.63	0.225
Has only natural teeth	3741	102	2.73	Ref				Ref				Ref			
Has neither natural teeth nor dentures	25	1	4.00	0.79	0.11	6.04	0.824	0.83	0.11	6.36	0.858	0.76	0.10	5.84	0.788
Missing	3	0													
^aEdentulism															
^a Dentate	5618	205	3.65	Ref				Ref				Ref			
^a Edentate	843	69	8.19	0.98	0.72	1.35	0.912	0.93	0.67	1.29	0.677	0.91	0.65	1.26	0.552
Missing	3	0													

^aEdentulism variable was derived from variable tooth conditions in table 6.2

^aDentate codes 2 or 3 derived from variable tooth conditions in table 6.2

^aEdentate codes 1 or 4 derived from variable tooth conditions in table 6.2

Stepwise logistic regression were run

Model 1: Adjusted for age, sex, education, income, marital status

Model 2: Adjusted for Model 1 plus smoking, alcohol drinking, BMI

Model 3: Adjusted for Model 2 plus high blood pressure, high cholesterol, diabetes, heart disease, stroke, Parkinson's disease, osteoporosis

6.5 Discussion

This chapter examined the data from the ELSA, adults aged ≥ 50 years in the UK, to assess the association of oral health with incident dementia. The results showed that SROH was significantly associated with an increased risk of dementia in older adults. These results are discussed in the following section.

Self-rated oral health

The results of the ELSA cohort study showed a significant association of poor SROH with incident dementia. A cohort study of 4,425 participants aged 65 years or older followed up for four years reported that poor SROH increased the risk of dementia. The HR of incident dementia was 1.85 (1.04–3.31) in those with few teeth and no dentures, 1.44 (1.04–2.01) in those who did not have a regular dentist, and 1.76 (0.96–3.20) in those who did not take care of their dental health (Yamamoto *et al.*, 2012). Similar results were observed in a national longitudinal study conducted on more than 9,853 white and African American adults of aged 45 years and older to study the association between SROH and cognitive function, using the incremental linear regression model. Moreover, when adjusted for socio-economic status (SES), no association between tooth loss and cognitive function was found, indicating the role of SES factors in the association between tooth loss and cognitive impairment (Matthews *et al.*, 2011). A recent case-control study conducted by Araujo *et al.* (2021) which examined the association between periodontitis and AD used the Geriatric Oral Health Assessment Index (GOHAI) questionnaire, in addition to an oral examination. The results indicated that periodontitis was strongly associated with AD (OR = 11.08, $p < 0.001$) (de Oliveira Araújo *et al.*, 2021).

Oral impacts

In the study, oral impact in different measures showed an overall positive but non-significant association with dementia. The results from the ELSA cohort study showed a positive but non-significant association of *difficulty in eating food* with dementia (OR 1.52, $p = 0.056$). It was consistent with results in a previous study that reported a non-significant association of ‘not able to chew food’ with dementia (adjusted HR 1.25, 0.81-1.93) (Yamamoto *et al.*, 2012).

The finding from the ELSA study showed a non-significant association of *difficulty in speaking* with dementia OR 2.0 (0.89-4.52) but in a positive direction. Previous studies have indicated that tooth loss can lead to poor speech, which in turn can lower quality of life and general health among older adults (Griffin *et al.*, 2012). Although most previous studies have explored speech difficulty due to poor oral health in the elderly, very limited literature is available for the influence of difficulty in speech on dementia risk. More studies are required to investigate incident dementia in relation to “*difficulty in speaking*” in terms of oral health indicators, including the validity of self-reported speaking difficulty in the older population.

The results of the ELSA showed a positive but non-significant association of *smiling without embarrassment* with incident dementia OR 1.75 (0.94-3.27). Previously data from the “National Health and Nutrition Examination Survey” (NHANES) in the USA, investigating the impact of poor oral health on the older population, reported similar findings (Griffin *et al.*, 2012). In addition, it showed that oral diseases restricted social contact and inhibited intimacy among the older population by lowering self-esteem (Starr and Hall, 2010), and they tended to avoid the company of others (Smith and Sheiham, 1979) due to concerns about physical appearance (Eli *et al.*, 2001). These findings support the result of ELSA which showed a positive but non-significant association between *enjoying company of others and dementia* (OR 1.12, 0.14-8.88). Similarly, *emotional stability* showed a positive but non-significant

association with dementia (OR 2.72, 0.77-9.63). The current literature on oral impact measures (difficulty in speaking, smiling without embarrassment, emotional stability and enjoying the company of others) associated with dementia is very limited.

Maintaining good oral health in the elderly is crucial as it not only improves the quality of life but also reduces the pain, poor self-esteem and loss of ability to laugh, smile or eat, which are associated with poor oral health (Pynn and Kolic, 2014). Few studies have explored OHRQoL in the older population; however, OHRQoL influence on dementia still needs to be explored, highlighting the need for further studies.

Tooth conditions

Tooth loss in older adults is quite common and is mainly caused by PD (Petersen and Yamamoto, 2005). Previous studies showed an association of tooth loss with an increased risk of cognitive impairment and dementia in older populations (Stein *et al.*, 2007; Kondo *et al.*, 1994; Takeuchi *et al.*, 2017). In this cohort study, data of four levels of having (no) teeth combined with wearing (no) dentures did not show any association of different levels of tooth conditions with incident dementia. The reasons for it could be (1) tooth loss was not categorised according to the number of teeth present or teeth extracted from the mouth as given in previous studies (Stein *et al.*, 2007; Yoo *et al.*, 2019; Takeuchi *et al.*, 2017) and (2) the number of participants in each level could be small. In combining them into “edentate” and “dentate” groups, the findings demonstrated the association of edentate was non-significant (adjusted OR 0.91, 0.65-1.26) with risk of incident dementia in older people versus dentate.

A previous cohort study conducted in Japan with a follow-up period of six years reported that the OR of dementia in edentulous without denture was 2.4 (0.9-6.5) (Shimazaki *et al.*, 2001). Another cohort study corroborated this and found that participants from community-dwelling adults without dementia aged 60 and older who were followed for five years had a non-

significant increase in the risk of dementia in those with no teeth (HR 1.63, 0.95-2.80) compared to participants with 20 teeth or more (Takeuchi *et al.*, 2017). However, a cohort study of 11,140 participants aged between 55-88 years reported that having no teeth was associated with the high risk of dementia (adjusted HR 1.48, 1.24-1.74) (Batty *et al.*, 2013). These results were similar to those in a recent USA study, which reported that edentulism was associated with an increased risk of dementia (HR was 1.90, 95% CI 1.40–2.58) (Demmer *et al.*, 2020). This shows there are inconsistent findings on the association between edentulism (tooth loss) and the risk of dementia.

Strengths and limitations

The strength of the study includes the use of cohort design with long follow-up (over 8 years) of older adults who were recruited from the community. A longer follow-up time for the impact of exposures on outcomes avoided problems of reverse causality. The oral health measurements in the study reflected different aspects of present and past oral health status which were comprehensively analysed. The study has adjusted for several important confounders, including comorbidities, which minimised their residual effects on the association of OH with dementia. This study also had some limitations. First, there was no clinical assessment of OH, and the available OH measures were limited to teeth status, self-rated oral health and OHRQoL. Second, this study focused on all types of dementia, and it was inappropriate to conduct further stratification analyses by subcategories of dementia such as AD due to small number of AD cases.

6.6 Implications and conclusions

The findings of this chapter have demonstrated significant prediction of poor SROH indicated incident dementia. It is important for policymaking and practice to prevent dementia in the population. The findings could be used to improve access to dental care in the general

population and to reduce the difficulties that older people face when they need dental treatment. The risk of dementia in the UK could be reduced through educational programs of OH. A qualitative study should be conducted to get in-depth information on the association of poor oral health with an increased risk of dementia.

CHAPTER 7: ASSOCIATION OF DEMENTIA WITH ORAL HEALTH: THE GUANGZHOU STUDY AND THE ELSA STUDY

7.1 Introduction

As the world population is becoming progressively older, the interest of healthcare professionals towards the quality of elderly life is increasing (WHO, 2021c). One of the most studied consequences of ageing is dementia (WHO, 2021b). It is generally known that once dementia is diagnosed, there is a decline in overall health as the disease progresses (WHO, 2021b). Consequently, poor cognition together with old age is a predictor of poor health outcomes (ADA, 2022).

It is poorly understood whether there is a relationship between decline in cognitive abilities and deterioration of patients' oral health. A longitudinal study conducted in 2017 explored several possible pathways leading to poor oral health in patients with dementia (Fereshtehnejad *et al.*, 2018). Dementia causes a progressive decline in cognition which can not only limit physical abilities, but also affect psycho-social behaviours in advanced stages. The resulting limitations in self-care can significantly impact oral hygiene and dental care (Zenthöfer *et al.*, 2014). This also leads to further care requirements and accentuates the risk of oral health conditions (Brennan and Strauss, 2014). Additionally, a few studies have proposed that decline in cognition and motor skills in dementia patients change their behaviour and perceptions regarding oral health (OH) (Ellefsen *et al.*, 2009; Syrjälä *et al.*, 2012).

The previous chapters (chapters 5 and 6) analysed the association of oral health with dementia using the Guangzhou case-control study and the ELSA cohort study, separately. However, in

this chapter, the data is analysed from case-control and cohort studies to evaluate the association of dementia or severe cognitive impairment with oral health.

7.2 Data analysis of the Guangzhou case-control study

7.2.1 Methods

The dataset was derived from the Guangzhou case-control study as explained in chapter 3, section 3.6.2. In this study, one participant did not answer the oral health questionnaire, leaving inputs from 465 participants for the analysis. In this chapter, the oral health measure was converted into three levels (good, fair and poor) for analysis, which looked at the relationship between dementia and self-rated oral health (SROH). Oral health measures such as SROH, SROH conditions, oral hygiene, and PD indicators were analysed.

7.2.2 Data collection

Data collection has been fully described in Chapter 3, section 3.6.2.4.

7.2.3 Data analysis

Distributions of different levels of SROH were examined with socio-demographic factors, dietary intake, oral health measures and comorbidities in participants. These analyses were performed using Chi-squared test for categorical variables, or one-way variance for continuous variables (e.g., age) (Tables 7.1 and 7.2). Multinomial regression or binary logistic regression models (where suitable) were employed to calculate odds ratio (OR) and its 95% confidence interval (95% CI) to assess oral health conditions in relation to dementia. In the multinomial logistic regression models, I adjusted for age, sex and covariates, including socio-demographic factors, dietary intake, cardiovascular diseases, other comorbidities, which were selected based on their potential relationship with three levels of SROH (see the footnotes of Table 7.4) to evaluate the association of dementia with three levels of SROH (see Table 7.3). Binary logistic regression models were used to compute the OR and its 95% CI of dementia with “fair SROH

versus poor SROH” (Table 7.5), and “all good and fair combined SROH versus poor SROH” (Table 7.6). Multivariate adjusted logistic models were used for oral health other measurements, such as brushing teeth, dental visit, number of teeth present and PD, where some subgroups were combined due to their small sample size to increase the statistical power mentioned in detail in the footnotes of Tables 7.6-7.10.

7.2.4 Results

7.2.4.1 Descriptive results

Of 465 participants, the average age was 73.6 years ($SD \pm 9.5$), and 63.4% of them were women. Table 7.1 shows the details of the characteristics of participants in three groups of SROH. Compared to those with good/fair SROH, participants with poor SROH were more likely to be older, illiterate and with a personal income below 10,000 RMB per annum. Furthermore, poor SROH participants compared to good/fair SROH participants were more likely to have stroke, chronic bronchitis, cancer, migraine, head hurt and dementia. There were no significant differences in smoking, alcohol drinking habits, marital status, family income, meat (pork, beef and lamb) consumption, fruit and vegetable consumption, hypertension, high blood cholesterol, diabetes, coronary heart disease, chronic kidney disease, Parkinson’s disease and depression among the three groups of SROH, which were provided in Table 7.1.

Table 7.2 shows the correlation between SROH and other oral health measures. Poor SROH compared to those with good/fair SROH were likely to have more SROH conditions, PD indicators (gingivitis/periodontitis), edentulous or 1-9 teeth in the mouth, and brush teeth less than once a day. However, there were no significant differences in wearing dentures, flossing teeth, dental visits, always use mouthwash and PD treatment among three groups of SROH.

7.2.4.2 Logistic regression analysis to examine the association between SROH and other co-variates

Age-sex adjusted analysis

Table 7.3 shows the age-sex adjusted ORs of fair and poor SROH participants in multinomial logistic regression models. It was found that participants with personal income under 10,000 RMB per annum had poor SROH (OR 5.78, 95%CI 1.99-16.79) and fair SROH (2.53, 1.09-5.86) versus good SROH. There was a significant association of pork consumed > a week or < daily with fair SROH (3.50, 1.61-7.58), but no significant association with poor SROH. Increased OR in poor SROH among those who had never consumed beef was significant (OR 3.66, 1.41-9.52), but not significant in fair SROH. There was a significant inverse-relation of daily intake of vegetables with poor SROH (OR 0.14, 0.03-0.73), and a high score of vegetable and fruit consumption (OR 0.32, 0.11-0.94). The overall p-value showed significant association with fair/poor OH of cancer (p = 0.022), chronic bronchitis (p = 0.002), stroke (p = 0.032) and dementia (p = 0.009). All the other variables in Table 7.3 were non-significantly associated with SROH.

Multivariate adjusted analysis

Table 7.4 illustrates the multivariate adjusted ORs of fair and poor SROH participants in multinomial logistic regression models. In the multivariate-adjusted analysis, a significant increase in poor SROH was found in participants whose personal income were under 10,000 RMB per annum. The data also showed that poor SROH was significantly associated with chronic bronchitis (OR 4.53, 1.42-14.47). All the remaining variables in Table 7.4 were non-significant.

7.2.4.3 Findings of dementia with SROH

In the multinomial regression model, age-sex adjustment analysis showed that dementia was associated with fair to poor SROH compared to good SROH (overall p = 0.009), although each

individual fair and poor SROH was not significantly related to dementia (Table 7.3). However, such an overall significant association disappeared in the multivariate adjustment analysis (Table 7.4).

Within the fair and poor SROH analysis, a binary logistic regression was used to examine the association of dementia with poor SROH (versus fair SROH). Table 7.5 shows a significant association of dementia with poor SROH when adjusted for age and sex in model 1 (OR 2.21, 1.27-3.85). In model 2 when further adjusted with income, education, marital status, consumption of meat, vegetable and fruits, the association with dementia became non-significant (OR 1.82, 0.96-3.45). In model 3 having more adjustment with comorbidities, OR was 1.33 (0.65-2.70).

In the analysis for the combinations of fair SROH with good SROH as a reference (Table 7.6), adjusted OR of poor SROH in relation to dementia was 1.31 (0.67-2.55), showing a similar trend to those in Table 7.5.

7.2.4.4 Findings of the association of dementia with oral health behaviour, oral hygiene, number of teeth present and PD

Table 7.7 shows the number and percentage of three groups of dental visits between people with and without dementia, and adjusted ORs of lower levels of visiting dentists. Participants with dementia had higher odds of every 2 years/> 2 years (OR 1.76, 0.81-3.86) and never/ tried avoiding the dental visit (OR 3.60, 1.65-7.83), with an overall p-value < 0.001.

Table 7.8 demonstrates the number and percentage of three groups of different levels of brushing of teeth between people with and without dementia, and adjusted ORs of lower levels of brushing of teeth. Findings reported that participants with dementia had significant higher odds of brushing teeth in once day (OR 6.01, 3.43-10.53) and in < once a day (OR 25.77, 11.66-56.96), and the overall p-value was <0.001.

Table 7.9 illustrates the number, percentage, and adjusted ORs of three groups of teeth number presented in the mouth between people with and without dementia. Findings showed that participants with dementia had increased odds of the 1-19 teeth (OR 2.22, 1.36-3.63) and edentulism (OR 3.33, 1.40-7.91), with an overall p-value <0.001.

Table 7.10 demonstrates the number, percentage and adjusted ORs of three groups of different levels of PD between people with and without dementia. Results reported that people with dementia had higher odds of mild PD (OR 1.98, 1.25-3.15) and moderate/severe PD (OR 2.70, 1.04-7.03), with and overall p-value= 0.004.

Table 7.1: Characteristics of participants with different levels of self-rated oral health in Guangzhou case-control study

Variables	Self-rated oral health								P Value
	All		Good (26.8%)		Fair (55.6%)		Poor (17.6%)		
	n=465	%	n=123	%	n=261	%	n=81	%	
<u>Demographic factors</u>									
Age (years)									
Mean (SD)	73.60	9.47	71.97	9.55	71.96	9.55	75.12	9.15	0.087
Age group									
<=60	29	6.2	13	10.6	12	4.6	4	4.9	0.054
61-70	169	36.3	48	39.0	100	38.3	21	25.9	
71-80	148	31.8	38	30.9	78	29.9	32	39.5	
81=>	119	25.6	24	19.5	71	27.2	24	29.6	
Gender									
Women	295	63.4	79	64.2	164	62.8	52	64.2	0.954
Men	170	36.6	44	35.8	97	37.2	29	35.8	
Smoking status									
Never	380	81.7	101	82.1	213	81.6	66	81.5	0.998
Former	48	10.3	12	9.8	27	10.3	9	11.1	
Current	37	8.0	10	8.1	21	8.0	6	7.4	
^aDrinking any alcohol during the past two years per 100 ml									
Never or less than once per month	439	94.4	114	92.7	248	95.0	77	95.1	0.624
More than once month/ weekly/daily	26	5.6	9	7.3	13	5.0	4	4.9	
<u>Socioeconomic status</u>									
Educational level									

University and above	50	10.8	13	10.6	29	11.1	8	9.9	0.127
Senior high school	60	12.9	21	17.1	34	13.0	5	6.2	
Junior high school	118	25.4	34	27.6	65	24.9	19	23.5	
Primary school	150	32.3	42	34.1	77	29.5	31	38.3	
Illiteracy	87	18.7	13	10.6	56	21.5	18	22.2	

Personal/Annual income (RMB)

≥70000	47	10.1	18	14.6	22	8.4	7	8.6	<0.001
50000-<70000	62	13.3	16	13.0	37	14.2	9	11.1	
30000-<50000	120	25.8	30	24.4	74	28.4	16	19.8	
10000-<30000	135	29.0	41	33.3	79	30.3	15	18.5	
< 10000	101	21.7	18	14.6	49	18.8	34	42.0	

Family income (RMB)

≥70000	70	15.1	14	14.6	38	14.6	18	17.3	0.678
50000-<70000	72	15.5	11	14.6	43	16.5	18	13.6	
30000-<50000	162	34.8	22	36.6	95	36.4	45	27.2	
<30000	161	34.6	34	34.1	85	32.6	42	42.0	

Social network

Marriage

Married or cohabiting	299	64.3	88	71.5	157	60.2	54	66.7	0.158
Separated,divorced and never married	32	6.9	10	8.1	17	6.5	5	6.2	
Widow	132	28.4	25	20.3	85	32.6	22	27.2	
*Missing	2	0.4	0	0	2	0.8	0	0	

Dietary intake

Meat consumption during the past two years

Pork

>= Twice a day	45	9.7	11	8.9	25	9.6	9	11.1	0.184
Once a day	148	31.8	42	34.1	83	31.8	23	28.4	
> Once a week and < daily	200	43.0	43	35.0	122	46.7	35	43.2	
=< Once a week	41	8.8	18	14.6	15	5.7	8	9.9	
Never or less than once per month	31	6.7	9	7.3	16	6.1	6	7.4	

Beef

Once a day/>= Twice a day	14	3.0	5	4.1	7	2.7	2	2.5	0.083
> Once a week and < daily	76	16.3	21	17.1	40	15.3	15	18.5	
=< Once a week	94	20.2	27	22.0	61	23.4	6	7.4	
Never or less than once per month	281	60.4	70	56.9	153	58.6	58	71.6	

Lamb

Once a day/>= Twice a day	15	3.2	5	4.1	8	3.1	2	2.5	0.471
> Once a week and < daily	33	7.1	6	4.9	21	8.0	6	7.4	
=< Once a week	57	12.3	15	12.2	37	14.2	5	6.2	
Never or less than once per month	360	77.4	97	78.9	195	74.7	68	84.0	

**^bScores of Meat
consumption**

0-2	290	62.4	77	62.6	158	60.5	55	67.9	0.504
3-5	116	24.9	31	25.2	71	27.2	14	17.3	
6-12	59	12.7	15	12.2	32	12.3	12	14.8	

**Consumption of
vegetables and
fruits during the
past two years****Vegetable**

>= Twice a day	190	40.9	45	36.6	113	43.3	32	39.5	0.123
Once a day	192	41.3	62	50.4	101	38.7	29	35.8	
> Once a week and < daily	55	11.8	12	9.8	32	12.3	11	13.6	
=< Once a week	17	3.7	2	1.6	8	3.1	7	8.6	
Never or less than once per month	11	2.4	2	1.6	7	2.7	2	2.5	

Fruit

>= Twice a day	37	8.0	8	6.5	18	6.9	11	13.6	0.293
Once a day	186	40.0	51	41.5	106	40.6	29	35.8	
> Once a week and < daily	172	37.0	43	35.0	104	39.8	25	30.9	
=< Once a week	46	9.9	15	12.2	22	8.4	9	11.1	
Never or less than once per month	24	5.2	6	4.9	11	4.2	7	8.6	

‘Scores of vegetables and fruits consumption

0-3	36	7.7	7	5.7	18	6.9	11	13.6	0.149
4-5	160	34.4	49	39.8	88	33.7	23	28.4	
6-8	269	57.8	67	54.5	155	59.4	47	58.0	

Cardiovascular disease and risk factors

Hypertension status

No	218	46.9	52	42.3	129	49.4	37	45.7	0.412
Yes	247	53.1	71	57.7	132	50.6	44	54.3	

High blood cholesterol

No	400	86.0	105	85.4	226	86.6	69	85.2	0.768
Yes	60	12.9	18	14.6	31	11.9	11	13.6	

*Missing	5	1.1	0	0	4	1.5	1	1.2	
Diabetes									
No	373	80.2	102	82.9	212	81.2	59	72.8	0.173
Yes	92	19.8	21	17.1	49	18.8	22	27.2	
Coronary heart disease									
No	423	91.0	108	87.8	238	91.2	77	95.1	0.205
Yes	42	9.0	15	12.2	23	8.8	4	4.9	
Stroke									
No	59	86.7	17	85.4	25	89.7	17	79.0	0.026
Yes	403	12.7	105	13.8	234	9.6	64	21.0	
*Missing	3	0.6	1	0.8	2	0.8	0	0	
Chronic bronchitis									
No	426	91.6	118	95.9	243	93.1	65	80.2	0.000
Yes	39	8.4	5	4.1	18	6.9	16	19.8	
*Missing									
Cancer									
No	457	98.3	120	97.6	260	99.6	77	95.1	0.017
Yes	8	1.7	3	2.4	1	0.4	4	4.9	
Chronic Kidney disease									
No	447	96.1	118	95.9	254	97.3	75	92.6	0.155
Yes	18	3.9	5	4.1	7	2.7	6	7.4	
Head hurt									
No	436	93.8	109	88.6	253	96.9	74	91.4	0.004
Yes	29	6.2	14	11.4	8	3.1	7	8.6	
Parkinson's disease									
No	434	93.3	115	93.5	247	94.6	72	88.9	0.202

Yes	27	5.8	7	5.7	12	4.6	8	9.9	
*Missing	4	0.9	1	0.8	2	0.8	1	1.2	
Migraine									
No	417	89.7	107	87.0	243	93.1	67	82.7	0.014
Yes	48	10.3	16	13.0	18	6.9	14	17.3	
Depression									
No	445	95.7	118	95.9	252	96.6	75	92.6	0.305
Yes	20	4.3	5	4.1	9	3.4	6	7.4	
Dementia									
No	232	49.9	60	48.8	143	54.8	29	35.8	0.011
Yes	233	50.1	63	51.2	118	45.2	52	64.2	

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

^aDrinking any alcohol during the past two years: Variables pooled were average frequency use wine (glass) during the past two years?; average frequency use beer (bottle) during the past two years? and average frequency use other alcohol (red wine, rice wine, fruit wine, etc.) during the past two years [100ml]?

^bScores of Meat consumption: Variables pooled from pork, beef, and lamb. Scoring was 0-2=Never or less than once per month/week; 3-5=> Once a week/< daily; 6-12=Once a day/>= Twice a day.

^cScores of fruits and vegetables consumption: Scoring was as 0-3= Never or less than once per month/< or >week; 4-5 = less than daily; 6-8 = Once a day/>= Twice a day

Table 7.2: Correlation between self-rated oral health (SROH) and other oral health measurements in Guangzhou case-control study.

Oral health variables	Self-rated oral health								P Value
	All participants		Good (26.8%)		Average (55.6%)		Poor (17.6%)		
	n=465	%	n=123	%	n=261	%	n=81	%	
<u><i>aSROH conditions</i></u>									
Teeth problems limit foods?									
Always	88	18.9	16	13.0	37	14.2	35	43.2	<0.001
Often	114	24.5	17	13.8	76	29.1	21	25.9	<0.001**
Occasionally	114	24.5	23	18.7	79	30.3	12	14.8	
Never	149	32.0	67	54.5	69	26.4	13	16.0	
Difficulties swallowing foods?									
Always	43	9.2	6	4.9	21	8.0	16	19.8	<0.001
Often	88	18.9	12	9.8	51	19.5	25	30.9	<0.056**
Occasionally	124	26.7	20	16.3	90	34.5	14	17.3	
Never	207	44.5	85	69.1	98	37.5	24	29.6	
*Missing	3	0.6	0		1	0.4	2	2.5	

Slip liquid to aid in swallowing foods?									
Always	52	11.2	9	7.3	29	11.1	14	17.3	<0.001
Often	75	16.1	15	12.2	40	15.3	20	24.7	0.103**
Occasionally	116	24.9	22	17.9	75	28.7	19	23.5	
Never	217	46.7	77	62.6	114	43.7	26	32.1	
*Missing	5	1.1	0	0	3	1.1	2	2.5	
Mouth feels dry when eating foods?									
Always	35	7.5	6	4.9	19	7.3	10	12.3	<0.001
Often	85	18.3	13	10.6	49	18.8	23	28.4	0.122**
Occasionally	119	25.6	25	20.3	76	29.1	18	22.2	
Never	220	47.3	79	64.2	113	43.3	28	34.6	
*Missing	6	1.3	0	0	4	1.5	2	2.5	
<u>Oral hygiene</u>									
^bDo you use dental floss to clean teeth/dentures?									
Never	365	78.5	102	82.9	200	76.6	63	77.8	0.299
Occasionally	59	12.7	10	8.1	40	15.3	9	11.1	0.942**

Often	32	6.9	11	8.9	16	6.1	5	6.2
*Missing	9	1.9	0	0	5	1.9	4	4.9

**^bDo you use dental
rinse or mouthwash
to clean your mouth?**

Never	329	70.8	99	80.5	176	67.4	54	66.7	0.095
Occasionally	75	16.1	11	8.9	49	18.8	15	18.5	0.075**
Often	56	12.0	13	10.6	32	12.3	11	13.6	
*Missing	5	1.1	0	0	4	1.5	1	1.2	

**How many times a
day do you brush
your teeth?**

Do not brush	57	12.3	8	6.5	30	11.5	19	23.5	0.002
Less than once a day	41	8.8	10	8.1	18	6.9	13	16.0	<0.001**
Once a day	180	38.7	48	39.0	104	39.8	28	34.6	
Twice	166	35.7	50	40.7	99	37.9	17	21.0	
More than twice a day	21	4.5	7	5.7	10	3.8	4	4.9	

**How often do you
visit a dentist**

Every 6 months	24	5.2	5	4.1	15	5.7	4	4.9	0.890
Once a year	34	7.3	12	9.8	18	6.9	4	4.9	0.677**

Every two year	34	7.3	7	5.7	19	7.3	8	9.9	
More than 2 years	152	32.7	42	34.1	84	32.2	26	32.1	
Try to avoid going to dentist	206	44.3	53	43.1	114	43.7	39	48.1	
*Missing	15	3.2	4	3.3	11	4.2	0	0	
<hr/>									
How many teeth do you have in your mouth									
0 edentulous	48	10.3	9	7.3	26	10.0	13	16.0	<0.001
1-9 teeth	68	14.6	11	8.9	40	15.3	17	21.0	<0.001**
10-19 teeth	93	20.0	18	14.6	50	19.2	25	30.9	
20 and above teeth	255	54.8	85	69.1	144	55.2	26	32.1	
*Missing	1	0.2	0	0	1	0.4	0	0	
<hr/>									
<u><i>PD problems (gingivitis/periodontitis)</i></u>									
Bleeding gums									
Always	31	6.7	4	3.3	19	7.3	8	9.9	<0.001
Sometimes	61	13.1	4	3.3	35	13.4	22	27.2	<0.001**
Rarely	137	29.5	37	30.1	72	27.6	28	34.6	
Never	233	50.1	77	62.6	134	51.3	22	27.2	

*Missing	3	0.6	1	0.8	1	0.4	1	1.2	
Swollen gums									
Always	28	6.0	3	2.4	17	6.5	8	9.9	<0.001
Sometimes	67	14.4	9	7.3	34	13.0	24	29.6	<0.001**
Rarely	123	26.5	24	19.5	74	28.4	25	30.9	
Never	245	52.7	87	70.7	135	51.7	23	28.4	
*Missing	2	0.4	0	0	1	0.4	1	1.2	
Painful gums									
Always	34	7.3	6	4.9	18	6.9	10	12.3	<0.001
Sometimes	69	14.8	7	5.7	39	14.9	23	28.4	<0.001**
Rarely	129	27.7	29	23.6	75	28.7	25	30.9	
Never	232	49.9	81	65.9	129	49.4	22	27.2	
*Missing	1	0.2	0	0	0	0	1	1.2	
Oral ulcers									
Always	31	6.7	7	5.7	17	6.5	7	8.6	0.003
Sometimes	57	12.3	6	4.9	37	14.2	14	17.3	<0.001**
Rarely	145	31.2	34	27.6	78	29.9	33	40.7	
Never	229	49.2	75	61.0	128	49.0	26	32.1	

*Missing	3	0.6	1	0.8	1	0.4	1	1.2	
<hr/>									
Bad breadth									
Always	48	10.3	11	8.9	27	10.3	10	12.3	0.015
Sometimes	73	15.7	8	6.5	50	19.2	15	18.5	0.003**
Rarely	149	32.0	40	32.5	79	30.3	30	37.0	
Never	190	40.9	62	50.4	104	39.8	24	29.6	
*Missing	5	1.1	2	1.6	1	0.4	2	2.5	
<hr/>									
<u>PD problems</u>									
<u>(periodontitis)</u>									
Noticed that your front teeth moved forward or that gaps have developed between your front teeth?									
No	272	58.5	84	68.3	150	57.5	38	46.9	0.049
Yes	86	18.5	17	13.8	49	18.8	20	24.7	0.039**
Unknown	107	23.0	22	17.9	62	23.8	23	28.4	
<hr/>									
Have you had your teeth that became loose on their own, without any injury?									

No	234	50.3	76	61.8	126	48.3	32	39.5	0.006
Yes	151	32.5	31	25.2	83	31.8	37	45.7	0.269**
Unknown	80	17.2	16	13.0	52	19.9	12	14.8	

Had treatment for gum disease, such as scaling and root planning, sometimes called ‘deep cleaning’

No	333	71.6	93	75.6	188	72.0	52	64.2	0.080
Yes	37	8.0	13	10.6	15	5.7	9	11.1	0.042**
Unknown	95	20.4	17	13.8	58	22.2	20	24.7	

Have you been told by a dental professional that you lost bone around your teeth?

No	324	69.7	91	74.0	184	70.5	49	60.5	0.035
Yes	26	5.6	6	4.9	10	3.8	10	12.3	0.292**
Unknown	114	24.5	26	21.1	67	25.7	21	25.9	
*Missing	1	0.2	0	0	0	0	1	1.2	

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

**Linear by Linear Association was calculated based on available data, not including those “missing” data.

^aSROH conditions four level were used for analysis (always, often, occasionally, never).

^bFlossing and mouth wash used for three levels for analyses (often, occasionally, never)

^cPD indicator (gingivitis/periodontitis) used four levels for analyses (always, sometimes, rarely, never).

Table 7.3: Age-sex adjusted ORs of co-variates in participants who had fair and poor self-rated oral health in Guangzhou case-control study.

Variables	Fair SROH				Poor SROH			Overall P-value**	
	OR ^a	95% CI	P	OR ^a	95% CI	P*			
<u>Demographic factors</u>									
Age group (years)									
<=60	0.44	0.19	1.04	0.062	0.70	0.21	2.41	0.574	0.056
61-70	Ref				Ref				
71-80	0.99	0.59	1.66	0.955	1.93	0.96	3.86	0.065	
81=>	1.44	0.81	2.56	0.221	2.30	1.07	4.95	0.033	
Gender									
Women	0.90	0.58	1.41	0.652	0.93	0.51	1.68	0.808	0.903
Men	Ref				Ref				
Smoking									
Never	0.99	0.42	2.34	0.981	0.98	0.31	3.13	0.979	0.999
Former	1.00	0.36	2.79	0.996	1.11	0.29	4.25	0.881	
Current	Ref				Ref				
^aDrinking any alcohol during the past two years (per 100 ml)									
Never or less than once per month	Ref				Ref				0.644
More than once month/week/daily	0.66	0.27	1.60	0.355	0.68	0.20	2.32	0.534	
<u>Socioeconomic status</u>									
Educational level									
University and above	Ref				Ref				0.186
Senior high school	0.80	0.42	1.910	0.620	0.46	0.12	1.74	0.253	
Junior high school	0.95	0.43	2.09	0.896	1.06	0.37	3.07	0.913	

Primary school	0.89	0.41	1.91	0.766	1.34	0.49	3.69	0.569	
Illiteracy	2.03	0.81	5.04	0.130	2.33	0.72	7.47	0.157	
Personal /annual income (RMB)									
≥70000	Ref				Ref				
50000-<70000	2.15	0.90	5.13	0.085	1.71	0.51	5.77	0.385	0.001
30000-<50000	2.39	1.10	5.18	0.027	1.72	0.58	5.12	0.327	
10000-<30000	1.87	0.88	3.96	0.102	1.18	0.40	3.47	0.763	
< 10000	2.53	1.09	5.86	0.030	5.78	1.99	16.79	0.001	
Family income (RMB)									
≥70000	Ref				Ref				
50000-<70000	1.27	0.57	2.82	0.563	0.95	0.33	2.70	0.922	0.673
30000-<50000	1.13	0.57	2.21	0.734	0.75	0.31	1.82	0.530	
<30000	1.10	0.55	2.19	0.788	1.29	0.55	3.03	0.563	
<u>Social network</u>									
Marriage									
Married or cohabiting	0.55	0.32	0.96	0.036	0.88	0.43	1.81	0.729	0.225
Separated, divorced, and never married	0.54	0.21	1.38	0.199	0.75	0.21	2.64	0.655	
Widow	Ref				Ref				
<u>Dietary intake</u>									
<u>Meat consumption</u>									
Pork intake frequency in the past two years									
≥= Twice a day	2.46	0.91	6.65	0.076	1.57	0.46	5.35	0.471	0.175
Once a day	2.32	1.06	5.09	0.036	1.19	0.45	3.20	0.725	
> Once a week and < daily	3.50	1.61	7.58	0.002	1.91	0.74	4.94	0.184	
=< Once a week	Ref				Ref				
Never or less than once per month	2.07	0.71	6.06	0.185	1.43	0.37	5.46	0.602	

Beef intake frequency in the past two years									
Once a day/>= Twice a day	0.52	0.15	1.83	0.309	1.39	0.21	9.19	0.730	0.036
> Once a week and < daily	0.78	0.38	1.58	0.489	2.85	0.93	8.70	0.066	
=< Once a week	Ref				Ref				
Never or less than once per month	0.96	0.56	1.64	0.868	3.66	1.41	9.52	0.008	
Lamb intake frequency in the past two years									
Once a day/>= Twice a day	0.60	0.17	2.14	0.426	1.05	0.15	7.32	0.962	0.432
> Once a week and < daily	1.34	0.45	4.01	0.604	2.73	0.59	12.62	0.198	
=< Once a week	Ref				Ref				
Never or less than once per month	0.78	0.41	1.50	0.458	1.96	0.67	5.70	0.216	
<u>Fruits and vegetable consumption</u>									
Vegetable intake frequency during the past two years									
>= Twice a day	0.65	0.13	3.16	0.589	0.21	0.04	1.09	0.064	0.248
Once a day	0.42	0.09	2.07	0.287	0.14	0.03	0.73	0.020	
> Once a week and < daily	0.65	0.12	3.50	0.613	0.25	0.04	1.47	0.124	
=< Once a week	Ref				Ref				
Never or less than once per month	0.84	0.09	7.66	0.877	0.27	0.02	3.32	0.305	
Fruit intake frequency during the past two years									
>= Twice a day	1.44	0.50	4.18	0.504	2.11	0.61	7.28	0.238	0.429
Once a day	1.46	0.70	3.07	0.316	0.99	0.38	2.56	0.983	
> Once a week and < daily	1.72	0.81	3.65	0.157	1.03	0.39	2.71	0.955	

=< Once a week	Ref				Ref				
Never or less than once per month	1.18	0.36	3.90	0.791	1.79	0.45	7.11	0.406	
^bScores of Meat consumption									
0-2	Ref				Ref				
3-5	0.96	0.49	1.90	0.913	0.98	0.42	2.29	0.964	0.458
6-12	1.08	0.65	1.79	0.772	0.60	0.29	1.23	0.163	
^cScores of vegetables and fruits consumption									
0-3	Ref				Ref				
4-5	0.94	0.37	2.36	0.892	0.47	0.17	1.33	0.156	0.227
6-8	0.73	0.29	1.88	0.517	0.32	0.11	0.94	0.038	
<u>Cardiovascular disease and risk factors</u>									
Hypertension status									
No	Ref				Ref				
Yes	0.71	0.46	1.10	0.126	0.81	0.46	1.43	0.468	0.309
High blood cholesterol									
No	Ref				Ref				
Yes	0.74	0.39	1.40	0.354	0.83	0.37	1.89	0.661	0.655
Missing									
Diabetes									
No	Ref				Ref				
Yes	1.12	0.63	1.97	0.701	1.79	0.90	3.56	0.096	0.208
Coronary heart disease									
No	Ref				Ref				
Yes	0.64	0.32	1.29	0.214	0.34	0.10	1.05	0.060	0.122
Stroke									
No	Ref				Ref				
Yes	0.59	0.30	1.16	0.128	1.46	0.68	3.13	0.326	0.032

*Missing

Chronic bronchitis									
No	Ref				Ref				
Yes	1.55	0.55	4.32	0.403	4.99	1.72	14.47	0.003	0.002
Cancer									
No	Ref				Ref				
Yes	0.13	0.01	1.26	0.078	1.63	0.35	7.74	0.536	0.022
Kidney disease									
No	Ref				Ref				
Yes	0.67	2.21	2.16	0.499	2.05	0.59	7.10	0.259	0.169
Depression									
No	Ref				Ref				
Yes	0.68	.217	2.13	0.510	1.39	0.40	4.91	0.610	0.439
Dementia									
No	Ref				Ref				
Yes	0.54	0.63	1.01	0.054	1.41	0.76	2.62	0.272	0.009

*Missing

OR^a adjusted for age and gender.

Reference category: Good self-rated oral health.

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

**Overall P value was calculated based on available data, not including those “missing” data.

^aDrinking any alcohol during the past two years: Variables pooled were average frequency use wine (glass) during the past two years?; average frequency use beer (bottle) during the past two years? and average frequency use other alcohol (red wine, rice wine, fruit wine, etc.) during the past two year [100ml]?

^bScores of Meat consumption: Variables pooled from pork, beef and lamb. Scoring was 0-2=Never or less than once per month/week; 3-5=> Once a week/< daily; 6-12=Once a day/>= Twice a day.

^cScores of fruits and vegetables consumption: Scoring was as 0-3= Never or less than once per month/< or >week; 4-5 = less than daily; 6-8 = Once a day/>= Twice a day

Table 7.4: Multivariate adjusted OR of fair SROH and poor SROH in Guangzhou case-control study.

Variables	Fair SROH			Poor SROH			Overall P value*		
	OR ^a	95% CI	P	OR ^a	95% CI	P			
<i>Socioeconomic factors</i>									
Educational level									
University and above	Ref			Ref					
Senior high school	0.70	0.28	1.75	0.441	0.38	0.09	1.64	0.195	0.430
Junior high school	0.82	0.35	1.94	0.647	0.74	0.22	2.47	0.629	
Primary school	0.78	0.32	1.91	0.580	1.14	0.33	3.93	0.833	
Illiteracy	1.50	0.52	4.36	0.454	1.30	0.31	5.37	0.722	
Personal/Annual income (RMB)									
≥70000	Ref			Ref					
50000-<70000	2.09	0.82	5.33	0.121	2.51	0.66	9.47	0.176	0.021
30000-<50000	2.45	1.03	5.84	0.044	2.39	0.67	8.54	0.181	
10000-<30000	1.69	0.70	4.04	0.243	0.93	0.26	3.33	0.909	
< 10000	2.49	0.94	6.59	0.067	4.28	1.20	15.33	0.025	

Social network

Marriage

Married or cohabiting	0.53	0.29	0.96	0.037	0.88	0.40	1.95	0.759	<i>0.183</i>
Separated, divorced, and never married	0.67	0.24	1.81	0.426	0.55	0.13	2.32	0.412	
Widowed	Ref				Ref				

Diet

^bScores of Meat consumption

0-2	Ref				Ref				
3-5	1.15	0.67	1.98	0.613	0.83	0.38	1.84	0.652	<i>0.863</i>
6-12	1.18	0.57	2.45	0.658	1.28	0.49	3.32	0.615	

^cScores of vegetables and fruits consumption

0-3	Ref				Ref				
4-5	0.72	0.27	1.94	0.511	0.39	0.12	1.29	0.122	<i>0.211</i>
6-8	1.13	0.42	3.03	0.814	0.77	0.24	2.46	0.653	

Cardiovascular disease and risk factors

Diabetes

No	Ref				Ref				
Yes	1.29	0.71	2.34	0.410	2.02	0.95	4.29	0.066	<i>0.183</i>

Coronary heart disease

No	Ref				Ref				
Yes	0.58	0.27	1.26	0.169	0.25	0.07	0.89	0.032	<i>0.068</i>

Stroke

No	Ref				Ref				
Yes	0.68	0.32	1.46	0.321	1.32	0.54	3.21	0.540	<i>0.244</i>

Missing

Chronic bronchitis

No	Ref				Ref				
Yes	1.48	0.51	4.33	0.475	4.53	1.42	14.47	0.011	<i>0.011</i>

Cancer

No	Ref				Ref				
Yes	0.15	0.02	1.63	0.119	1.65	0.30	9.22	0.570	<i>0.052</i>

Kidney disease

No	Ref				Ref				
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Yes	0.77	0.22	2.72	0.679	2.31	0.58	9.24	0.238	0.244
Dementia									
No	Ref				Ref				
Yes	0.67	0.38	1.18	0.166	1.06	0.49	2.30	0.883	0.245
Missing									

Reference category: Good self-rated oral health

*Overall P-value is likelihood ratio test

^aAdjusted OR for age (cont.), gender, personal income, education, marital status, score of vegetables and fruits, score of meat consumption, coronary heart disease, stroke, diabetes, chronic bronchitis, cancer, kidney disease, dementia

^b**Scores of Meat consumption: Variables pooled from pork, beef and lamb. Scoring was 0-2=Never or less than once per month/week; 3-5=> Once a week/< daily; 6-12=Once a day/>= Twice a day.**

^c**Scores of fruits and vegetables consumption: Scoring was as 0-3= Never or less than once per month/< or >week; 4-5 = less than daily; 6-8 = Once a day/>= Twice a day**

Table 7.5: Binary logistic analysis for dementia associated with self-rated oral health (Poor and Fair SROH) in Guangzhou case-control study.

Variable	Fair SROH		Poor SROH		*P	Model 1				Model 2			Model 3				
	n=261	(%)	n=81	(%)		OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
Dementia																	
No	143	54.8	29	35.8	0.003	Ref				Ref				Ref			
Yes	118	45.2	52	64.2		2.21	1.27	3.85	0.005	1.82	0.96	3.45	0.066	1.33	0.65	2.70	0.433

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Model 1 was adjusted with age, gender

Model 2 was adjusted with age, gender, personal income, education, marital status, score of vegetables and fruit, score of meat consumption

Model 3 was adjusted with age, gender, personal income, education, marital status, score of vegetables and fruit, score of meat consumption, coronary heart disease, stroke, diabetes, chronic bronchitis, cancer, kidney disease

Table 7.6: Binary logistic analysis for dementia associated with self-reported oral health (Poor and Good plus Fair SROH) in Guangzhou case-control study

Variable	^a Good SROH		Poor SROH		*P	Model 1			Model 2			Model 3					
	n=384	(%)	n=81	(%)		OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
Dementia																	
No	203	54.8	29	35.8	0.003	Ref			Ref			Ref					
Yes	181	45.2	52	64.2		1.91	1.12	3.25	0.018	1.58	0.85	2.92	0.145	1.31	0.67	2.55	0.436

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

^aGood SROH comprises of good and fair SROH participants from table 7.2

Model 1 was adjusted with age, gender

Model 2 was adjusted with age, gender, personal income, education, marital status, score of vegetables and fruit, score of meat consumption

Model 3 was adjusted with age, gender, personal income, education, marital status, score of vegetables and fruit, score of meat consumption, coronary heart disease, stroke, diabetes, chronic bronchitis, cancer, kidney disease

Table 7.7: Multivariate analyses for dementia associated with oral health behavior (dental visit) in Guangzhou case-control study.

Outcome variable: Dental visit	^a Dental visits															
	^b Every 6 months / once a year		Every 2 years/> 2 years		Try to avoid dentist/ never been to a dentist		*P	Every 2 years/> 2 years			Try to avoid dentist/ never been to a dentist			Overall P-value**		
	n=58	%	n=186	%	n=206	%		^c OR	95% CI	P	^c OR	95% CI	P			
Dementia																
No	37	63.8	102	54.8	78	37.9	<0.001	Ref				Ref				
Yes	21	36.2	84	45.2	128	62.1		1.76	0.81	3.86	0.156	3.60	1.65	7.83	0.001	<0.001

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data (15 missing values in dental visit variable)

**Overall P-value is likelihood ratio test

^aClassification of Oral hygiene variables were changed into three levels for analyses. How often do you go to the dentist (every six months, once a year, every two years, more than two years and try to avoid or never been to the dentist) from table 7.2 were derived as Every 6 months /Once a year, Every 2 years/> 2 years and Try to avoid the dentist or never been to a dentist

^bReference category: every six months / once a year

^c**OR adjusted with** age, gender, personal income, education, marital status, score of vegetables and fruit, score of meat consumption, coronary heart disease, stroke, diabetes, chronic bronchitis, cancer, kidney disease

Table 7.8: Multivariate analyses for dementia associated with oral health behavior (brushing teeth) in Guangzhou case-control study.

Outcome variable: brushing	^a Brushing teeth															
	^b More than once a day		Once a day		Less than once a day		P	Once a day			Less than once a day			Overall P value*		
	n=187	%	n=180	%	n=98	%		^c OR	95% CI	P	^c OR	95% CI	P			
Dementia																
No	145	77.5	75	41.7	12	12.2	<0.001	Ref				Ref				
Yes	42	22.5	105	58.3	86	87.8		6.01	3.43	10.53	0.000	25.77	11.66	56.96	0.000	<0.001

*Overall P-value is likelihood ratio test

^aClassification of Oral hygiene variables was changed into three levels for analyses. How often do you Brush teeth (Do not brush, Less than once a day, Once a day, Twice a day and More than twice a day) from table 7.2 were derived as More than once a day, Once a day and never or less than once a day.

^bReference category: More than once a day

^c**OR adjusted with** age, gender, personal income, education, marital status, scores of vegetables and fruit, scores of meat consumption, coronary heart disease, stroke, diabetes, chronic bronchitis, cancer, kidney disease

Table 7.9: Multivariate analyses for dementia associated with number of teeth present in the mouth in Guangzhou case-control study.

Outcome variable:	^a Number of teeth present															
	^b 20-32 teeth		1-19 teeth		Edentulous		P*	1-19 teeth			Edentulous			Overall P value**		
Number of teeth present	n=187	%	n=180	%	n=98	%		^c OR	95% CI	P	^c OR	95% CI	P			
Dementia																
No	167	65.5	55	34.2	10	20.8	<0.001	Ref					Ref			
Yes	88	34.5	106	65.8	38	79.2		2.22	1.36	3.63	0.002	3.33	1.40	7.91	0.006	<0.001

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data. 15 missing values in no dementia.

Excluded from analyses one missing value from variable number of teeth present

**Overall P-value is likelihood ratio test

^aClassification of number of teeth present variable 4 levels (Edentulous, 1-9 teeth, 10-19 teeth and 20-32 teeth) from table 7.2 were derived as Edentulous, 1-19 teeth and 20-32 teeth for analyses.

^bReference category: 20-32 teeth

^cOR adjusted with age, gender, personal income, education, marital status, scores of vegetables and fruit, scores of meat consumption, coronary heart disease, stroke, diabetes, chronic bronchitis, cancer, kidney disease

Table 7.10: Multivariate analyses for dementia associated with periodontal disease in Guangzhou case-control study.

Outcome variable: PD	^a Periodontal disease															
	^b Normal		Gingivitis (mild PD)		Periodontitis (moderate/severe)		Gingivitis (mild PD)			Periodontitis (moderate/severe)			Overall P value*			
	n=267	%	n=43	%	n=154	%	P	^c OR	95% CI	P	^c OR	95% CI		P		
Dementia																
No	158	59.0	64	38.1	10	34.5	<0.001	Ref				Ref				
Yes	110	41.0	104	61.9	19	65.5		1.98	1.25	3.15	0.004	2.70	1.04	7.03	0.041	0.004

*Overall P-value is likelihood ratio test

^aPD variable: Two variables from table 7.2 (had treatment for gum disease, such as scaling and root planning, sometimes called ‘deep cleaning’; been told by a dental professional that you lost bone around your teeth?) where ‘unknown’ and ‘missing’ values were changed into ‘no’ values and were pooled with other three variables bleeding gums, swollen gums, bad breadth together for PD variable.

^bReference category: Normal

^cOR adjusted with age, gender, personal income, education, marital status, scores of vegetables and fruit, scores of meat consumption, coronary heart disease, stroke, diabetes, chronic bronchitis, cancer, kidney disease

7.3. English Longitudinal Study of Aging (ELSA)

7.3.1 Methods

The studied populations were derived from the ELSA, fully described in Chapter 3, section 3.6.3.

7.3.1.1 Participant selection

The analytical sample used in this chapter was a subset of ELSA data, designed for examining the association of dementia or severe cognitive impairment at baseline with incident OH outcomes in the cohort follow-up. Participants were selected from those who were interviewed at wave 5 as baseline cohort members, since this survey had OH questionnaire measure and the participants could have a diagnosis of dementia from wave 3 and wave 4 which helped identified those with dementia. Also, to minimise a potential bias from lost to follow-up, the participants for analysis were required to have interviews at wave 3, wave 4, wave 6 and wave 7. Thus the total number of participants for this data analysis was 5,412, after excluding those who were below 50 years of age and had “poor SROH” at wave 5 (n=80). The number of participants analysed for different OH measures in the cohort follow-up (SROH, no teeth and oral impact) varied and was seen footnotes for detail in table 7.11-7.19. Incident poor SROH documented from waves 6-9 were n=564, and non-incident poor SROH were 4,848 participants. Similarly, in the data analysis for “no teeth” incidence, documented from waves 6-9, 670 participants at wave 5 and 7 missing values at wave 7 were excluded, leaving 4,949 participants for the analysis. For “none of these oral impact (total summed Q6)” incidence which was documented from waves 6-9, 663 participants at wave 5 were excluded, with 4,963 participants left for the analysis. Similarly, the oral impact from Q1-6, SROH, no teeth have been described in detail in footnotes of Tables 7.12-7.19.

7.3.1.2 Data collection

Data collection and questionnaire have been discussed in Chapter 3, section 3.6.3. A brief description of the data collection for the main questionnaire was completed by CAPI and a self-completion questionnaire. OH measures, SROH and oral impact data have been reported in waves 3, 5, 7, 8 and 9, except for tooth condition measure, which has been reported in waves 3, 5 and 7. BMI data, which was used for adjustment, was taken from wave 4 as it was not reported in wave 5.

7.3.2 Data analysis

The distributions of socio-demographic factors and comorbidities, and their differences between participants with and without incident poor SROH were examined using the Chi-squared test for categorical variables, or one-way variance for the continuous variable. Binary logistic regression models were employed to calculate OR and 95% CI of incident poor SROH. These models were also used to determine the incidence of “none of these oral impact” documented from waves 7- 9 (no oral data was present in wave 6) in relation to dementia (including cognitive impairment) at baseline from waves 3- 5. Similarly, binary logistic regression models were also used to examine the risk of the incidence of “no teeth” from wave 7 (as data for tooth conditions were not reported in waves 6, 8 and 9) in relation to dementia (including cognitive impairment) at baseline from waves 3-5. Stepwise logistic regression was used and three different sets of confounding variables which were adjusted (see tables 7.12- 7.19 footnotes) in the association of cognitive impairment /dementia with oral health.

7.3.3 Results

7.3.3.1 Characteristics of ELSA participants in the analysis

Of 5,412 participants, the average age was 66.9 years ($SD\pm 9.3$), and 57.2% of them were women. Participants with incident poor SROH were likely to be older, have no educational qualifications, sick or disabled, have the lowest equivalised total income, be widowed, current

smokers, and have BMI higher than 30 Kg/m². Participants with incidences of poor SROH had not consumed alcohol in the previous 12 months. All comorbidities had a significant association and are higher in poor incident SROH than non-incident SROH, except cancer which had no significant differences (Table 7.11).

7.3.3.2 Incident SROH, edentulism and oral impact (dental conditions) in relation to dementia/ cognitive impairment at baseline

Table 7.12 shows the number, percentage and OR of incident poor SROH across participants with different levels of cognitive impairment and dementia. Taking all participants with mild cognitive impairment or normal cognition as a reference for analysis, there was a significant association of severe cognitive impairment with incident poor SROH in model 1 which was adjusted for age, sex and education, the OR was 2.24 (95% CI 1.42-3.54), and in model 2 with additional adjustment for education, income, marital status, smoking, alcohol intake and BMI, OR was 1.98 (1.24-3.15). In model 3, which was further adjusted with comorbidities (hypertension, high blood cholesterol, diabetes, stroke, heart attack, lung disease, asthma, Parkinson's disease, psychiatric condition, and osteoporosis), there was a slight attenuation in the association of severe cognitive impairment with incident poor SROH, but the OR remained significant (1.91, 1.19-3.05).

An increased OR of moderate cognitive impairment in participants with incident poor SROH was significant, with OR 1.61 (1.20-2.16) in model 1, OR 1.50 (1.11-2.02) in model 2, and OR 1.49 (1.10-2.02) in model 3. All increased ORs of incident poor SROH in dementia were not significant, which could be due to the small number of patients in the group. The combined data of dementia and severe cognitive impairment have shown a significant OR with incident poor SROH (1.90, 1.22-2.98) in model 3 (Appendix 10).

Table 7.13 shows the number, percentage, and OR of incident “no teeth” across participants with different levels of cognitive impairment and dementia. Taking all participants with mild cognitive impairment or normal cognition as a reference, adjusted OR of “no teeth” in people with combined severe cognitive impairment and dementia was 2.39 (0.93-6.11) in model 1, 1.62 (0.61-4.31) in model 2 and 1.07 (0.39-2.93) in model 3. The data of moderate cognitive impairment showed a non-significant association with incident “no teeth” (OR 0.98, 0.50-1.92) in model 1, 0.84 (0.42-1.68) in model 2, and 0.80 (0.40-1.60) in model 3.

Tables 7.14-7.19 illustrates the number, percentage and OR of incident oral impact across participants with different cognitive impairment levels and dementia. The oral impact variables include five questions, and the sixth question is the total sum of questions (Q) from 1-5. The data showed a non-significant inverse association of dementia/ cognitive impairment with “difficulty in eating food” (Q.1, Table 7.14), “smiling, laughing and showing teeth without embarrassment” (Q.3, Table 7.16), and “problems enjoying other people’s company” (Q.5, Table 7.18). Moreover, there was a positive but non-significant association of dementia/ cognitive impairment with “difficulty in speaking” (Q.2, Table 7.15). However, data of dementia showed a significant association with emotional stability (Q.4, Table 7.17) (adjusted ORs 6.97, 1.83-26.11) in model 1, 6.54 (1.67-25.62) in model 2 and 4.32 (1.07-17.49) in model 3. Table 7.19 shows the data analysis for the last question (Q.6), “difficulties caused by dental conditions, none of these listed”, which was a summed finding of all the previous five questions (Q1-Q5). Participants who reported at least one oral impact were likely to have dental difficulties. The increased OR was not significant in models 1-3 (1.28, 0.54-3.02; 1.15, 0.49-2.74; 0.93, 0.39-2.23).

Table 7.11: Basic characteristics of participants with and without incident poor SROH in ELSA cohort study

Variables	All participants		Non-Incident poor SROH		Incident poor SROH		P value
	n=5412	%	n=4848	%	n=564	%	
Basic characteristics							
Age (years) Mean (SD)	66.89	(9.26)	66.79	(9.17)	67.79	(9.96)	0.008
Gender							
Men	2316	42.8	2057	42.4	259	45.9	0.113
Women	3096	57.2	2791	57.6	305	54.1	
Educational level							
Degree or equivalent	961	17.8	900	18.6	61	10.8	<0.001
Higher education	805	14.9	726	15.0	79	14.0	
Intermediate / low education	2366	43.7	2121	43.8	245	43.4	
No qualification	1236	22.8	1061	21.9	175	31.0	
*Missing	44	0.8	40	0.8	4	0.7	
Employment status							
Retired	3122	57.7	2790	57.5	332	58.9	<0.001
Employed +self employed	1702	31.4	1564	32.3	138	24.5	
Unemployed	44	0.8	37	0.8	7	1.2	
Sick or disabled	180	3.3	131	2.7	49	8.7	
Looking after home or family	345	6.4	309	6.4	36	6.4	
Others	18	0.3	16	0.3	2	0.4	
*Missing	1	0.0	1	0.0	0	0	
Equivalised total income in quintiles							

Lowest	864	16.0	744	15.3	120	21.3	<0.001
2	936	17.3	827	17.1	109	19.3	
3	955	17.6	845	17.4	110	19.5	
4	1011	18.7	921	19.0	90	16.0	
Highest	1092	20.2	1019	21.0	73	12.9	
*Missing	554	10.2	492	10.1	62	11.0	

Marriage

Married or cohabiting or civil partners	3913	72.3	3532	72.9	381	67.6	0.006
Unmarried/single	225	4.2	203	4.2	22	3.9	
Separated	799	14.8	705	14.5	94	16.7	
Widowed	414	7.6	360	7.4	54	9.6	
Divorced	61	1.1	48	1.0	13	2.3	

Cardiovascular disease risk factors

Smoking

Never smoker	2039	37.7	1897	39.1	142	25.2	<0.001
Ex-smoker	2728	50.4	2432	50.2	296	52.5	
Current smoker	597	11.0	476	9.8	121	21.5	
*Missing	48	0.9	43	0.9	5	0.9	

Drinking alcohol over the past 12 months

Daily or ≥ 5 times per week	1077	19.9	982	20.3	95	16.8	<0.001
≤ 4 and ≥ 1 times per week	1934	35.7	1774	36.6	160	28.4	
Once or twice per month	586	10.8	518	10.7	68	12.1	

Occasionally (couple of months or once or twice a year)	785	14.5	695	14.3	90	16.0	
Never	564	10.4	470	9.7	94	16.7	
*Missing	466	8.6	409	8.4	57	10.1	
*BMI (Kg/m²)							
< 18.5,	28	0.5	24	0.5	4	0.7	0.025
18.5-24.9	1114	20.6	1026	21.2	88	15.6	
25-29.9	1861	34.4	1673	34.5	188	33.3	
≥30	1377	25.4	1219	25.1	158	28.0	
*Missing	1032	19.1	906	18.7	126	22.3	
Hypertension							
No	3536	65.3	3205	66.1	331	58.7	<0.001
Yes	1876	34.7	1643	33.9	233	41.3	
High blood cholesterol							
No	3785	69.9	3415	70.4	370	65.6	0.018
Yes	1627	30.1	1433	29.6	194	34.4	
<u>Comorbidities</u>							
Diabetes							
No	4949	91.4	4464	92.1	485	86.0	<0.001
Yes	463	8.6	384	7.9	79	14.0	
Stroke							
No	5181	95.7	4657	96.1	524	92.9	<0.001
Yes	231	4.3	191	3.9	40	7.1	
Angina							
No	4787	88.5	4326	89.2	461	88.5	<0.001

Yes	625	11.5	522	10.8	103	11.5	
Heart attack							
No	5133	94.8	4615	95.2	518	91.8	<0.001
Yes	279	5.2	233	4.8	46	8.2	
Lung disease (Chronic bronchitis and emphysema)							
No	5246	96.9	4709	97.1	537	95.2	0.012
Yes	166	3.1	139	2.9	27	4.8	
Asthma							
No	4866	89.9	4375	90.2	491	87.1	0.017
Yes	546	10.1	473	9.8	73	12.9	
Parkinson's disease							
No	5392	99.6	4833	99.7	559	99.1	0.033
Yes	20	0.4	15	0.3	5	0.9	
^bPsychiatric condition							
No	4972	91.9	4477	92.3	495	87.8	<0.001
Yes	440	8.1	371	7.7	69	12.2	
Cancer							
No	5278	97.5	4733	97.6	545	96.6	0.149
Yes	134	2.5	115	2.4	19	3.4	
Osteoporosis							
No	5083	93.9	4565	94.2	518	91.8	0.029
Yes	329	6.1	283	5.8	46	8.2	

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

^a BMI (Body Mass Index) is taken from ELSA wave 4 as nurse data was not collected in ELSA wave 5. BMI grouped according to WHO definition. < 18.5: underweight; 18.5-24.9: normal range; 25-29.9: overweight; ≥ 30 : obese

^bPsychiatric problems include any psychiatric conditions such as depression, anxiety, hallucination.

Table 7.12: Baseline dementia (waves 3-5) associated with Poor SROH in the follow-up (waves 7-9) in ELSA cohort study.

Dementia/ cognitive impairment from waves 3- 5	^a All participa nts n=5412	Incident poor SROH n= 564	%	*P	Model 1				Model 2			Model 3				
					OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
^b Normal and MCI	936	57	6.09	<0.001	Ref											
Moderate cognitive impairment	3981	426	10.70		1.61	1.20	2.16	0.002	1.50	1.11	2.02	0.008	1.49	1.10	2.02	0.009
Severe cognitive impairment	264	42	15.91		2.24	1.42	3.54	<0.001	1.98	1.24	3.15	0.004	1.91	1.19	3.05	0.007
Dementia	51	8	15.69		2.23	0.98	5.05	0.055	2.14	0.92	4.97	0.078	1.89	0.81	4.41	0.144
*Missing	180	31	17.22													

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Stepwise logistic regression were run

Model 1: adjusted for age, gender, and education

Model 2: adjusted for Model 1 plus Equivalised total income in quintiles, Marital status, Smoking, Drinking alcohol over the past 12 months, BMI

Model 3: adjusted for Model 2 plus Hypertension, High blood cholesterol, Diabetes, Stroke, Heart attack, Lung disease, Asthma, Parkinson’s disease, Psychiatric condition, Osteoporosis.

^aTotal number of participants who were interviewed at both waves 3, 5 and wave 7 were n=5706. Excluded participants at w5 were n=294 (were aged <50 [n=80], poor SROH [n=214], leaving n= 5412 for analysis. No loss to follow up participants.

^bDue to the small number in the normal group (n=20) was combined with mild cognitive impairment as a reference group. *Normal group:* All participants in the non-incident poor SROH group were n=19; participants in incident poor SROH n=1.

Table 7.13: Baseline dementia (waves 3-5) associated with no tooth in the follow-up wave 7 [4 years follow-up] in ELSA cohort study.

Dementia/ cognitive impairment from waves 3-5	^a All participants	No teeth	Model 1					Model 2			Model 3			
	n= 4949	n= 82	%	*P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	
MCI	919	11	1.20	<0.001	Ref									
+Normal														
Moderate cognitive impairment	3642	55	1.51		0.98	0.50 1.92	0.940	0.84	0.42 1.68	0.625	0.80	0.40 1.60	0.523	
^b Severe cognitive impairment	202	11	5.45		2.39	0.93 6.11	0.070	1.62	0.61 4.31	0.335	1.07	0.39 2.93	0.896	
Dementia	43	0												
*Missing	143	5												

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Stepwise logistic regression were run

Model 1: adjusted for age, gender, and education

Model 2: adjusted for Model 1 plus Equivalised total income in quintiles, Marital status, Smoking, Drinking alcohol over the past 12 months, BMI

Model 3: adjusted for Model 2 plus Hypertension, High blood cholesterol, Diabetes, Stroke, Heart attack, Lung disease, Asthma, Parkinson’s disease, Psychiatric condition, Osteoporosis.

^aTotal number of participants who were interviewed at both waves 3, 5 and wave 7 were n=5706. Excluded participants at w5 were n=757 (aged < 50 years [n=80], edentate [n=669] and missing values [n=1]) and missing value at wave 7 (n=7) leaving n= 4949 for analysis. No loss to follow up participants.

^bDementia and severe cognitive impairment groups were combined for OR analyses.

Table 7.14: Baseline dementia (waves 3-5) associated with the dental condition- Difficulty eating food in w7-9 in ELSA cohort study.

Dementia/ cognitive impairment from waves 3-5	^a All participants	Difficulty eating food			Model 1			Model 2			Model 3					
	n= 5105	n= 674	%	*P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
Mild cognitive impairment + Normal	894	120	13.42	0.619	Ref			Ref			Ref					
Moderate cognitive impairment	3850	512	13.30		0.98	0.79 1.23	0.798	0.95	0.76 1.19	0.644	0.96	0.77 1.21	0.743			
Severe cognitive impairment	252	27	10.71		0.77	0.48 1.23	0.294	0.71	0.44 1.13	0.150	0.70	0.43 1.12	0.136			
Dementia	36	4	11.11		0.85	0.29 2.47	0.590	0.78	0.27 2.29	0.653	0.65	0.22 1.93	0.439			
*Missing	73	11														

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Stepwise logistic regression were run

Model 1: adjusted for age, gender, and education

Model 2: adjusted for Model 1 plus Equivalised total income in quintiles, Marital status, Smoking, Drinking alcohol over the past 12 months, BMI

Model 3: adjusted for Model 2 plus Hypertension, High blood cholesterol, Diabetes, Stroke, Heart attack, Lung disease, Asthma, Parkinson’s disease, Psychiatric condition, Osteoporosis.

^aTotal number of participants who were interviewed at both waves 3, 5 and wave 7 were n=5706. Excluded participants at w5 were n=601 (aged 50 years [n=80], above and mentioned difficulty in eating [n=404] and missing values [n=117]) leaving n=5105 for analysis. No loss to follow up participants.

Table 7.15: Baseline dementia (waves 3-5) associated with the dental condition - Difficulty speaking clearly_in waves 7-9 in ELSA cohort study.

Dementia/ cognitive impairment from waves 3-5	^a All participants n= 5420	Difficulty speaking clearly n=208					Model 1			Model 2			Model 3			
			%	*P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
MCI +Normal	945	35	3.70	0.671	Ref				Ref			Ref				
Moderate cognitive impairment	4075	157	3.85		0.97	0.66	1.43	0.870	0.87	0.59	1.30	0.499	0.88	0.59	1.31	0.521
Severe cognitive impairment	278	10	3.60		0.84	0.39	1.80	0.656	0.72	0.33	1.55	0.397	0.67	0.31	1.47	0.321
Dementia	39	3	7.69		2.02	0.58	7.02	0.270	1.68	0.47	5.97	0.425	1.25	0.35	4.50	0.736
*Missing	83	3	3.61													

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Stepwise logistic regression were run

Model 1: adjusted for age, gender, and education

Model 2: adjusted for Model 1 plus Equivalised total income in quintiles, Marital status, Smoking, Drinking alcohol over the past 12 months, BMI

Model 3: adjusted for Model 2 plus Hypertension, High blood cholesterol, Diabetes, Stroke, Heart attack, Lung disease, Asthma, Parkinson’s disease, Psychiatric condition, Osteoporosis.

^aTotal number of participants who were interviewed at both waves 3, 5 and wave 7 were n=5706. Excluded participants at w5 were n= 286 (aged < 50 years [n=80], mentioned difficulty in speaking clearly[n=89] and missing values [n=117]) leaving n=5420 for analysis. No loss to follow up participants.

Table 7.16: Baseline dementia (waves 3-5) associated with dental condition - Problems with smiling, laughing (SL) and showing teeth without embarrassment (STwE) (waves 7-9) in ELSA cohort study.

Dementia/ cognitive impairment from wave 3-5 from waves 3-5	^a All participants n= 5324	Problems with SL and STwE			Model 1			Model 2			Model 3				
		n= 300	%	*P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P		
MCI +Normal	931	45	4.83	0.056	Ref			Ref			Ref				
Moderate cognitive impairment	3998	244	6.10		1.35	0.96 1.89	0.083	1.25	0.89 1.75	0.208	1.25	0.89 1.77	0.198		
Severe cognitive impairment	273	7	2.56		0.65	0.28 1.51	0.320	0.54	0.23 1.25	0.151	0.52	0.23 1.22	0.135		
Dementia	39	2	5.13		1.28	0.29 5.57	0.743	1.04	0.24 4.60	0.959	0.83	0.19 3.69	0.805		
*Missing	83	2													

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Stepwise logistic regression were run

Model 1: adjusted for age, gender, and education

Model 2: adjusted for Model 1 plus Equivalised total income in quintiles, Marital status, Smoking, Drinking alcohol over the past 12 months, BMI

Model 3: adjusted for Model 2 plus Hypertension, High blood cholesterol, Diabetes, Stroke, Heart attack, Lung disease, Asthma, Parkinson’s disease, Psychiatric condition, Osteoporosis.

^aTotal number of participants which were interviewed at both waves 3, 5 and wave 7 were n=5706. Excluded participants at w5 were n=382 (aged < 50 [n =80], mentioned problems with smiling, laughing and showing teeth without embarrassment [n=185] and missing values [n=117]) leaving n=5324 for analysis. No loss to follow up participants.

Table 7.17: Baseline dementia (waves 3-5) associated with the dental condition - Problems with emotional stability (waves 7-9) in ELSA cohort study.

Dementia/ cognitive impairment from waves 3-5	^a All participants n= 5485	Problems with emotional stability n= 75			Model 1			Model 2			Model 3					
		%	*P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P				
MCI +Normal	951	14	1.47	0.009	Ref				Ref							
Moderate cognitive impairment	4128	56	1.36		0.96	0.52	1.78	0.907	0.88	0.47	1.64	0.690	0.89	0.48	1.66	0.705
Severe cognitive impairment	281	2	0.71		0.56	0.12	2.63	0.465	0.51	0.11	2.43	0.398	0.48	0.10	2.28	0.355
Dementia	41	3	7.32		6.97	1.83	26.61	0.004	6.54	1.67	25.62	0.007	4.32	1.07	17.49	0.040
*Missing	84	0	0.00													

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Stepwise logistic regression were run

Model 1: adjusted for age, gender, and education

Model 2: adjusted for Model 1 plus Equivalised total income in quintiles, Marital status, Smoking, Drinking alcohol over the past 12 months, BMI

Model 3: adjusted for Model 2 plus Hypertension, High blood cholesterol, Diabetes, Stroke, Heart attack, Lung disease, Asthma, Parkinson’s disease, Psychiatric condition, Osteoporosis.

^aExcluded participants from total number of participants at wave 5 were n=221(aged <50 [n =80], mentioned problems with emotional stability [n=24] and missing values [n=117]) leaving n=5485 for analysis. No loss to follow up participants.

Table 7.18: Baseline dementia (waves 3-5) associated with the dental condition - Problems in enjoying company of other people (waves 7-9) in ELSA cohort study.

Dementia/ cognitive impairment from waves 3-5	^a All participants n= 5489	Problems in enjoying company of other people n= 859	%	*P	Model 1				Model 2			Model 3				
					OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
MCI +Normal	957	148	15.46	0.953	Ref				Ref			Ref				
Moderate cognitive impairment	4125	649	15.73		1.00	0.81	1.22	0.977	0.96	0.78	1.18	0.698	0.98	0.80	1.20	0.841
Severe cognitive impairment	282	41	14.54		0.89	0.59	1.32	0.550	0.81	0.54	1.22	0.319	0.79	0.52	1.19	0.253
Dementia	41	6	14.63		0.95	0.39	2.31	0.902	0.87	0.36	2.14	0.765	0.71	0.29	1.76	0.462
*Missing	84	15	17.86													

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Stepwise logistic regression were run

Model 1: adjusted for age, gender, and education

Model 2: adjusted for Model 1 plus Equivalised total income in quintiles, Marital status, Smoking, Drinking alcohol over the past 12 months, BMI

Model 3: adjusted for Model 2 plus Hypertension, High blood cholesterol, Diabetes, Stroke, Heart attack, Lung disease, Asthma, Parkinson’s disease, Psychiatric condition, Osteoporosis.

^a Excluded participants from total number of participants at wave 5 were n=217 (aged <50 [n=80], above and mentioned problems enjoying company of other people [n= 20] and missing values [n=117]) leaving n=5489 for analysis. No loss to follow up participants.

Table 7.19 Baseline dementia (waves 3-5) associated with the dental condition - none of these above (difficulties present in Q. 1-5) (waves 7-9) in ELSA cohort study.

Dementia/ cognitive impairment from waves 3-5	^a All participants	Not mentioned					Model 1			Model 2			Model 3			
	n= 4963	n= 847	%	*P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P			
MCI +Normal	872	147	16.86	0.460	Ref			Ref			Ref					
Moderate cognitive impairment	3737	645	17.26		1.03	0.84 1.26	0.789	0.98	0.80 1.20	0.833	0.99	0.80 1.22	0.898			
Severe cognitive impairment	246	33	13.41		0.79	0.51 1.21	0.279	0.71	0.46 1.10	0.122	0.69	0.44 1.06	0.092			
Dementia	36	7	19.44		1.28	0.54 3.02	0.571	1.15	0.49 2.74	0.747	0.93	0.39 2.23	0.865			
*Missing	72	15	20.83													

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Stepwise logistic regression were run

Model 1: adjusted for age, gender, and education

Model 2: adjusted for Model 1 plus Equivalised total income in quintiles, Marital status, Smoking, Drinking alcohol over the past 12 months, BMI

Model 3: adjusted for Model 2 plus Hypertension, High blood cholesterol, Diabetes, Stroke, Heart attack, Lung disease, Asthma, Parkinson’s disease, Psychiatric condition, Osteoporosis.

^aExcluded participants from total number of participants at wave 5 were n= 743 (< aged 50 [n=80], not mentioned none of these [n=546] [difficulties present in Q. 1-5] and missing values [n=117]) leaving n=4963 for analysis. No loss to follow up participants.

7.4 Discussion

This chapter examined data from both the Guangzhou case-control study and the ELSA cohort study to assess the association of dementia/cognitive impairment with OH conditions. Oral health was evaluated using SROH, SROH conditions, number of teeth present, oral health habits and PD for a comprehensive analysis of their relations to dementia/cognitive impairment. The details of the findings from both studies are discussed below.

7.4.1 Self-rated oral health

The results from both the Guangzhou case-control study and the ELSA cohort study showed a statistically insignificant increase in the association of dementia with poor SROH (Tables 7.5 and 7.6, and Table 7.12). The cohort data analysis reported a significant association of moderate/severe cognitive impairment with incident poor SROH (Table 7.12), and when the data of combined severe cognitive impairment and dementia group was analysed, it reported significant association with SROH (adjusted OR 1.90, 1.22-2.98). These results are in line with a previous study which reported that the participants with a decline in cognitive test performance (when compared to participants without cognitive decline) had increased poor oral health due to the role of reduced salivation, dry mouth and decline in dental status (Sørensen *et al.*, 2018). A similar correlation was reported in previous systematic reviews confirming that older people with dementia tend to have poor oral health (Nangle *et al.*, 2019; Lauritano *et al.*, 2019).

Similarly, a study suggested that self-reported behaviours may not be very reliable in patients with dementia due to their memory impairment (Naorungroj *et al.*, 2013). A systematic review by Wu and colleagues also argued that whether cognitive status and oral health are related is unclear (Wu *et al.*, 2016). Therefore, under-reported oral health in people with dementia could partially explain why the results of SROH in the case-control study were non-significant.

7.4.2 Edentate or dentate

The data of the Guangzhou case-control study showed a significant association of dementia with a smaller number of teeth present and an edentulous state, while the ELSA cohort did not, probably due to its small number of participants with dementia at the baseline.

A previous study reported no significant association between cognitive decline and complete tooth loss (Naorungroj *et al.*, 2013); however, the recent studies have shown a significant association (Lopez-Jornet *et al.*, 2021; Jockusch *et al.*, 2021). A meta-analysis of six studies revealed that Alzheimer's disease patients have an increased risk of dental loss (HR 1.52, 95% CI 1.00–2.30) and edentulous condition (HR 2.26, 1.70–3.01) (Dioguardi *et al.*, 2019).

7.4.3 Oral impact on oral health quality of life

In the ELSA cohort study, the data of all oral impact questions related to oral health quality of life showed non-significant relations to dementia except for one question, “problems with emotional stability”. A recent meta-analysis conducted by Ming *et al.* (2020) also found no significant differences in GOHAI (Geriatric Oral Health Assessment Index) scores of 4 studies between participants with AD and controls (standard mean difference: 0.09, 95% CI –0.66 to 0.85) (Ming *et al.*, 2020).

7.4.4 Dental visits

The Guangzhou case-control study observed an OR of 3.60 (1.65-7.83) of not regularly, or never visiting a dentist in participants with dementia compared to those without dementia. A significant association was reported in previous studies (Dolan *et al.*, 1998; Avlund *et al.*, 2001; Silva *et al.*, 2014; Fereshtehnejad *et al.*, 2018). A study by Avlund *et al.* (2004) reported that people with poor cognition were at a five times higher risk of not having regular dentist visits (Avlund *et al.*, 2004). A similar association was reported in a study on nursing home residents

in Australia, where residents with dementia had poor access to professional oral care (Silva *et al.*, 2014).

7.4.5 Brushing of teeth

The Guangzhou case-control study indicated that the participants with dementia brushed less than once a day affected their oral health. Gao *et al.* (2020) have shown a significantly higher level of visible plaque (77%), difficulties in tooth brushing (57%) and in having a dentist visited (64%) in people with dementia than without dementia (Gao *et al.*, 2020). Another study found that inability to perform routine oral care might be an early indication of the decline in cognitive functions (Naorungroj *et al.*, 2013) and strongly influences oral health outcomes (Lopez-Jornet *et al.*, 2021). As the older adults with cognitive impairment progresses to dementia, they are more likely to have poorer oral health and less likely to brush and floss their teeth frequently (Lee *et al.*, 2016). It can be partially explained that individuals with lower cognitive function may not view dental care as a high priority and may have limited self-awareness of dental care needs.

7.4.6 Periodontal disease

The findings from the Guangzhou case-control study showed a significant association of dementia with moderate or severe PD (OR 2.70, 1.04-7.03). This was consistent with the results of a previous study conducted by Aragón *et al.* (2018), which concluded that AD patients had poor oral health (caries and PD) with a greater amount of oral mucosal lesions, and qualitative and quantitative deterioration of the saliva (Aragon *et al.*, 2018). Moreover, Lopez-Jornet *et al.* (2021) reported a significant association of dementia with a higher score of plaque index (OR 1.39, 1.07–1.47) and bleeding on probing (OR 1.26, 1.06–1.15). Similarly, a recently conducted retrospective cohort study reported that RR of PD in dementia patients was significantly higher than in the non-dementia group (OR 1.83, 1.72-1.94) (Ma *et al.*, 2021).

Furthermore, my meta-analysis, including updated literature, in Chapter 2 also supported this association.

7.4.7 Strengths and limitations

The strength of this study is the use of both case-control and cohort studies to examine dementia/severe cognitive impairment associated with poor oral health. The ELSA cohort study, used for analysis in this chapter, is one of the few cohort studies that examine the association of both cognitive impairment and dementia with oral health in a longitudinal study in the world. It is further strengthened by a large sample size and a long follow-up of over 8 years with detailed confounding variables available. This allowed a comprehensive exploration and analysis of the association between dementia/cognitive impairment, and an increased incidence of poor oral health. Furthermore, by using prospective cohort data, the time-based order of exposure-outcome relationship was preserved. Also, the oral health measures used in the ELSA cohort study were multi-dimensional and assessed patient perception with SROH. The dentate and edentulous teeth status tells us about the past accumulation of oral diseases over a patient's lifetime, while the oral impact questions cover overall health and oral habits to evaluate the quality of life. The Guangzhou case-control study enquires about additional oral health measures, different from and complementary to the ELSA study, to evaluate oral health in dementia patients, thus giving a comprehensive analysis of the association between dementia and oral health.

Both the case-control and cohort studies have their limitations. Although the case-control study helps examine the association, it is unable to ascertain the direction of causality. Other limitations of the case-control study can suffer from recall and selection bias. The ELSA cohort study evaluated tooth status, however, the follow-up period for dentate and edentulous was short, only four years at wave 7 (no data at waves 6, 8 and 9), compared to other oral health variables measured. Also, the memory index was used in ELSA to examine the cognitive

function and evaluate cognitive impairment participants who were grouped according to their cognitive function score. However, the questions used in the memory index were derived from three indexes which were similar to the Mini-Mental State Exam (MMSE) (Barret and Burns, 2014), thus giving reliability to the cognitive impairment found in participants. Furthermore, there might be some unmeasured covariates such as interleukin-6 (systemic inflammatory biomarker) in both the case-control and cohort studies, which may lead to confounding bias. In both the studies, the oral health assessed for patients was self-reported and clinical diagnosis was not done, which may cause misclassifications. More studies are required to use the multi-dimensional questionnaires to measure oral health to confirm the prediction of dementia/cognitive impairment to incident oral health.

Most of the existing studies regarding the association of cognitive impairment and dementia with poor oral health and PD are from HICs, while such analyses remained largely absent in LMICs, indicating the need for future prospective cohort studies, especially in LMICs and middle-income countries (MICs).

7.5 Implications and Conclusions

This chapter examined the data derived from the population of two different countries in China and the UK. The Guangzhou case-control study helps us identify that older Chinese participants with dementia were at higher risk of tooth loss, brushing of teeth less than once a day, the lack of routine dental visits, and consequently having a higher risk of severe PD compared to those without dementia. On the other hand, the ELSA cohort study addresses the prediction of severe cognitive impairment /dementia to incident poor SROH, but not significant to be associated with tooth loss and oral impact (OHRQoL). These results indicate variations in LMIC (China) and HIC (UK) studies. Hence the findings from this chapter can have several implications for policymaking, practice and further research to reduce the global burden of oral disease. By

promoting better access to professional dental care and increasing awareness regarding the importance of oral hygiene among dementia patients and carers, the burden of disease can be reduced. This points out the need for a qualitative study to understand and have an in-depth information on the association of dementia/cognitive impairment with oral health.

CHAPTER EIGHT: CAREGIVERS PERCEPTION ON ASSOCIATION BETWEEN ORAL HEALTH AND DEMENTIA: FOCUS GROUP RESEARCH

8.1 Introduction

This chapter outlines the use of the qualitative study method, followed by a description of participants, procedure, and data analysis. Next, findings from the thematic analysis are described, and finally, a discussion is offered.

A recent debate on whether there is a bidirectional relationship between oral health and dementia, given that they share common risk factors; the current literature has shown inconsistent findings regarding this association (Wu *et al.*, 2016; Kapellas Kostas 2019; Liccardo *et al.*, 2020). The existing knowledge from quantitative studies cannot reflect caregivers' experience and perceptions on the association between oral health and dementia. Few qualitative studies have been done to examine oral health in people with dementia. Hence, I carried out qualitative research in Wolverhampton for my PhD study. The findings of this chapter will contribute new knowledge on this topic and offer a deeper insight into the caregiver's perception on the association between oral health and dementia. It will also explore issues related to dementia care and the determining factors that can affect oral health and dementia risk or vice versa using a qualitative design approach. This chapter is aimed to complement the quantitative findings of my doctoral research project.

8.2 Method

8.2.1 Study design

This chapter employed a qualitative approach using focus groups. The rationale for using a focus group and qualitative study design is explained in chapter three (methodology). I conducted three focus groups to explore caregivers' views (including family caregivers) of people with dementia. The three focus groups had different participants but had the same focus group guide (Appendix 4), which was approved by the research ethics committee of the University of Wolverhampton (Appendix 1). The focus groups were used to explore caregivers' perceptions on whether poor oral health causes dementia or, conversely, whether people with dementia have poor oral health. It also inquired about the challenges faced and support provided to people with dementia by caregivers.

8.2.2 Study population

The participants for this study were selected from a population of caregivers residing or working in the Wolverhampton area of the West Midlands, UK, through purposive sampling. Caregivers included both family caregivers and professional caregivers, aged 18 and above, caring for people with dementia. Family caregivers were either providing in-home care or were the primary contact for their family members residing in care homes. Professional caregivers were from care homes in the Wolverhampton area. These caregivers were chosen because they were the primary health care providers responsible for people with dementia in residence or care homes. The intention was for the sample to cover a wide range of caregivers' perceptions along with different ages who have different relationships to the person with dementia which could give accurate information on the association between oral health and dementia. As a person who cares for people with dementia can play a vital role in providing information needed for improving the quality of life and care for those living with dementia. General population was not chosen as they would not been able to provide correct information. Many

of the participants might not have family members with dementia or they might not be primary caregiver of the person with dementia in family homes or care homes. Hence their knowledge on the research topic might be limited. People with dementia were not chosen for the focus group because of safeguarding issues that might arise. Also due to their memory issues they were not the ideal sample for this research project as they might not have been able to recall the required information.

8.2.3 Recruitment Procedure

The participants for the study were recruited from caregivers within the care homes in Wolverhampton through purposive sampling. Participants were approached by contacting the care homes in Wolverhampton, UK. Participants were recruited with the help of care home managers. An initial phone call was made to care homes asking whether they would participate in the focus group study. A face-to-face appointment was then arranged with the interested care home managers to explain the research procedure and what was expected from them. The study information sheet (Appendix 7) and invitation letter (Appendix 3), which included the researcher's contact email address and telephone number, were handed over to the care manager to be forwarded to the interested caregivers. People interested in the study contacted the researcher directly via telephone or email to inquire about the focus group participation. During initial talks, eligibility requirements (see Section 8.2.2) were reviewed, and the study was explained in more detail to potential participants. When they agreed to participate in it, they were told they would need to sign the informed consent form (Appendix 6) before starting the focus group discussion. The participants were informed that the focus group discussion would be held in a safe and private meeting room in Harrison Library, the University of Wolverhampton (UoW).

For the first focus group, nine participants agreed to participate and come to the UoW library (private room arranged), but only six turned up for the focus group discussion. All the participants who came to the first focus group were family caregivers. It took eight months to organise the first focus group meeting due to difficulties in arranging a time accommodating all participants' availability. For this reason, the second and third focus groups were conducted at local care homes in Wolverhampton (Appendix 9) after the care homes granted permission (Appendix 2). The care homes manager would also help recruit the potential participants by finding out when caregivers were not on duty and when all potential participants could be available for focus group discussion. Of 31 people identified for the three focus groups, 25 confirmed their interest in participating, and 17 took part in the focus groups.

8.2.4 Data collection tools and procedure

The data collection was done via the focus group topic guide and short questionnaire (Appendix 4 and 5). Before the focus group study, a very brief questionnaire was used to collect basic socio-demographic background information on the participants (Appendix 5). Focus group topic guide questions were semi-structured open-ended questions (Appendix 4). After developing the questions for the topic guide, it was tested and revised. A pilot focus group of 5 people was conducted initially to determine if the questions (of focus group topic guide) generated discussion and relevant information and ensure that the questions were not leading.

All focus groups ensured that the discussion was held in a quiet and safe room. Each session was facilitated by the researcher (moderator) while a co-moderator assisted with notetaking and arrangements at the venue. The room was arranged with a round table in the centre, comfortable chairs around it in a circle, and name plates of the participants on the desk. Refreshments were provided to make the atmosphere more conformable and friendly. The participants were once again provided with the information sheet and given the opportunity to

ask questions, which were addressed. They were then given a consent form to sign. They were also asked for permission to record the focus group discussion with a digital audio recorder before it began.

The focus group discussions were audio-recorded, and throughout the session, brief field notes were taken. The interviewer's (researcher's) function was to guide the respondents to talk freely about all the topics in the list and tell in their own words their past experiences (Polit and Beck, 2004). The probing questions were done carefully, and the probing questions were standardized for each focus group. The reason for using the probing questions was that the researcher wanted detailed information about the association between oral health and dementia (Oppenheim, 1992). All the focus group discussions were conducted in English. The three focus group sessions were held a month apart (Appendix 9), and each session took between 1 hour and 1.5 hours (73 min, 81 min and 62 min, respectively). Finally, the participants were asked again if they consented to the interview data being used in the study.

8.2.5 Ethical considerations

This research study was approved by the University of Wolverhampton institutional review board prior to commencing the study (see Appendix 1). There were no direct risks for the participants other than being unable to answer a question. If this occurred, the researchers were to support the participants. Before the focus group began, participants were informed that they could only withdraw their data consent within a week of the focus group discussion, that is, until the commencement of the data analysis. In addition, it was made clear that only the researcher and their supervisors would have access to audio recordings and transcripts following the GDPR. This was important for creating a nonthreatening environment for discussion (Krueger and Casey, 2015).

8.3 Data Analysis

The data of the three focus groups were analysed using Braun and Clarke thematic analysis approach (Braun and Clarke, 2006). Thematic analysis is a method for identifying, analysing, and reporting patterns within data, providing a flexible tool that can assist in the generation of a detailed account of data without requiring a theoretical framework to guide analysis (Braun and Clarke, 2006). It has been a widely used approach to find trends about people’s perceptions, views, opinions, knowledge, experiences or values from a qualitative data set (King, 2004, Braun and Clarke, 2006). Thematic analyses also highlight differences and similarities in the participants’ views on a topic and uncover unexpected insights produced from the study (Nowell *et al.*, 2017; Braun and Clarke, 2006). A series of six different phases have been outlined by Braun and Clarke (2006), as a qualitative analysis guideline to support the thematic analyses process (Table 8.1). The following section discusses how they have been adopted for this study.

Table 8.1: Braun and Clark (2006) six phases of thematic analysis (Braun and Clarke, 2006)

Phases of analyses	Description
1. Familiarization with dataset	Involves repeated reading of data in active way looking for meaning and patterns and making notes of ideas. Check the transcripts back against the original audio recordings for accuracy.
2. Generating Initial codes	Involves systematically coding the entire data set. Data is formed into meaningful groups, which are then organized into themes. The researcher considers if themes are to be analysed in an indicative (data-driven manner) or a theoretically oriented manner (analyst -drive, motivated by researchers’ interest). Thematic maps can be used to depict the relationship between codes and themes.

3. Searching for themes	Re-focuses on the analysis at the broader level of themes, rather than codes, involves sorting the different codes into potential themes, and collating all the relevant coded data extracts within the identified themes.
4. Reviewing themes	Reviewing the coded extracts by re-reading and considering if they appear in a coherent pattern. Also, it involves similar process which considers the validity of the themes in relation to the data set.
5. Defining and naming themes	Themes are further refined and defined. Generating clear definitions and name for each theme
6. Writing report	Begins when you have a set of fully worked-out themes and involves the final analysis. Vivid, compelling extract are selected as examples to showcase interpretation of data. Analysis of data relates back to research hypotheses and relevant literature. Producing a scholarly report.

8.3.1 Familiarization with focus group data

The collected data from the focus group were converted into verbatim transcription and kept anonymous. Original audio recordings were checked against transcripts for accuracy. After accurately transcribing the sessions, it was read and re-read through the text many times, initial notes were made, and I kept looking through the data to get familiar with them.

8.3.2 Initial codes

This phase generated initial codes to identify important data features that were relevant to answer the research question. According to Boyatzis (1998), codes are “the most basic segment, or element, of the raw data or information that can be assessed in a meaningful way regarding the phenomenon” (Boyatzis, 1998). In this phase, the first digital transcripts (word

document) were imported into NVivo software. I reread digital transcripts, and NVivo was used as a management tool to code more significant patterns. Although the focus group guide was used to ask specific questions in all focus group discussions, data-driven theme coding was done in the entire dataset during this phase, instead of coding around only the key questions. As many codes as possible were generated, and the coding included surrounding extracts of data to avoid the context of each code being lost. This process allowed the generation of more potential themes from the dataset (Braun and Clarke, 2006).

8.3.3 Looking for themes

A total of 135 codes were generated for all the data across the entire dataset. In this phase, codes were examined and collated, using NVivo as a management tool, identified significant broader patterns of meaning (potential themes). This was done for all recurrent themes; similar codes were collapsed, and then codes were grouped to make subthemes and later categorised into major themes. These codes were cross-referenced across the three-focus group, which resulted in a re-classification of 135 codes within 22 broader categories (subthemes). The codes were coloured according to the subthemes to help visual presentation. Thematic maps were used to help show the relationships between different codes, subthemes and potential major themes. At this stage, I had some codes that did not seem to belong anywhere, so I put them under a theme called “miscellaneous”.

8.3.4 Reviewing themes

In this phase, themes were refined. Some themes appeared to be finalized in the previous stage, while some had to be reviewed again and split, combined, or discarded, leaving a refined total of 10 subthemes from the initial 22. Data were rechecked for each theme, starting from the collated extracts and coded data for each theme. Some codes of subthemes were recoded again to make sure that they formed a coherent pattern. It was carefully examined whether themes

accurately reflected the data set as a “whole” when making overall themes. This process was repeated until I was satisfied with the themes.

8.3.6 Writing up

The final phase involved writing a report using relevant or direct data extracts to illustrate the emerging themes, support the findings of the report and contextualise the analysis with existing literature (Braun and Clarke, 2006). The details of this report are presented in the subsequent sections. Themes and subthemes generated from the data were then presented using this framework, which included the identification of any relevant interrelationships between dementia and oral health.

8.3.5 Defining and naming themes

The completed thematic map was carefully viewed after defining and refining the themes. I was able to identify the “essence” of each theme and what aspects of the data it captured. Each theme name would give the reader sense of what the themes are about. In doing so, I did not lose the original story of the data but only made it more credible by revisiting the dataset. Themes were also internally coherent, consistent, and distinctive. The themes were checked against each other and against the original data set to ensure that themes fit together with subthemes and code data extracts. As a whole, subthemes were refined from 10 to 7 and finally 3 major themes emerged.

8.4 Results

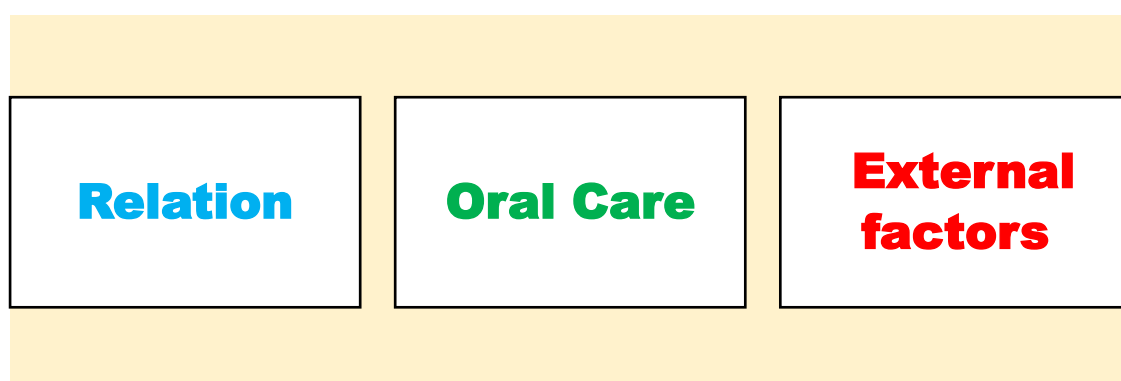
A total of 17 participants took part in the three focus group discussions, of whom five were men and twelve were women. The sample was diverse, with most of the participants being professional caregivers (eleven) (64.71%) and the rest family caregivers (six) (35.29%). Further details are given in Table 8.2, showing the participants' demographic characteristics.

Table 8.2: Demographic Characteristics of Participants for the Focus Group Study

Demographic characteristics	N =17 (%)
Age	
18-30 years	7 (41.18)
31-40 years	6 (35.29)
41-50 years	2 (11.76)
>51 years	2 (11.76)
Sex	
Male	5 (29.41)
Female	12 (70.59)
Education	
None	2 (11.76)
Primary	0
Secondary	6 (35.29)
Graduate	7 (41.18)
Other	2 (11.76)
Caregiver	
Family caregivers	6 (35.29)
Professional caregiver	11 (64.71)
Do you know anyone with dementia?	
Yes	17 (100)
No	
If yes, what is your relationship with them?	
Friend	1 (5.88)
Family	5 (29.41)
through work	11 (64.71)
others	0
Duration of caregiving to person with dementia	
1-2 Years	6 (35.29)
2-5 Years	3 (17.65)
5-10 Years	3 (17.65)
>10 Years	5 (29.41)
Smoking status	
Active	4 (23.53)
Passive	8 (47.06)
Both	5 (29.41)
Don't wish to disclose	0

The thematic analysis of the three focus groups discussion revealed three themes in caregivers' perception of an association between oral health and dementia. These include the themes relation, care and external factors (Figure 8.1). The first theme portrayed the caregiver's perception of the association between oral health and dementia (blue colour). The second theme suggested the caregivers' experiences on barriers and support regarding oral care of people with dementia (green colour). The third theme suggested that external factors influenced dementia and oral health association (red colour). Each of these themes is presented in detail below.

Figure 8.1 shows the three themes in the study of the caregiver's perception of association between oral health and dementia in people with dementia.



8.4.1 Theme 1: Relation

A major theme that emerged from the three focus group discussions is the theme “relation”. In the context of the study, the theme “relation” explores the participants' perception of the association between oral health and dementia. In the focus group discussion, participants had mixed perceptions which led the theme to be subdivided into two subthemes, “dementia influence on oral health” and “oral health influence on dementia”, which describes how they believe oral health influences dementia or vice versa. Figure 8.2 is given below.

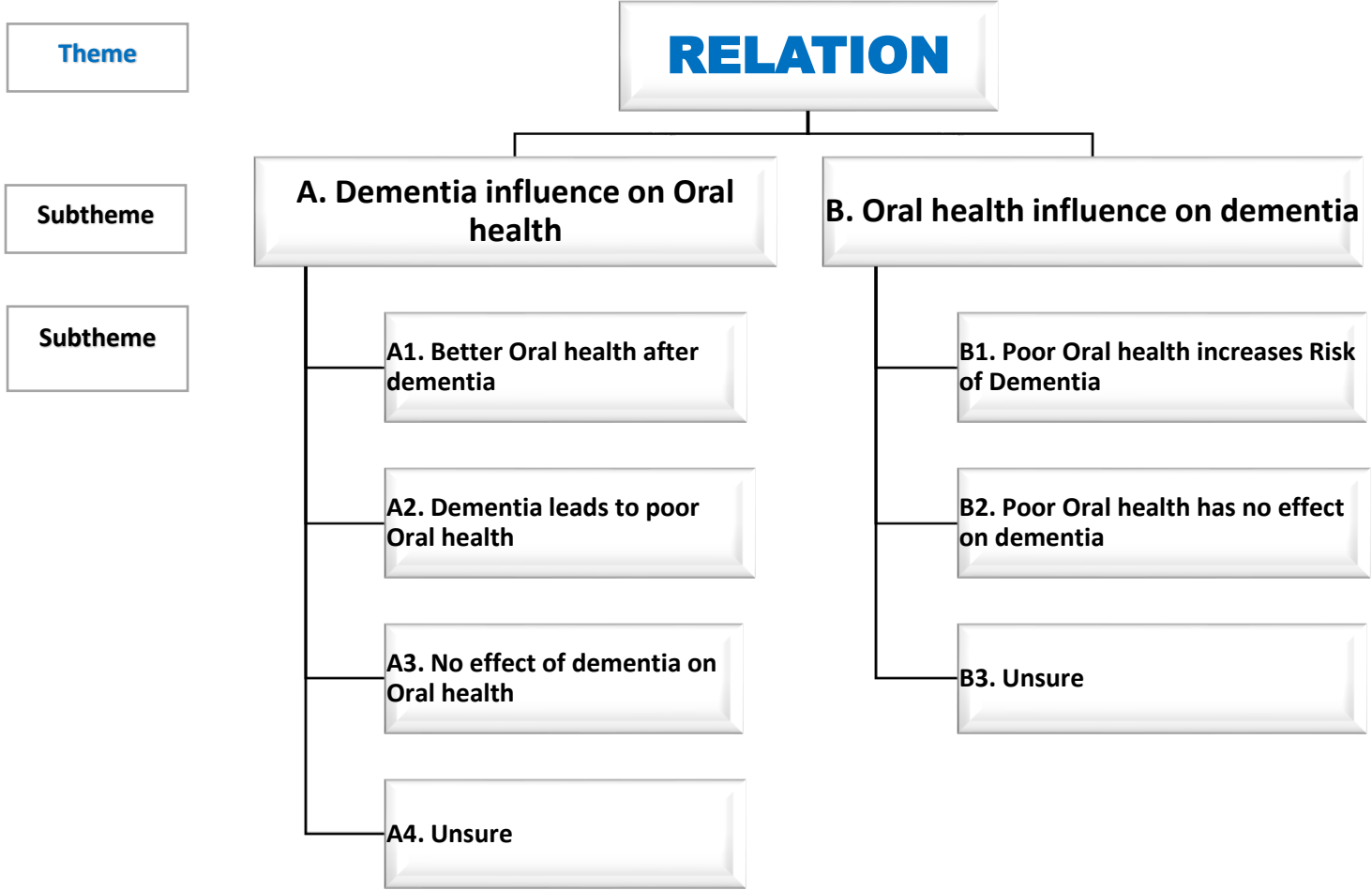


Figure 8.2: Thematic map showing subthemes emerging from theme Relation

8.4.1.1 Subtheme A: Dementia influence on oral health

The “subtheme A” revealed that dementia influences oral health, which was derived from four other subthemes: “better oral health after dementia”, “dementia leads to poor oral health”, “no effect of dementia on oral health” and “unsure” as represented by Figure 8.2. Participants comprehensively discussed their views on how the oral health status of people with dementia changed after being diagnosed with dementia, which is further discussed in subthemes below.

8.4.1.1.1 Subtheme A1: Better oral health after dementia

Some participants believed that oral health would be better in people with dementia as caregivers would be helping them in their oral care. One of the participants said:

“The positive effects could come in too, because the carers will be doing it for them where they're getting more support”. (P2, FG3)

A similar view was given by another participant who said:

“If I've never brushed my teeth in my life, but then I get Dementia and then the caregivers brushing my teeth, hasn't the oral care then got better rather than negative?”. (P1, FG3)

Within this study, it was considered that people with dementia would be looked after by caregivers who will help them brush their teeth, clean their dentures and with other oral hygiene procedures punctually every day.

8.4.1.1.2 Subtheme A2: Dementia leads to poor oral health

Most participants believed that oral health would get worse in people with dementia. They have experienced some difficulties in managing oral care. However, despite acknowledging the importance of oral health, caregivers felt that when people get dementia, they will usually have poor oral health. One of the participants commented:

“I think, I mean of course, when you've got the dementia then that impact the oral hygiene”. (P2, FG2)

Another participant commented:

*“I think it also depends on, you know, how much that progression that dementia had”.
(P3, FG1)*

Throughout the analysis, the evidence suggested that some caregivers believed that people with dementia would have poor oral health. As dementia progresses, people with dementia lose their ability to maintain oral care, deteriorating their oral hygiene.

8.4.1.1.3 Subtheme A3: No effect of dementia on oral health

Some participants believed that there was no association between dementia and oral health.

One of the participants explained this as:

“Couple of the residents on the top floor they got dementia, but they've still got good oral health”. (P1, FG2)

Another participant stated:

*“How often do we see people who have very good oral hygiene and they're still having dementia and people with really bad oral hygiene; we see them without dementia”.
(P5, FG3)*

The opinions evidenced within this “subtheme A3” suggested that dementia has no role in good/poor oral health. Participants felt that dementia is related to other risk factors as they have experienced previously in care homes.

8.4.1.1.4 Subtheme A4: Unsure

A few participants were not sure about whether dementia plays a role in the poor oral health of people with dementia or not. One of the participants commented:

"I don't know. I don't really know a lot about how Dementia affects... like, how it starts or what from?". (P5, FG3)

A few participants argued that dementia influences oral health but felt that they could not be sure that it is the only cause or influence for poor oral health.

"I don't think it's what I'd say causes poor oral health, cause it- it's always multi-factorial, but I think it does have an impact on it". (P3, FG3)

From the above expressions, it is clear that a few participants felt that there was a weak association between dementia and oral health but were not sure whether it was a positive or negative relationship, as they believed dementia is related to many underlying diseases.

8.4.1.2 Subtheme B: Oral health influence on dementia

The context of subtheme B, "oral health influence on dementia", is whether poor oral health increases the risk of dementia or not. It was derived from three subthemes "increased risk of dementia", "no effect on dementia" and "unsure", as represented in Figure 8.2 above.

8.4.1.2.1 Sub- subtheme B1: Poor oral health increases the risk of dementia

From caregivers' perspectives, most of them acknowledged that poor oral health is a risk factor for dementia. One participant commented:

"So, if we're talking about two people, one has poor oral health, one has good oral health, the poorer oral health one has higher chance of developing dementia than the good oral health". (P1, FG1)

Another participant had a similar view:

"I think poor oral health's going to cause Dementia". (P4, FG3)

From these comments, I realised that many participants felt that people with poor oral health would have a higher risk of dementia, as they believed poor oral affects general health.

8.4.1.2.2 Subtheme B2: Poor Oral health has no effect on dementia

Some of the participants believed that poor oral health impacts other non-communicable diseases such as cardiovascular diseases rather than influencing/causing dementia.

“I know the studies where it's linked to, um, like heart disease and things, but I've never, I've never read any research where poor oral hygiene will have an impact or influence somebody to get dementia”. (P2, FG2)

In focus group analyses, the data provided evidence from a few participants that poor oral health does not have any association with dementia. One of the participants commented:

“I don't think in the oral hygiene will have an impact on the dementia. If someone's got dementia, they have an impact on their oral hygiene well not the other way around”. (P4, FG1)

While the findings also showed that some participants believed dementia leads to poor oral health, they firmly believed that poor oral health has no role in the risk of dementia, as they had not read any research about it.

8.4.1.2.3 Sub- subtheme B3: Unsure

Not all participants had a clear opinion; some were unsure whether poor oral health can influence/cause dementia. One participant indicated this as follows:

“I'm not sure... I don't know about whether poor oral health can lead to dementia”. (P2, FG1)

One of the participants thought that brain-cell activity might be increased by tooth brushing. However, aside from this view, he was unsure if there is any relation between the two.

“Well, I feel like oral health can stimulate the brain. Like, for example, waking up every morning, brushing your teeth, that stimulates the brain a bit better, because obviously

you're waking up remembering that. But, in regard to Dementia, I feel like that's the only way I can see how it relates to it". (P1, FG3)

These expressions indicate that in view of some of the participants there was a lack of evidence, so they were unsure how to explain that poor oral health could affect dementia.

8.4.2 Theme 2: Care

Another theme that emerged from the three focus group discussions was “care”. “Care” highlights the caregivers’ perceptions on the barriers faced in providing oral care to people with dementia and on the support provided to overcome oral care problems. The “care” theme emerged from the two subthemes, “barriers to oral health” and “support provided for oral care”. These are represented in Figure 8.3 below.

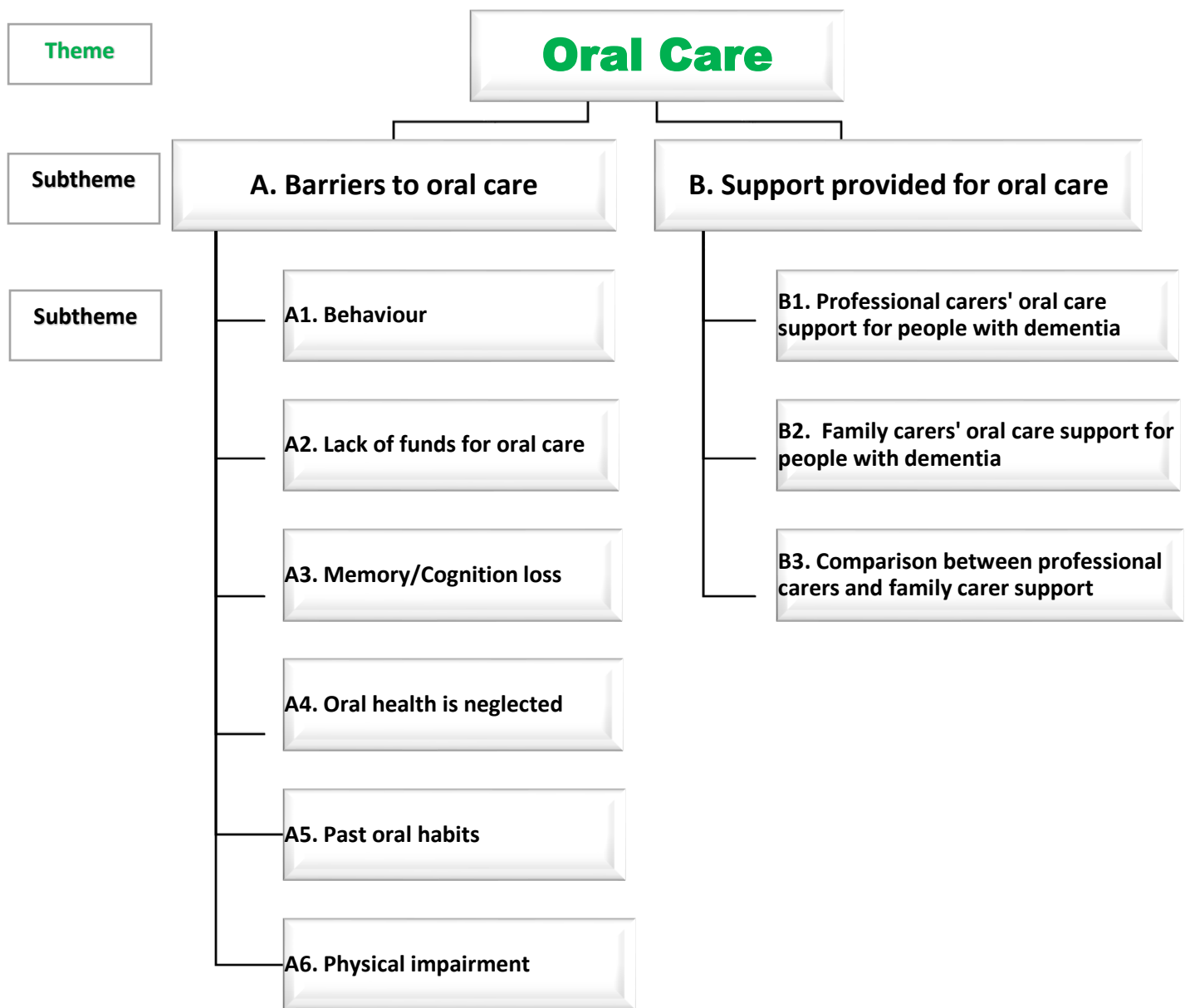


Figure 8.3: Thematic map showing the subthemes emerging from theme Care

8.4.2.1 Subtheme A: Barriers to oral care

Subtheme A “barriers to oral care” emerged from six subthemes: “due to behaviour of people with dementia”, “due to lack of funds for oral care”, “due to memory/cognition loss”, “due to neglected oral health”, “due to personal characteristic differences” and “due to physical impairment”.

8.4.2.1.1 Subtheme A1: Due to the behaviour of people with dementia

The majority of participants acknowledged behavioural issues in people with dementia as one of the main challenges in providing oral care. A few participants shared their views that people with dementia were uncooperative and aggressive. One of the participants commented:

“If they're very aggressive and stuff like that, it, it becomes a challenge. If they're declining their oral care, then they will not look after it. And then it becomes more challenging”. (P1, FG1)

Most participants reported that people with dementia clearly expressed their wish to remain independent and in control for as long as possible; thus, they want to make decisions about their care. Participants highlighted that all oral health care is carried out with the implicit permission of the people with dementia. One of the participants commented:

“We've got a lady, or we go into every morning give her the toothbrush with the toothpaste on and she says, no and we have to respect her wishes”. (P1, FG2)

One of the participants said:

“Sometimes it can be challenging because obviously, if you want to give them the best care by giving them the oral care and everything else, and they don't want to do it”. (P4, FG3)

Another participant believed that people with dementia do not want to see a dentist due to denture trials and are uncooperative.

“It’s stress of seeing the dentist sometimes. If they have denture, they don’t understand the process if somebody go in put something in the mouth to bite down it does not happen”. (P2, FG2)

Throughout the discussion, the behaviour was seen as a significant hindrance for caregivers. They felt that some residents became uncooperative, aggressive and did not consent to be appropriately managed, and, consequently, oral hygiene measures were neglected. Caregivers further explained that not enough information is provided to people with dementia about oral care procedures, making them feel stressed, anxious, and afraid of dental procedures.

8.4.2.1.2 Sub- subtheme A2: Due to lack of funds for oral care

The families' financial circumstances may influence the decision whether dental care is used or not, particularly if private payment is required. Participants further emphasized that the cost of dental treatment was a significant barrier to the families of residents:

“It’s just that not everybody could afford it basically”. (P1, FG1)

Participants expressed that the oral care level is different among residents due to differences in the support provided by family members in providing daily care items and oral care products needed for oral hygiene. Two participants stated:

“The families do provide them things. Like you do go into certain people's bathrooms, and they'll have like, I don't know, one kind of spray. Some have like fifteen”. (P3, FG2)

“Some people haven't got families to bring stuff in. So, I think then that goes on a budget”. (P5, FG2)

Some caregivers felt that, sometimes, families do not follow the recommendation given by care homes, and they felt powerless as money was spent on things that were not urgent, which made oral care more difficult. One of the participants commented:

“By recommendations? Obviously if they've got a power of attorney, the resident, you can say that I need this, and they should be spending money on it but there's nothing really we can do to make the families again they go and spend on the couch. I was just on, we can see we can recommend and ask, we need toothbrushes and toothpastes. Can you bring them in for us?”. (P4, FG2)

The analysis shows that some participants expressed that accessing existing funds through next of kin was an issue hindering care plans.

“Yeah, and the family might not live in the same country. They might have children who live abroad, who live very far away and can't visit regularly. They might visit on occasions like Christmas, Easter but they might not be here regularly to bring them stuff in here”. (P3, FG3)

Cost was a recurrent theme throughout the focus group discussions relating to the oral care of people with dementia. Caregivers considered that there were significant disparities in access to care between those who can fund the care themselves and those who seek funds from their families. From the caregivers' perspective, dental care is expensive, and many family members try to avoid it, which is not necessarily the family members fault, as they have limited budgets.

8.4.2.1.3 Subtheme A3: Memory/Cognition loss

The analysis reflected that dementia affects one's cognitive ability to make good decisions, which is an essential factor in oral health.

“If you have Dementia. You have um, certain qualities where, for example, you might forget stuff, and you may not... the capability you had before the Dementia... there's a lack of capability you know, to take care of yourself.” (P1, FG3)

Caregivers face many obstacles as dementia advances. They need to tailor the care as people with dementia begin to show memory loss. One of the caregivers expressed this severity of dementia as:

“Some of them still believe they've got teeth in there when they don't got teeth”. (P1, FG3)

From a caregiver's perspective, the subtheme “memory/cognition loss” was considered an important barrier in providing oral care.

8.4.2.1.4 Subtheme A4: Oral health is neglected

Most participants were aware of the need to help the residents to clean their teeth when providing personal care. Still, they also acknowledged that oral hygiene is often neglected because of other demands related to their general health. One of the participants commented:

“I think as well when people are getting older and they've got, other health conditions, sometimes their teeth is quite low priority compared to other things”. (P2, FG2)

Another participant said:

“If they get, ever get admitted to hospital, for any reason that they're unwell, people focus more on their physical health, rather than their oral health, so that gets even more neglected”. (P3, FG3)

In the focus group discussions, caregivers were aware that oral health is not a priority compared to general health because they don't have enough time and see other health care practices as more urgent.

8.4.2.1.5 Subtheme A5: Past oral habits

During the focus group discussion, the participants considered past oral habits of people with dementia as an important factor influencing whether or not they want to take care of their oral health. One of the participants said:

"And it might be more challenging for somebody who's never really been in the habit of brushing their teeth, but then make them get into that habit. They'll be like, "What are you doing?" because they've never done it". (P5, FG3)

Some participants believed that oral habits have an important link with dementia and oral health. One of the participants specified this as:

"Some people like take priority in their teeth and you know they want good oral hygiene and they go to the dentist every year, whenever or if they've got a problem, they go to the dentist, they may wash, the floss, whatever. Some people might have never done that." (P2, FG2)

In this focus group, the subtheme "past oral habits" suggests that earlier oral habits, before the diagnosis of dementia, can be a barrier for caregivers in giving regular oral care.

8.4.2.1.6 Subtheme A6: Physical impairment

Participants considered physical impairment as a crucial factor as it can affect a person's ability to hold and use cutlery and handle other objects such as a toothbrush.

“I definitely agree as in like, um, I think we could've touched on it earlier, how because of the anatomy impairments, they're not going to be able to kind of carry out the actual physical action of, um, brushing their teeth”. (P3, FG2)

People who require assistance with eating are at high risk of poor nutrition. Health status limits a person's ability to perform adequate oral care for maintaining a healthy mouth. Some participants believed that when taking care of people with dementia, they sometimes emphasize mobility and nutrition issues rather than oral health.

“Isn't that that oral health, yes, is always neglected, but once they have dementia, it's people start focusing on different things even if they're fall unwell, or even if they're not evaluated, they're being looked after in a care home. We focus more about their nutrition, and their mobility, because their mobility declines”. (P1, FG1)

Reliance on carers and their motivation, knowledge, skills or training necessary to carry out oral care (especially if an individual shows a challenging behaviour) is essential to prevent adverse oral hygiene impacts.

8.4.2.2 Subtheme B: Support provided for oral care

Subtheme B, “support provided for oral care”, was mentioned to some extent by almost all participating carers. Carers made frequent references to how they provided support to people with dementia in different situations. Subtheme B “support provided for oral care” emerged from three subthemes: “professional carers oral care support for people with dementia”, “family carers oral care support for people with dementia” and “comparison between family carers and professional carers support provided”. These subthemes are explained below.

8.4.2.2.1 Subtheme B1: Professional carers' oral care support

The analysis reflected that participants thought cooperating with families can enhance the condition of the person with dementia by sharing information about available services and financial support. One of the carers said:

“Well, we'll tell them the risk, we trying to encourage. And obviously that's part of what the care comprises then, isn't it? So, when you meet with families and stuff, you'll explain this is the risks of the, obviously they're not brushing the teeth.” (P2, FG2)

Most participants believed that they provided good oral care by doing risk assessments. One of the participants commented:

“Well, we do risk assessments within ours, we do oral hygiene risk assessments, don't we and it asks you questions on there that whether the medication, they are on causes them dry mouth and then that's how you have the high risk of needing to refer to a dentist or not. So, we call them on that, but we can only go so far and then have to pass it onto the family”. (P2, FG2)

One of the participants believed that social support from the community is crucial for dementia caregiving.

“In some patients, uh, oral health might actually improve after the diagnosis. Like you pointed out, that they have, receive more support from the, uh, community or the, uh, hospital.” (P2, FG1)

The majority of the participants mentioned that they aimed at establishing a personal relationship with the person with dementia by encouraging them to take care of their oral health.

A participant commented:

“Do you know the behavior you get to know your residents? And obviously we have mental capacity in place, so if they lack the capacity, you've act in their best interest so you can act in their best interest and go prompt them to brush the teeth and do that. But if they've refused you take that refusal”. (P2, FG2)

It was acknowledged during the discussion that caregivers support by continuing to send people with dementia to their dentist when they need it. One of the participants commented:

“People who are in our care we usually establish whether they got here own dentist which they attend which we continue to support”. (P1, FG3)

The findings of the emergent subtheme “Professional carers oral care support for people with dementia” reveals the support provided by caregivers. At an individual level, caregivers support with encouragement, perform oral care procedures, and inspire the residents to go to the dentist regularly. Moreover, they felt that they kept in touch and informed family members about the patient's needs, and recommended the essential care needed.

8.4.2.2.2 Subtheme B2: Family carers' influence on oral care support

The caregivers comprehensively discussed the influence of family carers on formal care, who felt that the role of family carers has some positive aspects. Participants highlighted that the family members of people with dementia in care homes were key in implementing oral health guidelines, as they were often required to consent to and help arrange dental care for the residents. Two of the participants expressed:

“In my personal opinion, from what I did see is that understanding and cooperative family members can help a lot in looking after patients with dementia”. (P1, FG1)

“Families might prioritize, you know, brushing their teeth”. (P6, FG1)

Another participant had a different view which he expressed as:

“Family support is good, but I feel like family's only, family support is only good within a professional setting”. (P1, FG3)

Participants reported that the level of care quality that people with dementia were receiving is also an important aspect. One of the participants commented:

“It's very individual. It depends upon the family, the family and the kind of, uh, support, uh, a person is getting from the, uh, carers”. (P3, FG2)

Throughout the data analysis, there was an overwhelming sense from the caregivers that family members and carers play a significant role in providing care to their loved ones.

8.4.2.2.3 Subtheme B3: Comparison between professional carers and family carers support

The caregivers discussed the comparison between support provided by professional carers and by family carers. One of the participants believed that family members could provide more care than professional carers.

“If the patient lives with a family, ah, it, that's supported by so many people in the family living in same house, you're more likely, you know, to be given... um, better care compared to when you lived by yourself, have only for ah, um, four times a day personal care”. (P2, FG1)

Participants believed that people with dementia are more comfortable in the presence of their loved ones compared to professional caregivers, and one participant expressed:

“And then suddenly somebody like mother or like daughter or a wife walks in and they're completely different and they'll be so calm and so relaxed”. (P1, FG1)

Another participant believed that more personalized care can be provided at home. Family carers can personalize the routine according to the habits of the person with dementia compared

to care homes, where they set a time to eat and sleep, which may not suit every person with dementia.

“Like with some of these with Dementia, they would not... they would get the same. I don't want to shower. I don't want that. Yeah, you've got enough time to sit there than keep going a push a meal. You don't with the caregivers in a care home.” (P1, FG3)

But another participant argued that in care homes, better care could be provided than at the resident's own home.

“Whereas if it's not in a professional setting, the consistency is not kept up”. (P3, FG3)

On the other hand, a participant believed that similar care could be given in care homes as well because of different facilities present at the care home and expressed it as:

“Well, what can the family do different to what the care staff can't do? There's nothing like the family can't”. (P3, FG2)

Our focus group analyses suggested that most professional caregivers believed they provided better care as they are more trained and responsible and provide better self-care to people with dementia. On the other hand, some caregivers felt the family caregivers were more compassionate, had a better understanding of their loved ones' behaviours and were more flexible when providing care. Moreover, participants also felt that the best situation was having both professional and family support as this was best for people with dementia.

8.4.3 Theme 3: External Factors

The third main theme that emerged from the focus groups was “external factors”. External factors highlight the phase of analysis which explores the participants' views about the caregivers' perceptions of factors affecting oral health and dementia. This main theme was drawn from three subthemes: (A) environmental and socio-cultural factors, (B) lifestyle factors

and (C) other multiple factors. These are represented in Figure 8.4 below.

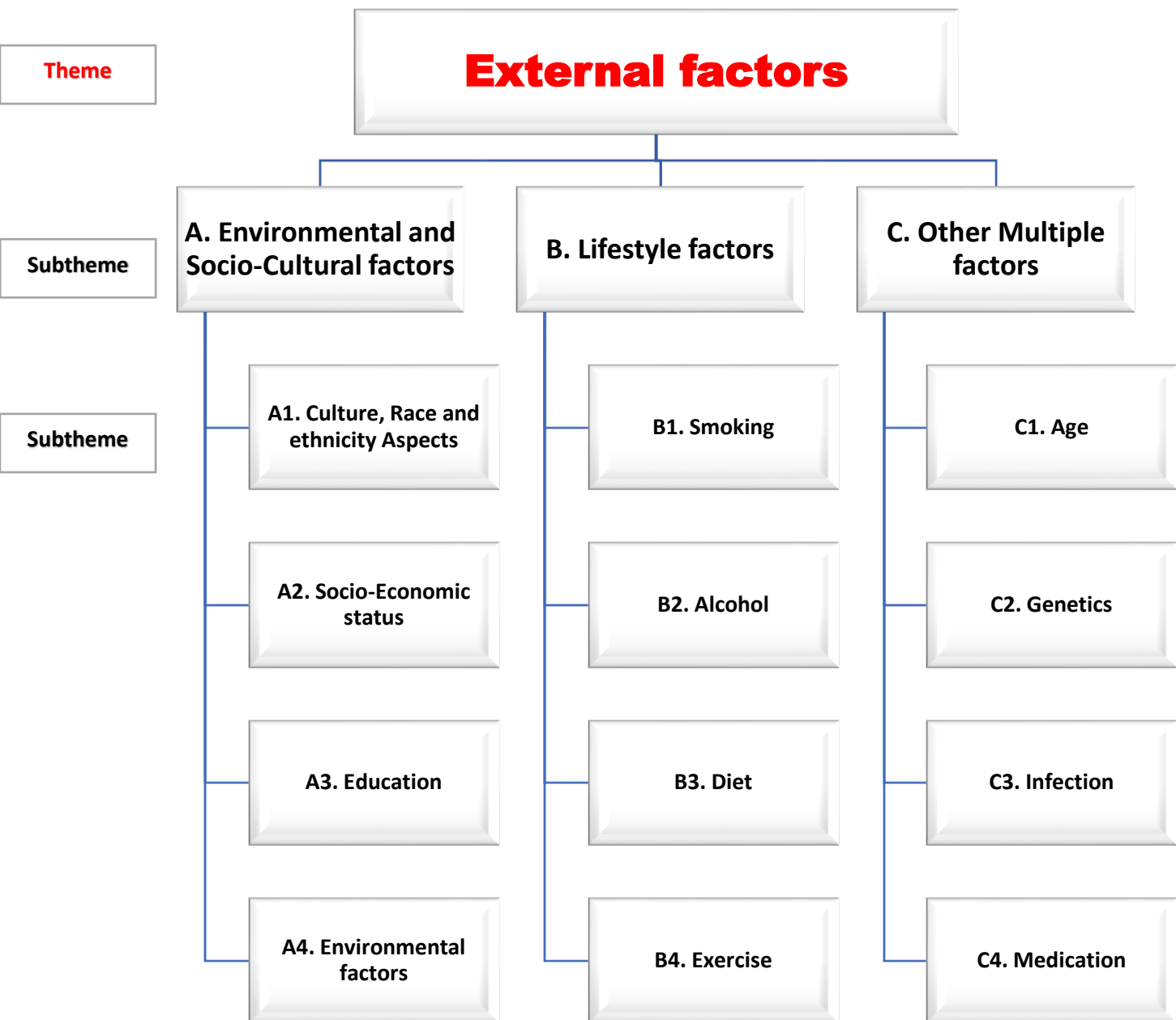


Figure 8.4: Thematic map showing the subthemes emerging from theme External factors

8.4.3.1 Subtheme A: Socio-Cultural and Environmental factors

Subtheme A “Socio-cultural and environmental factors” goes under the theme “External factors”. Subtheme A emerged from the other four subthemes: “culture, race and ethnicity aspects”, “socio-economic status”, “education”, and “environmental factors”. These four subthemes, which can be common risk factors between oral health and dementia, are described as follows.

8.4.3.1.1 Subtheme A1: Culture, race and ethnicity aspects

In discussing the association of culture and ethnicity with dementia risk and poor oral health, the majority of the participants believed that culture does play a role in poor oral health and dementia risk. One of the participants commented:

“Cultural influences on oral health and dementia”. (P2, FG1)

In contrast, some participants had a different opinion that culture may not be related to dementia. A participant commented:

“I think culture could influence oral health, but on dementia really don't know”. (P3, FG2)

Few participants were unsure whether there is any relation between ethnicity and dementia/oral health. One of them stated:

“I think, I don't know if, uh, so obviously there's ethnic correlations with dementia”. (P6, FG1)

It was also suggested that people of a different race might have stronger teeth.

“Like, people from the African background, the teeth are naturally stronger”. (P1, FG3)

In some cases, a few participants described how religious observance might improve oral health.

“I would give a personal example, like we're Muslims. And we pray at five every day. So, we brush and clean up outside five times a day. So, I don't think anybody else would be doing that”. (P1, FG1)

Another participant had a different opinion regarding the role of religion and described it as:

“I don't think it will have an effect because I think regardless of your culture or religion, you're either going to brush your teeth or you're not”. (P2, FG3)

Many participants in the focus group believed that whether culture influences dementia and oral health depends on how the residents perceive and value their cultural values. Some believed that culture and ethnicity do not affect oral health and dementia, while a few participants supported that it could influence. A unique point that came up in the discussion was religion, as many cultural values are related to religion, but participants had different opinions about this.

8.4.3.1.2 Subtheme A2: Socio-Economic Status

A majority of the participants had the opinion that socio-economic status (SES) is an important factor in causing both poor oral health and dementia. Some participants mentioned that living in a better socio-economic area may influence oral health. One of the participants commented:

“I like, more affluent area, generally are better”. (P3, FG2)

Another participant had a different opinion and expressed it as:

“It's down to the individual and I don't think it's got anything to do where you live. If you want to look after your teeth, you look after your teeth. If you don't, you don't, simple. Everybody has a choice”. (P6, FG2)

In the focus group, it was discussed that SES could be a risk factor for dementia. One participant stated:

“Uh, they said that people with socioeconomic conditions because they don't have good diet. They, uh, they have, they can more absolutely have high risk of getting vascular dementia.” (P1, FG1)

Some participants believed that SES is a risk factor for poor oral health, but it does not increase the risk of dementia. Two participants explained:

“Socioeconomic does affect oral health but not dementia”. (P5, FG3)

“Yes, for oral health. Like for example if you can afford, like something, like people on the street, they can't afford toothpaste, they're going to have bad oral health, but I don't think it has anything to do with Dementia. Where you come from. But oral health, if you can't afford it, you can't afford to maintain it, you're going to have bad oral health. So, if can't maintain oral health you are going to have bad oral health”. (P1, FG3)

Both, these focus group analyses and previous literature, have highlighted that dementia and oral health have multiple common risk factors that are interlinked, including SES, which is an important factor for both oral health and dementia, as participants concluded.

8.4.3.1.3 Subtheme A3: Education

The analysis of the focus group discussions found only two participants mentioning education as an important risk factor inversely related to poor oral health. Two participants held contrary views, reported as follows:

“Like a lower socioeconomic status, like, you're more likely to develop dementia. But also, you're more likely to have poor oral health. You're more likely to be smoking, or you just didn't have that kind of education on oral hygiene.” (P4, FG1)

"I don't think so. I think it depends on the individual whether they want to do oral health or not". (P6, FG2)

These opposite opinions indicate a possibility that education may be related to SES leading to dementia and poor oral health.

8.4.3.1.4 Subtheme A4: Environmental factors

Environmental factors were perceived by some participants as an essential factor that has a link with both oral health and dementia. One of the participants commented:

"It depends on where you live because it's if I lived in a forest somewhere, um, then obviously I was going to have clean air and compare to this. I don't think necessarily just smoking or passive smoking cause as they are loads of factors, I know down in Cornwall I, um, bricks and tyre abuse which is known to be more radioactive or something. So, if you lived there for long period, there other things like the cancer. So, it's all just again, environmental factor". (P5, FG2)

Another participant stated:

"Yes. Say, if I was a smoker, well I am... but like if I was pregnant and had a baby, that baby's going to be around smoke it's whole life. That baby would have more chance of Dementia than say a baby who's grown up in a healthy home with no smoke around it". (P3, FG3)

The subtheme "environmental factors" emerged as a less frequent subtheme. A few participants mentioned dementia is multifactorial and that the surroundings of a person play a role in increasing dementia risk.

8.4.3.2 Subtheme B: Lifestyle factors

Subtheme B “lifestyle factors comes under the theme 'external factors’’. This subtheme emerged from four subthemes: “diet”, “smoking”, “alcohol”, and “exercise’’, suggesting that oral health and dementia are linked to lifestyle factors described below.

8.4.3.2.1 Subtheme B1: Smoking

The analyses reflected that some of the participants highlighted smoking as a significant risk factor in causing dementia and having poor oral health. In addition, a few of the participants commented on *active smoking*:

“See, smoking causes heart attacks because smoking causes respiratory problems, and what, smoking affects everything. And all these things eventually lead to dementia. They like direct effect on like the brain”. (P1, FG1)

“And smoking because smoking can cut off circulation everywhere so if I'm cutting circulation off to my brain”. (P5, FG2)

Another participant responded that there was *no effect* of smoking on dementia:

“I don't think smokes got anything to do, I mean a lot my family I say I stayed at my family home, a lot of my uncles, grandparents, they all smoke and no one got dementia, I haven't heard anyone in my family whose got dementia they all smoke”. (P4, FG2)

One of the participants believed that occasional smoking might have *protective effects* and decrease the risk of dementia.

“I've just thought of is, kind of, if you talk about oral health metrics, smoking, and is actually, this weird links with smoking and dementia in that, social smokers who don't smoke a lot for a small part of their life are actually lower risk of dementia”. (P6, FG1)

Another participant commented:

"I think that's going to have a direct effect on your oral health, but that the overall health isn't going to have a direct effect on whether or not you're going to have Dementia". (P2, FG3)

From the analysis of the focus groups, it was found that participants also believed that *passive smoking* (second-hand smoke) has some role in dementia risk and poor oral health. One of the participants stated:

"I don't agree that passive smoking has a protective effect on dementia. I still would say passive smoking it's, it's bad." (P1, FG1)

The participants in the study also felt that exposure to passive smoking in limited amounts could result in a protective effect on dementia. For example, one of the participants expressed:

"I mean, if smoking has some kind of protective effect, then passive smoking might also have a protective effect." (P6, FG1)

Another participant believed that passive smoking could lead to poor oral health.

"I think smoking anyways poisons. Whether it's active or passive. And it would lead to poor effects, whether it's dementia, oral health". (P5, FG1)

The focus group discussion showed that most caregivers felt that smoking could increase the risk of dementia and poor oral health. By contrast, few participants believed that occasional smoking could reduce the risk of dementia whereas, interestingly, one of the participants felt it was not related at all.

8.4.3.2.2 Subtheme B2: Alcohol

Some participants believed that alcohol has an impact on oral health and can also increase the risk of dementia. One of the carers stated:

"I think drinking, it causes bad oral health and possibly causes dementia as well". (P5, FG3)

One participant also expressed that alcohol can be a risk factor for dementia.

"I think if you're alcoholic he can get dementia through like being alcoholic and stuff like that". (P2, FG2)

Although there was less evidence to support the view that alcohol may influence dementia and oral health, a few participants expressed that alcohol is an important lifestyle factor in relation to dementia and oral health.

8.4.3.2.3 Subtheme B3: Diet

Diet was discussed in focus group discussions, and participants had mixed opinions regarding its role. Many participants believed that it has a negative influence on the brain. They commented that an unhealthy diet could lead to a lack of nutrients, which may impact the proper functioning of the brain. Some participants discussed this negative impact of diet on dementia as below:

"I think it's a cause. So, if I ate just crisp the whole entire time, it could produce the protein that might affect my brain". (P5, FG2)

Another participant had an opposite view, as stated:

"I am not sure, if they are eating very little then that can make them weak both physically and mentally". (P5, FG3)

One of the participants strongly felt that poor oral health does not have any role in the increased risk of dementia.

"Due to the lack of poor oral health and hygiene and the high intake of food properly and due to that, but I feel like that won't cause Dementia". (P4, FG1)

Another participant felt unsure that dementia risk was linked to diet.

“With oral hygiene it does some things with the dentures and stuff. I doubt with I think if it has a role with dementia”. (P2, FG2)

Caregivers perceived that diet does play a role in causing dementia. They also thought that poor oral health could decrease diet intake, which could then cause dementia due to a deficiency in important nutrients. However, this perception was not agreed on by all participants.

8.4.3.2.4 Subtheme B4: Exercise

It was acknowledged from the analysis that exercise can be a significant risk factor for dementia and oral health. One of the participants stated:

“So, for me, if I've got a dementia in my family and if I start smoking, eat a bad diet, don't exercise, and don't allow that. I might have more risk of getting dementia compared to if I exercise and eat healthy in my opinion”. (P5, F2)

From this comment, it is apparent that lack of exercise can trigger dementia. It gives a unique perspective on how a lifestyle factor such as exercise can be a risk factor for dementia.

8.4.3.3 Subtheme C: Other Multiple factors

Subtheme C “other multiple factors” comes under the theme “external factors”. Subtheme C emerged from four subthemes: “age”, “genetics”, “infection” and “medication”. These subthemes are explained below.

8.4.3.4.1 Subtheme C1: Age

According to the participants' discussion, age is an important factor directly related to increased risk of dementia and poor oral health. One of the participants commented:

“I was thinking, obviously, uh, increasing age you will actually get dementia. That's how you, um, unless you have early onset dementia. But most, mostly in the older age group. And also with oral health, I think like... I'm wondering if there's any scientific correlation, but from what I understand that as you grow older, um, you are more likely uh, oral health problems”. (P4, FG1)

Some participants felt that old age increases the chance of having dementia if there is a family history of dementia.

“People in your family that have got dementia, you're probably more likely to getting when you are old”. (P3, FG2)

Another participant commented:

“Increasing age, you will actually get dementia, from what I understand that as you grow older, um, you are more likely have oral health problems”. (P3, FG1)

One of the participants reported that an increase in age is directly linked to poor oral health but not dementia.

“Um, well it depends on the person for oral health because obviously as they got older and more like, out of habits, their oral health might get worse. And not necessarily because of the Dementia”. (P2, FG3)

A deeper exploration shows that carers perceived that ageing played a significant role in both dementia and oral health. They commented that in their experience, dementia was more common in older people and felt that it is natural that as people grow older, they will have poorer oral health.

8.4.3.4.2 Subtheme C2: Genetics

An analysis of the participants' views revealed that most participants believe that dementia is hereditary, and its risk increases if someone in the family has suffered from it. One participant commented:

"I don't know. You honestly never know. My granddads got it and right now, my dad's kind of following the same path". (P1, FG3)

But the same participant also said:

"Not oral health. I don't think genetically you're going to have bad teeth or bad hygiene, but Dementia, if there is genetics here". (P1, FG3)

Another participant gave a contrary view:

"I agree. But it doesn't directly cause dementia". (P4, FG1)

The findings within the themes suggested that participants believed that dementia is directly or indirectly linked with genetics. However, participants did not feel that genetics has any role in causing poor oral health.

8.4.3.4.3 Subtheme C3: Infection

The focus group analysis of the participants' views showed that some participants knew that infections could lead to dementia and poor oral health. One of the participants argued that infections would cause poor oral health, which then will indirectly cause dementia due to a decrease in diet intake.

"Like, if they got... like candida thrush. Oral thrush. Like, any oral infection. If, uh, obviously if they've got, uh, a toothache. They will not eat anything". (P1, FG1)

Another participant commented:

“So, you know, you get the different types of dementia currently where you know someone who's got a UTI that can trigger like the delirium. Yeah. You know, somebody, I've known somebody before had a UTI and they ended up with dementia long term it's not got rid of the infection. So, any infection, might trigger in the brain?”. (P2, FG2).

Some participants felt that there was no association and described it as:

“I think that, say if you were to get an infection, like it could affect the brain, obviously. Couldn't it? But we don't know whether that's directly... because you haven't brushed your teeth, you're going to get Dementia or anything. I don't think there's a link”. (P2, FG3)

Hence, most caregivers considered that infections could cause poor oral health and increase the risk of dementia.

8.4.3.4.4 Subtheme C4: Medication

Some participants felt that medication is a major factor in causing poor oral health, as it can cause xerostomia (dry mouth) in people with dementia. One participant commented:

“Medication can dry mouth um stuff, you have to be careful, it's not good for their teeth”. (P5, FG3)

Caregivers explained that, in their experience, some medicines cause dry mouth, which leads to decreased diet intake due to difficulties in swallowing food, thus causing dementia.

8.5 Discussion

This chapter includes three focus group discussions of caregivers in Wolverhampton and investigates the caregivers' perception of the association between dementia and oral health in people with dementia. From the findings, there were seven main subthemes that were grouped

into three key themes which answer the research questions mentioned in Section 2.8.1. The findings of this study are discussed below in relation to the relevant literature.

8.5.1 Association between oral health and dementia

This part is divided into two sections, i.e., “oral health’s influence of dementia” and “dementia influence on oral health”.

8.5.1.1 Oral health’s influence on Dementia

In this focus group study, the findings reported by the caregivers of people with dementia suggest that poor oral health may have a weak association with an increased risk of dementia. Previous longitudinal studies have shown that poor oral hygiene, leading to the development of dental caries, periodontal diseases, and ultimately tooth loss, has been associated with an increased risk of dementia (Shimazaki *et al.*, 2001; Gatz *et al.*, 2006; Stewart *et al.*, 2013). Furthermore, reviews also found that poor oral health indicators such as periodontal disease and tooth loss are significant risk factors for increased risk of dementia (Nadim *et al.*, 2020; Chen *et al.*, 2018). A few studies did not find such association (Wu *et al.*, 2016; Pazos *et al.*, 2018).

The results of this study help answer the first research question; Does poor oral health increase the risk of dementia? Focus group discussions suggest that in some aspects, oral hygiene and oral health are worse among dependent elders who have dementia than those without dementia. Although some participants felt that there was a link between poor oral health and dementia, few participants believed that poor oral health was not linked to an increase in the risk of dementia.

8.5.1.2 Dementia influence on oral health

It is difficult to establish any causal relationship between oral health and dementia considering the limitations of this study design. However, the data emerging from this focus group study

show that dementia is linked to oral health thus answering the second research question: Do people with dementia or severe cognitive impairment have worse oral health than people without dementia? The relationship between dementia (including cognitive impairment) and poor oral health revealed in this study is consistent with previous studies. In the past, studies (Noble *et al.*, 2013; Foley *et al.*, 2017) reported that people with impaired cognition are expected to be more inattentive to oral hygiene as dementia progresses and experience poor oral health (Noble *et al.*, 2013; Foley *et al.*, 2017). Our results are corroborated by Daly *et al.*, who gave evidence that people with dementia may experience worse oral health and poor oral hygiene (Daly *et al.*, 2018). In another recent review, Lauritano *et al.* found that the elderly with dementia show a higher level of plaque, coronal and root caries, retained roots, gingival and periodontal disease when compared to the elderly population not diagnosed with dementia (Lauritano *et al.*, 2019). Therefore, the focus group findings suggest that there might be a bidirectional relationship between oral health and dementia in line with the most current literature (Kapellas Kostas 2019; Liccardo *et al.*, 2020).

8.5.2 Oral Care

This part is composed of two sections: the barriers faced, and the support provided for oral care of people with dementia. These are explained below.

8.5.2.1 Barriers faced in providing oral care to people with dementia

Due to behaviour and oral neglect

This study reports that behaviour is a critical factor. The behavioural problems such as aggression and lack of compliance make it more difficult for the carers to provide oral care. This in longer term contributes to oral neglect and leads to oral diseases as reported in previous studies (Sonde *et al.*, 2011; Yi Mohammadi *et al.*, 2015). Furthermore, the research corroborates previous findings which establish the importance of informed consent and

communication with carers of dementia patients (Chávez *et al.*, 2018). In this qualitative study, the participants understood that the ability to comply with oral hygiene procedures and dental care is often influenced by past dental behaviour and experiences (Hilton and Simons, 2003; Nordenram *et al.*, 1997).

Due to dental care

In this study, dental care also emerged as an important barrier in maintaining good oral health for people with dementia. These findings with previous study which reported that among the older Japanese population, aged 65 years and older, those without regular dental visits were more likely to have incident dementia HR of 1.44 (1.04-2.01) (Yamamoto *et al.*, 2012). Another study found that patients with AD and other types of dementia showed poor denture hygiene and had a greater proportion of moderate to heavy plaque compared to those without dementia (Syrjälä *et al.*, 2012). In contrast, the study by Ribeiro *et al.* (2012) reported no significant difference in the median plaque assessment scores were high (worse) for both groups (Ribeiro *et al.*, 2012). Another finding from this focus group discussion is that people with dementia suffer stress when seeing a dentist consistent with a previous study (Bharti *et al.*, 2015).

Due to lack of care support

Findings from the focus groups also help understand that carers' level of support is a significant factor in providing oral care. Also, this research has demonstrated that people with dementia and their informal carers used fewer services in comparison to other people in need of care (Vecchio *et al.*, 2016; Phillipson *et al.*, 2014). In UK caregivers of people with dementia were not favouring access to dental care despite being aware of dental problems or the need for regular dental attendance (Hilton and Simons, 2003).

Memory / Cognition loss and Physical impairment

This focus groups analysis reports that as dementia progresses, it makes oral hygiene care more difficult. Similarly, previous studies reported as dementia progresses it causes cognitive loss, decreased function and motor skills and reduced ability to self-care, including carrying out oral hygiene procedures (Warren *et al.*, 1997; Brennan and Strauss, 2014).

8.5.2.2 Support provided by caregivers for oral care in people with dementia

Professional carers' support for oral care

This is consistent with previous quantitative studies that showed a higher need for assistance with oral hygiene care in dementia patients, with an increase in severity of cognitive impairment (Gao *et al.*, 2020). A previous study found that caregivers were reluctant to take persons with dementia to use dental services and visits to a dentist for various reasons (Hilton and Simons, 2003). The findings from this focus group study also show that residents who did not have relatives/friends to support them were often reliant on care home personnel, which is consistent with the literature (Jones *et al.*, 2019).

Family carers' support for oral care

The focus group results show that the family caregivers were an integral part of the support for people with dementia, consistent with previous studies (Finkleman *et al.*, 2012; Paley *et al.*, 2009; Tham and Hardy, 2013). Family and friends were identified as co-supporters of oral care and had an active role in encouraging and supporting oral care and access to treatment (Jones *et al.*, 2019).

Comparison between professional carers' and family carers' support

The data from the focus group study reflect that participants had contradictory opinions; some caregivers felt that better oral care was given in care homes while others did not agree. Similarly, Ryan and Scullion (2000) documented how family members considered themselves

to have a more significant role in caring for relatives than that acknowledged by care home personnel (Ryan and Scullion, 2000). In addition, Nordenram *et al.* conducted a survey regarding priorities for oral health care in people with dementia (Nordenram *et al.*, 1997). They reported that nursing staff felt that being able to eat was important while relatives were much more concerned about social behaviour and communication, including aesthetics, speech and fresh breath. Similar to the results from this focus groups analysis, previous studies found no significant differences in oral health among people with dementia between those living in care homes and those living in their own homes (Chen *et al.*, 2013; Chalmers *et al.*, 2003) while others did not (Ribeiro *et al.*, 2012; Chalmers *et al.*, 2002).

8.5.3 External factors which play a role in dementia risk and poor oral health

This part is composed of three sections: environmental and socio-cultural factors, lifestyle factors, and other multiple factors explained below.

8.5.3.1 Environmental and socio-cultural factors

Culture, race and ethnicity aspects

Participants believed that culture and ethnicity play a role in causing dementia and poor oral health. This was consistent with previous studies in which culture was considered an internal determinant that influences dementia care at multiple levels through support-seeking and inadequate care service (Santos *et al.*, 2013; Calia *et al.*, 2019). Adelman *et al.* (2011) revealed an increased prevalence of dementia in people of black-Caribbean ethnicity in London (Adelman *et al.*, 2011). In this study, another link between dementia and oral care discussed by participants was religion. Little research has been done on cultural and religious barriers for people from black and minority ethnic groups in accessing a dentist and the impact this has on oral health (Marshaman *et al.*, 2013; Livingston *et al.*, 2017). Further research is needed in this area.

Education

Participants in this study believed that education levels are strongly and inversely associated with dementia. This is consistent with previous studies, which showed that a higher level of education in early life is associated with a reduced risk of dementia (Livingston *et al.*, 2017; Larsson *et al.*, 2017). Similarly, the poor oral health of the elderly could be due to caregivers' lack of adequate education, proper instruction in oral healthcare and person with dementia low formal education (Johnson, 2012; Bonfim Mde *et al.*, 2013).

Socio-economic status (SES)

This study reveals how participants believed that SES increases dementia risk and poor oral health, as they are inversely related to SES. Adelman *et al.* (2011) reported that socioeconomic status has long been seen as an independent predictor of dementia (Adelman *et al.*, 2011). Previous studies demonstrated that socioeconomic status is negatively associated with oral health and dental diseases (Mejia *et al.*, 2014; Peres *et al.*, 2019).

Environmental factors

Few participants (two) felt that environmental factors might increase the risk of dementia. This view is similar to a previous review, based on 13 longitudinal studies of air pollutants exposure and incident dementia, which found exposure to PM_{2.5}, NO₂, and carbon monoxide were all associated with increased dementia risk (Peters *et al.*, 2019).

8.5.3.2 Lifestyle factors

Alcohol

This focus group analysis shows that alcohol intake is another important lifestyle factor that significantly impacts cognition. A recent systematic review, incorporating 45 studies of light to moderate drinking, reported a reduced risk of dementia compared with not drinking (RR 0.7; 95% CI 0.6–0.91) (Ilomaki *et al.*, 2015). Similarly, these findings are consistent with previous

studies showing that alcohol can also increase the risk of poor oral health including oral cancer, periodontitis and halitosis (Suzuki *et al.*, 2009; Turati *et al.*, 2013).

Diet

Participants in this study revealed that diet plays a vital role in causing dementia, and the analysis also showed that it was linked with poor oral health. The latest research has shown that masticatory disorders due to tooth loss can lead to poor nutrition and reduce cerebral blood flow, which may be linked to memory deficits (Frenkel *et al.*, 2001). Furthermore, compromised oral health (e.g., tooth loss, xerostomia) may impair sensory and masticatory function; which can cause poor nutritional conditions, including deficiencies of micronutrients (vitamin B12 and thiamine) and weight loss, which are potentially important determinants of dementia (Tucker *et al.*, 2005; Krall *et al.*, 1998; Wahl *et al.*, 2018).

Smoking

The results are consistent with previous studies which reported that smokers are at higher risk of dementia than non-smokers (Livingston *et al.*, 2017; Choi *et al.*, 2018). Pan and colleagues indicated that in women aged 55–64 years, exposure to second-hand smoke was associated with more memory deterioration (Pan *et al.*, 2018). Smoking was also found to be a risk factor for poor oral health (Grossi *et al.*, 1995; Tomar and Asma, 2000).

Exercise

Another common factor for poor oral health and dementia risk is exercise. A meta-analysis that included 30 randomized trials found that exercise trail positively affects cognitive function (Heyn *et al.*, 2004). Similarly, the oral conditions that strongly influence physical strength are malocclusion and periodontal disease (Bramantoro *et al.*, 2020).

8.5.3.3 Other multiple factors

Age

Participants perceived that *age* is one of the most important risk factors for increased risk of dementia and poor oral health. (Kukull *et al.*, 2002). Marcenes *et al.* (2013) also reported that periodontal (gum) disease and tooth loss increase with age (Marcenes *et al.*, 2013). These patterns of increased risk in the ageing population in the UK and other countries have important public health implications, which are highlighted in this focus group study.

Genetic and hereditary factors

The evidence from the focus group study suggested that genetic factors such as family history increase the risk of dementia and mild cognitive impairment, which has been reported in previous studies as well (Locke *et al.*, 2009; Milne *et al.*, 2008). Carter *et al.* (2017) reported that AD-related genes from GWAS overlap with the PD genes. Thus suggesting the susceptible genes and pathogen may condition each other's effects (Carter *et al.*, 2017).

Infection

Participants suggested that infection could cause dementia. This view is consistent with previous studies that suspected infections, the most common of which are urinary tract infections (UTIs), often accompany advanced dementia (Mitchell *et al.*, 2014). Accumulation of plaque could cause PD (oral infection) which can become a systemic infection. Once the bacteria enter the blood, the resulting high inflammatory immune responses may contribute to the pathogenesis of dementia (Watts *et al.*, 2008; Socransky and Haffajee, 1994).

Medication

The effect of a dry mouth has severe consequences for a cognitively impaired older person who may be unaware of, or unable to articulate their difficulties (Ship *et al.*, 1990). In this focus

group study, it was also found that people with dementia had dry mouth due to medication they are taking.

8.5.4 Strengths, limitations and suggestions for future study

The main strength of this study is that limited research exists on this topic, so it will help to increase our knowledge and awareness about the problems faced by caregivers concerning oral care and enhance our understanding of them. To the best of my knowledge, this is the first qualitative research study based on focus group discussions that investigates the perception of both family and professional carers' on the association between oral health and dementia whether they influence each other or not. Unlike previous studies, this study not only found out about support and barriers for oral care but also explored their views on the relation between oral health/care and dementia risk, including common risk factors. The study has carried out three separate focus group discussion sessions using the same topic guide, which helped to reach data saturation according to Krueger (1994) and Morgan (1997). Another strength of this study is its diverse sample population, with respect to age, gender, carers' type (family and professional caregivers of people with dementia), duration of care, carers' relation to people with dementia and carers' education level, thus providing quality data (Onwuegbuzie *et al.* 2009). In addition, the researcher selected the widely used thematic analysis method by Braun and Clark (2006) that helps achieve trustworthiness criteria in thematic analysis (Nowell *et al.*, 2017). Triangulation was achieved as there was a constant analysis of the data and the different data collection modes, including audio recording devices, note-taking and confirming codes for themes by the co-moderator.

In this study, there are some *limitations* to be considered. Since the study was limited to caregivers' perceptions, the researcher has neither included the dementia patient's perspective nor their view on the association between oral health and dementia, which needs further

understanding. Future studies could explore the perception of people with dementia, yield more accurate results and test the validity of the results in this research. Furthermore, the findings are based on personal perspectives and therefore subject to potential bias. Hence, it is recommended that a future research design should be a prospective cohort study to find the causal relationship between oral health and dementia. There were also differences among the participants regarding primary caregivers, knowledge of dementia and information on oral health, which may be due to differences in education level and the number of years of experience in caring work. Future research should focus on family carers considering the oral care needs of homebound elderly with dementia and evaluating the interventions for all types of care to improve oral hygiene, which could further help in policy implementation. The last suggestion for future research includes expanding the study to include caregivers of people with dementia from across the region.

Another major limitation of the focus group study is its inability to establish or infer a causal link between dementia and oral health. For instance, some participants were sure while other participants felt unsure about the association between poor oral health and dementia. This may be due to a difference in education level or experience in caring work among the participants, as a few of them had only < 2 years of caring experience. Thus, the qualitative study can help by giving us the insight to understand how the phenomenon happens, but it cannot establish a causal link, which is best explained by cohort studies.

8.6 Implications and conclusions

The data collected in this research can be beneficial to both current and future caregivers. They also reveal that many caregivers are unaware of the relation between oral health and dementia and its confounding factors. By educating our future caregivers with courses and relevant training programs we can overcome these barriers. Also, through providing our current

caregivers with the necessary support and information, we believe that the dementia caregivers will be able to give oral care to all.

It also contributes to our understanding of barriers in providing oral care, including behaviour, level of support, dental care, memory and cognition loss, oral health neglect, personal characteristics and physical impairment, as well as the common risk factors for oral health and dementia. In conclusion, the focus group suggested that some carers believe that poor oral health could potentially be related to cognitive impairment and dementia, while people with dementia may have worse oral health.

CHAPTER NINE: GENERAL DISCUSSION AND CONCLUSIONS

9.1 Introduction

This chapter discusses and integrates the key findings from both qualitative and quantitative studies of the thesis. The various contributions to knowledge from all aspects of the research project are highlighted to support the conclusions to be drawn from this thesis. The chapter commences with a summary of key findings from the thesis. It then progresses into the integration of the findings from the quantitative and qualitative research, followed by the strengths and limitations of the thesis and suggestions for future studies. Furthermore, the implications and recommendations of the findings are presented. The answers to the research questions and an explanation of the research objectives, the contribution to knowledge and finally, the study's conclusions are given in the end.

9.2 Summary of key findings

This thesis has employed a mixed method approach to investigate the bidirectional association between oral health and dementia; that is, poor oral health predicts dementia, and dementia/cognitive impairment increases poor oral health in older adults aged 50 or above. The quantitative part had two studies; one case-control study of older people in hospital, conducted in China and one population-based cohort study with a long follow up over 8 years in people aged 50 or above years, conducted in the UK. In chapter 5, the analysis of the Guangzhou case-control study showed that poor oral health could be associated with an increased risk of dementia. Oral health measures, such as poor SROH, tooth loss, edentulism, bleeding gums, painful gums, bad breath, brushing teeth, dental visits and PD, all reported increased risk of dementia. The confounders were adjusted with factors including demographic, socio-economic, lifestyle, dietary intake and comorbidities. There were a few variables with unknown participants' responses, but this issue has been addressed in this chapter. In many LMICs, oral diseases

remain largely untreated because the treatment costs exceed available resources, which leads to untreated oral diseases and reduced quality of life (Peres *et al.*, 2019). Chapter 6 explored the association of poor oral health with incident dementia with a follow up over 8 years in a cohort study. The findings showed that various oral health measures were significantly associated with incident dementia.

The findings from two quantitative studies on the association of dementia/cognitive impairment with oral health have been discussed in chapter 7. The findings from the case-control study did not find a significant association of dementia with SROH. However, all other oral health measures (never or occasionally visiting dentist, < once per day brushing teeth, number of teeth present and PD) indicated that poor/fair SROH were significantly increased in people with dementia versus those without dementia. On the other hand, the results from over 8 years follow up ELSA study were different because they showed a significant association of combined dementia and severe cognitive impairment with incident poor SROH, while dementia was not significantly associated with SROH, no teeth and oral impact, which was probably due to small number of patients with dementia in the baseline.

In chapter 8, the three focus groups explored views and perceptions of caregivers on the association between dementia and oral health of people with dementia. The findings from three focus groups revealed three themes. The first theme was “relation” which explored caregivers’ perceived views on whether there is an association between dementia and oral health. The second theme was ‘care’, which highlighted caregiver perception about barriers and support on oral care provided to people with dementia. The third theme was “external factors” for dementia and oral health in people with dementia which discussed socio-cultural, lifestyle and other multiple factors. This study increases our understanding as some of the qualitative

findings were consistent with the quantitative findings of this thesis. This is discussed in the following section below (Section 9.3).

9.3 Integrating focus groups findings with quantitative studies

The findings from the quantitative and qualitative studies are discussed below to explore how they have contributed to or added new knowledge on the association between oral health and dementia. The following section provides an integrated summary of the key findings from the meta-analysis, the Guangzhou case-control study, the ELSA cohort study and the Wolverhampton based focus groups study considering the research questions. Oral health with dementia is discussed first, followed by the association of dementia and severe cognitive impairment with oral health and its reasons.

9.3.1 Poor oral health associated with increased risk of dementia

This thesis investigated the effect of poor oral health on incident dementia in the UK based on an over 8 years follow up cohort study and the association of oral health with increased risk of dementia in the Guangzhou case-control study conducted in China. Both quantitative studies have reported consistent findings that SROH is associated with an increased risk of dementia. A dose-response relationship was found between the number of teeth and dementia risk in the case-control study. This is similar to the findings in a recently published meta-analysis study (Qi *et al.*, 2021), which showed that the risk of dementia increased by 28% in each missed tooth. Furthermore, oral health measures such as brushing teeth less than once a day (Paganini-Hill *et al.*, 2012), never or occasional dentist visits (Yamamoto *et al.*, 2012) and severe PD showed an increased risk of dementia (Lee *et al.*, 2017b).

The qualitative study results supported the findings in the quantitative studies and showed that past oral habits like brushing teeth (never or less than once a day) and dental visits (try to avoid dentist or never been to a dentist) could lead to dementia. The qualitative study was done using

three focus groups on caregivers' perception of the association between dementia and oral health of people with dementia. The perceived view of the participants that came across all focus groups was that poor oral health could increase the risk of dementia, and some participants felt that multiple risk factors were responsible for poor oral health in people with dementia. These findings from the focus group were in line with quantitative results supporting that poor oral health increases the risk of dementia.

Qualitative study findings further explained how past oral habits could affect oral health of older adults. Similar findings in the case-control study reported that infrequent brushing habits and never or occasional dental visits are significantly associated with increased risk of dementia (Paganini-Hill *et al.*, 2011; Yamamoto *et al.*, 2012). Moreover, it can be explained that people who do not brush their teeth or visit dentists would have a higher chance of accumulation of plaque on teeth, leading to infection (PD) and eventually tooth loss (Van Dyke and van Winkelhoff, 2013; Page and Kornman, 1997).

Qualitative study revealed that oral health is often neglected in older adults with dementia as more focus is on general health. For instance, lack of funds or aggressive behaviour of dementia patients results in infrequent visits to the dentist, which leads to poor oral health. Similar findings are mentioned in quantitative results, that individuals who are not visiting a dentist have poor oral health.

9.3.2 Dementia and cognitive impairment associated with increased risk of poor oral health

The findings from this thesis showed that oral health measure results varied in the case-control and cohort studies. The ELSA, a prospective cohort study, found that combined dementia/cognitive impairment or cognitive impairment were significantly associated with oral health measure SROH. However, the ELSA study found a non-significant association of dementia with edentulism and oral impact. The evidence from the case-control study findings

showed that dementia had a non-significant association with SROH. However, it has significant association with other oral health measures including the number of teeth present, brushing teeth, dental visits, and PD.

Moreover, the qualitative study gave evidence that proved the association of dementia/cognitive impairment with *poor oral health*. In the subtheme “dementia leads to poor oral health”, the caregivers perceived that people with dementia have an increased risk of poor oral health. These focus group findings were consistent with the SROH measure in the cohort study. Hence, the qualitative study provided an in-depth understanding of why dementia/cognitive impairment increases the risk of poor oral health. The qualitative study findings clarify the results found in quantitative studies and at the same time, increased understanding of the research topic. The results of quantitative and qualitative studies have added new knowledge which could help to understand the detailed picture of how dementia is associated with oral health.

Furthermore, the findings from the qualitative study demonstrated some reasons why people with dementia had *poor oral hygiene*, as found in the quantitative studies. These views were mentioned in the theme ‘care’, which related to the barriers faced by caregivers in providing oral care. It was revealed in the focus group study that uncooperative and aggressive behaviour prevented caregivers from providing oral care (e.g., brushing teeth) (Ettinger, 2000). It was also reported that people with dementia were reluctant to go to the dentist due to fear of dental procedures, cost and anxiety, similar to the previous study in the literature (Bharti *et al.*, 2015). These results were similar to the Guangzhou case-control findings, which showed a significant association of people with dementia who brushed their teeth less than once day and never or tried to avoid a dental visit leading to poor oral health. Lack of funds, poor memory, cognitive and physical impairment were other factors identified in focus groups results, which relate to

case-control findings. These factors cause poor oral hygiene in people with dementia (Ribeiro *et al.*, 2012; Warren *et al.*, 1997). Previous studies have also suggested these factors could lead to poor oral health in people with dementia (Gil-Montoya *et al.*, 2017; Aragon *et al.*, 2018; Naorungroj *et al.*, 2013).

In the focus groups, caregivers perceived that *past oral habits* played an important role; for instance, people with dementia who brushed teeth regularly in the past will continue to do so compared to those who did not. These focus group findings could be related to the Guangzhou case-control study, which reported that people with dementia had a higher risk of not brushing teeth, and this could be due to past oral habits. The focus group study also reveals the reasons why some people with dementia could have better oral health than before diagnosis of dementia. The findings showed that different factors, such as better support from carers and family members, risk assessment plan in care homes, support from the community, motivation and encouragement from caregivers and support to go to the dentist, could lead to maintaining or improving oral health. These findings are similar to these in previous findings (Housing, 2009; Hilton and Simons, 2003; Jones *et al.*, 2019).

The findings from the case-control study were similar to meta-analysis results in chapter 2, showing PD in relation to dementia/cognitive impairment. In addition, findings from the focus group were similar to ELSA cohort study showing poor oral health in relation to dementia/cognitive impairment. On the other hand, the focus group results explained the reasons for dementia leading to poor oral hygiene. The use of prospective cohort data ensured that the temporal order of the exposure and outcome relationship was established. These findings from the different designed studies have added strength to the thesis results and increased new knowledge on this topic.

9.3.3 Risk factors for poor oral health and dementia

The findings across focus groups reported risk factors that influenced both oral health and dementia. These risk factors are explained in the theme ‘external factors’ (Chapter 8). These risk factors were adjusted in quantitative studies as well to avoid confounding bias on the association. In this section, the bidirectional association of oral health with dementia is discussed by considering the risk factors common to both conditions.

In focus group findings, the subtheme ‘*culture, race and ethnicity*’ gives an interesting aspect to the research, which associated influence of culture on oral health. Although culture was not observed in quantitative studies, findings were consistent when two culturally different countries explored poor oral health association with dementia. Similar results have been reported in a previous study (Adelman *et al.*, 2011).

The focus group study found that dementia was associated with *smoking*, which is consistent with that in cohort study but not in with the case-control study. Previously, several studies have found strong evidence that *smoking* increases the risk of cognitive decline and possibly dementia as well, and can have a negative effect on oral hygiene (Singh *et al.*, 2013; Livingston *et al.*, 2017; Harding *et al.*, 2017). *Diet* impact on oral health was not found in the focus group study. This is contrary to the findings in a recent meta-analysis of 16 studies, which reported that the circulating 25(OH)D levels were significantly lower in chronic periodontitis patients (pooled MD = -6.80, 95% CI: -10.59 to -3.02) as compared to controls (Machado *et al.*, 2020). However, the association of diet with dementia was indicated, and dementia, in turn, could lead to poor oral health (Frenkel *et al.*, 2001; Harding *et al.*, 2017). VDD significantly increases the risk of all-cause dementia and Alzheimer disease as reported by a cohort study which showed that the adjusted hazard ratios (95% confidence interval [CI]) for incident dementia in participants who had 25(OH)D deficiency at ≥ 25 to < 50 nmol/L and

severe deficiency (<25 nmol/L) were 1.53 (95% CI: 1.06–2.21) and 2.25 (95% CI: 1.23–4.13) compared to participants with sufficient concentrations (\geq 50 nmol/L) (Littlejohns *et al.*, 2014). *Age* was considered as an important risk factor for both dementia and poor oral health in all quantitative studies and focus group discussions and has been discussed in previous studies too (Kukull *et al.*, 2002; Harding *et al.*, 2017). *Genetics* was discussed in detail in the focus group. It was perceived to be related to dementia but not to oral health, which was contrary to previous studies that reported the role of genetic polymorphisms in AD and periodontitis (Carter *et al.*, 2017; Harding *et al.*, 2017). Furthermore, the role of *infections* in causing dementia (Harding *et al.*, 2017) was also revealed in focus groups discussion which is discussed in infection – inflammation pathways. The case-control study reported that people with dementia had an increased risk of severe PD or vice versa. Its pathways were explained below.

9.3.4 Pathways for the bidirectional association between oral health and dementia

In this thesis, the bidirectional association between poor oral health and dementia was explored, which can be explained in light of the modified conceptual framework by Noble *et al.* (2013) in chapter 1 (Noble *et al.*, 2013).

Pathways explaining poor oral health causes dementia

In this research work, poor oral health, poor oral hygiene and PD increased the risk of dementia, probably in a causal response relationship. Several longitudinal studies have found that poor oral hygiene leads to the development of dental caries and PD, which induce soft-tissue inflammation and ultimately result in tooth loss (Tzeng *et al.*, 2016; Chen *et al.*, 2017). Tooth loss has been associated with an increased risk of dementia (Qi *et al.*, 2021; Stein *et al.*, 2007). Two pathways that could explain the association of oral health with dementia are the inflammatory pathway and diet-mastication pathway.

First, the inflammatory pathways explained the role of periodontal pathogens and the resulting host immune response. This increases the proinflammatory cytokines such as IL-1, IL-6, and TNF-a, which might compromise the blood-brain barrier and cause inflammatory reactions in the central nervous system resulting in cognitive impairment and dementia (Lee *et al.*, 2017b). Second, diet-mastication pathway is another possibility. It explored how poor nutrition caused by periodontitis and tooth loss (Abbaya *et al.*, 2015) and reduced ability to masticate due to tooth loss (Tucker *et al.*, 2005; Krall *et al.*, 1998) would lead to decreased cerebral blood circulation and neurotransmitter secretion, which in turn can increase risk of dementia.

Pathway explaining dementia/cognitive impairment leading to poor oral health:

This thesis also found that dementia and cognitive impairment could increase the risk of poor oral health. The diet/mastication pathway explores how people with dementia can develop physical impairment and dry mouth (Ship, 1992; Tucker *et al.*, 2005), leading to poor oral hygiene. As explained before, poor oral hygiene causes caries and PD and eventually tooth loss. Tooth loss together with dry mouth can reduce cerebral circulation (as explained above). The inflammatory pathways explain that xerostomia and poor oral hygiene due to the motor and cognitive impairment of dementia would lead to PD. PD then increases the proinflammatory cytokines (as explained above). Thus, it is not surprising that dementia/cognitive impairment could increase the risk of oral health problems. The resulting two-way links form a cycle, thus highlighting a bidirectional relation between oral health and dementia. All these factors and the pathways mentioned above further support the evidence that poor oral health measures and PD are related to increased risk of dementia and vice versa.

9.4 Study strengths and limitations, and future research

9.4.1 Strengths of the study

The strengths of this research work are explained in detail below:

1. Mixed method research

In this thesis, the mixed method convergent design was employed, which provides a detailed view. The quantitative findings from the case-control study and cohort study provide a clear picture of whether there is a bidirectional association between oral health and dementia. The qualitative findings from focus groups explore and discuss the participants' perspectives, providing rich detail to the picture. Therefore, the use of both quantitative and qualitative methods allowed a complete understanding of the bidirectional association between oral health and dementia. Moreover, the studies from China and the UK were in different study designs; they would be complementary to each other and indicate that the relationship between poor oral health and dementia could be bidirectional. The results from the focus group study were also consistent with the quantitative findings. Since the results from all studies were only integrated in the discussion stage, the separate findings add new knowledge regarding the association between oral health and dementia.

2. Longitudinal ELSA cohort data and analysis

ELSA cohort study investigated the research question using different waves data extracted from the ELSA dataset, which is representative of a national sample of older adults, aged 50 years and above, living in England. The availability of high-quality longitudinal data in the ELSA provided an excellent setting for a deeper assessment of the research question. This allowed the use of longitudinal data to analyse the association of poor oral health with dementia and the association of dementia/cognitive impairment with poor oral health. The strengths of such longitudinal data in enabling stronger inference in relation to the key research question of the thesis have already been discussed previously.

Furthermore, for the analyses of poor oral health associated with dementia, follow up duration was of over 8 years, having participants interviewed at both wave 3 and wave 5 (2010-11) to

wave 9 (2018-19) (chapter 6). Similarly, for analysis of whether people with dementia/cognitive impairment poor oral health have, follow up was over 8 years for participants interviewed at wave 3 (2006-07), wave 5 and wave 7 (2014-15) to wave 9 (2018-19) (chapter 7). There are very few prospective cohort studies conducted with a long follow up period of over 8 years. The length of follow up duration strengthens the findings, which can have implications for policymaking and practices to decrease poor oral health and dementia.

3. Diversity of oral health measures

Oral health measures were analysed in this thesis to assess different aspects of current and historical oral health. In the cohort study and case-control study, oral health was assessed using different measures, with each measure showing a particular aspect of oral health. Both studies had assessed SROH, tooth conditions, edentulism and oral impact. Oral health was also assessed by evaluating oral health behaviour/hygiene and PD in the case-control study. These measures reflect a contemporary account of both self-report measures and clinical aspects of oral health. A study found that those with better dental health, established by clinical examination, tend to self-report good oral health compared to others with poor clinical oral health (Airila-Månsson *et al.*, 2007). Furthermore, oral health measures from cohort and case-control studies have been validated in previous studies (Tsakos *et al.*, 2015; Wu *et al.*, 2013).

4. Controlling for relevant confounders

A strength of this thesis is the range of potential confounders that were controlled during analysis in the cohort study and case-control study. The availability of several potential confounding factors and health behaviours provided in both the cohort study and case-control study helped in conducting multivariable analyses for association between oral health and dementia/cognitive impairment.

5. Focus group study

One of the strengths of this doctoral research work is drawn from the focus group study conducted in the UK. Most of the risk factors that came across in this focus group study were adjusted for in the quantitative studies. Three focus groups discussions were conducted to reach saturation of the data as suggested in the literature. The focus group study process was made rigorous and trustworthy using suggestions from Nowell *et al.* (Nowell *et al.*, 2017), which is important for meaningful and valuable findings.

9.4.2. Limitations of the study

Although all the studies in this thesis were effectively conducted and provided new insight into the association between oral health and dementia, they have limitations that should be recognised.

1. Measures of oral health status

In this thesis, there is a risk of low specificity because oral health measures were self-reported only, and there is no clinical data to confirm the findings. Additionally, the analysis of tooth loss employs a very crude measure of total tooth loss (presence or absence of edentulism). It does not allow for testing a more refined measure that would reflect the extent of tooth loss. The case-control study used validated self-reported PD and oral hygiene questions, but there was no clinical data to validate. Furthermore, the lack of PD measures limited the analyses. In the future, detailed information from clinical parameters will confirm the association of oral health and dementia.

2. Cognitive impairment measure

Although the ELSA dataset is rich in cognitive measures, memory index was used to measure cognitive impairment at wave 5 (explained in Chapter 7) instead of Modified Telephone Interview for Cognitive Status (mTICS) as it was first collected at wave 7. Hence, mTICS was

not used during analysis to assess the relationship of dementia/cognitive impairment with poor oral health at wave 5 (baseline). It should be noted that mTICS has not been used in previous studies that assessed the association between oral and cognitive impairment. Most of the studies used the Mini-Mental State Examination (MMSE), which is not available in the ELSA dataset. Therefore, in this thesis, comparing the findings regarding the association of cognitive impairment was difficult. The cut-off points for memory index score out of 30 were taken as 27 and above as normal, 21-26 mild cognitive impairment, 20-10 moderate cognitive impairment, and 9 or less as severe cognitive impairment for analyses to overcome this problem.

3. Case-control study design limitations

These have been discussed in detail in chapter 5.

4. Focus group study limitations

The focus group study limitations have been discussed in detail in chapter 8 (focus group study).

9.4.3 Suggestions for the future research

The research findings presented in this thesis provides valuable information about the links between oral health and dementia among older adults. However, further research on this topic needs to be undertaken before the association between oral health and dementia is more clearly understood.

- In terms of methodology, future research should be undertaken to investigate the biological and molecular aspects of inflammation caused by bacterial infections. Diet-mastication pathway could be further explored to see the impact of tooth loss on dietary intake patterns, and it's influence on the intestinal microbiome environment. This

regulates various mechanisms of transmission throughout the microbiota-gut-brain axis, which could have an effect on brain.

- The findings from the cohort and case-control studies were inconsistent regarding dementia/cognitive impairment associated with poor oral health. This could be due to differences in the study design, questionnaire, and study setting. There is a gap in knowledge, and more cohort studies with long follow up periods are needed. Another aspect that needs attention is that the number of participants in the ELSA study is not large enough to do subgroup data analysis for answering some questions and a large cohort study with a long time follow- up is required.
- Due to no clinical assessment of oral health in the studies included in this thesis, further studies, which take a clinical evaluation of oral health of dementia patients into account, will need to be undertaken to validate the thesis findings.
- There has been no standard method for PD diagnosis so far. Further work is required to establish standardised diagnostic criteria for PD and maintain the same criteria across the studies as it will increase the reliability of the results.
- The findings of this thesis suggest that there might be unmeasured covariates, such as genetic, culture, religious beliefs, etc., that could impact dementia. Future studies on the current topic are therefore recommended.
- Future studies need to be focused on the impact of oral health treatment on dementia risk. The findings from this research work show that poor oral health could predict dementia. There is much room for further progress in determining whether oral treatment (PD treatment) could reduce the risk of dementia. These future studies will also confirm whether reducing local inflammation and infection in the mouth could reduce systematic inflammation in the brain, thus reducing dementia risk.

- Findings from focus groups were based on carers of people with dementia only. In future investigations, it might be possible to use people with dementia and health professionals so that their beliefs and perceptions can also be taken into consideration.
- In future investigations, it might be possible to use different populations to study the impact difference in socio-cultural and lifestyle factors. For instance, another suggestion for future research includes expanding the study to include caregivers of people with dementia from China.

9.5 Implications of findings

This research has demonstrated the bidirectional association between oral health and dementia through quantitative and qualitative data analysis. Dementia has emerged as a major public health concern associated with high morbidity and mortality (WHO, 2021a). This thesis has explored that dementia has multiple modifiable and non-modifiable risk factors, as discussed in chapter 2 (literature review). Since non-modifiable risk factors such as age, gender, genetics, etc., are beyond one's control, all future studies should explore the ways to control and reduce the impact of modifiable risk factors to reduce dementia related GBD (UN, 2020). Of all the modifiable risk factors, this thesis explores the role of oral health in detail. Oral diseases account for almost 3.9 billion people globally (GBD, 2017). PD affects almost half of the world's population, with 11.2% suffering from severe PD (Kassebaum *et al.*, 2014). PD is also a known risk factor for dementia, as mentioned in a previous study (Nadim *et al.*, 2020). Through this thesis, the role of poor oral health variables (SROH, tooth loss, edentulism, poor oral hygiene habits and PD) in causing dementia has been explored in detail. These results highlight the need for public health policies and interventions to reduce oral health diseases. Furthermore, by controlling treatable conditions like PD, the global burden associated with dementia can be lowered.

The research findings from the quantitative and qualitative studies in this thesis indicated a possible association of dementia with poor oral health. Although the results varied between the cohort, case-control and focus group studies, the overall results supported the role of dementia in causing poor oral health and PD. This thesis indicates that people with dementia have an increased risk of poor oral health due to neglected oral health, including lack of regular teeth brushing, lack of funds, infrequent dental visits, and more importance to general health care. These can help the government in future public health policymaking; by channeling resources and funding towards improving oral health education among carers for dementia people as well as the general population, the economic burden associated with oral diseases can be significantly reduced.

Overall, strategies needed to reduce the GBD related to both dementia and oral health diseases should aim to eliminate barriers to providing oral care to dementia patients as well as the general population by arranging better oral care facilities, financial aids, carers' education and increasing awareness regarding the importance of oral hygiene behaviour.

9.6 Recommendations

The results from this thesis can have a significant impact on future policymaking, practices and research. This research work reports that a modifiable risk factor and treatable condition like PD can lower the risk of dementia, which is associated with high morbidity and mortality and is responsible for a high economic burden. Consequently, health practitioners and policymakers should globally aim to improve oral health care worldwide to ensure better cognition in the older population.

Furthermore, proper cognitive assessment and routine health checks in an older population can allow early detection of cognitive decline, thereby allowing oral health care and interventions to target these individuals, thus reducing their risk of progression to dementia. This, in turn,

will not only reduce dementia prevalence but will also decrease the costs associated with the care of people with dementia.

Future policies should encourage people to adopt a healthier lifestyle by improving oral health hygiene behaviour such as regular teeth brushing, routine and frequent dentist visits, fluoride toothpaste, floss, mouthwash and maintain denture hygiene. In addition, medical and dental practitioners should also aim to educate people regarding better diet and oral hygiene, as this will reduce their risk of cognitive decline in older ages.

9.7 Research questions and objectives

The research question and objectives are mentioned in chapter 2 (literature review). The section below explains how the research questions were answered and how the study's objectives were achieved.

Research question 1: Does poor oral health increase the risk of dementia? If yes, which oral health measure significantly predicted the risk of dementia?

It is clear from this research work that poor oral health predicts the risk of dementia. Different oral health variables including SROH, SROH conditions, number of teeth present, edentulism, brushing teeth, dental visits, bleeding gums, bad breath, painful gums, and PD variable; reported their poor oral health status was significantly associated with increased risk of dementia. Furthermore, the results in the case-control study (chapter 5) reported that severe PD increases the risk of dementia. This was confirmed with the current systematic review and meta-analysis (chapter 4), which achieves the first research objective, '*To investigate the influence of periodontal disease and oral hygiene conditions on the increased risk of dementia*'. The second objective was '*To examine the impact of poor oral health on incident dementia*'; it was confirmed over 8 years follow up cohort study (chapter 6), which further proves results from Guangzhou case-control study (chapter 5).

Research question 2: Do people with dementia or severe cognitive impairment have worse oral health than people without dementia? If yes, what are the reasons for it?

This thesis has shown that dementia or severe cognitive impairment could lead to poor oral health. The findings from the case-control study showed a significant association of dementia with various oral health measures such as the number of teeth present, PD and oral hygiene variables (chapter 7). It showed that people with dementia had a higher risk of brushing teeth less than once a day and never or occasional dental visits. The systematic review and meta-analysis findings (chapter 2) also reported that dementia increased the risk of PD (third objective: *influence of dementia on periodontal disease and oral hygiene conditions*). In the ELSA dataset, combined dementia and cognitive impairment or cognitive impairment data showed a significant association with incident poor SROH (fourth objective: *To investigate whether people with dementia or cognitive impairment had increased risk of incident oral health problems*). The evidence collectively with meta-analysis (chapter 2) highlights the association of dementia/cognitive impairment with incident poor oral health. Overall, these results indicate that dementia and cognitive impairment increases the risk of poor oral health. The reasons for this association include poor oral hygiene, past oral habits, aggressive behaviour and non-compliance of dementia patients, lack of funds and support to carers; all of these have been discussed in detail in chapter 7 and chapter 8.

In the thesis, the focus groups study helped to understand the quantitative findings by achieving the fifth objective (*To explore caregiver perception on the bidirectional association between oral health and dementia*). The findings from theme “relation” showed caregivers' perceptions on the association between oral health and dementia. The theme “care” explained barriers to why people with dementia had poor oral health due to cognitive and physical impairment, memory loss and past oral habits. The caregivers explained that due to behavioural problems, lack of funds and oral health is neglected compared to general health. Some of the common

risk factors were discussed in the theme “external factors” in focus groups. These risk factors give caregivers perceived views and shed new light to improve the understanding of this topic.

9.8 Summary of contributions to knowledge

The findings from this thesis make several contributions to the current literature. The mixed method approach led to findings that increased the understanding of the association of poor oral health with dementia. The thesis generated further evidence that poor SROH increased the risk of dementia and incident dementia in older adults aged 50 or above in China and the UK. In the Guangzhou case-control study, it was comprehensively explored that tooth status (in terms of the number of teeth present) was also associated with increased dementia risk. The evidence showed a dose-response relation, reflecting dementia risk increased around three to six folds as the number of teeth lowered from more to no teeth (edentulous). The case-control study presented additional evidence that poor oral hygiene (SROH conditions, brushing teeth and dental visits) and PD were significantly associated with an increased risk of dementia.

On the other hand, the findings from the cohort and case-control studies add a new knowledge to dementia/cognitive impairment association with oral health. The cohort study with a follow-up of over 8 years showed combined dementia and cognitive impairment or cognitive impairment are associated with incident poor SROH. The case-control study and focus group study findings support the limited evidence present in the literature that dementia is associated with poor oral health. In the case-control study, people with dementia had a higher risk of poor oral hygiene (brushing less than once a day, never or occasionally visiting the dentist and edentulism), demonstrating that they were at increased risk of having PD.

In the thesis, focus group findings enhance understanding of the bidirectional association of dementia with oral health by exploring the views and perceptions of caregivers of people with

dementia. It supported that oral health and dementia have common risk factors not explained before in a qualitative study.

9.9 Conclusion

The increase in population ageing would be an increase in the risks of poor oral health and dementia. Hence poor oral health and dementia have become major public health issues associated with high morbidity and global economic burden. This thesis has addressed the bidirectional association between poor oral health and dementia in detail. This study has demonstrated that poor oral health is associated with dementia and indicates a possible association of dementia with poor oral health. It is important to develop public health policies and strategies to improve oral health and prevent oral diseases, thus reducing the dementia epidemic. The focus group analysis also revealed that oral health care of the people with dementia, living in institutions or homes, has been given a low priority, even though it is as important as general health care needs. This highlights the need for public health campaign to increase awareness regarding the importance of oral health and oral hygiene behaviour, not only among dementia carers but also the general population, to reduce the risk of dementia in older age. The role of other risk factors contributing to poor oral health and dementia risk have also been discussed throughout this research work.

In short, maintaining better oral health and cognitive function in old age is critical to ensure a better quality of life in later years. This research work has indicated that controlling any conditions of oral health and dementia can lower the global burden of diseases in the world and reduce the financial burden on the global healthcare facility.

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APPENDICES

APPENDIX 1: THE APPROVAL LETTER FROM THE RESEARCH ETHICS COMMITTEE OF THE FACULTY OF EDUCATION, HEALTH AND WELLBEING, UNIVERSITY OF WOLVERHAMPTON UK FOR FOCUS GROUPS



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Re: Minor Amendments to Study

10 December 2019

Rizwan Nadim
University of Wolverhampton
Faculty of Education, Health & Wellbeing

Dear Rizwan

Re: "Perceptions of caregivers on association between dementia and oral health" (new title) submitted to The Faculty of Education, Health and Wellbeing Ethics Panel (Health Professions, Psychology, Social Work & Social Care)

The Faculty Ethics Panel (Health Professions, Psychology, Social Work & Social Care) has considered and reviewed your proposed minor amendments submitted 6 December 2019.

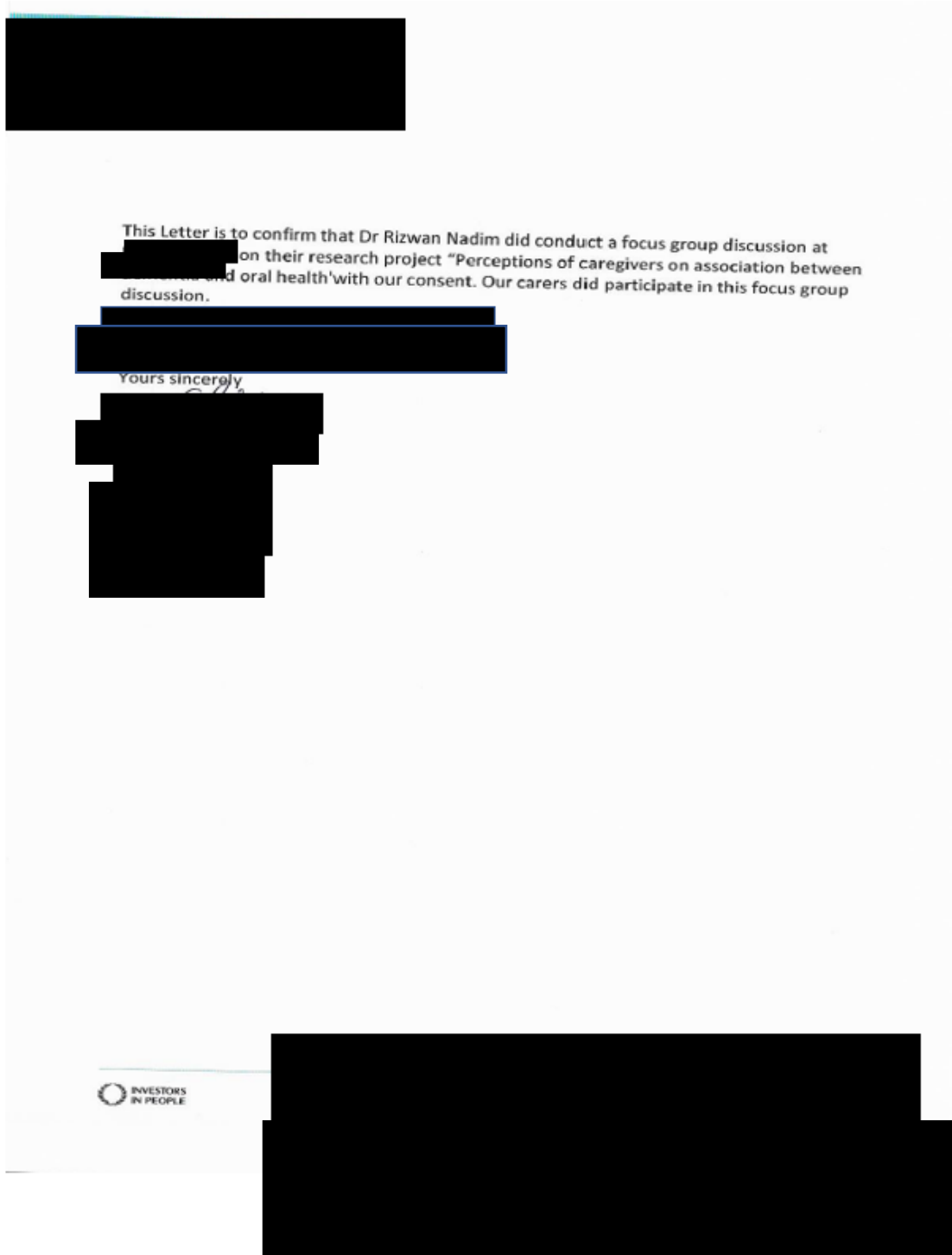
On review your Revised Research Proposal was passed and the Panel believes that the ethical issues inherent in your study remain adequately considered and addressed. Therefore the Panel is giving you full ethical approval for your revised study (**Code 1 - Approved**). We would like to wish you every success with the project.

Yours sincerely

Angela Clifford
Dr Angela Clifford (BSc, MSc, PhD, FHEA)
Chair – Ethics Panel

APPENDIX 2: PROOF OF CORRESPONDENCE/APPROVAL WITH CARE HOME FOR PARTICIPANTS (CAREGIVERS) RECRUITMENT

Letter redacted due to confidentiality considerations.



APPENDIX 3: SAMPLE LETTERS TO PARTICIPANTS.



SAMPLE LETTER 1 TO PARTICIPANTS

Dear Participants,

I am writing to invite you to participate in a research project, which I am conducting as part of a PhD in Public Health at the University of Wolverhampton. I am enclosing an information sheet which explains the title and aims of the project and what taking part will involve.

If you are willing to participate in a focus group, the focus group would take approximately 60-90 minutes including filling in a short questionnaire. Anything you say would be confidential, any notes and short questionnaire made as a result of the focus group would be destroyed afterward. The focus group discussion will take place in the meeting room in the [REDACTED] of the University of Wolverhampton, situated in the West Midlands, UK. The time and date will be arranged in advance. A report will be written on the findings and numbers will replace all names so that you cannot be identified.

If you feel that you would like to take part in a focus group please indicate on the attached sheet and either email or hand the letter to the researcher next time he visits you. If you would prefer not to be involved, please destroy/ignore this letter. If you decide not to be involved I would like to assure you that you will not be affected in any way.

Yours sincerely,

Rizwan Nadim

SAMPLE LETTER 2 TO PARTICIPANTS

Dear Participants,

I am writing to invite you to participate in a research project, which I am conducting as part of a PhD in Public Health at the University of Wolverhampton. I am enclosing an information sheet which explains the title and aims of the project and what taking part will involve.

If you are willing to participate in a focus group, the focus group would take approximately 60-90 minutes including filling in a short questionnaire. Anything you say would be confidential, any notes and short questionnaire made as a result of the focus group would be destroyed afterward. The focus group discussion will take place in the meeting room in the care home [REDACTED] situated in the Wolverhampton, West Midlands, UK. The time and date will be arranged in advance. A report will be written on the findings and numbers will replace all names so that you cannot be identified.

If you feel that you would like to take part in a focus group please indicate on the attached sheet and either email or hand the letter to the researcher next time he visits you. If you would prefer not to be involved, please destroy/ignore this letter. If you decide not to be involved, I would like to assure you that you will not be affected in any way.

Yours sincerely,

Rizwan Nadim

APPENDIX 4: FOCUS GROUP GUIDE

Title: “Perceptions of caregivers on association between dementia and oral health”

Opening statement:

Good morning/afternoon. Thanks for taking the time to join us to talk about perceptions of people who care for family members with dementia on passive smoking association with dementia and oral health. My name is Dr. Rizwan Nadim and I am doing PhD at the University of Wolverhampton. Please kindly fill the short questionnaire as it is part of the focus group study. After you have completed, we will start the focus group discussion.

In today’s session, the most important rule is that only one person speaks at a time. There are no right or wrong answers, only differing points of view. You do not have to speak in any particular order. We're audio recording today’s session so we don’t miss any comments. Despite being audio recorded, I would like to assure you that the discussion will be anonymous. The information you give us is completely confidential. I would like to begin today session by asking you:

Key Questions:

Focus group Questions

Q1. In your view, is there any relation between dementia and oral health?

- **If positive relation:** how and why there is a link between the two.
- **If negative or no or one way:** why there is one way/no/negative relation, can you explain.

Q2. In your opinion, do you think that dementia can influence oral health?

Follow up questions

- **If it influences:** how significant is the impact in person with dementia (good or poor oral health).
- **If it does not have impact/influence:** what made you believe that dementia has no influence on oral health.

Q3. Do you believe that in person with dementia oral health status changes after being diagnosed with dementia? Do you think that a person with dementia has bad or good or no change in oral health?

Follow up question

- What do you mean please explain more?

Q4. In your view, do you think oral health has a role in developing dementia?

Follow up questions

- Can you tell me more what do you mean by this in detail?

Q5. Can you tell me how you cope with oral care for a person with dementia on a daily basis? Do you think it is more challenging because they have dementia?

Follow up question

- What you mean by that can you elaborate more?
- What are the reasons behind can you explain?

Q6. In your opinion, does passive smoking cause dementia by causing poor oral health?

Follow up question:

- **If yes** –How are they related?
- **If not**- Why do you think they are not related?

Probing questions for all focus groups:

- Can you give an example?
- Can you elaborate on what you said?
- Please tell me more about it?
- Please help me understand what you said?
- What else can you say about that?
- Is there anything else you can add?
- Can someone build on that?
- On a scale of 1-5, how important is this?
- Why?
- Can you tell me more about how you felt about X?
- Why do you think you feel this way?
- What do you mean when you say X is ['no good']?
- I want to make sure I understand, can you explain more

Prompt questions for all focus groups:

- Anything else
- Does anyone else have something to add
- How about this side of the group
- How do others feel about that point?

- Who has a different perspective on that?
- Can someone build on that?

Closing statement:

Thanks for coming today and talking about these issues. Your comments have given us lots of different ways to see this issue. I would like to remind you that any comments featuring in this research will be anonymous. I thank you for your time.

APPENDIX 5: FOCUS GROUP QUESTIONNAIRE

“Perceptions of caregivers on association between dementia and oral health”

This questionnaire is a part of focus group study. Any information provided here will be kept confidential and anonymous. Please answer the following questions in the spaces provided, circle or tick the most appropriate options.

Basic characteristics

1. Age of caregiver:

18-30 years 31-40 years 41-50 years 51-65 years 65 years or above

2. Gender of caregiver: Male Female

3. Education of caregiver:

None Primary Secondary Graduate Other: _____

4. Do you know anyone with dementia?

Yes no

If yes, what is your relationship with them?

Friend Family through work other _____

5. Would you describe yourself as caregiver for others?

Yes No

6. Time spent caregiving of person with dementia per week:

<1 Year 1-2 Years
 2-5 Years 5-10 Years
 >10 Years

7. Smoking status:

Active passive both don't wish to disclose

8. Time exposed to active/ passive smoking:

1-4 hrs. per week 5-10 hrs. per week
 11-15 hrs. per week 16 hrs. or more per week

Thank you for taking the time to complete this questionnaire.

APPENDIX 6: PARTICIPANT CONSENT FORM



CONSENT FORM

CONSENT FORM

Title of Project: “Perceptions of caregivers on association between dementia and oral health”

Name of Researcher: Dr. Rizwan Nadim

Please initial boxes

1. I confirm that I have read and understand the information sheet dated 05-12-19 (version 4 minor amendment) for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw within 1 week after the focus group has been conducted, without giving any reason.
3. I understand that my data will be stored securely and confidentially and that I will not be identifiable in any report or publication.
4. I understand that the researcher may wish to publish this study and any results found, for which I give my permission.
5. I agree to be audio recorded during the focus group and for the data to be used for the purpose of this study.
6. I agree to take part in the above study.

.....
 Name Date Signature

.....
 Name of person taking Date Signature
 consent (if different from researcher, state position)

.....
 Researcher Date Signature

APPENDIX 7: INFORMATION SHEET FOR PARTICIPANTS

Study title

“Perceptions of caregivers on association between dementia and oral health”

Invitation

You are being invited to take part in a research study. Before you decide to participate, it is important for you to understand why this particular research is being undertaken and what it would involve. Please take some time to read the following information carefully and discuss it with family/ friends. Please feel free to ask us questions and clarify any doubts. Learning about the study will help you to decide whether you wish to take part. Thank you for your time and patience.

What is the purpose of the study?

The purpose of this study is to explore the perceptions of caregivers who care for people with dementia regarding the association between dementia and oral health is: to determine whether the two conditions influence each other or not.

Dementia is a big health problem worldwide. It is a condition marked by loss of memory and difficulty in thinking, problem-solving or language. In the United Kingdom, estimates show that there are around 850,000 people live with dementia, and 700,000 friends and family are caring for a person with dementia. Oral health is the health of your mouth, including your teeth, gums, throat, and bones around the mouth.

It is not yet clear what is the association between oral health and dementia as little information is present. Currently, there are no treatments available to cure or alter the progressive course of dementia. Therefore, identifying any treatable risk factor for dementia could greatly benefit efforts to promote public health. As a person who cares for people with dementia can play a vital role in improving the quality of life and care for those living with dementia, we want to know their perceptions whether there is an association between oral health and dementia.

Why have I been chosen?

You have been chosen because you have met the inclusion criteria based on age, experience with caring for a person with dementia, capacity to provide consent and because we believe you can make an important contribution to the research. There will be a total of 4-8 participants in the study including you.

Do I have to take part?

Participation is voluntary. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. Participants can withdraw from the study however if you decide that you want to withdraw your data or the contribution you made during the discussion, it should be done within a week of the focus group discussion, before data analysis begins. A decision to withdraw or not to take part, will not affect the standard of care you receive.

What will happen if I decide to take part?

You will be invited to participate in a focus group discussion (in-depth interview) that will involve a meeting of a group of 4 to 8 people. You will be informed of the time and date in advance. The group discussion will last approximately 60-90 minutes. In the focus group discussion, we will ask you about your views and perceptions on the association between dementia and oral health. The focus group will be audio-recorded throughout the session and brief notes will be taken.

What are the potential benefits and risks of taking part?

Though there are no direct benefits for you if you take part, by taking part you will help us to find out about perceptions of a person who care for people with dementia regarding oral health and dementia which will help in improving the lifestyle and health of elderly people in future.

There are no risks for you in taking part outside of those you would experience in everyday life. However, by taking part, you may remember things that you may find upsetting. If this occurs, the researcher will ask you if you want to continue to participate in the focus group. Any decision you make will be respected.

Will my taking part in the study be kept confidential?

Yes, all the information about your participation in this study will be kept confidential. The transcription of the focus group you participated in will be stored on a password-protected computer and locked cabinet in the office. Only the researcher and the supervisors working on the project will have access to the information. You will not be identifiable in any publication or report as the data will be grouped together and all identifying information will be removed.

What will happen at the end of the research study?

The results will form part of a research dissertation towards my Ph.D. Also, the results will be presented at international conferences and published in scientific journals. The collected information will be securely kept in a locked location for 2 years according to the university regulation on data storage and subsequently destroyed.

What if I have a problem or concern?

If you have concerns or complaints about any aspect of this study, you should ask to speak with the researcher who will do his best to answer your questions. You can contact Prof. Ruoling Chen on [REDACTED] or [REDACTED]

If you remain unhappy and wish to complain formally you can do this by contacting [REDACTED] who is independent from the research team and will investigate the matter fully.

[REDACTED]
Professor of Corporate Governance and Dean of Research
The Research Hub, MD150, Ambika Paul Building
Faculty of Social Sciences
University of Wolverhampton Business School
[REDACTED]

Who has reviewed the study?

The Faculty of Education, Health and Wellbeing Research Ethics Committee at University of Wolverhampton has reviewed and approved this study.

Contact for further information

If you wish to participate you will be given a copy of this information sheet and a copy of the signed consent form to keep.

If you require further information about this study, please contact:

Dr. Rizwan Nadim

Centre for Health and Social Care Improvement (CHSCI)
Faculty of Education, Health and Wellbeing
University of Wolverhampton
[REDACTED]

APPENDIX 8: FOCUS GROUP DISCUSSION TRANSCRIPT SAMPLE

In your view, is there any relationship between dementia and oral health?

P 1: Hi, I'm xxxx. Um, I think yes, the two can be related, um, 'cause um, poor oral health, obviously dementia, if somebody has dementia, they won't be able to look after their oral health. That would be the least of their... on their mind. So, they won't be looking after their general health. They won't be brushing. They'll have carers probably helping them, but still their oral health will get worse. On the other hand, um, poor oral health, um, probably it won't get... they won't chew their food properly, so it won't get properly digested and the nutrients won't get absorbed, so some nutritional limit, like, vitamin deficiency can lead to dementia I suppose.

P2: Hi, my name is xxxx. I'm not sure... I don't know about whether poor, poor oral health can lead to dementia but, uh, definitely if some, some person has dementia, that has effect in a person's oral, health, uh, as well as oral health and general physical health. Um, so per- persons with dementia may be less likely to look after their oral health, so that, that I, I agree with. Yep.

P 3: So I agree with both what P 1 and P 2 both said, um, in terms of how oral health will... it's like your teeth deteriorate in someone with dementia. Um, as P1 has mentioned, I think it's not like they have... they intentionally not taking care of their health, their oral health, as in brushing and washing et cetera. But I think as their memory kind of deteriorates, they're less able to kind of take care of themselves and, um, kind of get on with their normal activities or getting, getting, uh, um, in, just caring for themselves, especially if they're quite, um, kind of frail patients, and we don't actually have the support, in terms of like carers, etc. Um, I think those patients are more at risk of having worse oral health, compared to through other patients.

P 4: Um, so, so on top of what everyone has to say, I think it also depends on how person, you know, how much that progression that dementia had. And ho- is for that patient, and obviously if they're not that, um, bad then they can still, um, do the basic oral health hygiene stuff.

P 5: In my view, yes, there is a relationship to dementia and oral health.

**Can you tell me how you cope with oral care for a person with dementia on a daily basis?
Do you think it is more challenging because they have dementia?**

P 2: Prompting and encouraging. Do you know the behaviour you get to know your residents? And obviously we have mental capacity in place, so if they lack the capacity, you've act in their best interest so you can act in their best interest and go prompt them to brush the teeth and do that. But if they've refused you take that refusal.

P 6: We've got a lady or we go into every morning give her the toothbrush with the toothpaste on and she says, no and we have to respect her wishes.

P1: Um, we've got a lady on ground floor that will not wear no dentures and they're brand new. She was fitted for them. She won't wear them.

P2: Well we'll tell them the risk, we trying to encourage. And obviously that's part of what the care comprises then, isn't it? So when you meet with families and stuff, you'll explain this is the risks of the, obviously they're not brushing the teeth, but it's easy when someone's just got dentures. Cause if they've got the dentures, you start the dentures and you clean the dentures rather than the teeth. It's hard to move the teeth if they've got the dementia. Just reminding them to take care of the gums. Obviously you've got to remember the gums and it's about medication and stuff like that. You have to remember.

P 6: medication can dry mouth um stuff, you have to be careful, it's not good for their teeth.

P4: yeah

P5: By recommendations. Obviously if they've got a power of attorney, the resident, you can say that I need this and they should be spending money on it but there's nothing really we can do to make the families again they go and spend on the couch. I was just on, we can see we can recommend and ask, we need toothbrushes and toothpastes. Can you bring them in for us?

P3: Yes. We've got residents that won't, won't wear their dentures. So we modify the diet so that they're still so that they're still eating. So they'll have lot of softer foods and it's not because medically they need softer foods, it's just so that they can eat them without the dentures.

P4: I will agree with what RE 3 was saying.

P4: Uh, one person in the past. Yeah. But again, you have to just change the diet they are eating to make sure they're still getting all the nutrients and stuff for the needs are met as well.

Do you believe that in person with dementia oral health status changes after being diagnosed with dementia? Do you think that a person with dementia has bad or good or no change in oral health?

P1: I think yeah, uh, we just talked about it earlier. isn't that that oral health, yes, is always neglected, but once they have dementia, it's people start focusing on different things even if they're fall unwell, or even if they're not evaluated, they're being looked after in a care home. We focus more about their nutrition, and their mobility, because their mobility declines. At- At one point they get so depressed they don't even want to talk to anybody. So I think oral health is never the, on top priority lists as to look after

P 3: But I think in terms of, like, if you focused more, uh, on the oral health, yes, you do. Once you get diagnosed, I think the... chances that it is their oral health is better because of the support they get. So for example, now they have more carers or family's now more aware of, like, uh, if, this, um, this patient needs more contents.

P 4: oral care and oral health and how that needs to be reviewed? And so, like, in patients who don't have a proper diagnosis, it'd probably be worse, I think, in them, than someone who actually has a diagnosis.

P 5: Patients can be in such different positions of either neglect or... well, they even, the patient be diagnosed with dementia when they're... pretty well and taking quite good care of themselves, But all patients are diagnosed with dementia when they're at the point of no return, really, and they're in quite like a desperate state.

P 2: Yeah, I know, the thing is that I agree with both of... my, my colleagues, both point of views. That... that after the, after the diagnosis it can be positive correlation as well as negative correlation. Some people, and in some cases, uh, uh, the oral health might deteriorate after the diagnosis if they are not being, uh, supported well? And in some cases, in some patients, uh, oral health might actually improve after the diagnosis. Like you pointed out, that they have, uh, receive more support from the, uh, community or the, uh, hospital. So, there may, may be a possibility. I haven't determined yet.

P 6: I don't know if there is actually any relationship between the diagnosis

APPENDIX 9: LOCATIONS, DATES AND TIMES OF FOCUS GROUPS

FOCUS GROUP 1:

Location: [REDACTED]

Date: 12/11/2019

Time: 18:30

FOCUS GROUP 2:

Location [REDACTED]

Date: 16/01/2020

Time: 14:30 pm

FOCUS GROUP 3:

Location: [REDACTED]

Date: 06/02/2020

Time: 14:30 pm

APPENDIX 10: BASELINE DEMENTIA (WAVES 3-5) ASSOCIATED WITH POOR SROH IN THE FOLLOW-UP (WAVES 7-9). COMBINED DEMENTIA AND SEVERE COGNITIVE AS ONE GROUP.

Dementia/ Cognitive impairment from waves 3- 5	^a All participa nts n=5412	^a Incident poor SROH n= 564	%	*P	Model 1			Model 2			Model 3					
					OR	95%CI	P	OR	95%CI	P	OR	95%CI	P			
[‡] Normal and MCI	936	57	6.09	0.000	Ref											
Moderate Cognitive impairment	3981	426	10.70		1.61	1.20	2.16	0.002	1.50	1.11	2.02	0.008	1.49	1.10	2.02	0.009
Severe Cognitive impairment + dementia	315	50	15.87		2.24	1.45	3.46	0.000	2.00	1.28	3.13	0.002	1.90	1.22	2.98	0.005
Missing	180	31														

*P-value in the Chi-square test was calculated based on available data, not including those “missing” data.

Model 1: adjusted for age, gender, and education

Model 2: adjusted for Model 1 plus Equivalised total income in quintiles, Marital status, Smoking, Drinking alcohol over the past 12 months, BMI

Model 3: adjusted for Model 2 plus Hypertension, High blood cholesterol, Diabetes, Stroke, Heart attack, Lung disease, Asthma, Parkinson’s disease, Psychiatric condition, Osteoporosis.

^aTotal number of participants who were interviewed at both waves 3, 5 and 7 were n=5706. Excluded participants at w5 were n=294 (were aged <50 [n=80], poor SROH [n=214], leaving n= 5412 for analysis. No loss to follow up participants.

[‡] Due to the small number in the normal group (n=20) was combined with mild CI as a reference group. *Normal group:* All participants in the non-incident poor SROH group were n=19; participants in incident poor SROH n

APPENDIX 11: QUESTIONNAIRE FOR THE CASE-CONTROL STUDY

HEALTH & FACTOR QUESTIONNAIRE

This survey is about dementia and factors related to dementia. Don't be concerned if some questions appear a little odd or strange, some of them will not apply to you, but we have to ask the same sort of questions.

Please tell us if you do not understand the questions or do not wish to answer them.

The whole questionnaire will take about 45 minutes. We encourage a family member or a caregiver to help you complete the survey. **All of the information you provide will be entirely confidential.**

Interviewer No.

Participant No.

Date of Survey (DD/MM/YY): //

This interview was conducted with:

Participant only=1

Participant and the relative/friend=2

Part 1. Person history

Q1. What is your gender:

- Female=1
- Male=2

Q2. Date of Birth (DD/MM/YY): //

Q3. Where were you born? Town/place: _____

County: _____

Country: _____

Q4. What is your present marital status:

- Single=1
- Married or cohabitating=2
- Separated, but not divorced=3

- Widowed=4
- Divorced=5

Q5. What is the highest level of education you have completed?

- University degree course=1
- Other professional or technical qualification or diploma after leaving school=2
- Secondary school=3
- Primary School=4

Q6. How many years altogether have you gone to school or studied full time from the age of 5 years? Years:

Q7. Please give full and precise details of you and your husband/wife's occupation.

(if presently unemployed give details of last job)

- Your occupation: _____
- Description of your work: _____

- Husband/wife's occupation: _____
- Description of your work: _____

Q8. What are you and your husband/wife's employment status?

(if presently unemployed give details of the last job)=1 your:

- Employee not supervising other employees=2 your wife/husband's
- Employee supervising other employees=3
- Self-employed not employing others=4
- Self-employed employing others=5

Q9. How do you and your household occupy your accommodation?

- As an owner occupier (including purchase by mortgage) =1
- Rent free from local authority=2
- Rent from a private landlord, or in some other way by lease=3

Part 2. History of your home address: Please tell us your home addresses your earliest one which you know, as much as you are able to.

No	Home Address(house number, Street, county, city, country, Postcode)	Start date	End data
1			

2			
3			
4			
5			
6			
7			
8			
9			
10			
11			

12			
----	--	--	--

Part 3. Smoking

Q1. Do you smoke cigarettes now?

- Yes, regularly=1 (Go to Q2)
- No=2 (Go to Q5)
- Occasionally (Go to Q3)

Q2. On average, about how many cigarettes do you now smoke a day?

(Go to 7) Number:

Q3. On how many days a week do you smoke cigarettes?

- Usually on one day or less=1
- Usually on 2 to 4 days=2
- Almost every day=3

Q4. On average, how many cigarettes do you smoke a day?

Number:

Q5. Did you ever smoke cigarettes regularly in the past?

- Yes=1 (Go to 6)
- No=2 (Go to 9)

Q6. When did you stop smoking cigarettes regularly? Year:

If in the last 12 months

- Less than 1 month ago=1
- 1-6 months ago=2
- 6-12 months ago=3

Q7. What is the highest average daily number of cigarettes you have ever smoked for as long as a year? Number:

Q8. How old were you when began to smoke cigarettes regularly? Age:

Q9. Have you ever smoked cigars/cigarillos?

- Now smoke regularly=1 (Go to 10)
- No=2 (Go to 11)
- Now smoke occasionally (less than one/day)=3 (Go to 10)
- Used to, but not now=4 (Go to 11)

Q10. How many do you smoke per week? Number:

Q11. Have you ever smoked a pipe?

- No smoke regularly=1 (Go to 12)
- No=2 (Go to 13)
- No smoke occasionally (less than once a day) =3 (Go to 12)
- Used to, but not now=4 (Go to 13)

Q12. About how many grams of tobacco do you smoke per week?

Grams:

Part 4. Exposure to tobacco smoke

Q1. Have you been exposed to tobacco smoke from other people?

- No, none at all=1 (Go to Part 5)
- Yes, a little=2
- Yes, some=3
- Yes, a lot=4

if a lot, about how many years:

Q2. Have you been exposure to tobacco smoke from someone else at home?

- No, none at all=1
- Yes, a little=2
- Yes, some=3
- Yes, a lot=4

if a lot, about how many years:

Q3. Have you been exposure to tobacco smoke from someone else at work?

- No, none at all=1
- Yes, a little=2
- Yes, some=3
- Yes, a lot=4

if a lot, about how many years:

Q4. Have you been exposure to tobacco smoke from someone else outsidess other than work?

- No, none at all=1
- Yes, a little=2
- Yes, some=3
- Yes, a lot=4

if a lot, about how many years:

Part 5. Diet intake questionnaire

Vitamin

Q1. How often did you take multi-vitamins during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q2. How often did you take vitamin B during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q3. How often did you take vitamin E during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q4. How often did you take vitamin D during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Drink

Q5. How often did you drink cup of coffee during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q6. How often did you drink a glass of wine during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q7. How often did you drink a half pint of beer during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q8. How often did you drink a single measure of spirits or sherry during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Fish and meat

Q9. How often did you take white fish (cod, haddock, hake, plaice or fish fingers, etc.) during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q10. How often did you take kippers, herrings, pilchards, tuna, sardines, salmon or mackerel (including tinned) during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q11. How often did you take beef (including minced beef, beef burgers) during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q12. How often did you take lamb during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q13. How often did you pork or bacon or ham during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q14. How often did you take chicken, turkey, or other poultry during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q15. How often did you take liver or kidney or heart during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q16. How often did you take butter, soft margarine, or hard margarine during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q17. How often did you eat home-fried food (including chips) during the past two years?

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Vegetables and fruit

Q18. How often did you take a serving of vegetables during the past two years?

(Note that one portion of salad or vegetables counts as a serving)

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Q19. How often did you take a serving of fruit during the past two years?

(Note that one fruit counts as a serving)

- Never take=1
- =<Once a week=2
- >Once a week and < Daily=3
- Once a day=4
- >= Twice a day=5

Part 6. Oral health (Please check ✓ one best answer for each question)

Q1. Would you say your dental health (mouth, teeth and/or dentures) is?

- Very Good 1
- Good 2
- Fair 3
- Poor 4
- Very Poor 5

Q2. Related to self-reported oral health questions:

	Did you ever had	Always	Frequently	Often	Occasionally	Never
		1	2	3	4	5
2.1	Teeth problems limit foods	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2.2	Difficulties swallowing food	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2.3	Sip liquid to aid swallowing food	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2.4	Mouth feel dry when eating food	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Q3. Questions on oral hygiene:

		Always	Frequently	Often	Occasionally	Never
		1	2	3	4	5
3.1	Do you wear denture	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.2	Do you use dental floss to clean teeth / denture	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.3	Do you use dental rinse product or mouthwash to clean your mouth	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Q4. How many times a day do you brush your teeth?

- Do not brush 1
- Less than once 2
- once 3
- twice 4
- more than twice 5

Q5. How often do you visit a dentist?

- Every six months 1
- Once a year 2
- Every two years 3
- More than 2 years 4
- Try to avoid or never been to dentist 5

Q6. How many natural teeth do you have in your mouth?

- _____ 1
- Unknown 2

Q7. Do you think you have gum disease?

- Yes 1
- No 2

Q8. (Please check ✓ one best answer for each line)

Gum related questions						
Have you ever had:		Always	Often	Sometimes	Rarely	Never
		1	2	3	4	5
8.1	Bleeding gums	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8.2	Swollen gums	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8.3	Painful gums	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8.4	Oral ulcers	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8.5	Bad breadth or taste	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Q9. Self-reported periodontal problems related questions:

Have you ever:	
9.1	Noticed that your front teeth have moved forward (toward the lip) or that gaps have developed between your front teeth? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know
9.2	Had any teeth that became loose on their own, without any injury? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know
9.3	Had treatment for gum disease, such as scaling and root planning, sometimes called "deep cleaning" <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know
9.4	Been told by a dental professional that you lost bone around your teeth

	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know
9.5	Had any tooth decay/caries <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know
9.6	Had Felt cold/hot sensation in teeth <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Don't know

Q10. Have you ever had lost teeth without injury or being extracted by dentist?

Yes No Don't know

If yes, please check ✓ below for any oral disease problems:

Oral problems	No. of tooth loss
• 1 <input type="checkbox"/> Tooth decay/caries	1 <input type="checkbox"/> ____ . 2 <input type="checkbox"/> unknown
• 2 <input type="checkbox"/> Gum disease (<i>bleeding, swollen, painful gums</i>)	1 <input type="checkbox"/> ____ . 2 <input type="checkbox"/> unknown
• 3 <input type="checkbox"/> Periodontal problems (<i>Bone lose around teeth or Loose tooth</i>)	1 <input type="checkbox"/> ____ . 2 <input type="checkbox"/> unknown
• 4 <input type="checkbox"/> Trauma or injury	1 <input type="checkbox"/> ____ . 2 <input type="checkbox"/> unknown
• 5 <input type="checkbox"/> other condition _____	1 <input type="checkbox"/> ____ . 2 <input type="checkbox"/> unknown
	1 <input type="checkbox"/> ____ . 2 <input type="checkbox"/> unknown

Part 7. Medical condition and diseases

Q1. Have you ever been told that you had high blood pressure?

- Yes=1 (Go to 2)
- No=2 (Go to 5)
- Unknown=9 (Go to 5)

Q2. When you were first told?

- 0 to 5 years ago=1
- 5 to 10 years ago=2

• 10 or more years ago=3
Q3. Were you started on treatment?

- Yes=1
- No=2

Q4. Are you still on treatment?

- Yes=1
- No=2

Q5. Have you ever been told that you had heart trouble?

- Yes =1 (Go to 6)
- No =2 (Go to 8)
- Unknown=9(Go to 8)

Q6. When you were first told?

- 0 to 5 years ago=1
- 5 to 10 years ago=2
- 10 or more years ago=3

Q7. What did the doctor say it was?

- Heart attack=1
- Angina=2
- Heart failure=3
- Valve disease=4
- Other=5

Q8. Have you ever been told that you had high blood cholesterol?

- Yes=1 (Go to 9)
- No=2 (Go to 11)
- Unknown=9 (go to 11)

Q9. When you were first told?

- 0 to 5 years ago=1
- 5 to 10 years ago=2
- 10 or more years ago=3

Q10. Are you taking pills to lower your blood cholesterol level during last two weeks?

- Yes=1
- No=2

Q11. Have you ever had a stroke that needed medical attention?

(Note only if clear history of sudden onset of unilateral paralysis, and/or loss of speech, and/or blindness lasting for at least 2 days)

- Yes =1 (Go to 12)
- No =2 (Go to 13)
- Unknown=9 (Go to 13)

Q12. Who diagnosed this stroke?

- No one=0
- GP=1
- Specialist=2

Q13. Have you ever developed sudden weakness of a limb, loss of speech, or partial blindness which got better quickly, in less than one day? (*Doctors sometimes call these attacks transient ischemic attack, TIAs*).

- Yes=1
- No=2
- Unknown=9

Q14. Have you ever had a serious head injury in which you were knocked out?

- Yes=1
- No=2 (Go to 17)
- Unknown=9 (Go to 17)

Q15. How long were you unconscious? (in hours and or minutes) _____

Q16. When was this happen?

- 0 to 5 years ago=1
- 5 to 10 years ago=2
- 10 or more years ago=3

Q17. Have you ever been told that you had diabetes?

- Yes=1
- No=2 (Go to 19)
- Unknown=9 (Go to 19)

Q18. Do you need a special diet, take tablets, or have insulin injections?

- Diet alone=1
- Oral hypoglycaemics=2
- Insulin=3
- No treatment= 4

Q19. Have you ever been told that you had Parkinson's disease?

- Yes=1 (Go to 20)
- No=2 (Go to 21)
- Unknown=9 (go to 21)

Q20. When was the first diagnosed?

- 0 to 5 years ago=1
- 5to 10 years ago=2
- 10 or more years ago=3

Q21. Have you been told that you had chronic obstructive pulmonary disease (COPD)?

- Yes=1
- No=2 (Go to 23)
- Unknown=9(Go to 23)

Q22. When was the first diagnosed?

- 0 to 5 years ago=1
- 5 to 10 years ago=2
- 10 or more years ago=3

Q23. Have you ever been told that you had depression?

- Yes=1
- No=2
- Unknown=9

Q24. Have you even been told that you had kidney disease?

- Yes=1
- No=2
- Unknown=9

Q25. Have you ever been told that you have dementia?

- Yes=1 (Go to 26)
- No=2 (Go to social support part)

Q26. What type of dementia do you have?

- Alzheimer disease=1
- Vascular dementia=2
- Mixed dementia=3
- Other=4
- Do not know=9

Q27. When you have a diagnosis?

- Within 12 months=1
- More than 12 months ago=2

Q28. Did your mother or father have dementia?

- Yes=1
- No=2
- Don't know=9

Q29. Did your brothers and sisters have dementia?

- Yes=1
- No=2
- Don't know=9

Q30. Did any of relatives have dementia?

- Yes=1
- No=2
- Don't know=9

Part 7. Social network

Q1. How far away in distance does your nearest (in terms of distance) relative live?

Excluding spouse

- Same house/0.5mile=1
- 0.5-4 mile=2
- 4-10mile=3
- 10-30 mile=4
- 30 mile+=5
- No relatives=9

Q2. If you have any children, where does your nearest child live?

- Same house/0.5mile=1
- 0.5-4 mile=2
- 4-10mile=3
- 10-30 mile=4
- 30 mile+=5
- No children=9

Q3. If you have any living sisters or brothers, where does your nearest sister of brother live?

- Same house/0.5mile=1
- 0.5-4 mile=2
- 4-10mile=3
- 10-30 mile=4
- 30 mile+=5
- No siblings=9

Q4. How often do you see any of your children or other relatives to speak to?

- Daily=1
- 2-3 times a week=2
- At least weekly=3
- At least monthly=4
- Less often=5
- Never/no relatives=9

Q5. If you have friends in this community/ neighborhood, how often do you have a chat or do something with one of your friends?

- Daily=1
- 2-3 times a week=2
- At least weekly=3
- At least monthly=4
- Less often=5
- Never/No friends=9

Q6. How often do you see any of your neighbors to have a chat with or do something with?

- Daily=1
- 2-3 times a week=2
- At least weekly=3
- At least monthly=4
- Less often=5
- No contact with neighbors=9

Q7. Do you attend any religious meeting?

- Yes, regularly=1
- Yes, occasionally=2
- No=3

Q8. Do you attend meetings of any community/ social groups, such as clubs, or lecture?

- Yes, regularly=1
- Yes, occasionally=2
- No=3

Thank you for participation

APPENDIX 12: CHARACTERISTICS AND FINDINGS OF THE COHORT STUDIES IDENTIFIED FOR SYSTEMATIC REVIEW (DEMENTIA AND COGNITIVE IMPAIRMENT ASSOCIATED WITH PD RISK STUDIES)

Authors (publication year); study location	Type of study, participants' characteristics and recruitment	Sample size and follow-up	Baseline dementia /cognitive impairment diagnosis criteria and endpoint outcome: PD diagnosis criteria	Adjustment for confounders and main findings	Comments
Ship and Puckett et al. (1994); U.S.A	Age: 65 or above Recruited community-dwelling persons who were participants of a National Institute on Aging study.	Sample size 42 subjects recruited: - 21 AD - 21 without AD matched for age and gender Follow up AD: 23±11 months Controls: 36±1.5 months	Baseline AD: NINCDS-ADRDA and MMSE for severity Endpoint outcome PD: GB, PPD, and CAL	Student t-test and Mann-Witney U procedure and a two-way Fisher exact test for prevalence were used. Pocket depth decreased significantly over time in both control ($p < 0.01$) and AD individuals ($p = 0.04$). However, no significant differences were found between the two groups <i>CAL</i> : the control group showed improvement over the 3-year follow-up period ($p = 0.00$) but AD subjects did not.	The study had a short follow-up period of 2-3 years, which was insufficient for gingivitis leading to periodontitis. Moreover, it was unable to examine the effects on oral health status owing to a limited sample size. Therefore, the study does not determine whether AD progression leads to PD. Furthermore, it was not adjusted for confounders (e.g., smoking, alcohol, education etc.) which might have resulted in non-significant association.
Chen et al. (2010); USA	Age: 44-102 years 1,626 older adults who received dental care as new patients from the Wilder Senior Dental Clinic in St. Paul, Minnesota, were selected.	Sample size 491 participants were recruited: - 119 dementia - 372 without dementia Follow up Mean: 3.2 years	Baseline AD, other dementia: CBS or ICD-9CM-R codes 290.x, 294.1, 331.2 Medical, cognitive and functional assessment: dental records Endpoint outcome	Cox, Poisson, and negative-binomial regressions were used for analysis. Oral health remains poor in older adults with dementia. More than 30% of participants with dementia presented with heavy calculus, dental plaque or GBI.	The criteria used by the dentist for measuring PD are not explained, and there was no calibration of intra- or inter-dental examiners. Poor oral health of participants with dementia on arrival will lead to a comprehensive dental treatment plan to prevent caries and PD. Thus, dementia alone had no statistically significant effect on tooth survival under the current models of dental care.

			Calculus, plaque, and gingival bleeding were diagnosed by the dentist	Crude OR, calculated from the data given in the article, was 1.61 (0.19-13.77).	
Kamer <i>et al.</i> (2012); Denmark	Age 70 or above 698 participants selected from Copenhagen County Hospital and the County Mental Hospital in Glostrup, Copenhagen, Denmark, 1964	Sample size 152 participants were present for final analyses Follow up 20 years	Baseline Clinical: WAIS, which measures several domains of cognitive function: DST and BDT Endpoint outcome MCPI	Multivariate logistic regression adjusted for education, cognitive test at age 50, gender, ECG signs of cardiac ischemia, CVDR score, smoking, alcohol, DFT scores and PI. OR for a low versus high DST score with PD was 7.00 (1.74-28.16), p=0.006	Although homogeneity of the study population was generally considered a strength of this study, it may limit the generalisability of the findings. PD diagnosis could be performed using a more reliable method, as MCPI is not sensitive enough to differentiate between gingivitis and less severe forms of periodontitis.
Naorungroj <i>et al.</i> (2013); USA	Age: 46-64 years Participants were selected from the ARIC study. In 1990-1992 (visit 1) and in 1996-1998 (visit 4), 10,050 participants answered dental screening questions, and 8,782 dentate participants received oral examination.	Sample size 5,878 dentate participants with complete forms were included in final analyses Follow up Six years	Baseline DWR, WF, DSST Endpoint outcome CDC/AAP 'severe' definition and gingival inflammation	Multiple logistic regression (binary, multinomial and linear regression models) adjusted for age, gender, race, education, smoking, alcohol and medical history. Cognitive decline over six years was reported along with oral health conditions Adjusted OR DST: 1.05 (0.97, 1.13) Adjusted OR DWR: 0.99 (0.92-1.06) Adjusted OR WF: 0.98 (0.91-1.05)	Self-reported behaviours are less reliable in people who experience cognitive decline, as non-compliance with routine oral hygiene care may be an initial sign of altered cognitive processes. Dentate participants who received periodontal examinations were more likely to have better cognitive ability than those who did not, leading to an overestimation of the association between cognitive decline and periodontitis.
Zenthofer <i>et al.</i> (2016);	Age: 54-102 Mean age: non-	Sample size 219 participants recruited for final	Baseline Cognitive impairment: MMSE	Linear regression models were used with confounders (age, gender, dementia, number of co-morbidities, coagulation inhibitors, and	Dementia evaluation was not detailed enough: only MMSE was used to examine the participants which is used for screening not for diagnosing

Germany	<p>dementia 80.7 years, dementia 84.6 years</p> <p>277 participants were selected from 14 nursing homes chosen to be representative of all nursing homes in Baden-Württemberg</p>	<p>analysis</p> <p>-136 dementia participants - 83 non-dementia participants</p> <p>Follow up Six months</p>	<p>Endpoint outcome CPITN, GBI</p>	<p>number of permanent medications).</p> <p>Prevalence of severe Periodontitis: higher risk for cognitive impairment participants to suffer from severe periodontitis</p> <p>CPITN: OR 2.9 (1.37-6.15), p = 0.006</p>	<p>dementia. That is why in this study it was used as cognitive impairment study.</p> <p>The study had a short follow-up period of 6 months. The target population was taken from nursing homes in Germany, and therefore represented a particular group and not the general population.</p>
<p>Ma et al. (2021); Taiwan (China)</p>	<p>Age: ≥ 50 years</p> <p>42,269 participants were selected from LHID.</p>	<p>Sample size</p> <p>- Dementia patients n=8640 and AD patients among dementia patients n=606 - Non-dementia patients n= 8640 and non-AD patients among non-dementia patients n=606</p> <p>Follow up 13 years</p>	<p>Baseline Dementia: DSM-5</p> <p>Endpoint outcome PD, CAL and BOP</p>	<p>Cox regression hazard model adjusted for age, sex, income, urbanisation, co-morbidities (diabetes, stroke, hypertension, traumatic brain injury, COPD, CVD, HLD), and socioeconomic status.</p> <p>HR of developing PD in dementia patients compared to non-dementia patients was:</p> <p>Dementia: 1.92 (1.77-2.08) AD: 1.67 (1.24-2.23)</p>	<p>This study was well planned and is of high quality, according to NOS. However, the severity of PD could not be recorded because full-mouth examination data was not included. Furthermore, the possibility of overestimation of the impact of dementia on PD risk cannot be ignored; further studies to validate these results are required so that these results can be generalised.</p>

APPENDIX 13: CHARACTERISTICS AND FINDINGS OF THE CASE-CONTROL STUDIES IDENTIFIED FOR SYSTEMATIC REVIEW (DEMENTIA AND COGNITIVE IMPAIRMENT ASSOCIATED WITH PD RISK)

Authors (publication year); study location	Type of study; participants' characteristics and recruitment	Sample size	Baseline dementia/cognitive impairment diagnosis criteria and endpoint outcome PD diagnosis criteria		Comments
Aragon <i>et al.</i> (2017); Spain	Mean age of AD patients = 77.4 ± 10.6 years; healthy controls = 62.6 ± 7.1 years 106 AD participants were recruited at the Alzheimer Centre Reina Sofia Foundation and at the Alzheimer State Reference Centre (and other dementias). The healthy control were selected from patients' caregivers	106 participants - 70 AD cases - 36 healthy controls	Baseline: AD: NINCDS-ADRDA criteria Endpoint outcome CPI	Student t-test, chi-square, Spearman's correlation coefficients and stepwise linear regression were used for analysis. Sextants of AD and control groups were observed. Healthy sextants coded as CPI = 0 (0.1 ± 0.4 vs 1.4 ± 2.1) and sextants with bleeding on probing, coded as CPI = 1 (0.0 ± 0.3 vs 1.0 ± 1.4)	Participants selected for the control were younger in age. Therefore, linear regression analyses for assessing the influence of age and the presence of AD within the clinical outcome variables findings might reduce the scientific evidence found. Also, findings indicating poor OH in AD patients may be due to caregivers not prioritising daily oral hygiene routines as AD progresses.
Gil Montoya (2017); Spain	Control mean age: 79.8 years (8.3 years); Case: group 1 and 2 mean age 78.25 years (7.6 years) 324 cases were elderly individuals selected from the neurology departments of two	Without cognitive impairment (n=324) Group 1: MCI /mild dementia (n=107) Group 2:	Baseline Dementia: DSM-IVR AD: NINCDS-ADRDA MCI criteria: Neurological, behavioural and dementia study group of Spanish society, and photo-test	Bivariate associations between the sociodemographic, health behaviour, and oral health variables and mild cognitive impairment/mild dementia, moderate/severe dementia, and controls. Logistic regression (brushing) and linear regression (PI and BI index) for gums was adj. for age, gender, SES, schooling, tobacco and alcohol.	It is difficult to find a causal relationship, and the results can be seen as a bidirectional relationship between dementia/ cognitive impairment and oral health/PD. It is unclear from this study if poor oral hygiene was due to dementia or lack of support from caregivers in providing oral care. Another limitation

	hospitals. 240 controls were selected from different primary care centres	Moderate/severe dementia (n=133)	Endpoint outcome CAL, BOP, PPD	Periodontitis was severe in 79.5% of cases and 49.2% of controls. For cases of severe cognitive impairment, BI was higher Crude OR was calculated from the data given in the article. Cognitive impairment was 2.71 (1.32-5.57) and Dementia was 2.90 (1.45-5.80)	was that, apart from the bleeding index, oral measures such as CAL and PPD were not adjusted with covariates
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APPENDIX 14: CHARACTERISTICS AND FINDINGS OF ALL COHORT STUDIES IDENTIFIED FOR THE SYSTEMATIC LITERATURE REVIEW EXAMINING THE ASSOCIATION OF PD WITH DEMENTIA RISK

Authors (publication year); study location	Participants' recruitment and sample size	A baseline measure of PD; Follow up and Endpoint outcomes: Dementia cases and diagnosis criteria	Adjustments for confounders and main findings	Comments
Arrive <i>et al.</i> (2012); France	Age: 66-80 years 2792 participants were recruited from PAQUID. Sample size 405 participants were selected for final analyses	Baseline: CPI Follow up: Over 10 years Endpoint outcomes: 72 participants developed dementia, including 61 AD. <i>Dementia:</i> DSM-III R criteria <i>AD:</i> NINCDS-ADRDA criteria <i>Vascular dementia:</i> Hachinski score.	Cox proportional hazard regression adj. for gender, BMI, diabetes, depression, hypertension, and ischemic cardiopathy/ history of brain stroke. Adj. HR for dementia in high educated patients (n=312) with tooth bleeding/calculus was 0.71(0.31-1.63) and periodontal pockets 0.42 (0.15-1.15). The matched HRs of dementia in low educated patients (n=92) were 1.24 (0.39-3.88) and 0.97 (0.29-3.19).	Poor dental conditions were not associated with reduced dementia risk in the higher and lower education. Further investigation is warranted and the generalization of the results of the study should be carried out with caution.
Tzeng <i>et al.</i> (2016); Taiwan (China)	Age: ≥ 20 years 2,888 patients with newly diagnosed CP and gingivitis, and age-sex matched controls without CP and gingivitis; both recruited from the LHID. Sample size: A total of 8,828 participants including: - 2,207 patients with CP and gingivitis - 6,621 controls without CP and gingivitis	Baseline: ICD-9-CM codes 523.4 (CP) and 523.1 (CG) Follow up: 10 years Endpoint outcome: 86 patients diagnosed with dementia include: 25 patients with CP and gingivitis and 61 patients without CP or gingivitis <i>Dementia:</i> DSM-IV or DSM IV Text Revision including AD, vascular dementia, and non-vascular dementia: ICD-9-CM codes 290.0, 290.10–290.13, 290.20–290.21, or 290.3, 331.0, 290.41–290.43 and 290.8–290.9	Cox proportional hazard regression adj. for age, gender, co-morbidities geographical area of residence, urbanisation level of the residence, and monthly income. Adj. HR for dementia in patients with CP and gingivitis was 2.54 (95% CI 1.55–4.16)	The NHIRD database might not have recorded all data accurately as this data was recorded in stages. Educational levels of the insured were not included in the NHIRD, and potential selection bias could exist. Also, it was unable to examine the effects in participants according to age as a combined analysis was done for participant's aged 20 to 102 years.

<p>Lee Y.L et al. (2017); Taiwan (China)</p>	<p>Age: ≥ 45 years 285,835 subjects were selected from the LHID</p> <p>Sample size 182,747 participants had PD according to ICD-9-CM diagnosis</p>	<p>Baseline: ICD-9-CM codes</p> <p>Follow up: 10 years</p> <p>Endpoint outcome: 6,133 participants developed dementia. <i>Pre-senile dementia, vascular dementia, senile dementia, or AD:</i> ICD-9-CM codes 290.X, 331.0</p>	<p>Cox proportional hazard regression adj. for age, sex, socio-economic status, residential area, and comorbidity variables</p> <p>Adj. HR for dementia in PD patients who had teeth extracted was 1.10 (1.04-1.16) and 1.14 (1.04-1.24) respectively, in those who did not have treatments compared to 1.18 (0.97-1.43) in patients who received intensive treatments.</p>	<p>The treatment codes in the data may reflect the level of inflammation (dental prophylaxis, PD intensive treatment, and PD with tooth extraction) as ICD-9-CM codes do not classify the level of inflammation or severity of PD. Tooth loss number was given, which could have confirmed the IR and dental effect of dental prophylaxis in protecting against dementia which may have been underestimated in the older age groups.</p>
<p>Lee Y.T et al. (2017); Taiwan (China)</p>	<p>Age: ≥ 65 years Equal numbers of patients with newly diagnosed periodontitis and age-sex matched controls were recruited from LHID.</p> <p>Sample size 6,056 participants in total, including: -3,028 participants with periodontitis -3,028 participants without periodontitis</p>	<p>Baseline: ICD-9-CM codes 523.3–5</p> <p>Follow up: 10 years approximately</p> <p>Endpoint outcome: <i>Dementia :</i> ICD-9-CM codes 290.0–290.4, 294.1, 331.0–331.2</p>	<p>Cox proportional hazard regression adj. for age, sex, geographic region, urbanisation level, periodontitis, hypertension, diabetes mellitus, stroke, cardiovascular disease, and chronic kidney disorder and comorbidities</p> <p>Adj. HR for dementia in participants with PD versus those without PD was 1.16 (1.01–1.32).</p>	<p>Data extracted contained many factors, but it still lacked a few variables like genetic factors, education level, more-complex socio-demographic characteristics, and lifestyle factors e.g. smoking and alcohol. Therefore, it is likely that if they were considered, the significance of the results would have been non-significant.</p> <p>ICD codes do not inform about the severity of PD and the development of dementia; thus, the study cannot find sub-group analyses.</p>
<p>Chen et al. (2017); Taiwan (China)</p>	<p>Age: ≥ 50 years 10,592 patients newly diagnosed with CP. Age, sex, index year, comorbidity, and urbanisation level matched controls without CP, both recruited from the NHIRD.</p>	<p>Baseline: ICD-9-CM codee 523.4</p> <p>Follow up: 11.9 years (± 2.6) in participants with CP and 12.2 years (± 2.6) in participants without CP.</p> <p>Endpoint outcome: 115 participants with CP and 208 participants without CP were diagnosed with AD.</p>	<p>Cox proportional hazards regression adj. for hypertension, hyperlipidaemia, chronic kidney disease, depression, stroke, traumatic brain injury, diabetes mellitus, Charlson co-morbidity index score and urbanisation level</p> <p>In patients with 10 years of CP exposure, the adj. HR for AD was 1.71 (1.15–2.53).</p>	<p>AD and dementia may overlap in this study because authors could not clarify from the medical records of all defined AD which may overestimate results as there were not able to sub-analyse dementia and all types of dementia groups from AD.</p> <p>NHIRD did not provide personal information regarding specific and definite variables relevant</p>

	<p>Sample size 27,963 participants including: -9291 participants with CP -18,672 patients without CP.</p>	AD: ICD-9-CM code 331.0		to this association, such as education level and smoking which may cause residual confounding.
<p>Choi et al. (2019); South Korea</p>	<p>Age :50_≥ years 262,349 participants were selected from the Korean National Health Insurance Service (NHIS) database</p> <p>Sample size Cases n=46,344 Control n=216,005</p>	<p>Baseline: ICD-10 code K05.3 and having undergone at least one of the CP treatments.</p> <p>Follow up: 11 years</p> <p>Endpoint outcome AD: ICD-10 codes (F00, G30) VaD: ICD-10 code (F01)</p>	<p>Cox proportional hazard regression adj. for age, gender, household income, smoking status, alcohol consumption, physical activity, BMI, systolic blood pressure, fasting serum glucose, total cholesterol, and Charlson Comorbidity Index.</p> <p>Adj. HR for dementia in CP patients</p> <p>Overall dementia: 1.06 (1.01-1.11) AD: 1.05(1.00-1.11) VaD: 1.10 (0.98-1.22)</p>	One of the main links between PD and dementia risk is inflammation. In this study, the inclusion criteria of participants included having any PD treatment might recently have led to more conservative findings due to less severe PD present in patients when analysed.
<p>Demmer et al. (2020); USA</p>	<p>Age: 63 years; SD (6 years)</p> <p>Participants were selected from 4th visit n=11,656 were eligible for inclusion taken from ARIC study</p> <p>Sample size 4,559 participants for final sample analysis</p>	<p>Baseline: <i>Periodontal profile class:</i> PD, AL, BOP</p> <p>Follow up: 18 years approximately</p> <p>Endpoint outcome: <i>Dementia:</i> DSM-V <i>AD:</i> NIA-AA <i>Vascular MCI/dementia:</i> NINDS-AIREN</p>	<p>Cox proportional hazards models adjusted for age, sex, education, and race-centre (5-level variable), income, and insurance time-dependent BMI, physical activity, and time-dependent cigarette smoking, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, heart failure, and APOE genotype, antihypertension medication, systolic blood pressure, prevalent CHD and stroke at visit 4, dental visit requery, longitudinal BMI, and smoking information at visits 5 and 6</p> <p>Multivariable adj. HR for incident dementia among participants with severe PPC or edentulism (vs periodontal healthy) were HR 1.22 (1.01–1.47) and HR 1.21 (0.99–1.48), respectively.</p>	This study might have participants with cognitive decline before the diagnosis of PD and tooth loss, which could influence the results, as assessment of PD was done at a mean age of 63 years. This study had more MCI cases than dementia cases at the end of follow up, and results were not given separately to observe PD impact on dementia risk, which could have overestimated the results.

<p>Lee Y.C et al. (2020); Taiwan (China)</p>	<p>Age: ≥ 50 years</p> <p>Equal numbers of patients with newly diagnosed periodontitis and controls with age-sex matched controls were recruited.</p> <p>Sample size Cases: 56,018 with PD and Controls: 56,018 without PD</p>	<p>Baseline: ICD-9-CM code 523.4</p> <p>Follow up: 13 years</p> <p>Endpoint outcome: <i>Dementia:</i> ICD-9-CM codes 290.0 and 331.0</p>	<p>Cox proportional hazard regression adjusted for age, gender, income, medical conditions, (hypertension, mental disorder, diabetes, ischemic heart disease, stroke, hyperlipidaemia, COPD, heart failure, traumatic brain injury), influenza vaccination, use of statins and metformin.</p> <p>Adjusted HR for dementia in participants with PD versus those without PD was 1.73 (1.61–1.86).</p>	<p>The severity of periodontitis was not provided in detail as it was not available in NHI database. Definition of periodontitis was based on the physician's diagnosis and treatment during medical visits. The potential for misclassification of PD is present because some people with mild periodontitis might not seek medical care. This dataset lacked information on the patients' detailed socioeconomic status, lifestyle, laboratory data, and medication compliance which could increase the possibility of residual confounding.</p>
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APPENDIX 15: CHARACTERISTICS AND FINDINGS OF CASE-CONTROL STUDIES IDENTIFIED FOR THE SYSTEMATIC LITERATURE REVIEW EXAMINING THE ASSOCIATION OF PD WITH DEMENTIA RISK

Authors (publication year); study location	Participants' characteristics, recruitment and sample size	A baseline measure of PD/ Endpoint outcomes: Dementia cases and diagnosis criteria	Statistical analysis; Adjustment for confounders and Findings	Comments
<p>Stein et al. (2012); U.S.A</p>	<p><i>Mean age of Controls = 70 years; MCI=72.1 years; AD=74.1 years.</i></p> <p><i>Participants were recruited from a subset of the BRAINS research.</i></p> <p>Sample size 158 participants</p>	<p>Baseline BOP and AAP classification used for diagnosis of CP</p> <p><i>Serum Sample:</i> Venous blood draws of the study participants</p> <p>Endpoint outcome In 81 cases, 35 participants developed AD, and 77 controls were cognitively intact</p> <p><i>AD: NINCDS-ADRDA</i> <i>Serum Sample:</i> IgG antibody were analysed using enzyme-linked immunosorbent assay.</p>	<p>Wilcoxon rank-sum test and general linear regression adj. for baseline age, baseline MMSE, years of education, gender, diabetes, smoking status and apolipoprotein epsilon 4</p> <p>Bonferroni correction for multiple comparisons was used.</p> <p>Antibody levels to F. nucleatum and P. intermedia were significantly increased (p=0.05) at baseline serum draw in the patients with AD compared with controls.</p>	<p>As this was a case-control study design, there is further need for additional cohort studies, profiling related oral clinical parameters with systemic response and AD, to evaluate whether any cause-and-effect association are warranted.</p>
<p>Chu et al. (2014); China</p>	<p>Age \geq60 years</p> <p><i>Recruited cases from day-care centres of the Hong Kong Alzheimer's Disease Association and St. James' Settlement Kin Chi Dementia Care support service centre. Healthy controls without dementia</i></p>	<p>Baseline CPI</p> <p>Endpoint outcome 59 dementia cases and 59 controls were matched for sex and age.</p> <p><i>Dementia:</i> 47 dementia cases and 50 controls were examined for PD evaluation.</p>	<p>A parametric t-test and chi-square were used for analysis.</p> <p>Adjusted RR was not presented. RRs* in dementia patients compared to non- dementia patients were as follows:</p> <p>-Moderate PD: 1.10 (0.58-1.68) -Severe PD: 1.25 (0.63-1.81)</p>	<p>It has not been mentioned why they were 21 missing participants in periodontal status examinations results. There is a chance of residual confounding as it was not adjusted with different covariates.</p>

	<p>from the registered list who attended Prince Philip dental hospital were invited</p> <p>Sample size 118 participants</p>			
De Souza et al. (2014); Brazil	<p>Mean ages: 75.17 years in cases and 61.17 years in controls</p> <p>Patients were recruited from the Cognitive Neurology and Behaviour Group of the Neurology Department of the University of Sao Paulo. Controls were older people without AD (relatives of the patients).</p> <p>Sample size 59 participants</p>	<p>Baseline: GBI, PPD and CAL</p> <p>Endpoint outcome: 29 AD cases and 30 controls were matched for age and gender</p> <p>AD: NINCDS-ADRDA and MMSE score for severity.</p>	<p>One way ANOVA and non-parametric tests (Chi-square and Fisher's exact tests) were used.</p> <p>Adj. RR was not presented.</p> <p>RRs* in AD patients compared with control group were as follows:</p> <p>-Mild PD: 2.12 (1.15-2.63) -Moderate PD: 1.13(0.25-2.32) -Severe PD: 2.12 (0.97-2.68)</p>	<p>Adjustments for confounding factors were not done for the analysis, which could lead to bias or confounding.</p> <p>In addition, mild AD patients were chosen because they were able to answer the questionnaires, which may not be the case for more severe patients. The dentist was not blinded to participant status as a case or control subject, leading to bias.</p>
Bramanti et al. (2015); Italy	<p>Recruited participant's from IRCSS staying at "Neurolesi Bonini-Pulejo" in Messina having mean age in the VaD group was 86.7±6.2 years and control group was 80.2 ± 7.4 years.</p> <p>Sample size 168 participants</p>	<p>Baseline: BOP and PPD</p> <p>Endpoint outcome 86 VaD cases and 82 healthy controls</p> <p>VaD: Imaging evidence of cerebrovascular disease and additional clinical features, MMSE (Italy version)</p>	<p>Chi-square and Fisher exact test were applied for categorical variables</p> <p>Adjusted RR was not presented. RR* in VaD patients compared with the control group was as follows: BOP positive: 4.22 (3.10-5.03)</p>	<p>The data analysis did not consider additional covariates apart from age. Therefore, it is likely that other essential determinants like smoking, alcohol, education, dietary habits etc., have been missed. The control subjects were reported to be younger than the cases. Thus, it is difficult to rule out the fact that it might have affected the results since increased age is associated with cognitive impairment.</p>
Gil-Montoya et al. (2015); Spain	<p>Age: 51 to 98 years</p> <p>Cases were recruited from the Neurology Departments of two hospitals. Controls</p>	<p>Baseline: PPD, CAL and BI</p> <p>Endpoint outcome 180 cases and 229 controls</p>	<p>Multiple logistic regression analysis was used and adj. for age, sex, CAL, number of teeth, oral hygiene habits and hyperlipidaemia.</p>	<p>Separate findings for dementia and cognitive impairment in the final analyses were not given. Also, the reference group was not separated from mild PD, which lowers the significance of the results.</p>

	were patients being seen in primary healthcare for problems other than dental or neurological problems. Sample size 409 participants	<i>Dementia:</i> DSM-IV including AD: NINCDS-ADRDA	RRs* for cognitive impairment with or without dementia with CAL >3mm was as follows: -Moderate CAL: 1.89 (1.13-2.69) -Severe CAL: 1.75 (1.11-2.46)	In the PD diagnosis, not all teeth were examined in patients with >12 teeth present. A partial mouth periodontal examination was done for the convenience of the patients, which may underestimate the prevalence and severity of the disease as PD may not be evenly distributed in the mouth.
Holmer et al. (2018); Sweden	Age: 50-80 years. Cases were screened at the Karolinska Memory Clinic. Controls were recruited by a random sample from the Swedish population register. Sample size 220 participants	Baseline: PPD, BOP, suppuration, tooth mobility, furcation involvement and MABL using panoramic radiograph. Endpoint outcome 154 cases (including 52 participants with AD, 51 with MCI and 51 with SCD) and 76 controls. <i>All cases:</i> ICD-10 th criteria including <i>AD</i> using NIA-AA diagnostic guidelines; and <i>Mild AD</i> using MMSE.	Multivariate logistic regression was used and adjusted for age, gender, marital status, education, smoking, BMI, and diabetes mellitus. RR* in AD patients compared with the control group was 3.05 (4.07 - 4.70) for those with more than one tooth with PPD ≥6mm.	The self-reported questionnaire might have introduced bias, and fewer covariates were used with no control for medical co-morbidities and apolipoprotein (ApoE). If they were considered, the significance of the results would have tended to be more conservative and significant. Although PD is chronic and slowly progressive in nature, severe MABL generally takes many years to develop. Similarly, AD often has a long latent period or pre-symptomatic phase. The risk remains that the results were affected by temporal bias. The sample size was modest, which could have resulted in the loss of precision in subgroup analyses of AD.
Araujo et al. (2021); Brazil	Mean age: Cases: 72.6 ±1.1/ Controls 69.8±1.0 Cases were selected from the Centre of Alzheimer's Disease of the Psychiatric Institute of the Federal University of Rio de Janeiro. Controls were selected age and gender-matched and recruited from the same place.	Baseline: PPD, CAL, BOP Endpoint outcome 34 cases with AD and 9 in controls <i>Dementia:</i> DSM and CDR	Binary logistic regression adjusted for age, gender, income, and educational level RR* in AD patients compared with the control group was 2.58 (2.03-2.74) for those with periodontitis.	This study did not adjust with enough confounders to prevent residual confounding, and important factors such as co-morbidities (e.g., CVD), smoking, alcohol and diet were not adjusted for. The sample size was small, and the presence of sample type two error cannot be ruled out.

	Sample size 102 participants (Cases: 50; Control: 52)			
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*Based on the original data, we calculated crude OR and converted OR to RR for dementia, AD and VaD based on following formula (Zhang and Yu, 1998)

$$RR = \frac{\text{odds ratio}}{1 - \text{risk}_0 + \text{risk}_0 \times \text{odds ratio}}$$