Risk Factors and Health Effects of Overweight and Obesity in Older adults

Isaac Moses Danat

B. Pharm, MBA, MPH.

Faculty of Education, Health and Wellbeing

University of Wolverhampton

United Kingdom

A thesis submitted in partial fulfilment of the requirements of the University of Wolverhampton for the degree of Doctor of Philosophy

February 2020

DECLARATION

I certify that this work or any part thereof has not previously been presented in any form to the University or to any other body whether for the purposes of assessment, publication or for any other purpose (unless otherwise indicated). Save for any express acknowledgements, references and/or bibliographies cited in the work, I confirm that the intellectual content of the work is the result of my own efforts, with supervisory assistance from Professor Ruoling Chen, Professor Jiaji Wang, and Dr Martin Partridge and of no other person.

Signature……Isaac Moses Danat……………………

Date…28th Feb 2020…………………………………

DEDICATION

This thesis is dedicated to God Almighty for His endless mercy, love, and faithfulness throughout my doctoral study in the United Kingdom. It is dedicated to my parents Mr Moses Vreng Danat and Mrs Fidelia Nape Danat for laying their hands of blessings upon me to succeed in my PhD study.

ACKNOWLEDGEMENT

My greatest gratitude goes to God Almighty for shining His glorious light on my path from the start to the end of the PhD study.

I am particularly very grateful to my director of studies Professor Ruoling Chen who provided the best possible supervision and support throughout the doctoral study. It was clear that without his guidance and encouragement it would have been extremely difficult to complete all the research work and the thesis. I am also very grateful for and delighted with the support and supervision from Professor Jiaji Wang and Dr Martin Partridge which guided me through PhD research work. May God bless, keep and strengthen all of you.

I would also like to thank Dr Angela Clifford for her support and contribution towards the completion of the qualitative part of this research, Dr Yuhui Wan, and Dr Yuyou Yao for the Chinese dataset management, and Dr James J Tang for the advice on data analysis. My appreciation also goes to Carol Bailey and Dr Danielle Mcfeeters for the academic English language support during the write-up stages of the doctoral study.

My deep appreciation goes to the Principal investigators of the prospective cohort studies conducted in Anhui and four-Provinces in China for the approval and access to use their datasets for the study. I am also very grateful to all participants in the focus group studies conducted in Wolverhampton UK.

I wish to express my deepest gratitude to my parents, Mr and Mrs Moses Danat, for their huge support towards my doctoral study. May God bless and keep you strong and healthy. To all my siblings, including my dear ones Joy Yashim and Nori-Nansat, I say very big thanks to you. I would not forget colleagues and friends in the UK, Canada and Nigeria for their encouragement and support in different ways; may God in his infinite mercy and goodness reward you all.

Funding: I obtained conference travel grants from the Faculty of Education, Health and Wellbeing at the University of Wolverhampton. This supported me in attending and orally presenting my research work at international conferences. These include (1) the Epidemiology and Public Health conference in Paris, France (October 2017), (2) the 14th World Summit on Alzheimer's disease, dementia care and awareness in Boston, USA (August 2018), and (3) the 9th European Epidemiology and Public Health Congress in Helsinki, Finland (June 2019).

ABSTRACT

Introduction: The older adult population is rapidly increasing, and overweight and obesity prevalence is fast rising in older people globally**.** It is unclear whether excess body weight in older age reduces or increases the risk of incident dementia and whether it prolongs survival. Evidence of the risk factors for overweight and obesity in older age is scarce. This thesis investigated the risk factors and health effects of overweight and obesity in older age, with a focus on their impacts on incident dementia and all-cause mortality.

Methodology: This study employed a mixed method of quantitative and qualitative approaches that are based on a large cohort study dataset from China and two focus group discussions from the United Kingdom. The cohort consisted of 3,336 participants in total: 1,736 aged >= 65 years recruited from urban areas in 2001 and 1,600 aged>=60 years from rural areas in 2003 in Anhui province, China. In the standard methods of interview, they were documented for sociodemographic, lifestyle, social network, disease, and other risk factors at the baseline survey. Body Mass Index (BMI) and waist circumference (WC) were measured, and dementia was diagnosed by the GMS-AGECAT for each of the participants. The cohort members were followed up for 10 years to monitor mortality and examine the cause of death. There were three waves of interview for surviving cohort members during the follow up to document incident dementia apart from the causes of mortality. The data of the Anhui cohort study were analysed in multivariate Logistic and Cox regression models. Two focus groups research were conducted in Wolverhampton UK. It

included 12 twelve older adults who were recruited from the community through their place of worship. The focus group data were collected in a digital audiotape. They were transcribed verbatim and analysed thematically.

Findings: The data from the cohort wave three surveys showed that the risk factors for overweight and obesity in older people included female gender, low education, low income, residing in urban areas, being married, watching TV/reading newspapers, and hypertension at baseline. Over the 10-year follow-up, 271 participants were diagnosed as having incident dementia. The continuous BMI at baseline increased the risk of incident dementia (multivariate-adjusted odds ratio (OR) 1.06, 95%CI 1.00-1.11). There was no significant increase in OR in participants who were overweight (1.34, 0.91-1.98) and obese (1.52, 0.86-2.70) when compared to normal weight, but separate data by gender showed that dementia risk was significantly increased in men with overweight (3.09, 1.65-5.77) and obesity (4.19, 1.75-10.03) and not in women (0.74, 0.43-1.27; 0.72, 0.32-1.64). The prediction was similar regardless of different adiposity measures used; the risk of dementia was elevated in non-smokers with obesity measured by BMI (4.28, 1.46-12.53) and in non-smokers with waist circumference classed as action level two (3.19, 1.04-9.77). The Anhui cohort data did not show significantly reduced mortality in older people with overweight (HR 0.78, 95%CI 0.56-1.08) and obese BMI (0.79, 0.47-1.33) when compared to normal BMI. There were no gender differences. But the risk of all-cause mortality was significantly increased in older people with underweight (2.04, 1.25-3.33), and the sex-stratified data analysis showed a stronger effect in men (2.31, 1.21-4.42) and not in women (1.59, 0.73-3.44). The focus group data also supported such findings of deleterious effects of

overweight and obesity by major themes including theme-harm, impairment, and mortality.

Conclusions: Overweight and obesity in older age increased the risk of incident dementia. They were not significantly associated with reduced risk of mortality although underweight increased the risk. Curtailing overweight and obesity and maintaining normal weight in older age could help reduce the risk of developing dementia and extend survival

MY PUBLICATIONS AND PRESENTATIONS DURING PHD STUDY

Journal papers

Danat, I.M., Clifford, A., Partridge, M., Zhou, W., Bakre, A.T., Chen, A., McFeeters, D., Smith, T., Wan, Y., Copeland, J. and Anstey, K.J (2019). Impacts of Overweight and Obesity in Older Age on the Risk of Dementia*:* A Systematic Literature Review and a Meta-Analysis*. Journal of Alzheimer's disease.* vol. 70, no. s1, pp. S87-S99.

Bakre, A.T., Chen, R., Khutan, R., Wei, L., Smith, T., Qin, G., **Danat, I.M.,** Zhou, W., Schofield, P., Clifford, A., and Wang, J. (2018) Association between fish consumption and risk of dementia: a new study from China and a systematic literature review and meta-analysis. *Public Health Nutrition Journal*, 21(10), pp.1921-1932.

Bakre, A.T., Song, Y., Clifford, A., Chen, A., Smith, T., Wan, Y., Devlin L., Jie Tang, J., Zhou, W., **Danat, I.M.,** Hu Z., Chen, R. (2018) Determinants of fish consumption in older people: a community-based cohort study. *Journal of Aging Research & Clinical Practice,* 7, pp.163-175.

Lang, L., Clifford, A., Wei, L., Zhang, D., Leung, D., Augustine, G., **Danat, I.M.,** Zhou, W., Copeland, J.R., Anstey, K.J. and Chen, R., (2017). Prevalence and determinants of undetected dementia in the community: a systematic literature review and a meta-analysis. *BMJ Open*, *7* (2), p.e011146.

Papers presented at major conferences

Danat, I.M., Chen, R., Tang, J. (June 2019) All-cause mortality in relation to overweight and obesity in older people: A community-based cohort study from

China. Speaker presentation at the 9th European Epidemiology and Public Health Conference, Helsinki, Finland.

Danat I.M. and Chen R (August 2018) Do older adult obesity and overweight prevent dementia risk? - A new population-based cohort study from China. Speaker Presentation at the 14th World Summit on Alzheimer's disease, dementia care and awareness, Boston, USA.

Danat I.M., and Chen R (Aug 2018). The impacts of overweight and obesity on dementia risk: A systematic literature review and meta-analysis. Speaker presentation at the Global epidemiology and Public Health conference, Telford, University of Wolverhampton United Kingdom.

Danat I.M., and Chen R (Oct 2017) Risk factors for abnormal weight in older adults: A community-based cohort study from China. Speaker presentation at the 6th International Conference on Epidemiology and Public Health, Paris, France.

Danat I.M., and Chen R (Oct 2016). The prediction of Body Mass Index to dementia: A new cohort study from China and Worldwide systematic review. Speaker presentation at The International Conference on Geriatrics and gerontological Nursing, London, United Kingdom.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

WHO:	World Health Organisation
WC:	Waist Circumference
WC/√ height:	Waist circumference divided by the square root of height
WtHR:	Waist to Hip Ratio
HDI:	Human Development Index
HR:	Hazard Ratio
RR:	Relative Risk
CVD:	Cardiovascular Disease
LMIC:	Low-Middle-Income Countries
AD:	Alzheimer's disease
MHO:	Metabolically Healthy Obese
MMSE:	Mini-Mental State Examination
DSM:	Diagnostic and Statistical Manual of Mental Disorders
ADDTC:	Alzheimer's Disease Diagnostic and Treatment Centre criteria -
AGECAT:	Automated Geriatric Examination for Computer Assisted Taxonomy
GMS:	Geriatric Mental Status
ICD:	International Classification of Diseases
NINCDS-	National Institute of Neurological and Communicative Diseases and
ADRDA:	Stroke Alzheimer's disease and Related Disorders Association
WADLS:	Western Australia Database linked system
TICS:	Telephone Interview for Cognitive Status
IQCode:	Informant Questionnaire on Cognitive Decline in the Elderly
BMI:	Body Mass Index

WHR:	Waist to Height Ratio
GDP:	Gross Domestic Products
SEP:	Socio Economic Position
OR:	Odds Ratio
ADL:	Activity of Daily Living
CVDRF:	Cardiovascular Disease risk Factors
CHD:	Coronary Heart Disease
VaD:	Vascular Dementia
MUO:	Metabolically unhealthy Obese
APOE:	Apolipoprotein E

CHAPTER ONE: INTRODUCTION

The chapter presents an overview and background of the thesis. It includes an overview of overweight and obesity as public health issues and the theoretical background of the research. The research question and specific objectives are presented with contributions to knowledge from the thesis. The conceptual model and research design used for the study are presented and the chapter concludes with an outline of the entire thesis.

1.1 Overweight and obesity as public health issues

1.1.1 The health issues

Overweight and obesity are complex problems of surplus body weight and fats which predispose people to illnesses and early death. They are commonly assessed using Body Mass Index (BMI) and Waist Circumference (WHO, 2000; Villareal *et al.,* 2005). Overweight and obesity have been linked with increased risk of several chronic illnesses, poor life quality and premature death (WHO, 2000; Guh *et al.,* 2009; Fahouri *et al.,* 2012). For instance, overweight and obesity are associated with increased cardiovascular diseases (CVDs), which are the major causes (30.3%) of morbidity, disability and mortality in older adults (Prince et al., 2015). Evidence showed that overweight and obesity increases the risks of other chronic non-communicable diseases including Cancers (Bhaskaran *et al.,* 2014), depression (Luppino *et al.,* 2010), Chronic Obstructive Pulmonary Diseases (COPD) and asthma (Beuther *et al.,* 2007; Franssen *et al.,* 2008). These major illnesses contribute to disability, reduced quality of life and high mortality; and they significantly increase the burden on medical care and social services.

1.1.2 The prevalence of overweight and obesity

Evidence from a large global research (Ng *et al.,* 2014) showed that over the past three decades overweight and obesity prevalence have increased in all age brackets across all countries and regions of the world. Notably, excess BMI (≥25Kg/m²) increased from 29% to 37% for men and 30% to 38% in women. Despite the declaration of overweight and obesity as huge public health problems by the WHO in 1997 and the efforts to curb the epidemic (WHO 2000, James, 2008), their prevalence rates have continued to rise. The evidence of obesity in US older adults (65 years and above) by Fakhouri *et al* (2012) showed that in just three years (2007-2010) one in every three persons (35%) were obese and this consisted of 8 million older adults of age 65-74 years and 5 million of those aged 75 years and above (Vincent and Velkof, 2010; Fakhouri *et al.,* 2012). Findings from Europe including the UK suggested that in 2015 alone there were already 32 million obese older adults with prevalence ranging from 20% to 30% depending on the statistical model used for quantification (Mathus-Vliegen *et al.,* 2012).

Evidence suggests there is a more rapid increase in overweight and obesity prevalence in low and middle-income countries when compared to high come countries despite indications of lower prevalence (Chan and Woo, 2010; Seidell and Halberstadt, 2015). It was also argued from the Asian perspective (Ng *et al.,* 2014; Bao *et al.,* 2015) that the absolute number of those with overweight and obesity in China is higher despite the prevalence in older adults is lower compared to the USA and the UK. This is because China has a huge population of about 1.4 billion people which includes about 155 million older adults (≥65 years) and this significant proportion is fast ageing due to increased life expectancy. This was boosted by rapid socio-economic development, advance in medicine and health care (Mai and Chen, 2013; Bao *et al.,* 2015). It was projected that by the year 2050 older adults of the age 65 years and above would account for 20%-33% of the entire population of China (Mai and Chen, 2013). Similarly, from the European perspective (Eurostat, 2014), it was projected that by the year 2060 older adults would occupy 30% of the entire population of Europe. This suggests that if excess body weight is not curtailed the future burden of overweight and obesity-related illnesses on healthcare and social services would be very massive.

1.1.3 Cost of overweight and obesity

The cost of obesity is enormous, internationally, and nationally. In the literature, it is described as a direct cost, which implies all healthcare cost that is associated with obesity (Thompson and Wolf, 2001; Withrow and Alter, 2011). According to Thompson and Wolf (2001), "the cost burden of obesity is measured in terms of attributable expenditures on other diseases for which excess body weight plays an aetiological role". The assessment are the population-attributable risk or population-attributable fraction methods based on modelling using data from epidemiological and economic sources. Another approach is the individual level data method from database studies which track the costs of comorbidities associated with obesity (Withrow and Alter, 2011).

The USA has amassed a total annual cost of between $147 billion to $210 billion as medical cost associated with overweight and obesity. This accounts for about 21% of all health care costs for the US (Smith and Smith, 2016; Kim and Basu, 2016). The findings from Canada showed annual cost of obesity ranging from $1.27 to 11.08 billion accounting for 2.2-12% total health care cost of which 37%-54.5 % is the direct cost of obesity (Tran *et al.,* 2013). Evidence from the UK revealed annual spending of £6.3 Billion on overweight and obesity by the NHS and this is estimated to increase to £9.7 billion by 2050. To the wider society, it costs the UK a total of £27 billion and will hit $49.9 billion by 2050 (PHE, 2017). The recent data from China (Qin and Pan, 2016) also suggests huge spending of USD 3.5 billion on overweight and obesity annually and this represents 2.46% of all healthcare costs. These findings, therefore, shows that overweight and obesity are huge public health issues in developed and developing countries.

1.2 The research background

1.2.1 Risk factors for overweight and obesity

The continuous spread of overweight and obesity in the world and threats to the health of populations made the research to investigate the risk factors for overweight and obesity a top priority to curb the epidemic (Ng *et al.,* 2014). This is imperative since curbing the rising overweight and obesity prevalence could reduce morbidity, improve quality of life, and prolong survival in older adults. However, there is limited data for older adults, and the evidence of risk factors for overweight and obesity in older adults particularly from social determinants of health perspective is lacking (Zamboni *et al.,* 2005: Decaria *et al.,* 2012). As a result, public health strategies for curbing excess body weight in older population tends to rely on data of the general or younger/middle-age population. This may not be appropriate for older adults who may present with different risk factors due to retirement-related transition from active to sedentary lifestyle and age-related changes in body fat composition and distribution (Zamboni *et al.,* 2005; Chan and Woo, 2010; Walters *et al.,* 2013). Also, findings have predominantly emanated from cross-sectional studies with only a few from longitudinal research to examine overweight and obesity risk factors over long-term follow-up. Therefore, research of risk factors for overweight/obesity in older adults (≥65 years) is needed.

1.2.2 Health effects of overweight and obesity

There is substantial evidence in the literature on the health effects of overweight and obesity in midlife (<65 years) in terms of incident dementia and all-cause mortality outcomes. Evidence from a meta-analysis of cohort studies (Pedditiz *et al.,* 2016; Albanese *et al.,* 2017) has shown that excess body weight in midlife significantly increased the risk of incident dementia. Similarly, midlife overweight and obesity are significantly associated with harmful effects in terms of all-cause mortality risk (Adams *et al.,* 2006; Aunne *et al.,* 2016; Di Angelantonio *et al.,* 2016).

However, despite the evidence of the harmful consequences of excess body weight in midlife, the health impacts of overweight and obesity in late life (≥65 years) is an issue of controversy which has persisted for more than 20 years (Zamboni *et al.,* 2005: Villareal *et al.,* 2005; Decaria *et al.,* 2012; Brown and Kuk, 2015; Keith *et al.,* 2016). The evidence has been so conflicting that public health strategies on obesity prevention and clinical management of body weight in older age are problematic at present (Walters *et al.,* 2013; Starr and Bales, 2015; Gill *et al.,* 2015).

One major area needing research evidence is the impacts of older age overweight and obesity on incident dementia (Anstey *et al.,* 2011; Shah *et al.,* 2016; Danat et al., 2019) and all-cause mortality risk (Winter *et al.,* 2014; Keith *et al.,* 2016; Wang *et al.,* 2016). For instance, the evidence from the meta-analysis (Danat et al., 2019) for the thesis showed that reduced risk of developing dementia is reduced in older adults with excess body weight. However, this protective effect was only observed in short term cohort studies and not over a long follow-up. Therefore, high quality research of the health effects in terms of incident dementia and all-cause mortality over a long follow-up would help clarify whether older adult overweight and obesity confer beneficial health effects.

1.2.2.1 Impacts of overweight and obesity on incident dementia

Dementia is a global public health challenge that affects about 50 million people, of which most are older adults, with the disorder setting in as early as 60 years and estimated cost of 1 trillion USD in 2018. Dementia affects cerebral structure and function and is marked by loss of memory, difficulties in thinking and solving problems and negative behaviours (Prince *et al.,* 2016; Wimo *et al.,* 2017; WHO, 2019). Dementia is also known as a worrisome chronic illness without a cure, making independent living tough for affected individuals, and there is relentless reliance on care and support from their caregivers, families and society. Therefore, it conveys a huge burden to the society across several cost domains including medical care and social services (WHO, 2019). Therefore, as an urgent public health priority

(Shah *et al.,* 2016), the evidence of the risk factors for incident dementia is needed to inform prevention strategies and measures.

The quest to unravel the modifiable risk factors for incident dementia led to the identification of overweight and obesity as a research focus area, since adiposity-linked morbidities such as cardiovascular diseases, diabetes and hyperlipidemia is associated with increased risk of dementia (Newman *et al.,* 2005; Kloppenborg *et al.,* 2008). Indeed, the evidence from recent systematic review and meta-regression analysis of 589,649 participants from 12 studies with BMI measured in midlife and followed up for 42 years (Albanese *et al.,* 2017) suggested that obesity increased the risk of incident dementia by 47% (RR 1.47, 95%CI: 1.06-2.03). However, overweight did not significantly predict incident dementia (1.07, 0.96-1.20). This finding supported a previous report that increased midlife obesity was associated with incident dementia (Anstey *et al.,* 2011), and confirmed that obesity in middle and younger age is a risk factor for dementia, but not overweight. However, most research including primary prospective cohort studies, and systematic literature reviews and meta-analysis (Fitzpatrick *et al.,* 2009; Neergaard *et al.,* 2016; Emerzaal *et al.,* 2015; Pedditizi *et al.,* 2016) of the impacts of overweight and obesity in older age (≥65 years) on incident dementia risk exhibits the opposite effect in support of beneficial health effects of adiposity against the illness.

Furthermore, the findings from research of BMI trajectory or change of body weight from midlife to late life in relation to the risk of dementia is also unclear (Gustafson *et al.,* 2012; Stewart *et al.,* 2005; Tolppanem et al., 2014; Singh-Manoux *et al.,* 2018). For instance, the previous research by Stewart *et al* (2005) on change in body weight and incident dementia, based on a prospective cohort with 32 years follow-up, showed that neither baseline BMI nor change of weight from midlife to late life had significant impact on incident dementia. Though dementia-associated weight loss was detected prior to clinical diagnosis of dementia, and it worsened at the period of ascertainment. Besides, the study of the Swedish cohort by Gustafson *et al* (2012) found a lesser increase in BMI from the age of 38 to 70 years in women who developed dementia compared to those who did not. Besides, it was observed that after 70 years there was a decrease in BMI that was similar in the two groups regardless of dementia diagnosis. The findings suggest a negative association of midlife BMI with dementia risk while weight loss tends to occur from midlife to late life regardless of cognitive state. In contrast, the study of a Finish population by Tolppanem *et al* (2014) confirm that apart from midlife obesity being significantly related to dementia, on the contrary, every decrease in BMI from midlife to late life elevated the risk of dementia (1.14, 1.03-1.25) and Alzheimer's disease (1.20, 1.09-1.33).

It is unknown if midlife to late life weight loss is causally linked with incident dementia however, there is a consensus (Stewart *et al.,* 2005; Johnson *et al.,* 2006; Knopman *et al.,* 2007; Singh-Manoux *et al.,* 2018) that weight loss precedes dementia diagnosis by several years (from 2 to 10 years in most studies). The mechanisms of weight loss are complex however there are evidence (White *et al.,* 1998; Poehlman *et al.,* 2000) suggesting that behavioural disturbances and forgetting to eat leading to undernutrition contributes to weight loss. While this is important, research of the causal relation of weight loss and dementia risk is needed.

It is clear from above that while evidence supports increased risk of dementia for midlife obesity, the research findings of overweight/obesity and dementia risk is unclear in late life. In addition, most of the evidence springs from cohort studies that were conducted in developed countries, and little research has been done in low and middle-income countries (LMICs). Therefore, research is needed to investigate the impacts of overweight and obesity on incident dementia risk using data from different populations, particularly in LMICs.

1.2.2.2 Impacts of overweight and obesity on all-cause mortality

There is a large body of evidence from epidemiological research showing that overweight and obesity in midlife is associated with all-cause mortality (Adams *et al.,* 2006; Aunne *et al.,* 2016; Di Angelantonio *et al.,* 2016). For instance, the systematic review and meta-analysis by Aunne *et al* (2016), which included 230 cohort studies with 30 million participants and over 3.7 million deaths, found that for every 5 unit increase in BMI the risk of all-cause mortality was elevated by 21% in never smokers (1.21, 1.18-1.25) and by 27% in the analysis that excluded the first 1-6 years of follow-up (1.27, 1.21-1.33). This showed that excess body weight in midlife reduce survival.

The reduced survival associated with excess body weight in midlife is supported by the evidence from previous study in mice which examined the impact of dietary restriction on longevity, cancer, and immunity (Weindruch *et al.,* 1986). The study found that Calorie Restriction (CR) was associated with increased survival in mice, and that longevity increases with severity of dietary restriction. Besides, the CR positively impacts on late-life disease patterns and delay immunologic aging. This calorie restriction and survival hypothesis is supported by the evidence in humans from the blue zone based on the Okinawa cohort study (Willcox *et al.,* 2007). The epidemiological study used six decades of archived population data of elderly cohort of Okinawans (≥aged 65) with the highest functional capacity and longest survival in Japan, the country with the world's longest-lived population (Willcox *et al.,* 2007). It examined the current survival patterns, and association of mortality from age-related illnesses and traditional diet composition, energy intake, energy expenditure, anthropometry, and plasma Dehydroepiandrosterone (DHEA). It found an extended average and maximum life span in human population that was associated with calorie restriction (without malnutrition) at least until midlife and reflected by lower BMI (below overweight). These findings suggest that calorie restriction is associated with survival.

The evidence of the association of adiposity in late life and all-cause mortality is unclear. Older adults are susceptible to overweight and obesity due to the influence of ageing on fat distribution and accrual to abdominal regions. Older adults are also vulnerable to multiple morbidities, of which several are adiposity related and reduce survival (Guh *et al.,* 2009; Beuther *et al.,* 2007; Bhaskaran *et al.,* 2014). However, the finding of the impacts of overweight and obesity in late life on all-cause mortality has been conflicting (Flegal *et al.,* 2013: Keith *et al.,* 2016) with suggestions that excess weight reduces health risks and prolong survival (Wang *et al.,* 2016). For instance, the review of evidence on the association of overweight, obesity and all-cause mortality by Flegal *et al* (2013) showed protective effects of overweight against all-cause mortality risk (0.90, 0.86-0.96) while obesity had no harmful effect (1.02, 0.81-1.29). Also, the study by Wang *et al* (2016) found a lower mortality risk

(0.80, 0.78-0.82) in overweight people after 10 years follow-up of a USA cohort and concluded that there was no evidence to suggest that the beneficial effects were products of methodological bias. It was also observed that even when findings of increased mortality are reported (Donini et al., 2012: De Hollander *et al.,* 2012; Winter *et al.,* 2014) the BMI associated with lowest all-cause mortality risk tend to lie beyond the normal BMI range. This suggests that adiposity confers beneficial health effects.

Therefore, the impacts of overweight and obesity on all-cause mortality remains controversial and more studies are needed to increase knowledge and understanding.

1.2.2.3 Overweigh, obesity and survival in population of patients

The evidence of overweight, obesity and all-cause mortality in the population of patients tends to support the 'obesity paradox hypothesis' (García-Ptacek *et al.,*2014; Sharma *et al.,* 2015; Dhana *et al.,* 2016). This posits that overweight and obese older adults with an established major illness such as dementia (Garcia-Ptacek *et al.,* 2014) or cardiovascular disease (Sharma *et al.,* 2015; Dhana *et al.,* 2016) have better survival than their normal weight counterparts. For instance, the study by Garcia-Ptacek *et al* (2014) used Swedish cohort data of 11,398 patients with incident dementia and BMI data to test the obesity paradox hypothesis of beneficial health effects. The study found that each unit increase in BMI resulted in a 3% dementia risk reduction in overweight patients. The study also reported a lower risk of mortality in men with obesity but not in women. This finding suggested overweight and obesity prolongs survival in older age. Therefore, more research is needed to clarify the association of adiposity with all-cause mortality in older adults.

Overall, little is known of the risk factors for excess weight in older people and there is controversy on the health effects in older age with some studies evidence suggesting beneficial rather than deleterious effects. These tend to challenge the official recommendations (WHO, 2011) of the same cut-offs for indices of adiposity in all adults regardless of age. It, therefore, raises an important and yet unclarified question of whether weight management and even prevention of overweight and obesity are necessary for older age. The thesis, therefore, investigates the risk factors and health effects of overweight and obesity in older adults focusing on the impacts on incident dementia risk and all-cause mortality risk.

1.3 Research question and objectives

1.3.1 Research questions

What are the risk factors for, and health effects of, obesity in older adults?

1.3.2 Specific objectives

- To investigate risk factors for obesity in the older population
- To investigate the impacts of overweight and obesity in older age on health in terms of incident dementia risk
- To investigate the impacts of overweight and obesity in older age on all-cause mortality risk
- To examine all-cause mortality risks in overweight and obese older adults with and without heart diseases, stroke, diabetes, and depression/dementia

1.4 The conceptual model and research design for the study

The thesis used a conceptual pathway model of overweight and obesity which was previously proposed by Kim and Popkin (2006) and recommended in obesity epidemiology for the understanding of causes and effect relationship but slightly modified for the research work (Figure 1). In the thesis, it was 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 included quantitative research based on data from prospective cohort studies conducted in China and a qualitative study using data generated from focus group discussions in the UK (Figure 1).

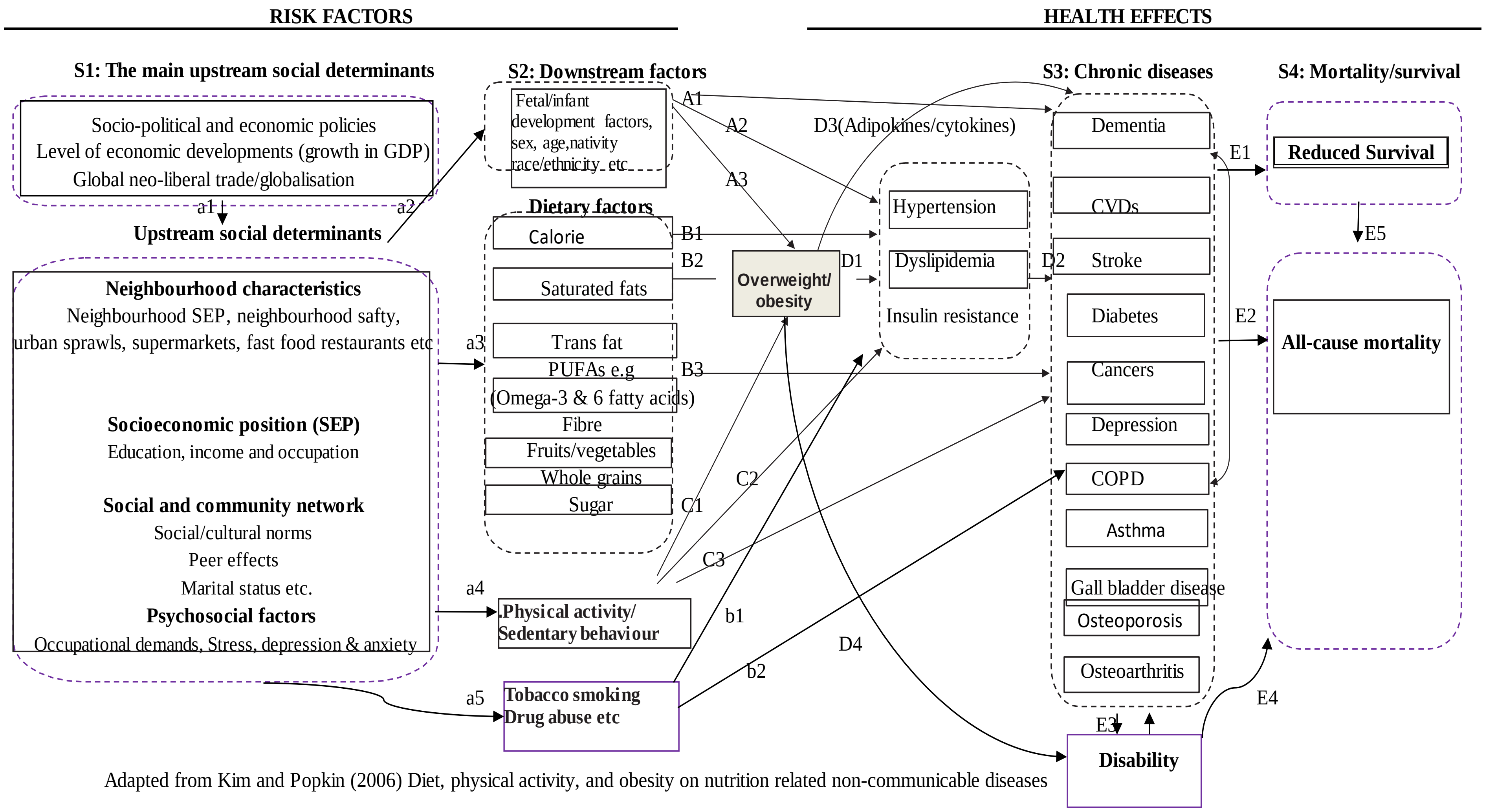
The conceptual model (Figure 1) portrays the possible factors involved in the aetiology and health consequences of overweight and obesity. **The original model** considered overweight and obesity as intermediate outcomes located in the causal pathway linking their determinants or causal factors to the development of morbidity outcomes. The determinants of obesity included factors such as genetics, foetal and infant development factors, dietary factors, physical activity, and sociocultural variables. The morbidity included chronic diseases like diabetes, cardiovascular diseases like CHD and stroke, cancers, osteoarthritis. According to the model, the harmful health effects of overweight/obesity on chronic diseases are mediated via hypertension, dyslipidaemia, and insulin resistance.

In terms of **modification of the model** for the thesis (additions in the purple colour of figure 1 below), another column (S4) was added to the health outcome side on chronic diseases (S3). This is to ensure the model also captured all-cause mortality or survival as an outcome that may result from the health effects of overweight/obesity. In the causes of overweight/obesity side, S2 was labelled as downstream social determinants (suggesting proximal factors) and this included more lifestyle factors like smoking at the bottom that have effects on chronic diseases and mortality and could confound the associations of body weight and health outcomes. The column S1 is another addition to the risk factors side on S2. The S1 depicts upstream social determinants and is subdivided into upper (main upstream social determinants) part and lower part (upstream social determinants). According to the risk factors side of the model (S1 and S2), the determinants of overweight/obesity included the main upstream, upstream, and downstream social determinants. It suggests that in the causal pathway between the main upstream determinants and overweight/obesity, there are upstream (e.g. neighbourhood characteristics) and downstream (e.g. diet and physical activity) factors.

One major aspect of the main upstream social determinants is the Global neo-liberal trade/globalisation. This global neo-liberal trade refers to the agreements adopted and backed by policies in different countries which may impact on obesity epidemic (Dahlgren and Whitehead, 2007; Vogli *et al.,* 2014). These trade agreements have led to the expansion of global markets which have liberalized the economic activities of the exchange of goods, services, data, technology, and funds (Dahlgren and Whitehead, 2007). Their negative negative impacts are hypothesised to be through new technologies, nutritional transitions, and urbanisation shaped by prevailing local environments (Swinburne *et al.,* 2011; Popkin, Adair and Ng, 2012). For instance, the evidence from large research found a global increase in BMI in relation economic globalisation and inequality between countries (Vogli *et al*., 2014). Therefore, the Global neo-liberal trade/globalisation in the model in figure 1 is important.

On the other side for health effects of overweight/obesity (S3 and S4), hypertension, dyslipidaemia, and insulin resistance (metabolic factors) are intermediary factors located (D1 and D2) in the causal pathway between overweight/obesity (predictor) and chronic disease outcomes (S3), while the impacts on chronic diseases may involve alternate pathways involving adipokines/cytokines (D3) and (D4). In addition, between the causal pathway of overweight/obesity and all-cause mortality/survival, there are metabolic factors (hypertension, dyslipidaemia, and insulin resistance) and chronic diseases (S3) as intermediates. Furthermore, the model suggests that the S1 and S2 (social determinants) may impact directly (A1, B3, b2, C3) on chronic diseases (S3) independently of overweight/obesity to act via metabolic factors (A2, C2, b1).

Figure 1 Conceptual pathway Model of Risk Factors and health effects of Overweight and Obesity in older adults

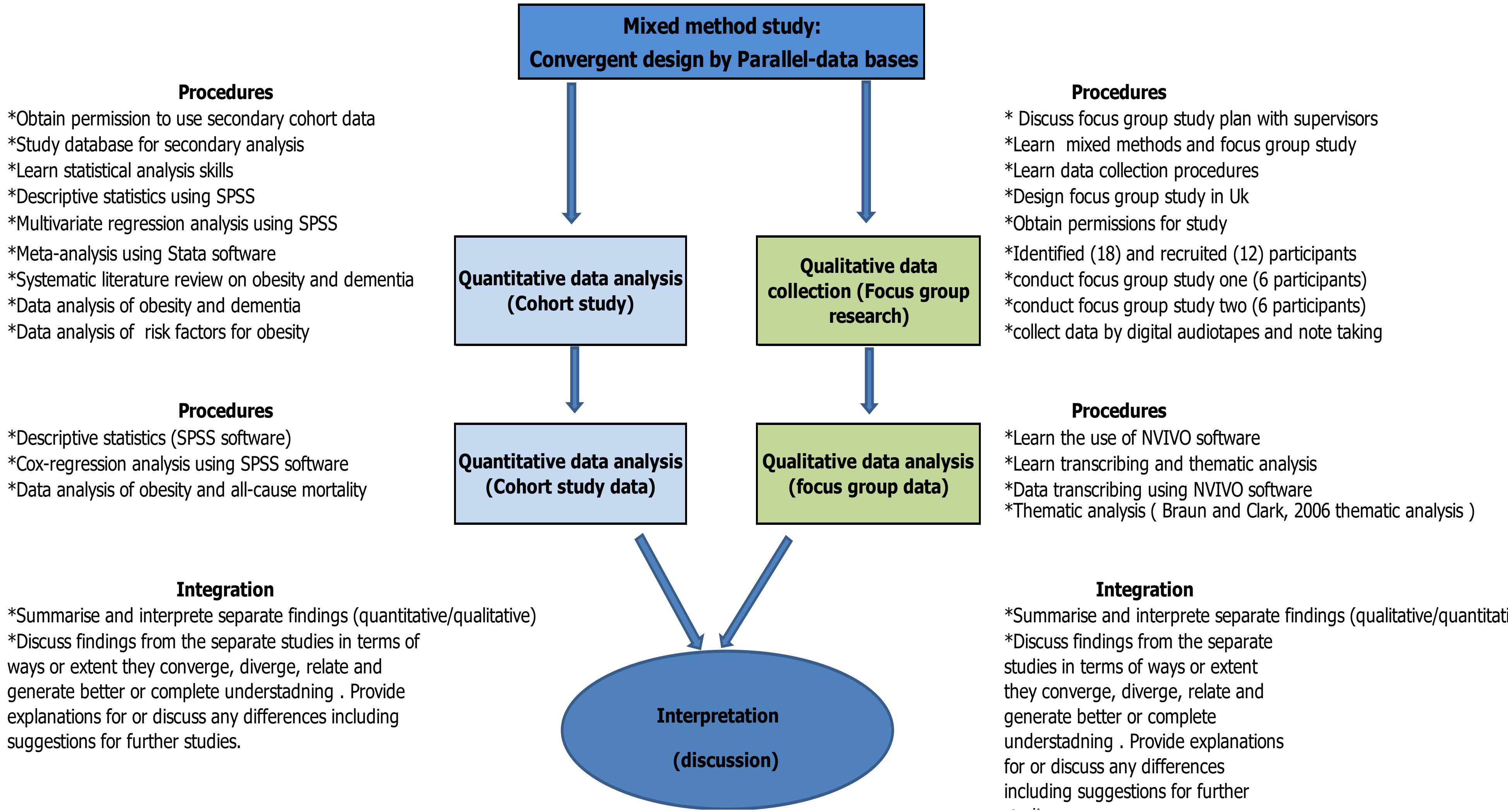


Adapted from Kim and Popkin (2006) Diet, physical activity, and obesity on nutrition related non-communicable diseases

1.5 Significance of the research

The findings from this thesis would help clarify whether overweight and obesity in older age are associated with beneficial or harmful effects on health. In addition, the evidence of the impacts of overweight and obesity on incident dementia risk will be useful for public health prevention of incident dementia. Older age is often associated with decreasing quality of life due to several underlying diseases and increased risk of mortality. Therefore, investigating the impacts of overweight and obesity on all-cause mortality would inform strategies on managing body weight to reduce morbidities thereby improving quality of life and increase survival in older age. The evidence of the major risk factors for overweight and obesity in older adults from the thesis will be crucial in the design of public health strategies to reduce the rising obesity epidemic and management of body weight in older age. Overall, the thesis will contribute significantly to knowledge and understanding of risk factors and health effects of overweight and obesity in older age and provide evidence to inform policies and practice.

Figure 2 Mixed method convergent design by parallel databases



1.6 Outline of the thesis

The thesis consists of nine chapters. **Chapter one** introduced the thesis. **Chapter two** presents a critical review of the literature on the risk factors and health effects of obesity and included summary of the main gaps and rationale for the PhD study, research question and objectives as well as the conceptual model for the research. **Chapter three** is a systematic literature review and meta-analysis on the impacts of overweight and obesity on dementia risk. **Chapter four** provides an account of the methodology; it included justifications for the research approach, study design for the project and procedures involved in the quantitative and qualitative studies including rationale for the choices made. **Chapter five** focuses on the risk factors for overweight and obesity in older adults. **Chapter six** is on the impact of overweight and obesity on dementia risk based on the prospective cohort study from China. **Chapter seven** examines the impact of overweight and obesity on all-cause mortality risk in older adults using data from a prospective cohort study in China. **Chapter eight** is on the impacts of overweight and obesity on dementia risk and survival in older adults based on qualitative research from a focus group study of UK older adults. **Chapter nine** covers the general discussion for the thesis and this included summary of the findings from each chapter of the thesis, discussions of the combined findings from the quantitative and qualitative studies of the Chinese population and UK older adults, it included the summary of main contributions to knowledge and recommendations for policy and practice. It also covers the strengths, limitations and suggestions for future study and general conclusions of the thesis.

CHAPTER TWO: RISK FACTORS AND HEALTH EFFECTS OF OVERWEIGHT AND OBESITY - LITERATURE REVIEW

This chapter provides an overall review of the literature on risk factors and the health effects of overweight and obesity. It commences with measures of overweight and obesity and their possible aetiology from a public health perspective. The risk factors for overweight and obesity are critically discussed as subthemes under downstream and upstream social determinants. The health effects in terms of morbidities and all-cause mortality are discussed with key knowledge gaps highlighted. The summary of the gaps, the rationale and the proposed conceptual model for the study are also presented.

2.1 Measures of overweight and obesity in older adults

2.1.1 Body Mass Index (BMI)

BMI is computed by dividing body weight in Kilograms (Kg) by the square of height in meters (m^2). Overweight and obesity are measures of excess body weight and fats and they are defined by Body Mass Index (BMI) of 25-<30 kg/m^2 and ≥30 kg/m^2 respectively while underweight and normal weight are defined by BMI of <18.5 kg/m^2 and 18.5-<25 Kg/m^2 (WHO, 2004; 2011). Most countries including the UK, USA and Canada use the above WHO cutoffs to classify overweight and obesity. However, research showed that the amounts of body fats per unit BMI vary according to ethnicity and race and this has led to the recommendation of country-specific BMI cut-offs (WHO, 2011). For instance, the Chinese from Asia have lower BMI cut-offs when compared with the Caucasians and are at higher risk of cardiovascular diseases and other health-related risks for similar BMI (Misra *et al.,* 2005; Chan *et al.,* 2009; Huxley *et al.,* 2010). Therefore, the Chinese government defined overweight and obesity as BMI of 24-27.9kg/m² and ≥28kg/m² while underweight and normal weight were defined by BMI <18.5kg/m² and 18.5-<23.9kg/m² respectively (Chen *et al.,* 2008).

2.1.2 Waist circumference (WC)

The waist circumference (WC) is a surrogate measure of central fat distribution which captures localised body fats in the abdomen (Zamboni *et al.,* 2005; WHO, 2011). The WHO recommended WC classification groups defines three action levels of waist circumference: for men no action<94cm, action level one 94-<102cm and action level two ≥102cm and for women<80cm, 80-<88cm and ≥88cm (WHO, 2011). The corresponding WC values for the Chinese men are <85, 85-95 and ≥95cm and for the Chinese women are <80, 80-90 and ≥90cm respectively (Chen *et al.,* 2008). WC is preferably measured using a plastic tape placed mid-way between the lowest rib and the iliac crest (Klein *et al.,* 2007). Findings showed intra-class correlation coefficients of r=0.998 and r=0.999 for men and women which indicated high reproducibility with WC measurements at the iliac crest (Klein *et al.,* 2007).

There are two types of abdominal fats which play important roles in the body. These are the white and brown fats. The review of evidence by Saely, Geiger and Drexel (2012) showed that, while White Adipose Tissue (WAT) stores energy, the Brown Adipose Tissue (BAT) increases energy expenditure. High amount of WAT is known to elevate the risk of obesity associated disorders while the opposite effect is elicited by high BAT (Saely, Geiger and Drexel, 2012). Besides, there is usually an increase in WAT with age while the BAT decreases relative to the total body weight. It is also documented that the metabolically active BAT is found in new-born and adults (BAT (Virtanen et al., 2009; Peirce et *al.*, 2014). However, the dwindling amount of BAT with age while the WAT increases, is an indication that the white adipose tissue is the major fat captured by use of WC in older adults.

The excess of fat is considered harmful to health. The build-up of abdominal fats is accompanied by accrual of ectopic fats in various organs including the skeletal muscles, heart, liver, pancreas, and blood vessels which leads to lipotoxicity (Jura and Kozak (2016). Intra-abdominal fat deposits from excess body weight are associated with comorbid conditions including insulin resistance, dyslipidaemia and hypertension, cognition impairment and elevated dementia risk (Power and Shulkin, 2007). For instance, obesity at midlife is a well-established predictor of late life dementia (Albanese et al., 2018). Physiopathologic theories like neurochemical, hormonal, atherosclerosis, and inflammatory pathways have been proposed as the possible mechanisms of the association between adiposity and dementia (Cereda et *al.*, 2007)). The amount and secretory capacity of the white adipose tissue (WAT) is proposed as the possible link with dementia. WAT being a large endocrine organ secretes adipokines, and this denote the immunomodulatory cytokines and related compounds. These are hundreds of cell-signalling molecules that play key role in the aetiology of dementia. The most popular adipokines capable of altering peripheral and CNS processes and linked with dementia are leptin, adiponectin, and interleukin 6 (Kiliaan et *al.,* 2014). Besides, there is the vascular mechanism where dementia may be triggered by the clustering of vascular factors such as total cholesterol, high blood pressure, diabetes, and midlife obesity (Kivipelto et *al*., 2005).

The WC is preferred to the BMI as a measure of abdominal adiposity. Evidence from the literature showed that the WC predicts cardiometabolic risks better than the BMI (Klein *et al.,* 2007; Lee *et al.,* 2008). The WC provides a measure of excess fats accumulated in the abdomen, making it different from the BMI (Lee *et al.,* 2008). The BMI, being an index of excess weight, is unable to accurately distinguish between lean or high body mass and body fats, and this limits its validity in differentiating visceral fat from subcutaneous fat (Rothman, 2008). Therefore, the BMI captures excess body weight and is predictive of general adiposity while the WC measures abdominal obesity which is implicated in CVDs. It was also argued that the stronger link of visceral abdominal fats with cardiovascular risk, and higher adipokines which play important role in neuropathology (Klein *et al.,* 2007; Lee *et al.,* 2008), makes the WC a better indicator of dementia risk than the BMI (Cereda et *al*., 2007; Kiliaan et al., 2014). Therefore, the WC is an important and preferred measure of adiposity and health risk.

2.1.3 Waist-to-Height Ratio (WHR) and Waist-to-Hip Ratio (WtHR)

The waist-to-height ratio provides a measure of waist circumference in relation to height and it is also recommended by the WHO (2011). There is evidence in support of the use of WHR to estimate surplus body weight and fats (Lee *et al.,* 2008; Gelber *et al.,* 2008; Correa *et al.,* 2016). For instance, the recent systematic review in the elderly population by Correa *et al* (2016) demonstrated that the WHR was better than other adiposity measures in detecting obesity and predicting non-communicable diseases. The findings support Waist-to-Height Ratio as a reliable measure of central adiposity for predicting cardiovascular disease risk factors such as diabetes, hyperlipidaemia, and hypertension. In addition, it was hypothesised that waist circumference divided by the square root of height (WC/√height) could provide a good measure of adiposity and show good predictability of obesity-related chronic diseases (Burton, 2010). However, the use of WC/√height from epidemiological research is sparse.

The Waist-to-Hip Ratio (WtHR) is another recommended adiposity measure (WHO, 2011). This is defined by values of ≥0.90cm and ≥0.85cm for men and women, respectively. Hip circumference is measured using a stretch-resistant tape at the largest circumference of the buttock at a level of measurement parallel to the floor. Findings from a systematic review (Lee *et al.,* 2008) showed that WtHR and WC predicted cardiovascular risk factors better than BMI. Similarly, other evidence (De Koning *et al.,* 2007) supported the use of WtHR as a measure of adiposity particularly for the assessment of regional body fats.

2.2 The aetiology of overweight and obesity: Public health perspective

The literature of obesity epidemiology (Egger and Swinburn, 1997; Hill., 2006; Kim and Popkin, 2006; Hu, 2008; Hruby and Hu, 2015) suggests that the aetiology of overweight and obesity is complex. It may be viewed as a consequence of complicated interactions involving the environmental, behavioural, biological or genetic factors which alter the balance between energy intake and expenditure thereby culminating in positive energy difference stored as body fats. There are three relevant perspectives in public health that pertain the aetiology of overweight and obesity. These include the life-course model, ecological model and the social determinants of health perspectives.

2.2.1 The life course Model of obesity

Evidence from the developmental and epigenetic pathways supports the life course model of obesity which is well-rooted in the developmental origins of health and diseases. According to this perspective, overweight and obesity emanate from long-term unfavourable life events, disadvantages or negative exposures during prenatal to infancy and over the life course (Hu, 2008; Gluckman *et al.,* 2008; Herrera *et al.,* 2011; Van Dijk *et al.,* 2015). This suggests a possible intergenerational transmission of obesity risks (Drake *et al.,* 2010). Therefore, according to this perspective, the critical aspects associated with the aetiology of obesity may be dated back to the early life changes within the intrauterine environment and early childhood. This also extends into adult life including older age. This model, therefore, emphasised the importance of identifying the risk factors for overweight and obesity over the entire lifespan.

2.2.2 The ecological model of obesity

The ecological model proposed by Egger and Swinburn (1997) is a public health model that is famous and still relevant in the design of strategies for obesity prevention but contains explanations on aetiology of obesity (Egger, Swinburn and Rossener, 2003; Swinburn, Gill and Kumanyika, 2005; Gortmaker *et al.,* 2011). The model was developed from old-fashioned epidemiologic triad for causation in infectious disease epidemiology. According to this model, obesity results from interactions of the array of host, vector, and environment-related factors. Importantly, the predisposing environment for obesity was viewed in terms of the political, economic, physical, and socio-cultural settings (Egger, Swinburn and Rossener, 2003). This model is marked by wider level factors including policy, legislation, and city planning as crucial determinants of overweight and obesity that guides interventions.

2.2.3 The social determinants of overweight and obesity

The public health perspective is well-rooted in the social determinant of health and it focuses on what was described as 'the causes of the causes' (Bennett *et al.,* 2008) and it conceptualises obesity as a complicated health problem well beyond the control of the individual. These are determined by wider policy factors which impact on the general socioeconomic, cultural, and environmental conditions (Hu, 2008; Bennett *et al.,* 2008; Dahlgren and Whitehead, 2006; Dugravot *et al.,* 2010). Therefore, according to this perspective, overweight and obesity are largely determined by the social determinants of health (Bennett *et al.,* 2008). These social determinants are viewed in terms of the downstream and upstream factors which may act via several mechanisms to influence behaviour towards excess energy intake and less expenditure (Christakri *et al.,* 2007; Torres and Nowson, 2007; Galster, 2012). The downstream factors in the literature (Bennett *et al.,* 2008) includes socio-demographic and psychosocial factors, while the upstream factors capture neighbourhood characteristics, the social structures and social environments as well as the level of socio-economic developments of the society people live. These are shaped by wider polices and globalisation as global drivers associated with overweight and obesity epidemic.

It was argued that the empirical measurements of social determinants of health are challenging due to differences in the determinants themselves (Bennett *et al.,* 2008). This has remained an area of continuous research to measure their impacts and to provide evidence in support of policies and public health strategies. The challenge for public health and obesity epidemiology as pointed out by Hruby and Hu (2015) includes identifying the risk factors and understanding the contribution of each factor to the obesity epidemic.

2.3 The risk factors for overweight and obesity

The risk factors for overweight and obesity are discussed as subthemes under downstream and upstream social determinants.

2.3.1 The downstream Factors

The downstream factors include the individual or biological factors. They play a vital role in predicting overweight and obesity but their effects from theoretical point of view are influenced by higher level factors outside their immediate domain. These individual factors may involve interactions with other factors to impact on overweight and obesity.

2.3.1.1 Biological /individual factors

This includes mainly age, sex, and hormonal factors. The literature suggests that age is an important factor that influences the risks of overweight and obesity (Zamboni *et al.,* 2005; Jura and Kozak, 2016). However, most research on predictors of overweight and obesity have focused on children and adolescents or the general population (Franks *et al.,* 2010) with little attention on older adults. There is compelling evidence that abdominal body fat called white adipose tissue increases with ageing (Miard and Picard, 2008; Brasilia *et al.,* 2012). It tends to increase at middle age, followed by a decline and redistribution to other parts of the body with further ageing (Jura and Kozak, 2016). Evidence showed that only about 25% of body weight in older age is attributed to muscle mass as compared to about 50% in the younger and middle age adults (Short *et al.,* 2004; Jura and Kozak, 2016). This suggests that older adults have higher body fats percentage as compared younger/middle age people. Also, compared to younger and middle age people, older adults tend to experience sedentary life and are less active as they enter retirement age thereby predisposing them to increased risk of overweight and obesity (Sebastiao *et al.,* 2019).

Sex is an important obesity risk factor. Evidence from prevalence studies reflects sex disparity in overweight and obesity with higher prevalence rates reported for women compared to men (Ng *et al.,* 2014). This suggests that sex may play a role in the aetiology of overweight and obesity. Indeed, differences in sex hormones have been linked to obesity risks with women more likely to be overweight or obese (Lovejoy, 1998*)*. While the causes and mechanism are poorly understood, it was proposed that the physiological demands of extra energy for reproduction and lactation exposes women to the evolutionary pressure of excess body fat storage (Lovejoy *et al.,* 2009). Research has also shown that for the same Body Mass Index (BMI) men have higher metabolic rates by about 20% more than women (Arciero *et al.,* 1993; Sharma and Padwal, 2010). This sex disparity accounts to a larger extent for the differences in fat-free mass. It is also well documented that there is additional weight gain associated with pregnancy and menopause in women, which again may be explained by hormonal changes (Arciero et al., 1993; Al-Safi and Polotsky, 2015).

Sex steroid hormones are hypothesised to be linked with both the peripheral and central mechanisms of appetite and weight control in women (Lovelady et al, 2008). In the case of pregnancy, there are physiological and behavioural changes such as changes in taste and food intake. Essentially, the sex steroids hormones called eostrogen and progesterone are increased to support the growth and development of healthy foetus, and marternal wellbeing by stimulating more food intake (Faas *et al,* 2010). Though the precise mechanism involved is poorly understood, it is postulated to be through the actions of leptin, ghrelin, cholecystokinin, and Peptide YY which have all be linked with adiposity in pregnancy (Sagawa et al., 2002; Pusztai et al., 2008; Faas *et al,* 2010). On the other hand, during menopause and post-menopause there is a decrease in estrogen levels (Lovelady *et al,* 2008; Zore et al., 2018). Evidence from studies in humans (Aloi et *al..,* 1995)) and female animals (Asarian *et al.,* 2006) have showed increased in body weight in relation to reduced estrogen. The accrual of visceral White Adipose Tissue (WAT) in post-menopausal women is often treated with hormone replacement therapy. However, the cellular mechanisms underlying the effects of menopause on total body fat and fat distribution is poorly understood even though the role of cholecystokinin has been postulated (Lovelady *et al.,* 2008; Newell-Fugate, 2017). While sex steroids are strongly associated with excess weight in women, the evidence from studies (Kruger *et al.,* 2009) suggests that the risks for overweight and obesity in women and men may also be at variance because of social and behavioural disparity in dietary choices and physical activity.

2.3.1.2 Lifestyle/Behavioural factors

The behavioural or lifestyle factors include diet, physical activity, watching TV, smoking, alcohol consumption etc. Evidence from research shows that older men whose lifestyles were sedentary or inactive were 39% more likely to be obese compared to men who were active; and those women were 28% more likely to be obese as compared to their active female counterparts (Kruger *et al.,* 2009). According to the energy balance perspective, poor diet intake involving high energy calorie and poor physical activity or less energy expenditure amounts to excess energy storage as body fats (Hill, 2006).

A major and relevant lifestyle factor in older age is watching TV. The watching of TV as sedentary life behaviour is poorly researched in older age, perhaps due to an impression that it reflects media exposure appropriate for the younger population. However, findings from developed countries (Gómez-Cabello *et al.,* 2012) suggest that at an older age the impact may be related to sedentary behaviour accompanied by the lifestyle such as sitting for several hours. The study by Xie *et al* (2014) found that TV watching impacted obesity risk in Chinese adults, but it was limited to 18-34 years adults. A study in a similar population found that more calories are consumed, and physical activity was reduced when watching TV (Williams *et al.,* 2008). However, research on the association of older age watching TV with risk overweight/obesity is lacking. Therefore, research using cohort studies, including in developing countries would be needed to provide evidence and inform public health strategies. Furthermore, association of overweight/obesity with smoking and alcohol has been investigated, however, findings are inconsistent across different settings (John *et al.,* 2005; Winslow *et al.,* 2015). Therefore, research is needed to clarify these lifestyle factors on the risk of overweight and obesity in older age.

2.3.1.3 Psychosocial and disease factors

Psychosocial factors include occupational stress, anxiety, and depression, while disease factors could include hypertension and cardiovascular disease risks (Bennett, Wolin and Duncan, 2008). They are sometimes viewed as midstream factors serving as mechanisms through which upstream factors may impact on downstream determinants and health outcome (Dahlgren and Whitehead, 2007). The literature suggests that poor income is linked to obesity through psychosocial pathway. According to this perspective, low income allocates people to the lower end of the social ladder in the society which predisposes people to feelings of low self-esteem and uneasiness due to their relative unfavourable position within the social ladder (Marmot, 2004, Graham 2009; Wilkinson and Pickett, 2006). These individuals often end up in some health-damaging behaviours like unhealthy food eating. For instance, high density foods are cheap and filling (e.g. a bag of chips in Iceland feeds a family for £1). Therefore, it is more likely to be chosen by those on low budgets. There is also reduced physical activity which contributes to a psychologically linked process of the mind-body pathways with decreased feeling of safety and locus of control (Marmot, 2004; Marmot and Wilkinson, 2006; Wilkinson and Pickett, 2006). Through such a pathway, it could increase depression, hypertension, and even cardiovascular diseases over time. Therefore, hypertension in older adults and subsequent relationship with overweight/obesity might reflect the wider context within which such persistent high blood pressure develops. This could be related to income which is an upstream social determinant. However, there is lack of evidence from research to inform policies and guide interventions.

2.3.2 Upstream social determinants

Upstream determinants include social and community network, socioeconomic position, neighbourhood characteristics, level of economic developments and globalization.

2.3.2.1 Social and community network

The literature suggests that social network including socio-cultural norms, peer effects, marital status, family etc. are possible mechanisms through which dietary and physical activity behaviours or choices may impact on the prevalence of obesity (Christakis *et al.,* 2007; Ball *et al.,* 2010; Napier *et al.,* 2014). According to Napier *et al* (2014), the influence of culture is so strong that neglect of culture in health may impact negatively on health outcome internationally. Findings from studies showed that dietary behaviours and physical activity may be culturally patterned (Brewis, 2010; Ball *et al.,* 2010; Biddle *et al.,* 2010) and obesity transmitted via social network (Christakis *et al.,* 2007). For instance, the evidence from the study by Christakis *et al* (2007) found that obesity may be spread through social networks (peer groups, spouse, and family) in a measurable and noticeable pattern depending on the type of social ties. These means that while culture could reinforce people's tradition, belief systems and behavioural patterns (Sharma and Padwal 2010), social ties like peer groups, spouse and family could encourage more calorie consumption (Fowler and Christakis 2008; Sobal *et al.,* 2009; Scherr, Brenchley and Gorin, 2013).

The findings on marital status from a cohort study in a developed country (Switzerland) suggest that living in couple reduced weight gain after 5.5 years of follow-up (Guerra *et al.,* 2015), while some studies found that higher calorie intake may be enhanced by influence of spouse (Sobal *et al.,* 2009; Scherr, Brenchley and Gorin, 2013). These findings show that even though marital status is associated with overweight/obesity, the direction of association is inconsistent. Besides, the literature suggests that these effects are modified by gender (Worsley et al., 1988; Rapp and Schneider, 2013; Mata et al., 2015). For instance, married men are healthier and married women tend to be more obese than single women, as shown by findings that cohabitation enhances healthy diet in men and unhealthy diet in women (Worsley et al., 1988). Married women also partake in fewer exercise than never-married women (Rapp and Schneider, 2013).

A study in the US by Sobal *et al* (2009) suggested that the positive association of marriage with obesity may be related to the broader trends of involvement of the society in marriage including commitment to family and the norms and expectations regarding body weight which may differ for married and unmarried/divorced people. However, it was argued (Cole and Fletcher, 2008) that the environment people live may be dominant over social factors that affect individual behaviour and choices. While this is considerable, socioeconomic factors could be more crucial to behaviours that predict overweight and obesity.

2.3.2.2 Socioeconomic position (SEP)

Evidence supports a link between socioeconomic position and risk of morbidities and mortality (Herd *et al.,* 2007). This suggests that socioeconomic position may shape access to resources influencing obesity risks. The measures of SEP including education, income and occupation are viewed as upstream social determinants associated with overweight/obesity. However, most evidence from research that inform policies emanates from studies of younger/middle populations, from high-income countries (Hajek *et al.,* 2015; Dugravot *et al.,* 2015) and using data of cross-sectional designs (Zhang *et al.,* 2008; Dinsa *et al.,* 2012; Wang *et al.,* 2012).

Older adults are predisposed to obesity for several reasons including age and lifestyle-related changes. However, the lack of evidence from studies in this population makes it difficult to design and streamline strategies to reduce the prevalence. Evidence from a previous systematic review of obesity in older adults (Samper-Trend and Snih 2012) was limited to countries in North America (the USA and Canada), Europe and Latin America with no study from continents like Asia which has a fast growing population of older people. Also, the risk factors for obesity may be shaped by local environments or settings across different countries (Swinburne *et al.,* 2011). Thus, the findings of obesity risk factors identified from studies in developed countries may not apply to different populations from low-middle income countries.

Furthermore, findings from research of SEP and overweight/obesity across different countries (Sobal *et al.,* 1989; Monteiro *et al.,* 2004; McLaren, 2007; Dinsa *et al.,* 2012) have shown lack of consistency. For instance, the evidence from studies in developed countries (Sobal *et al.,* 1989; Wang *et al.,* 2007) suggested that overweight and obesity are problems of the lower socioeconomic class as defined by education and income. In contrast, previous review (Cohen et al., 2013) suggested that higher SEP was associated with obesity in developing countries. It was also documented that the findings from developing countries tend to be mixed though most of the studies reviewed were cross-sectional studies (Monteiro *et al.,* 2004; McLaren, 2007; Dinsa *et al.,* 2012). These suggest a lack of clarity in the direction of the association and the need for further research using cohort data from different populations.

The possibility of reverse causality in the association of low SEP and obesity is one critical perspective that is rarely considered (Kim et al., 2017; Kim and Knesebeck, 2018). Reverse causality in the context of lower SEP and obesity relationship refers to a situation where instead of obesity emerging as the consequence, it becomes the cause of lower income (Kim and Knesebeck, 2018). For instance, a recent systematic review and meta-analysis (Kim et al., 2017) found that while low education increased overweight/obesity in developed settings (OR 1.33, 95%CI: 1.21-1.47), conversely, overweight/obesity was related to lower education (1.57, 1.0-2.25). Another study by Kim and Knesebeck (2018) also observed reverse effect for association of lower income with overweight/obesity.

The explanation for the vulnerability of low-income people to obesity is in terms of the limited access to food and healthcare, poor dietary and physical activity behaviours, insecurity, stress, reduced control over life events and social isolation. However, overweight/obesity results in low income (reverse causality) and the explanation in the literature is related to the obesity stigma theory linked to the social determinants of health (Kim and Knesebeck, 2018). This theory suggests untoward stereotyping of obese people as lazy, unsuccessful, and lacking self-control resulting in weight penalty in the form of less income, fewer job opportunities and greater job insecurity. There is also indulgence in health damaging behaviour such as poor diet and physical activity due to discrimination, and self-stigma that impacts on self-esteem and moods (Kim et al., 2017; Kim and Knesebeck, 2018). All these elevate the risk of obesity.

The need for longitudinal studies to ascertain the link of SEP and overweight/obesity is underlined by the fact that there are more cross-sectional studies in the literature, with only a few cohort studies available. Reliance on evidence from cross-sectional studies might be misleading since they are prone to reverse causality, and it is difficult to establish temporal order of exposure and outcome to ascertain causality (Hu, 2008, P.35; Caruana et al., 2015). Besides, studying the cohort data of different population is necessary since culture tends to influence the association of SEP and overweight/obesity (Napier et al., 2014), as evidenced by the cultural patterning of dietary behaviours and physical activity across different settings (Brewis, 2010; Ball et al., 2010; Biddle et al., 2010).

2.3.2.3 Neighbourhood characteristics

The notion that health risks are influenced by where people live is well supported. For instance, it is established that overweight and obesity are prevalent in people residing in settings with a high density of supermarkets and fast food outlets (Popkin, Adair and Ng, 2012). This notwithstanding, it is still not fully understood how neighbourhood characteristics including neighbourhood SEP, urban sprawls and food outlets impacts on health problems like overweight and obesity (Braveman, Egerter and Williams, 2011). The findings in developed countries linked poor neighbourhood with a high prevalence of overweight/obesity (Sheehan *et al.,* 2017). However, living in the urban areas in developing countries might be associated with higher risk due to rapid urbanisation and lifestyle changes including the nutritional transitions brought about by rapid economic development (Yang et al., 2008; Popkin, 2010; 2014; Fox, Fen and Asal, 2019). Research showed dietary behaviour within China varies according to the neighbourhood environment (Zhang *et al.,* 2015) perhaps due to differences in prevailing norms across settings. This suggests that the cultural patterning of overweight and obesity may be evident. Therefore, research is needed to help investigate the impacts of the neighbourhood features on overweight and obesity to inform strategies to reduce the epidemic.

2.3.2.4 Globalisation

The literature suggests that the wider causes of overweight and obesity are located in the main upstream determinants including socio-political and economic policies (Dahlgren and Whitehead, 2007; Vogli *et al.,* 2014). It is documented that global neo-liberal trade agreements adopted and backed by policies in different countries have impacted on obesity epidemic (Dahlgren and Whitehead, 2007; Vogli *et al.,* 2014). These have negative impacts through new technologies, nutritional transitions, and urbanisation shaped by prevailing local environments (Swinburne *et al.,* 2011; Popkin, Adair and Ng, 2012) (Swinburne *et al.,* 2011). The evidence from large research on economic globalisation and obesity by Vogli *et al* (2014) found a global increase in BMI in relation to economic globalisation and inequality between countries. However, while economic globalisation increases BMI, the impact of economic inequality was only detected in high-income countries and not low-and middle-income countries. Another theory that underpins globalisation is westernisation (Fox, Fen and Asal, 2019). This suggests that apart from the unjust trade laws that encourage unhealthy foods (economic globalisation), there is increased consumption of unhealthy or fast foods as part of modernity or cultural appeal of western lifestyles described as cultural globalisation.

2.3.2.5 Level of economic development

The Gross Domestic Product (GDP) and Human Development Index (HDI) are used as level of economic development in countries and applied in research of overweight and obesity (McLaren, 2007; Fox, Fen and Asal, 2019). A previous study by McLaren (2007) which used the Human Development Index (HDI) (per capita income, literacy rate and life expectancy as index of SEP) found that the association of SEP and overweight/obesity was inverse in high income countries. However, it observed a positive association with decreasing level of economic development from middle income to low-income countries. In addition, recent data supportive of the modernisation theory (Fox, Fen and Asal, 2019) from a study of 190 countries over 30 years suggested that domestic processes involving economic development (in GDP per capita), urbanisation and women's empowerment within countries play a significant role in driving the obesity epidemic internationally.

The study by Fox, Fen and Asal (2019) found that higher Gross Domestic Products (GDP) was associated with lower BMI in developed countries while growth in GDP in Low-and Middle-Income Countries (LMICs) predicted increase in BMI. However, since the findings were disaggregated by high income countries and LMICs, it was unclear from the studies if the impact in middle income countries may differ from low income settings. This is important since the literature suggests that differences among countries may exist due to variation in stages of epidemiological transition impacting on health risks (Bennett, Wolin and Duncan, 2008). A typical example is a country like China that witnessed huge and fast economic developments in the past three to four decades and has evidence suggestive of epidemiological transitions in disease and risk factors due to such changes (Yang *et al.,* 2008; Popkin, 2010; 2014). The risk factors for overweight and obesity might likely be different from that of the Caucasians. Therefore, research using data from China would contribute to understanding of overweight and obesity risk factors and develop and support new prevention strategies.

2.4 The health effects of overweight and obesity

This section is on the health effects of overweight and obesity in terms of incident dementia and all-cause mortality. It critically discusses the impacts of overweight and obesity on incident dementia and other morbidities including cardiovascular diseases, hypertension, diabetes, dyslipidaemia, depression, and mobility disability. The discussion on the association of overweight and obesity with all-cause mortality is in general population and extends briefly in people with co-morbidities.

2.4.1 Overweight, obesity, and incident dementia risk

The epidemiology of dementia is briefly introduced. It includes the prevalence, incidence, impacts, types, and possible aetiology of dementia. This is followed by a critical review of the impacts of overweight and obesity on incident dementia.

2.4.1.1 Definition, prevalence, and incidence of dementia

2.4.1.1.1 Definition: Dementia is a serious morbidity that is common from the age of 60 years. It was recently declared by the WHO as a huge public health challenge of urgent research priority (Shah *et al.,* 2016). Dementia is defined as a chronic disorder that affects cerebral structures and function leading to continuous worsening of memory, thinking and behaviour. Dementia is typically marked by inability to cope with daily activities thereby rendering independent living difficult (WHO, 2019). Dementia syndrome transcends the normal ageing process despite its increasing prevalence with advancing age. Its manifestations include amnesia at early stages and progresses with further memory loss, disorientation, agitation, mood swings, wandering, and speaking and swallowing difficulties. Further changes in behaviour may occur depending on the impacts of the disorder and the individual personality prior to the illness (Winblad *et al.,* 2016; WHO, 2019).

2.4.1.1.2 The dementia types and aetiology

The aetiology of dementia is complex and poorly understood. There are different types of dementia; the commonest is Alzheimer's disease (AD) which accounts for 60-70% of all dementias (Reitx, 2011), vascular dementia (VaD) accounts for 14.5% to 20%, Lewy Body Dementia (LBD) accounts for 15-20% and this comprised of Dementia with Lewy Bodies (DLB) and Parkinson's Disease Dementia (PDD) while the frontotemporal dementia (FTD) resulting from group of diseases that contribute to degeneration of the frontal lobe of the brain occupy about 1% (Aarsland *et al.,* 2001; Rizzi *et al.,* 2014; Jones and O'brien, 2014; Jellinger and Attems, 2011; Kane *et al.,* 2018; WHO, 2019). In terms of neuropathology, AD is marked by atrophy of the brain and aggregation of extracellular amyloid plaques and intracellular neurofibrillary tangles (Karch, Cruchaga and Goate, 2014) and is well known to be associated with APOEε4 status as a risk factor (Elias-Sonnenschein *et al.,* 2011). Vascular dementia (VaD) describes a diverse collection of the clinical syndrome including all dementia from ischemic, hemorrhagic, anoxic, or hypoxic brain damage (Rizzi *et al.,* 2014). Dementia often present as mixed forms although some research tries to focus on the subtypes to improve understanding of the aetiology. It is documented (Winblad *et al.,* 2016) that mixed dementia from neurodegenerative and cerebral mixed vascular pathology has remained the most diagnosed dementia cases and confirmed only at pathological level. Therefore, it is common for epidemiological research to investigate all dementia (or mixed dementia).

The risk factors for dementia are poorly understood. However, several factors are thought to be associated with the development of dementia. This may include factors such as APOEε4 carrier status, midlife obesity, depression, cardiovascular diseases (CVDS), diabetes, hypertension, dyslipidaemia, air pollution, and smoking (Saczynski *et al.,* 2010; Li and Singh, 2014; Shah *et al.,* 2016). Research is still ongoing to understand the association of these factors with dementia and mechanisms involved to guide prevention.

2.4.1.1.2 Prevalence and incidence of dementia

The WHO (2019) reckoned that nearly 50 million people are currently affected by dementia globally, which is more than the 46.8 million living with dementia reported in 2015 (Prince *et al.,* 2015). Internationally, 10 million cases of incident dementia occur annually, with Low-and Middle-income countries (LMIC) harbouring about 60% (WHO, 2019). The World Alzheimer's Report revealed that Asia accounts for nearly 50% of world dementia cases, which doubled the figures for Europe and surpassed those for North and Latin America put together (Prince *et al.,* 2015). Evidence suggests that these are largely driven by longevity or increased ageing population (Prince *et al.,* 2016). In China older adults (≥65 years) would account for 20%-33% of the population by 2050 (Mai and Chen, 2013). Similarly, from the European perspective (Eurostat, 2014), it was projected that by the year 2060 older adults (≥65 years) would occupy 30% of the population of Europe including the UK. It is therefore not surprising that it was estimated (WHO, 2019) that by 2050 there will be 152 million dementia cases globally, with 68% expected to come from LMICs.

2.4.1.1.2.1 The evidence in UK and China

In the UK with about 66 million population, there are 954, 099 people (≥65 years) with dementia (Prince *et al.,* 2014). The study by Matthews *et al* (2016) reported about 210,000 new dementia cases annually in older adults (≥65 years) in the UK, with more cases in women (135,000) compared to men. The number of dementia cases in the UK has been projected to reach 2,092,945 by the year 2051 (Prince *et al.,* 2014). These show that dementia is a problem of urgent attention.

Recent research (GDB 2019; Jia *et al.,* 2019) suggest that China with about 1.4 billion population accounts for 25% of global dementia cases. Findings from large studies within China (Jia *et al.,* 2014; Wu *et al.,* 2018; Huang *et al.,* 2019) indicated that dementia prevalence among older adults (≥65 years) in 2014 was 5.14% (95%CI: 4.71-5.57) and in 2019 it was 5.6% (3.5-7.5). The study by Wu *et al* (2018) found a prevalence of 5.3% (4.30-6.30) from a meta-analysis of 96 observational studies in China for those aged 60 years or more. This study included data from only mainland China, Hong Kong and Taiwan and yet it estimated 9.5 million people with dementia. The reported incidence of dementia for older adults (≥65 years) in China ranged from 18.2 to 30.4 per 1000 person-years according to 10/66 Dementia research group (Prince *et al.,* 2012), which was higher than 12.14 per 1000 person-years using the DSM 1V criteria (Yuan *et al.,* 2016). Though the 10/66 dementia algorithm, includes the GMS as a significant component and was initially validated in developed countries, it tends to make over-diagnosis of dementia in LMICs due to bias associated with low educational level (Prince et al., 2012). Notwithstanding, it is clear from all these data that regardless of the method of diagnosis, the burden of dementia is growing rapidly internationally and could get worse with severe impacts on affected countries.

2.4.1.2 The impacts of dementia

Dementia has far-reaching consequences for individuals, being a main cause of disability, reducing the quality of life, and greater reliance on care. The health of people affected by dementia often deteriorates and culminates in mortality. This, therefore, triggers huge demand for support from carers, families, and the society at large. This could be very overwhelming in terms of the emotional, physical, social, and economic burden making it a worrisome public health issue of urgent attention (WHO, 2019).

The cost of dementia to society is high. It includes direct government expenditure and indirect costs resulting from health and social care for dementia (Prince et al., 2014; Wimo et al., 2017). In 2015, the global cost of dementia amounted to about 818 billion USD and grew to 1 trillion USD in 2018 according to earlier projections (Wimo *et al.,* 2017). It was projected that by 2030 dementia will cost the world 2 trillion USD (Prince *et al.,* 2015). In the UK, the cost of dementia is £26.3 billion annually. The analysis showed the highest cost is currently £11.6 billion from work of unpaid carers of people with dementia; social care consumes £10.3 billion whilst healthcare cost is £4.3 billion (Prince *et al.,* 2014). In China, the socioeconomic costs required 19,144.36 USD per person and 167.74 billion USD in 2015 (Jia *et al.,* 2019). It was estimated that by 2030 it will rise to 507.49 billion USD with the figures projected to reach 1.89 USD trillion by the year 2050 (Jia *et al.,* 2019). These show clearly that dementia is one of the worst public health problems affecting the human population and deserving the urgent research attention as declared by the WHO (Shah *et al.,* 2016)

2.4.1.3 Impacts of overweight and obesity on incident dementia risk

There has been an increased focus from research to identify and investigate dementia risk and protective factors to guide public health for prevention since it currently lacks a cure. One of the areas of research interest is overweight and obesity since their associated morbidities such as cardiovascular diseases and related risk factors (hypertension, diabetes and dyslipidaemia) have been implicated in dementia (Newman *et al.,* 2005; Kloppenborg *et al.,* 2008). Research suggests that midlife obesity (<65 years) increases incident dementia risk (Anstey *et al.,* 2011; Albanese *et al.,* 2017). However, the impact of overweight and obesity in older age (≥65 years) on incident dementia is poorly understood with most findings (Pedditizi *et al.,* 2016) suggesting excess body weight slow the development or confer protection. These literatures, including sex differences in findings, are critically discussed.

2.4.1.3.1 Impact of overweight and obesity in middle age on dementia risk

The evidence from systematic reviews and meta-analysis of prospective cohort studies conducted internationally supports positive association of BMI in middle age with incident dementia risk. The increased dementia risk was frequently reported for obesity and not overweight at middle age. The early meta-analysis by Anstey *et al* (2011) investigated BMI and dementia risk relationship and found 64% increased risk for mid-life obesity (RR 1.64, 95%CI: 1.34-2.00) and 26% for overweight (1.26, 1.10-1.44). These findings were based on data of 11,800 and 18,046 participants involved in the respective pooled analysis of three cohort studies. Subsequent updated systematic literature review and meta-analysis by Pedditzi, Peters and Beckett (2016) found that whilst obesity at middle age (<65 years) increased dementia risk by 41% (1.20-1.65) there was no significant association with overweight (1.10, 0.99-1.22). This study used the data from five and seven cohort studies respectively for the meta-analysis. The recent systematic review and meta-regression analysis of 589,649 participants from 12 studies on BMI in midlife and dementia (aged 35-<65 years) with 42 years follow-up also confirmed that obesity increased the risk by 33% (1.33, 1.08-1.63) with higher risk detected (1.47, 1.06-2.03) is purposely designed cohort studies (not routine data). However, overweight was not a significant risk factor for incident dementia (1.07, 0.96-1.20). These findings suggest overweight in midlife does not impact on dementia risk except for those categorised as obesity. Obviously, the lack of association of overweight with dementia needs further research. This is important since larger proportion of most populations with excess body weight is overweight.

2.4.1.3.2 Impact overweight and obesity in older age on dementia risk

Research of overweight and obesity in older adults and incident dementia risk have generated controversial findings, with most recent studies suggesting protective effects. The early prospective cohort studies on the subject conducted in Japan, USA and France (Yoshitake *et al.,* 1995; Borenstein-Graves *et al.,* 2001: Nourhashemi *et al.,* 2003) found no association of excess body weight with incident dementia. One previous study conducted in 382 women from Sweden (Gustafson et al., 2003) found that excess BMI increased the risk of dementia (1.13, 1.04-1.24) after adjusting for several covariates. However, subsequent studies (Atti *et al.,* 2008; Fitzpatrick *et al.,* 2009) had challenged this finding and concluded that overweight and obesity in older age was protective against dementia risk. For instance, the study of a Swedish cohort of 1,255 elderly participants (age 75 years) found that higher BMI reduced the risk of dementia by 25% (0.75, 0.59-0.96) after nine years of follow-up (Atti *et al.,* 2008). In addition, the research of Cardiovascular Cognition Study in the USA by Fitzpatrick *et al* (2009) followed 2,798 older adults

(65-97 years) for incident dementia over 5.4 years and also found reduced risk for continuous BMI (0.95, 0.92-0.98) and no association for categorical BMI except underweight (1.62, 1.02-2.64). These findings suggest that excess body weight confers protection against the risk of dementia, and it is unclear if overweight and obesity is associated with a harmful effect in older age.

The meta-analysis by Anstey *et al* (2011) summarised the evidence from prospective cohort studies of BMI in older age and dementia risk. They did not observe any significant dementia risk for continuous BMI (0.98, 0.92-1.04) using data of 6,913 older adults from 6 studies. The systematic review by Emmerzaal *et al* (2015) found that the overweight and obesity in older age (≥65 years) were associated with reduced risk of dementia while harmful effects were observed from overweight and obesity in middle age (<65 years). In the same vein, the review and meta-analysis by Pedditizi *et al* (2016) confirmed the same hypothesis that obesity in older age ≥65 years significantly reduced dementia risk (0.83, 0.74-0.94) and the opposite effect for obesity in middle age (1.41, 1.20-1.65).

Considering limited understanding on the topic, and more studies published, an updated systematic review of all prospective studies on the impact of overweight and obesity on dementia risk (Danat *et al.,* 2019) was conducted as presented in Chapter three. Consistent with the previous reviews (Emmerzaal *et al.,* 2015; Pedditzi *et al.,* 2016), It was found that most studies reported inverse associations of excess weight with incident dementia risk, with few suggesting harmful or no associations (Gustafson *et al.,* 2003; Nourashemi *et al.,* 2003: Hayden *et al.,* 2006).

However, several methodological issues were observed with implications for further research, which is suggested in Chapter three.

2.4.1.3.3 Sex disparity in the association of obesity and dementia risk

Evidence supports sex differences in prevalence and incidence of dementia (Li and Singh, 2014; Neu *et al.,* 2017). In addition, the literature (Hogervorst *et al.,* 2012) suggests that several Alzheimer's disease risk factors are congruent with those for cardiovascular and cerebrovascular diseases such as midlife obesity. There is also sex-disparity in these risk factors predicting Alzheimer's disease with reported risks often higher in females compared to men (Hayden *et al.,* 2006; Neu *et al.,* 2017). The risk factors as summarised by Li and Singh (2014) include APOEε4 carrier status, midlife obesity, cardiovascular diseases (CVDS), CVD risks factors (diabetes, hypertension, dyslipidaemia) and sex hormone reduction due to ageing. Others sex disparity exists in terms of brain anatomy, brain volume decline associated with ageing, and sex difference in brain metabolism (Li and Singh, 2014; Gurvich *et al.,* 2018). For instance, Alzheimer's disease is linked with APOEε4 status as a risk factor (Elias-Sonnenschein *et al.,* 2011) which may contribute to dementia by enhancing cerebral amyloid angiopathy and cognitive decline (Liu *et al.,* 2013). Recent evidence (Neu *et al.,* 2017) from a meta-analysis of 27 separate research including data of 58,000 prospective participants found a greater risk of Alzheimer's disease in APOEε4 female carriers (4.37, 3.82-5.00) compared to their male counterparts (3.14, 2.68-3.67) of 65-75 years of age. Therefore, sex may also impact differently on dementia risk associated with overweight and obesity for older women and men.

There is a possible sex disparity in the association of overweight/obesity in older age and dementia risk due to several reasons. Evidence from the literature suggest that the second most prevalent cause of dementia is the Vascular Contributions to Cognitive Impairment and Dementia (VCID) (Li and Singh, 2014; Gannon *et al.,* 2019). The VCID refers to group of risk factors that are known to vary by sex and these include midlife obesity, diabetes, late Hormonal Replacement Therapy (HRT), Menopause, preeclampsia, hyperlipidemia, heart disease and myocardial infarction (Gannon et al., 2019). For instance, midlife obesity, diabetes, and hypertension are well established vascular risk factors associated with dementia (Kloppenborg *et al* 2008; Sharp *et al.,* 2011; Albanese *et al.,* 2017). However, evidence from research suggests these risks are greater in women compared to men (Jutilainen *et al.,* 2004). Conversely, stroke and hyperlipidemia are well known to predict the risk of dementia however the risks of these factors are higher in men than women (Giroud *et al.,* 2017). Besides, some VCIDs like late HRT, menopause and eclampsia are only applicable to women (Li and Singh, 2014) and heart disease and myocardial infarction are prevalent in men (Gannon *et al.,* 2019). One important standpoint is that adiposity increases with aging (Jura and Kozak, 2016) and is strongly associated with most VCIDs (Gannon *et al.,* 2019), while age is an independent risk factor for dementia (Prince *et al.,* 2016). Therefore, stratifying analysis of overweight/obesity and dementia by age and sex is vital.

However, little is known of the sex disparity in the impact of older age overweight and obesity on incident dementia risk. The most recent systematic review and meta-analysis on the impacts of overweight and obesity in older age (≥65 years) on incident dementia risk (Danat *et al.,* 2019) revealed a lack of focus by cohort studies in examining gender effect as confirmed by very few included studies (four out of sixteen) which performed sex-stratified analysis. The study by Haden *et al* (2006) investigated all types of dementia using data of 3,264 US older adults (age ≥65 years) with 3.2 years follow-up and included subgroup analysis for sex disparity in obesity and AD association. They found the significant risk for women (2·23, 1·09-4·30) and not men (1·48, 0·41-4·18). This finding was however contrary to the absence of sex difference in the association of continuous BMI with AD risk in American men (1.05, 0.82-1.34) and women (1.06, 0.87-1.31) after 3.8 years follow-up reported previously by Borenstein Graves et al (2001). Contrary to these findings, the study by Dahl et al (2008) of 605 Finish population (age 65-92 years) found a significant protective effect of continuous BMI against dementia risk after 8 years in women (0.90, 0.84-0.96) and not in men (0.95, 0.84-1.07). Similarly, the study by Atti et al (2008) of the Swedish cohort of 1,255 (age 75 years) with 9 years follow-up found reduced dementia risk for overweight women (0.73, 0.55-0.95) and none in men (0.62, 0.36-1.08). These findings suggest gender differences in association of obesity and incident dementia, however, more studies supported beneficial health effects.

One notable difference among the studies which might impact differently on findings is the duration of follow-up. The evidence from studies showed that the mean length of follow-up to detect dementia risk in older age is 7-8 years (Johnson, 2006), and 10 years or more in midlife (Knopman et al., 2007). The effect of reverse causality might influence Late-life studies such as Hayden et al (2006) and Borenstein Graves et al (2001) with short follow-up of 3.2 and 3.8 years respectively since dementia diagnosis happens too close to the baseline and the consequence of obesity takes a long time to develop (Kizimaki et al., 2018). However, it should be noted that longer duration of follow-up may be associated with lost to follow-up and survivor bias which presents the challenge of selection bias that often limits the validity of findings from cohort studies (Howe et al.,2016). Therefore, it is important to take into consideration these limitations in the interpretation of findings.

At the same time, while the duration of follow-up is essential, the baseline investigation of morbidities is also crucial. Pre-existing illnesses are known to confound the association of overweight/obesity and health outcomes (Aunne et al., 2016), and older adults are susceptible to multiple morbidities due to ageing (Guh et al., 2009). Therefore, while research is needed to examine the sex-disparity in the impact of overweight and obesity in older age on incident dementia risk, it is crucial to consider the length of follow-up, and morbidities confounding the relationship.

2.4.2 Obesity and other morbidities

The impacts of overweight and obesity on hypertension, diabetes, dyslipidemia, cardiovascular diseases, depression, and mobility disability are briefly discussed in this section. This is because of their relevance in the study of dementia and all-cause mortality in older adults.

2.4.2.1 Hypertension

Evidence showed that overweight and obesity directly impact on the risks of hypertension, with population attributable risk estimates suggesting that over 75% of hypertension can be directly attributed to obesity (Garrison *et al.,* 1987; Krauss *et al.,* 1998; Hall *et al.,* 2001). Evidence from the Framingham Heart study of 4,394 adults of age 20-49 years (2,027 men and 2,267 women) with 8 years follow-up revealed that 78% of the risk of essential hypertension in men and 65% in women are attributed to obesity (Garrison *et al.,* 1987).

Central obesity measured by waist circumference or waist-to-hip ratio is also often and strongly implicated in the risk of hypertension (Canoy *et al.,* 2004; Chrostowska *et al.,* 2011). To further buttress evidence of the impact of excess body weight on hypertension, a meta-analysis of 25 randomised controlled trials by Neter *et al* (2003) demonstrated that a net weight decrease of 5.1kg (95%CI: 6.03-42.5) reduces systolic and diastolic blood pressures by 4.44mmHg (5.93-2.95) and 3.57mmHg (4.88-2.25) respectively. Though the precise mechanism involved in the link of excess weight and hypertension is not fully known, the stimulation of the renin-angiotensin-aldosterone and sympathetic nervous systems have been proposed (Rahmouni *et al.,* 2005) which has been targeted for treatment by drug molecules (James *et al.,* 2014). In addition, recent evidence from systematic review and meta-analysis (Ettehad *et al.,* 2016) demonstrated that reducing blood pressure every 10 mmHg prevents a major CVD event (0.80, 0.77-0.83) and mortality (0.87, 0.84-0.91). This suggests that CVDs is mediated through high blood pressure. The association is so strong that the risks of CVDs due to high blood pressures have been confirmed in 12 different types of CVDs including CHD, stroke, heart failure and atrial fibrillation (Rapsomaniki *et al.,* 2014).

The evidence of the association of obesity with hypertension is of importance for the understanding of adiposity and incident dementia relationship. Evidence from a meta-analysis (Sharp *et al.,* 2011) of six cohort studies that included data of 8,123 participants and 425 cases (mean age 57.9-80.6 years) found that hypertension increased incident vascular dementia risk by 59% (1.59, 1.29-1.95) after median follow-up of 4.9 (3.2-10) years. In addition, hypertension is associated with poor cardiovascular health which is a determinant of cognitive decline and dementia risk in older adults (Samieri *et al.,* 2018). Therefore, it is likely that overweight and obesity in older adults may contribute to increased dementia risk via hypertension and poor cardiovascular health.

2.4.2.2 Dyslipidaemia

Dyslipidaemia is abnormal levels of blood lipids which include elevated triglycerides (TG), low-density lipoprotein (LDL), and decreased high-density lipoprotein (HDL) levels (Bays *et al.,* 2013). The association of obesity with increased risk of dyslipidaemia is well documented (Lee *et al.,* 2008; Huxley *et al.,* 2010; Bays *et al.,* 2013). Though the mechanisms involved are yet to be completely disentangled, there is growing evidence (Klop *et al.,* 2013; Verkic *et al.,* 2018) in support of insulin resistance as the chief pathway whilst pro-inflammatory adipokines are also implicated. These suggest that obesity may impacts on dyslipidaemia and diabetes via a similar mechanism involving insulin resistance and inflammation.

Evidence also showed that dyslipidaemia is a major risk factor for CVDs (Anum and Adera, 2004). For instance, the findings from a meta-analysis of prospective studies by Anum and Adera (2004) showed increased CHD risk (1.24, 1.1–1.37) in relation to hypercholesterolemia in those 65 years and above. Evidence also showed increasing recoveries from cardiovascular outcomes in those treated with low density lipoprotein lowering agents (Biagent *et al.,* 2005; Sabestine *et al.,*2015) confirming that dyslipidaemia impacts on CVD risks. These findings support dyslipidaemia as an indirect pathway between obesity and CVDs. Therefore, it is not surprising for hyperlipidaemia to contribute to increased risk of incident dementia since they are also one of the chief risk factors for CVDs.

There are several mechanisms proposed for the role of lipids in dementia (Reitz, 2012; Chew et *al.,* 2020). One mechanism that underpins the role of lipids in dementia is the effects of Metabolic Syndrome (MetS). MetS and its components, which includes dyslipidaemia, glucose metabolism and high BP have been associated with central obesity and linked with risk of cognitive impairment and dementia (Frisardi *et al.,* 2010). The co-existence of these vascular factors contributes to a heightened risk of dementia (Li *et al.,* 2011).

Lipids are involved in the blood-brain barrier, processing of the Amyloid Precursor Protein (APP), myelination, cell membrane formation, receptor signalling, inflammation, oxidation and energy storage or balance (Chew *et al.,* 2020). Dementias are linked to lipid metabolism with cholesterol, sphingolipids, phospholipids, glycerolipids and gangliosides being the ones implicated (Wong *et al.,* 2017). For instance, the main cholesterol carrier protein that facilitates the delivery of cholesterol to neurons from astrocytes, where it is synthesized, is the Apolipoprotein. Evidence showed that APOE ε4 carriers with altered cholesterol and sphingolipid metabolism develop Alzheimer's disease (Bandaru *et al.,* 2009).

Though the precise mechanism involved in cholesterol and the risk of dementia is yet to be clarified, cholesterol might bind to amyloid precursor protein and facilitate its processing by β-site amyloid precursor protein–cleaving enzyme 1 (BACE1 or βsecretase) and g-secretase (Chew *et al.,* 2020). It also documented that cholesterol links with sphingolipids in membranes to form lipid raft, which anchors numerous essential transmembrane proteins implicated in AD pathogenesis (Ehehalt *et al.,* 2003. Begum et al., 2016)

2.4.2.3 Diabetes

Findings support the link between obesity and diabetes (Vazquez *et al.,* 2007; Hartemink *et al.,* 2006; Abdullah *et al.,* 2011). Evidence from a meta-analysis of 18 prospective cohort studies (Abdullah *et al.,* 2010) found that, compared to normal weight people, the relative risk (RR) of type 2 diabetes in the obese was 7.19 (5.74-9.00) and in the overweight, it was 2.99 (2.42-3.72). The pooled estimates were based on included studies with measured BMI and clinical diagnosis of diabetes in those of age 18-80 years and which adjusted for at least three key covariates including age, family history of type 2 diabetes and physical activity. In addition, recent evidence (Riaz *et al.,* 2018) from meta-analysis of Mendelian Randomization Studies (age 50-64 years) found that obesity was associated with increased risks of diabetes (1.67, 1.30-2.14) and Coronary artery disease (1.20, 1.02-1.41). The aetiology of diabetes is not completely known. However, type 2 diabetes may be triggered by obesity via mechanisms of inflammation, oxidative stress, and insulin resistance (Cheung and li 2012).

The research evidence (Jutilainen *et al.,* 2004; Woodall *et al.,* 2006; Kloppenborg *et al*., 2008; Lazano *et al.,* 2010; Cui *et al.,* 2011; Chatterjee et al., 2016) showed that diabetes is associated with several health consequences. Diabetes was associated with heightened (2-4 times) risk of stroke (Cui *et al.,* 2011) which is a major cause of cardiovascular mortality in the Asian population (Woodall et al., 2006; Lazano *et al.,* 2010). Findings from Finland also showed an increased risk of CHD in type 2 diabetic men (2.8, 2.0-3.7) and women (9.5, 5.5-16.9) compared to those without diabetes after 13 years of follow-up of a cohort of age 45- 65 years (Jutilainen *et al.,* 2004). The systematic review by Kloppenborg *et al* (2008) found that diabetes in older age conveyed the greatest risk of incident dementia among the vascular risk factors. A recent meta-analysis of over 2.3 million people with 102,274 dementia cases (Chatterjee et al., 2016) showed that people with type 2 diabetes had over 60% increased risk of developing dementia (1.62, 1.45-1.80) compared with those without diabetes.

The biological mechanisms that underpins the association of diabetes and dementia is unclear. However, evidence from research (Ahtiluoto *et al.,* 2010; Callisaya *et al.,* 2013; Ninomiya, 2014) suggest that insulin metabolism, high blood glucose toxicity, inflammatory processes, and vascular changes play important roles dementia pathogenesis. Insulin resistance, secondary to overweight/obesity, is the chief driver of hyperglycaemia in type 2 diabetes (Callisaya *et al.,* 2013). Pancreatic failure to handle insulin requirement is associated with elevated levels of blood glucose, and insulin also play a direct role in neuronal communication, memory formation and in regulating inflammatory pathways linked with increased expression of interleukin-6 in the central nervous system (Craft and Watson, 2004; Callisaya *et al.,* 2013). Evidence suggests that vascular associated cognitive impairment and dementia emanates from atherosclerosis and altered cerebral energy metabolism triggered by insulin resistance (Ahtiluoto *et al.,* 2010).

Furthermore, the prolonged build-up of excess blood glucose exerts toxic effect through oxidative stress which culminate in vascular changes in the nervous system and accumulation of end products of advanced glycation as detected in Alzheimer's disease. The reaction of sugars, other dicarbonyl compounds and cellular proteins results in the advanced glycation end products (AGEs) which triggers microvascular and macrovascular complications of type 2 diabetes through proinflammatory pathways (Radoi *et al.,* 2012; Callisaya *et al.,* 2013). Oppositely, cognitive impairment may result from increased coagulation factors and neuronal death due to acute hypoglycaemia (Ninomiya, 2014; Chatterjee et al., 2016). The risk of AD is known to be elevated by both the inflammatory process in the brain and oxidative stress, and these contribute to neurodegeneration by promoting formation of neurofibrillary tangles and beta-amyloid plaques (Arvanitakis *et al.,* 2004; Ahtiluoto *et al.,* 2010; Srikanth *et al.,* 2011).

2.4.2.4 Cardiovascular diseases (CVDs)

Cardiovascular diseases (CVDs) are the major causes (30.3%) of morbidity, disability, and mortality in older adults internationally (Prince *et al.,* 2015). Overweight and obesity are modifiable risk factors for CVDs such as Coronary Heart Disease (CHD), stroke, heart failure, atrial fibrillation, and sudden cardiac deaths (De Koning *et al.,* 2007; Guh *et al.,* 2009). For instance, the evidence from a systematic review and meta-analysis (Guh *et al.,* 2009) showed an increased risk of coronary artery disease in people with overweight (1.29, 1.18-141) and obesity (1.72, 151-1.96) using measured BMI. The pooled estimates were from eleven cohort studies (age 27-84 years) with a mean follow-up of 12.5 years. This study also found a higher corresponding risk of 1.41 (1.16-1.72) and 1.81 (1.45-2.25) using WC. The higher risk observed for WC compared to use of BMI as measure of adiposity may be explained by WC being a better surrogate measure of abdominal fats which consists of predominantly the White Adipose Tissue (WAT). The effects of intra-abdominal fats are exerted through insulin resistance, chronic hyperglycaemia, inflammatory processes, and vascular changes (Callisaya *et al.,* 2013). Evidence from the literature (Power and Shulkin, 2007) showed that the WC, which captures the WAT, predicts cardiometabolic risks better than the BMI which is unable to accurately distinguish between lean mass and visceral fats (Rothman, 2008). In addition, the meta-regression of prospective studies and randomised control trials by De Koning *et al* (2007) found that CVD events were predicted by adiposity measured by waist circumference (1.63, 1.31-2.04) and waist-to-hip ratio (1.95, 1.55-2.44). These findings were based on data of 258,114 participants (mean age 57 years), with 4,355 CVD events from 15 studies (12 studied CHD and 3 on strokes) and over 1,520,864 person-years of follow-up.

The mechanisms involving obesity and CVDs are complex. The literature (Chrostowska *et al.,* 2013) suggests a direct pathophysiological link of obesity and CVDs through obesity-induced cardiovascular changes, dysfunctional adipose tissue, and roles of adipokines. There is also indirect pathway via CVD risk factors such as hypertension, dyslipidaemia and diabetes which is well supported by substantial epidemiological evidence from the literature (Lu *et al.,* 2014; Koliaki *et al.,* 2018). In fact, study by Lu *et al* (2014) used data of 1.8 million adult participants from 97 cohorts to confirm that blood pressure, cholesterol and blood glucose not only act as mediators but partly explain the link between obesity and CVDs.

It may be argued that most evidence on the association of obesity with CVD came from data of the general population including older adults. However, the findings are important in understanding the impacts of older adult adiposity on incident dementia. The study by Newman *et al* (2005) which used data from prospective cohort of 3,602 male and female US older adults (≥65 years) with 5.4 years follow-up showed that CVD increases the risks of incident dementia (1.3, 1.00-1.06) and AD (1.3, 1.0-1.80) after adjustments for several covariates including; age, race, education, income, APOEε4 allele, 3MSE. The subgroup of those with Peripheral Artery Disease (PAD) showed a higher risk for dementia (2.4, 1.40-4.00) and AD (2.2, 1.10-4.50). PAD is established by a low value (<0.90) of the ratio of the ankle to the arm systolic blood pressure known as the Ankle to Arm Index (AAI) using Doppler. It is indicative of the extent of the vascular disease with low AAI reflecting extensive and diffuse atherosclerosis (Newman *et al*., 2005). This also explains why the risk of dementia is higher for PAD. Notably, the study detected a gradient of increasing risk of incident dementia depending on the extent of the CVDs. In support of this view, a recent study (Samieri *et al.,* 2018) demonstrated that better cardiovascular health in older adults (mean age 73.7 years) reduced cognitive decline and dementia risk after 8.5 years of follow-up of 745 people. These suggest increased risk of incident dementia in sicker populations who developed CVDs and CVD risk factors like diabetes, hypertension, and hyperlipidaemia. Therefore, it is difficult to rule out the hypothesis that overweight and obesity in older age increases the risk of incident dementia. This is because the evidence clearly supports a causal link of obesity and CVDs. Research is however needed to test this hypothesis since most current epidemiological evidence supports an inverse association of adiposity in older age and incident dementia risk.

2.4.2.5 Depression

Obesity and depression are both huge public health problems that affect older adults internationally. The link between obesity and depression has been well researched (Luppino *et al.,* 2010; Faith *et al.,* 2011; Jantaratnotai *et al.,* 2017.). Evidence from systematic review and meta-analysis of 15 longitudinal studies with 58, 745 participants by Luppino *et al* (2010) showed that obesity increased the risk of depression (1.57, 1.23-2.01); but conversely, depression was associated with increased risk of obesity (1.40, 1.15-1.71) in what was described as a reciprocal link between depression and obesity. A similar review by Faith *et al* (2011) which involved 25 cohort studies also found evidence of increased risk of depression by obesity though the findings for the opposite effect was less consistent. The reciprocal effects between obesity and depression were suggestive of possible biological relationship however the mechanisms involved in the association are not clearly understood.

Several mechanisms behind the reciprocal link were proposed by Luppino et al (2010). They postulated that in terms of the obesity-to-depression pathway, inflammation plays a key role in both obesity and depression, serving as a mediator of the relationship (Shoelson et al., 2007; Bremmer et al., 2008). Also, Insulin resistance in type 2 diabetes modifies the functions in the brain, thereby culminating in depression (Craft and Watson, 2004; Shoelson et al., 2007). Another pathway is via dysregulation of the hypothalamic-pituitary-adrenal axis (HPA axis), which occurs in both obesity and depression (Walker, 2001).

The literature suggests that the dysfunction of the hypothalamic-pituitary-adrenal axis (HPA axis) and elevated levels of cortisol related with the pathophysiology of both obesity and depression (Hryhorczuk et al., 2013). In terms of the obesity-to-depression pathway, fat mass is related to elevated cortisol levels at the time of waking and high cortisol reactivity under stressful circumstances (Therrien et al., 2008; Mujica-Parodi et al., 2009). Besides, chronic stress is associated with high visceral fats (Adam and Epel, 2007; Kyrou and Tsigos, 2009). Evidence showed that fat distribution and excessive fat accumulation in the central regions is more strongly and consistently related to excess cortisol owing to dysregulation of the HPA axis activity (Brown et al., 2004; Lasikiewicz et al., 2008).

Elevated cortisol from activated HPA axis is known to perform the adaptive role of energy balance restoration by increasing insulin levels and motivation for appetising food while mobilising stored energy to the major stores (Piazza and Le Moal, 1997; Mann and Thakore, 1999; Dallman et al., 2006). High cortisol in the blood is frequently associated with the subclinical depression called melancholic depression encountered in weight loss (Hryhorczuk et al., 2013). Conversely, there is evidence in support of the depression-to-obesity pathway (Weber-Hamann et al., 2002; Juruena and Cleare, 2007) through the association of hypercortisolemia depression with abdominal adiposity (Weber-Hamann et al., 2002). This is linked with reduced glucocorticoid-mediated negative feedback and increased release of corticotrophin-releasing hormone from the paraventricular nucleus (Holsboer, 2000). Besides, the most typical form of depression, marked by decreased HPA axis activity, results in weight gain from craving for carbohydrates enhanced by appetite, and mood (Juruena and Cleare, 2007; Hryhorczuk et al., 2013).

The proposed biological mechanisms involving dysregulation of the HPA axis activity and hypercortisolemia tends to support the findings of reciprocal link between depression and obesity (Hryhorczuk et al., 2013). However, the epidemiological evidence is not completely convincing. For instance, the meta-analysis by Luppino et al (2010) could not adjust for potential covariates except age and sex. It is therefore difficult to rule out confounding biases in the reported reciprocal association. Besides, another systematic review by Faith et al (2011) could not perform a meta-analysis because the included cohort studies had large differences in the covariates adjusted. There was also uncertainty about the covariates that should be adjusted by studies examining the association of depression and obesity and verse visa. The importance of confounders is further emphasised by the fact that medications such as antidepressants have been significantly associated with weight gain (Gafoor et al., 2018), while physical inactivity and dietary pattern may strongly influence the bi-directional association (Sahle et al., 2019). Therefore, more research is needed to confirm this relationship.

Evidence suggests that chronic inflammatory changes associated with oxidative stress are implicated in both obesity and depression and may serve as a pathway to incident dementia (Bornstein *et al.,* 2006; Hryhorczuk *et al.,* 2013). The findings from a major meta-analysis (Palta *et al.,* 2014) supported the link between depression and increased oxidative stress; which was proposed as a pathway to brain damage leading to dementia and serving as a target for neuroprotective treatments (Chen et al., 2011). There is also evidence in support of vascular depression hypothesis (Steffens *et al.,* 2002; Taylor *et al.,* 2013) on the role of vascular risk factors (including obesity) in the aetiology of depression which increases dementia risk. Indeed, evidence by Saczynski *et al* (2010) from prospective cohort data of 949 members from the Framingham Heart Study (mean age 79 years) with 17 years followed up for incident dementia showed that depression significantly increased incident dementia risk (1.72, 1.04-2.84) and AD risk (1.76, 1.03-3.01). The study adjusted for age, sex, education, homocysteine and APOEε4 and even when mild cognitive impairment cases were excluded to address reverse causality the results were similar.

As a whole, it is clear that while most of the evidence from epidemiological studies support beneficial effects of overweight and obesity in terms of reducing the risk of dementia, several obesity-related morbidities in older age have notable links with dementia risk. Therefore, more research is needed to clarify the impacts of overweight and obesity in older adults on the risk of dementia. In addition, whether gender has a significant impact on the magnitude and direction of the relationship needs further research.

2.4.2.6 Mobility disability

Mobility disability is a major public health issue that affects older adults (WHO, 2018). It commonly affects walking, climbing the stairs, transferring body weight and production of average walking speed in older adults (Owsley *et al.,* 2018) and it is prevalent from the age ≥60 years (Vincent, Vincent, and Lamb, 2010). It was argued (Vincent, Vincent, and Lamb, 2010) that mobility remains a critical factor in curtailing risks of CVDs, disability and mortality in older adults. It is also documented (Webber, Porter and Menec, 2010; Ul-Haq *et al.,* 2013) that mobility serves as major indicator of independent living among older adults and importantly providing a measure of health-related quality of life and survival. Overweight and obesity was postulated to impact on disability due to several health risks associated with excess weight such as CVDs, diabetes, stroke, osteoarthritis etc. (*Guh et al.,* 2009; Ul-Haq *et al.,* 2013) and this has been a subject of increased research internationally (Vincent, Vincent, and Lamb, 2010; Samper-Ternent and Al Snih, 2012; Strandberg *et al.,* 2013). A major systematic review and meta-analysis of 15 cohorts and 13 cross-sectional studies (Vincent, Vincent, and Lamb, 2010) demonstrated that mobility disability was increased by overweight and obesity in older adults with health consequences higher for women compared to men. However, the mechanism by which excess weight impacts on mobility disability is still largely unknown. For instance, it is still unclear how overweight, and obesity may bypass a disease process in older age to impact on mobility disability (Ferrucci and Alley, 2007; Strandberg *et al.,* 2013). In addition, the previous study suggests that losing excess weight at middle age to a normal weight at an older age was associated with increased health risk (Strandberg *et al.,* 2013), with risk of mobility disability and mortality higher compared to those of stable normal weight. This finding, therefore, suggests that maintaining excess weight may be beneficial in reducing disability and prolonging survival. However, the evidence is lacking to increase knowledge and understanding. Therefore, research is needed to clarify the association of body weight, mobility disability and mortality in older age.

2.4.3 Impacts of overweight and obesity on all-cause mortality

This section critically reviews the literature on the impact of overweight and obesity in older age on all-cause mortality risk. It briefly introduces the evidence of midlife obesity (<65 years) and all-cause mortality before discussion on the impacts in older age (≥65 years). These are followed by the next two sections on overweight/obesity and survival in population with major comorbidities, and the methodological issues in studies examining the association of obesity and all-cause mortality.

2.4.3.1 Obesity in younger age (<65 years) and all-cause mortality risk

The association of obesity at younger/middle age (<65 years) and all-cause mortality is less contested in the literature because of substantial evidence supporting the harmful effects (Calle *et al.,* 1999; Adams *et al.,* 2006; Aunne *et al.,* 2016; Di Angelantonio *et al.,* 2016). However, one systematic review and meta-analysis by Flegal et al (2013) triggered debates about the obesity paradox hypothesis in all adult population (≥25 years) by suggesting that, though obesity grade 2 and 3 (BMI ≥35) are harmful (1.29, 1.18-1.41), obesity grade 1 (BMI 30-<35) had no association (0.95, 0.88-1.01) and overweight (BMI 25-<30) conferred protection (0.94, 0.91-0.96) against all-cause mortality risk. However, this overweight paradox which shows protective effect, rather than harmful effects, against all-cause mortality may be due to reverse causality. Reverse causality, springs from lower BMI, underweight or sarcopenia observed at baseline due to pre-existing chronic morbidities and smoking rather than lower BMI itself being the cause of morbidities leading to death (Yu *et al.,* 2017). This weight loss linked with baseline chronic diseases such as cancer, CVDs, COPD etc. and smoking is a potential bias that may affect findings of adiposity and all-cause mortality since the loss of weight prior to mortality can lead to inverse association (Willett et al., 2013; Di Angelantonio *et al.,* 2016; Yu *et al.,* 2017).

The most recent evidence in younger/middle age was a systematic review and meta-analysis conducted by Aunne *et al* (2016), which included 230 cohort studies of over 30 million participants and more than 3.7 million deaths. The meta-analysis showed that the relative risk of all-cause mortality was 1.21 (1.18-1.25) in every 5 unit increase in BMI in the whole sample analysis of never smokers; and in studies that excluded first 1-6 years follow-up it was 1.27 (1.21-1.33), and in the never smokers of age <65 years the effect was similar (1.27, 1.22-1.34). This evidence was further supported by findings from another large study based on individual participant data from 239 prospective cohort studies across four continents, which showed an increased risk of all-cause mortality (1.52, 1.47-1.56) for excess BMI in those of age 35-49 years. This evidence showed that the large BMI was associated with an increased risk of all-cause mortality in the younger and middle age (<65 years).

2.4.3.2 Overweight/obesity in older age (≥65 years) and all-cause mortality risk

The impacts of overweight and obesity in older age on all-cause mortality has been less investigated, and the reported findings have generated controversy on the magnitude and direction of the association. The evidence from some studies that detected positive associations (De Hollander et al., 2012; Donini et al., 2012) also included suggestions that excess body weight might confer a survival advantage. Though no association between overweight and obesity in older age and all-cause mortality risk was often reported in the literature, substantial findings from cohort studies suggested that all-cause mortality risk could be reduced by overweight and obesity in older age. These conflicting literatures are discussed below

2.4.3.2.1 Positive associations of overweight and obesity with all-cause mortality

Few studies have shown a positive association of excess body weight in older adults with all-cause mortality risk. Some previous studies suggested that all-cause mortality risk was reduced by adiposity in older age (De Hollander *et al.,* 2012; Donini *et al.,* 2012; Partel *et al.,* 2014). However, the studies in the same report (De Hollander *et al.,* 2012; Donini *et al.,* 2012) have concluded that the recommended limits of adiposity indices particularly the BMI might too restrictive for older adults since the reduced risk of all-cause mortality was located within the excess body weight range. For instance, the study by De Hollander *et al* (2012) investigated the impact of continuous BMI in older age on all-cause mortality and found an increased risk. The study examined data of a 7-year follow-up cohort of 1,970 older Europeans of age 70-77 years and found that while categorical BMI had no association with all-cause mortality, the risk of all-cause mortality was increased with continuous BMI and the lowest risk (RRs not reported) was at BMI of 27.1 (95% 24.1-29.3) Kg/m^2 after adjusting for age, smoking and educational levels. Another study by Partel et al (2014) of a US cohort of white and black people found no association of overweight and obese BMI with all-cause mortality risk after 8 years follow-up in men of age ≥70 years who were never smokers and without prevalent diseases such as cancer, heart disease, stroke, respiratory disease. However, in the women counterpart, they observed significant increased risk of all-cause mortality across different overweight and obese BMI ranges including RR of 1.07 (1.02-1.12), 1.13 (1.08-1.19), 1.33 (1.19-1.49) and 1.29 (1.03-1.61) for BMI 27.5-29,9, BMI 30.0-34.9, BMI 35.0-39.9 and BMI ≥40 Kg/m^2 respectively. In contrast, a study in Spain by Guallar-Castillón et al (2009) found that over the 7 years follow-up of 3,536 older adults, the all-cause mortality risk was increased in upper quartile of WC compared to lower quartile (1.48, 1.07-2.05), while the risk was reduced in upper BMI quartile versus lower quartile (0.63, 0.45-0.88).

In a systematic review and meta-analysis by of 32 cohort studies (mean follow-up 12 years) undertaken in developed countries including 197,940 older adults (≥65 years), Winter et al (2014) found a U-shape association of BMI and all-cause mortality. It showed excess risk of mortality at both extremes of BMI range for underweight (20.0-20.9 Kg/m^2) and obesity (>33 Kg/m^2), and the nadir of the U-shape curve was between 24.0-30.9 Kg/m^2 with lowest risk (0.90, 0.88-0.92) in the overweight BMI (of 27.0-27.9 Kg/^{2}). The lack of evidence to demonstrate the strength and direction of the association was also underscored in the findings of only little effect size (1.04, 1.01-1.07) for mortality risk from a recent systematic review and meta-analysis by Aune et al (2016), which included 6 eligible cohort studies with late-life BMI out of the 230 cohorts. Therefore more evidence in older adults is needed to investigate the impact of overweight and obesity on all-cause mortality risk.

2.4.3.2.2 No associations of overweight and obesity with all-cause mortality

One notable observation about studies of excess weight in older age and all-cause mortality risk is findings suggesting no associations (Berraho et al., 2010; Takata et al., 2013; Clark et al., 2014). Analysing data of a 13 years follow-up of the cohort of 3,646 older French population (≥65 years) Berraho et al (2010) found that overweight and obesity were not associated with all-cause mortality except underweight (<18.5Kg/m²) which increased the risk by 45% (1.45, 1.17-1.78) after adjusting for co-morbidities, smoking and demographic variables. Similarly, Clark et al (2014) examined data of 10-year mortality in very old African Americans and Yoruba-Nigerians of age ≥70 years and found no association of overweight and obesity with all-cause mortality. However, all-cause mortality risk was increased in underweight African Americans (2.49, 1.40-4.43) and Yoruba, Nigerians (1.35, 1.12-1.63). The study of 675 Japanese of age 80 years in 12 years follow up showed increased all-cause mortality in older people with underweight, but not in those with obesity, while normal and overweight groups had the lowest all-cause mortality risk (Takata et al., 2013). These findings in older adults, therefore, supported lack of associations.

2.4.3.2.3 Inverse associations of overweight and obesity with all-cause mortality

The literature is also dominated by findings of inverse associations which suggest that overweight and obesity in older age may confer a survival advantage. For instance, the study by Beleigoli *et al* (2012) found that continuous BMI was associated with reduced risk of all-cause mortality after 10 years of follow-up of a cohort of 1,450 older adults from Brazil. They found reduced risk (0.85, 0.80-0.90) for continuous BMI after adjusting for several covariates, including in analysis of non-smokers (0.85, 0.80-0.90) and it was stronger (0.83, 0.73-0.94) after excluding first 5 years mortality and those with weight change. The study also found overweight BMI (25-30) was inversely related to all-cause mortality (0.76, 0.61-0.93) but not obesity (BMI ≥30) (0.85, 0.64-1.14). Similarly, the study by Dahl et al (2013) of a Swedish cohort of 882 older adults (age 70-92 years) also found an inverse association of overweight with all-cause mortality over the 18 years follow up (0.80, 0,67-0.95) though no effect was observed in obesity (0.93, 0.72-1,22). The meta-analysis by Flegal *et al* (2013) using WHO BMI categories found an inverse association of overweight with all-cause mortality (0.90, 0.84-0.90) in older adults (≥65 years), but no significant association of obesity (1.02, 0.81-1.29). This set of studies, therefore, suggest that overweight and obesity confer beneficial health effects against all-cause mortality risk. However, the protective effects were mostly detected in overweight and not obesity. This suggests that what is often observed is more of an overweight paradox that the general term obesity paradox in the epidemiological literature.

In all, the literature of overweight and obesity with all-cause mortality revealed several inconsistencies with most findings suggesting that excess weight may confer health benefits against death. It may be argued that the four unresolved issues in the literature of adiposity in older adults and all-cause mortality (Partel *et al.,* 2014) need further scrutiny. These are 1) whether overweight is beneficial or harmful for survival in late life, 2)the degree of influence of smoking and pre-existing morbidities on the association of overweight/obesity with all-cause mortality, 3) age of BMI assessment and all-cause mortality risk, and 4) racial disparity in the association of BMI with mortality.

2.4.4 Association of overweight and obesity with all-cause mortality in people with co-morbidities

In most of the epidemiology literature of obesity and all-cause mortality or survival in population of patients, the term "obesity paradox", which is technically coined as reverse epidemiology, describes better survival or reduced all-cause mortality risk detected in overweight and obese patients with established chronic diseases including dementia (García-Ptacek *et al.,* 2014) and cardiovascular disease (Dhana *et al.,* 2016; Koliaki *et al.,* 2018). Since the paradox in the findings of overweight, obesity and survival was first reported (Fleischmann et al., 1999), there has been a surge in research with numerous studies (Schmidt and Abdulla, 2007; Larvie et al., 2013; Sharma et al., 2015) including recent findings buttressing the hypothesis in the older population (Wang et al., 2015). The findings from a meta-analysis (Sharma *et al.,* 2015) of 6 studies on the association of BMI with all-cause and cardiovascular mortality in 12,807 patients (mean age 65.6 years) with established chronic heart failure showed that the lowest risks of CVD mortality (0.79, 0.70-0.90) and hospitalisation (0.92, 0.86-0.97) were in the overweight patients (BMI 25-29.9) compared to normal weight patients (BMI 20-24.9). The findings for the obese (BMI 30-34.9) and severely obese patients (BMI≥35) were not significant, while underweight exhibited increased risks of all-cause mortality (1.27, 1.17 – 1.37), CV mortality (1.20, 1.01 -1.43), and hospitalization (1.19, 1.09 – 1.30) after 2.85 mean years of follow-up.

The largest study on the subject (Wang *et al.,* 2015), which pooled the data from 89 studies in a meta-analysis of 1,300,794 patients with cardiovascular events of coronary artery disease with a mean follow-up of 3.2 years, examined the effects of BMI on mortality and cardiovascular events and reported J-shape associations. The findings showed inverse association of overweight (0.69, 0.64 - 0.75) and obesity (0.68, 0.61 to 0.75) with short term mortality (<6 months), also with long term (≥6 months) mortality (0.78, 0.74-0.82; 0.79, 0.73-0.85). However, after 5 years follow-up the association was no longer significant for obesity (0.99, 0.91-1.08). Instead, an increased risk (1.25, 1.14-1.38) was observed for Class II/III obesity (BMI ≥35) even though it was lowered in short term (0.76, 0.62- 0.91). This evidence showed that despite findings of excess body weight conferring protection against mortality, the length of follow-up is important in detecting the deleterious effects of overweight and obesity.

2.4.5 Methodological issues in studies examining the impact of overweight and obesity on all-cause mortality

There are several methodological issues from the literature on the study of the impact of overweight and obesity on all-cause mortality. This includes effects of smoking and pre-existing morbidities on the association, reverse causation, length of follow-up, use of BMI and collider stratification bias.

2.4.4.1 Smoking

Smoking has lingered at the centre stage of the debate on BMI and all-cause mortality relationship (Stoke and Preston, 2014; Partel *et al.,* 2014; Wang et al., 2016; Di Angelatonio *et al.,* 2016). In older adults, smoking is strongly and clearly associated with all-cause mortality (Gellert *et al.,* 2012; Müezzinler *et al.,* 2015), and evidence suggests it may jointly combine with obesity to predict early mortality (Roos *et al.,* 2016). In fact, the systematic review and meta-analysis of cohort studies in older adults (≥60 years) from 17 countries (Gellert *et al.,* 2012) showed that it significantly elevated the risk of mortality by 83%. In addition, smoking affects body weight itself, with significant weight loss in smokers compared to non-smokers, leading to lower BMI (Winslow *et al.,* 2015). Therefore, failure to adequately account for smoking in studies of adiposity and all-cause mortality would bias the risk estimates.

One challenge is addressing bias due to smoking. Some researchers adopt exclusions of smokers or perform a subgroup analysis of smokers and non-smokers (Aune *et al.,* 2016; Di Angelantiono *et al.,* 2016), while others prefer to account for smoking by adjustment in statistical models (Flegal *et al.,* 2013). However, it was contended that adjustments for smoking in the statistical models do not address residual confounding associated with smoking (Winslow *et al.,* 2015). Therefore, separate or sub-group analysis for non-smokers and smokers may preferably deal with residual confounding.

2.4.4.2 Pre-existing morbidities

It was argued (Joshy *et al.,* 2014; Partel *et al.,* 2014) that the inverse associations between adiposity and all-cause mortality springs from pre-existing morbidities effect. Recent evidence (Joshy *et al.,* 2014) of methodological issues underlying the conflicting findings of BMI and all-cause mortality relationship showed that the most reliable risk estimates of the impact of overweight and obesity on mortality are from studies that accounted for baseline morbidities. This is true since older adults are prone to multiple morbidities due to ageing and may impact on their body weight and predispose them to health risks (Guh *et al,* 2009). While the extent of confounding by pre-existing morbidities on adiposity and mortality relation remains debatable, there is no agreement on the best approach to handle the inherent bias. A common approach by most studies is adjustment for chronic illnesses in the models. However, caution in the choice of covariates particularly those considered to be on the causal pathway of obesity and all-cause mortality such as diabetes and physical activity is important (Di Angelantonio *et al.,* 2016). In addition, there is growing evidence, building on the analytical approaches deployed by previous studies, that excluded participants with pre-existing chronic illnesses from the study or limiting the analysis to relatively "healthier" participants improve the validity of results (Aunne *et al.,* 2016; Di Angelantonio *et al.,* 2016). Although this approach was contested for its extent of validity (Flegal et al., 2010), some studies that excluded pre-existing chronic diseases and data of first few years of follow-up in limiting inverse associations have reported harmful effect of overweight and obesity on all-cause mortality (Calle *et al.,* 1999; Adams *et al.,* 2006; Aune *et al.,* 2016; Aunne *et al.,* 2016; Di Angelantonio *et al.,* 2016).

2.4.4.3 Reverse causality

Reverse causality, in the context of the relationship between BMI and all-cause mortality, emanates from lower BMI observed at baseline due to pre-existing morbidities and smoking rather than lower BMI itself being the cause of morbidities leading to death (Yu *et al.,* 2017). This weight loss associated with baseline chronic diseases and smoking is a potential bias that may affect findings of adiposity and all-cause mortality since the loss of weight prior to mortality can lead to inverse association (Willett et al., 2013; Di Angelantonio *et al.,* 2016; Yu *et al.,* 2017). The approach to reducing the effect of reverse causality is excluding the first few years' data and those with pre-existing illness (Calle *et al.,* 1999; Adams *et al.,* 2006; Aune *et al.,* 2016). However, there is no consensus on how many years' data should be excluded. One older review proposed that 1-2 years could be enough (Zamboni *et al.,* 2005) whilst some studies over the years (Freeman *et al.*, 2006) and more recently (GBMC 2016) have excluded 3 or 5 years data to reduce reverse causality. The recent study by Di Angelantonio *et al* (2016) based on individual participant prospective cohort data in over 10 million people addressed the issue of confounding and reverse causality. They excluded pre-existing illness, first 5 years of follow-up data, and also limited the analysis to never-smokers and found 21% increased risk (1.21, 1.27-1.35) of all-cause mortality for higher BMI at baseline age of 70-89 years. This suggests that the approach could be useful in the study of body weight and all-cause mortality. However, this also requires caution since there is concern of ending up with reduced samples sizes which limit statistical power or reduces significance (Flegal *et al.,* 2011).

2.4.4.4 Length of follow-up

The impacts of overweight and obesity on all-cause mortality is hard to observe in <10 years follow-up studies but the effects could manifest with longer-term (≥ 10 years) Follow-up (Aunne *et al.,* 2016). This is because unlike other diseases such as infectious diseases or even some chronic health conditions (e.g. incident dementia) the risk of death associated with overweight and obesity takes time to unfold. In fact, evidence suggests that over the life span, longer duration of follow-ups is required to observe deleterious effects of adiposity (Calle *et al.,* 1999; Adams *et al.,* 2006; Wang *et al.,* 2015; *Aunne et al.,* 2016). Even evidence from obesity and all-cause mortality in population of patients suggest that the duration of follow-up could explain differences in outcome from cohort studies. For example, the largest review of obesity and survival in population of patients by Wang *et al* (2015) clearly found that the inverse association for obesity in short term follow-up (0.79, 0.73-0.85) vanished with longer follow-up (0.99, 0.91-1.08) while increased mortality risk was detected in those with excessive weight class II/III (1.25, 1.14-1.38). Therefore, prolong follow-up is crucial to the detection of health effects of overweight and obesity.

2.4.4.5 Use of BMI

It was argued that BMI does not accurately distinguish between body fats and lean mass or unable to account for body composition patterns and regional fats (Rothman, 2008). This, therefore, makes it highly susceptible to underestimation of CVD and mortality risks. A recent study by Iliodromiti *et al* (2018) including 296, 535 adults of white European descent showed that compared to other adiposity measures like WC, the BMI was more susceptible to confounding by baseline chronic illnesses. Besides, the BMI calculations require height and body weight measures and could be challenging when measure errors occurred and also older adults are liable to loss of height with ageing due to vertebra disc compression (Groot *et al.,* 2002; Zamboni *et al.,* 2005).

2.4.4.6 Collider stratification bias

Collider stratification is the conditioning upon a common effect of exposure and outcome which may occur while designing a study or at analysis stage via regression adjustments, restriction or stratification (Hernan et al., 2004; Cole *et al.,* 2010). It is postulated as a possible methodological explanation for the paradoxical findings in the study of adiposity and all-cause mortality particularly in population of patients (Banack and Kaufman 2014; Lajous *et al.,* 2014; Stoke and Preston, 2014). The literature suggests false associations, or reverse association may result from conditioning on a variable affected by exposure and outcome (Rothman *et al.,* 2008; Banack and Kaufman 2014; Lajous *et al.,* 2014; Stoke and Preston, 2014). For instance, studies of BMI (exposure) and mortality (outcome) are often conditioned on a variable (CVD) by restricting participation at baseline to those with confirmed CVD. The collider is the CVD because it could be a consequence of obesity, and CVD is associated with increased risk of mortality. Therefore, in the study of obesity and all-cause mortality, the common effect of the collider (CVD) on the relationship between BMI and mortality is may be unmeasured and yet large enough to falsify association between the exposure and outcome. However, while this presents a useful explanation, it is unclear from research how this unmeasured effect of the collider may be correctly estimated. While this is an area for future research, addressing most of the methodological issues discussed so far would help minimise bias in epidemiological studies or enhance the validity of findings.

2.5 Summary of findings, gaps and rationale for the study

Prevalence of overweight and obesity has increased more in Low- and Middle-Income Countries (LMICs) like China than those in high-income countries that bear greater prevalence. However, knowledge of the risk factors for overweight/obesity in older people were predominantly derived from studies undertaken in high-income countries. Most findings were from the studies of the general population, and this may not apply to older adults who could present with different risk factors from the rest of the population, owing to different body characteristics and lifestyle changes associated with both ageing and retirement. The literature suggested that overweight/obesity may involve several risk factors combining to increase the prevalence in older age. This may include socioeconomic factors lifestyle factors, social network, etc. However, the magnitude and direction of the association in older adults are poorly understood. Besides, evidence from prospective cohort studies to help investigate the long-term risk factors for overweight and obesity are scarce, while cross-sectional studies are limited by temporal order issue or prone to reverse causality. Importantly, investigating the risk factors from a public health and social determinant perspectives would help identify risk and protective factors for the prevention of excess weight in older age.

The knowledge and understanding of the association of older adult overweight and obesity and incident dementia are limited. Most evidence supported beneficial health effects of excess body weight against incident dementia risk. The large body of evidence in support of the inverse associations of overweight, obesity and incident dementia included individual cohort studies, systematic reviews and meta-analysis. This is regardless of evidence of obesity-related co-morbidities being strongly linked with dementia including hypertension, dyslipidaemia, diabetes, and CVDs. However, most of these studies are from high-income countries with a lack of data from LMIC like China that present different risk factors since adiposity varies with age, sex, ethnicity and race. Besides, different population may also present unique risk factors for several other reasons including the level of social support, depression and cardiovascular health etc. Several issues were identified which may explain the findings from cohort studies which needs to be addressed through further research, including the type of adiposity indices, confounders, pre-existing diseases, length of follow-up, reverse causation, gender effect.

The evidence of the association of older adult overweight and obesity with all-cause mortality is weak compared to the substantial evidence for midlife obesity. Most evidence in older adults (≥65 years) reinforces the medical hypothesis that overweight and obesity in older age confers protection against the risk of all-cause mortality or prolong survival. The review showed that some studies, although having detected harmful effects, concluded that excess weight in older adults should be encouraged since minimum BMI for survival were located in the overweight to the obese range. Similarly, several studies reporting no association also found support for the beneficial health effects of excess body weight. Therefore, whether overweight is beneficial or harmful for late-life survival is unclear and need to be further studied. Furthermore, several methodological issues identified from the literature needs to be addressed in testing the 'obesity paradox hypotheses' in research using prospective cohort data from a different population. These include adiposity indicator, smoking, pre-existing morbidities, reverse causation, length of follow-up, and effect modification by gender. In addition, most findings in the literature on health effects of overweight and obesity in terms of incident dementia and survival have come from quantitative research internationally and there is lack qualitative data generated from the views of older adults to increase knowledge and understanding of the health effects of excess body weight. Such evidence would also guide public health strategies on prevention and management of body weight in older age to reduce morbidities and extend survival.

2.8 Conclusion

The review of the literature on risk factors and health effects of overweight and obesity in older adults revealed several gaps. The knowledge of the major risk factors for overweight and obesity in older adults is lacking. It is unknown whether overweight and obesity in older age confer beneficial or harmful effects on incident dementia and all-cause mortality. To help advance knowledge and understanding, a mixed methodology approach using data from quantitative research by prospective cohort design and qualitative study by focus group discussion would be employed for the study.

CHAPTER THREE: IMPACTS OF OVERWEIGHT AND OBESITY ON DEMENTIA RISK: A SYSTEMATIC LITERATURE REVIEW AND A META-ANALYSIS

3.1 Introduction

Dementia is an age related chronic ill health condition that affects older people. More than 90% of the dementia cases manifests from the age of 60 years, while 32% are found in those of age ≥85 years (Prince et al., 2015; Alzheimer's Association, 2016). Dementia has no cure; therefore, identifying and understanding its risk or protective factors is an urgent research priority to guide public health strategies on preventing or delaying the onset of the disorder (Shah et al., 2016). The term "incident dementia" describes newly diagnosed cases which manifests in a population after exposures to certain risk factors. One of such factors of interest is overweight and obesity since there is substantial evidence (Meng *et al.,* 2014) that midlife vascular factors predict incident dementia risk.

There is a difference between midlife and late life overweight/obesity and incident dementia risk. The evidence from research of midlife obesity (aged 35-<65 years) showed a strong association with incident dementia (Whitmer *et al.,* 2005; Albanese *et al.,* 2017). For instance, a recent systematic review and meta-regression analysis by Albanese et al (2017) of 589,649 participants from 12 cohort studies on midlife BMI and dementia found that obesity increased the risk by 47% (RR 1.47, 95%CI: 1.06-2.03). However, the findings from studies in older adults (≥65 years) are conflicting with most studies suggesting reduced risks (Anstey et al., 2011; Emmerzaal *et al.,* 2015; Pedditzi *et al.,* 2016). For instance, the previous review and meta-analysis by Anstey *et al* (2011) found no association of late life BMI with incident dementia (0.98, 0.92-1.04) but midlife obesity increased the risk of dementia (1.26, 1.10-1.44). The review of cohort studies conducted from 2003 to 2013 on the association of BMI with incident dementia (Emmerzaal *et al.,* 2015) concluded that large BMI in middle age increased the risk of dementia, while in older age it reduced the risk. In 2016 Pedditzi *et al* published a systematic review paper, which pooled data of 3,262 older adults (≥65 years) from four prospective cohort studies with 362 cases. The data showed that obesity reduced the risk of incident dementia by 17% (0.83, 0.74-0.94), and overweight had no significant association (0.88, 0.76-1.02). In the paper, however they found that obesity in younger/middle age (<65 years) increased the risk of dementia by 41% (1.41, 1.20-1.66). Their findings were consistent with those in previous systematic reviews (Anstey et al., 2011; Emmerzaal *et al.,* 2015). The current literature and systematic reviews therefore supported the harmful effects of midlife overweight and obesity on dementia risk. However, in late life the evidence suggested beneficial health effects of excess body weight in older age of reducing the risk of dementia.

However, since the last review (Pedditizi *et al.,* 2016) more studies were published, which showed other findings, while the previous literature review (Pedditizi *et al.,* 2016) missed a few studies (Buchman et al., 2005; Lucca et al., 2012; Tolppanem *et al.,* 2014; Neergaard *et al.,* 2016). In addition, there was lack of research on the impact of WC on incident dementia risk since most studies focused on BMI as overweight and obesity indicators. Therefore, there is need to update the current knowledge of the association of overweight and obesity in older age with incident dementia risk. This Chapter presents an updated and comprehensive systematic literature review. It included new data from Anhui cohort study from China in meta-analyses to examine the impact of overweight and obesity measured by BMI and WC in older age on incident dementia risk, and whether the association differ by the duration of the cohort follow-up.

3.2 Methods

3.2.1 Search strategy

A search strategy was developed to ensure a comprehensive search of the literature using Population, Exposure and Outcome framework (PEO) (Khan *et al.,* 2003; Bettany-Saltikov *et al.,* 2012). The following search terms were developed; ("dementia" OR "Alzheimer's, vascular dementia, cognitive impairment and cognitive decline") AND ("BMI, 'Body Mass Index'" OR "Overweight, Obesity, Adiposity and Waist Circumference"). The search terms were for all fields and included MeSH terms, abstract, title or text words. The following databases were searched; Embase, Medline, PubMed, CINAHL, Psych-info and Cochrane library. The search of the literature was done until 31st July 2016 starting from the earliest dates of each of the databases without language restriction. To ensure all searches were done according to planned protocol, two other colleagues (Aishat Bakre, Zhou Weiju) used the same key terms to search all databases.

3.2.2 Inclusion and exclusion criteria

There was a total of 14,529 records from completed search in all databases. They were screened using Endnote software to identify and remove 2,498 duplicates. 12,031 records were left for further screening. Of them, 11,960 were excluded due to non-relevance, and there were 71 left for full text reading after screening for title and abstracts. The full text of the 71 journal articles were read and a manual reference search was also conducted to find articles missed from the database search. The grey literature was also explored by identifying abstracts from conferences (Lucca *et al.,* 2012; 16). E-mails were sent to authors of potential articles for more information to judge their eligibilities. For inclusion, studies selected for the review were required to be of prospective cohort design that investigated incidence of all dementia or specific type of dementia such as Alzheimer's disease or Vascular dementia in relation to overweight or obesity. Studies were included whether they used BMI or Waist Circumference (WC) as measures of adiposity, while the study participants must be community-based older adults with baseline age of ≥65 years. Studies of cross-sectional and case control study designs were not included. Articles that assessed only cognitive impairment as an outcome without formal diagnosis of dementia were excluded. The total eligible original studies for the literature review after assessment according to inclusion and exclusion criteria was sixteen (16); three out of these came from manual reference and grey literature search. Figure 4 shows a flow chart of the process involved.

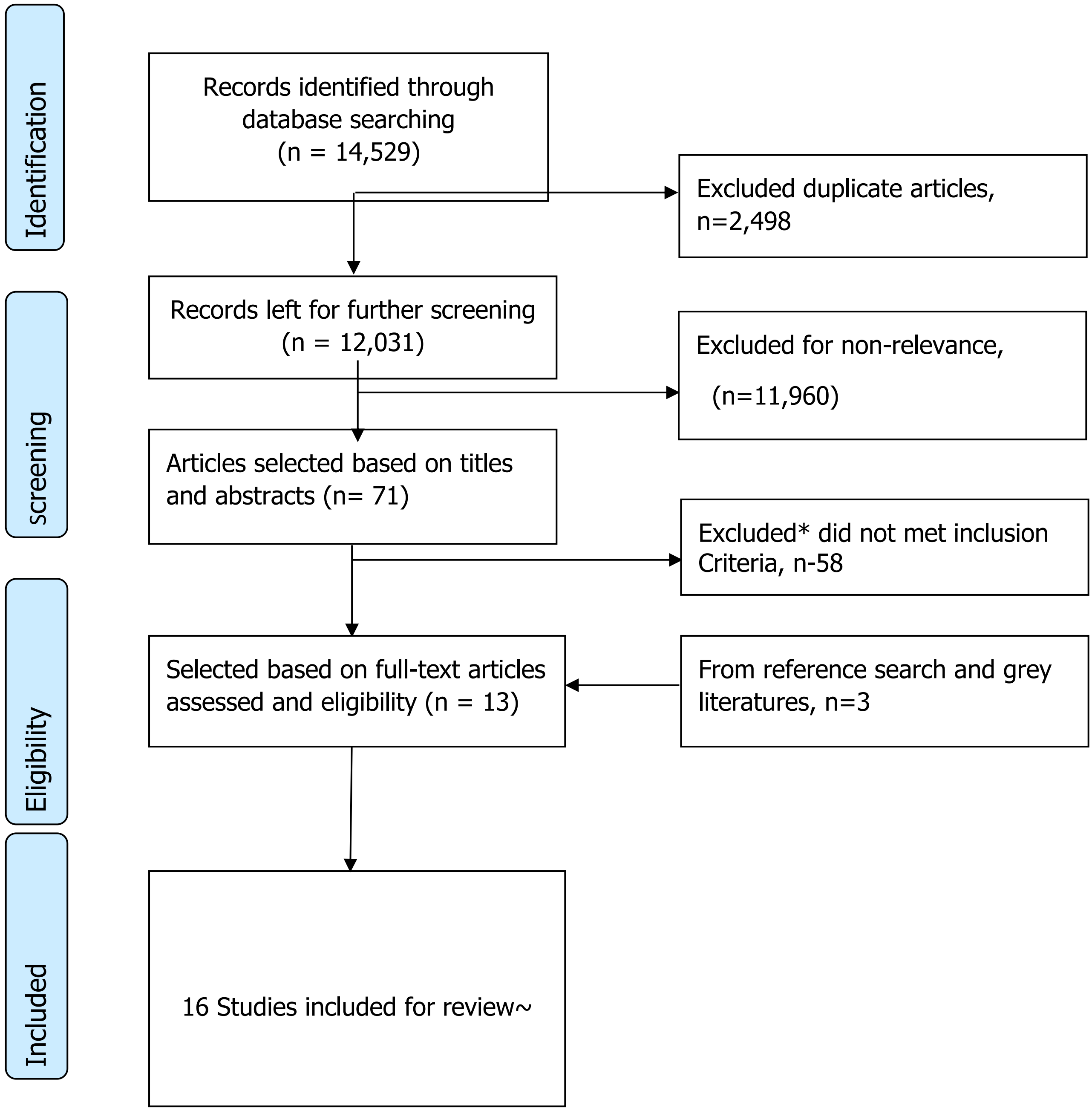


Figure 3 The flow chart for the literature search and inclusion of studies for systematic literature review

*reasons included; studied midlife or younger baseline age <65 years, other outcome variables such as MCI, dementia+MCI, did not assess the key predictor (BMI or WC), different study design (such as cross-sectional or case control) etc.

3.2.3 Data extraction and quality assessment

The conduct of the systematic literature review followed the PRISMA guidelines (Liberati *et al.,* 2009). Each of the 16 articles was reviewed by two reviewers (Isaac Danat and Aisha Bakre /Weiju Zhou) and assessed independently using a predesigned data extraction form to extract the necessary information from the chosen studies. Data extraction included participants' recruitment and characteristics, Sample size and follow up, baseline measure of overweight and obesity, endpoint outcomes with dementia cases and diagnosis criteria, 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 the differences remained the 3rd reviewer discussed with them to reach agreement. The quality assessment of each article was conducted by employing the Newcastle-Ottawa Scale (Wells *et al.,* 2018).

3.2.4 Meta-analysis

Eligible data from 14 out of the 16 studies in the systematic literature review and this new data from the Anhui cohort study (Chapter six) were pooled in a meta-analysis. 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 separately for AD and VaD. The studied population was each sample in the study based on place, time (years) and person (gender, etc) where applicable. For the analysis, only reported relative risk (eg, RRs, Hazard ratio, or Odds ratio) and 95% CIs from confounder adjusted models were included. 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. Funnel plot and Egger's tests were used to assess the risk of publication bias.

The first meta-analysis provided a general picture of the association between elevated BMI and incident dementia. It included the RR (95%CI) for continuous BMI from each studied population or if the study did not investigate continuous BMI in relation to dementia risk, the highest BMI category was used. Of 14 studies which were used in the meta-analysis, three studies (Nourhashemi *et al* 2003; Hayden *et al.,*2006; Lucca *et al.,* 2012) used self-reported BMI in their analyses, which might have a potential source of bias, and thus the analysis was repeated in all studies with measured BMI, after excluding the three studies.

The second analysis examined continuous BMI associated with incident dementia. The third analysis was for data of continuous BMI associated with incident dementia stratified by length of follow-up using 9 years as cut off for short term (< 9 years) and long term (≥9 years) studies. This was based on the theory that the duration of follow up would account for or contribute to the differences in findings from cohort studies (Zamboni *et al.,* 2005). In addition, the findings from research showed that the health effects of excess weights may take time to manifest (Zamboni *et al.,* 2005; Johnson *et al.,* 2006), and a duration of 9 years was considered in this meta-analysis as a cut-off point time for the impacts of overweight and obesity on development of dementia to be evident. This was informed by previous evidence which showed that the mean duration of follow-up needed for incident dementia to be detected after exposure to risk factors like excess weights in older age varies between seven to eight years, and this is inclusive of the prodromal stages of the disease (Johnson *et al.,* 2006). Previous studies in middle age population also showed that this could be up to ten years or more (Knopman *et al.,* 2007).

The fourth set of meta-analyses pertained to categorized BMI and incident dementia. This included separate pooled risk estimates for obese, overweight, underweight people in relation to all dementia, Alzheimer's disease and vascular dementia using reference categories in respective primary studies. The fifth set of meta-analyses assessed the impact of Waist Circumference (WC) on incident dementia and in this analysis, the term 'large WC' was used to define its third quartile or the action level 1 while the term 'larger WC' refers the fourth quartile or the action level 2 based on WC classifications from existing literature. These groupings were necessary since included studies used different WC cut-offs or quantiles in their analysis. The Stata/IC 14.0 statistical software package (Stata Corp, College Station, Texas, USA) was used for all meta-analyses.

3.3 Results

3.3.1 Quality assessment of included studies

Table 1 shows the study quality assessed by the Newcastle Ottawa assessment scale for 16 cohort studies in the review. The details of the individual score for each item assessed on the quality assessment scale are shown for studies that examined the association of overweight and obesity with dementia risk in older adults. The ratings were based on the total of each score (denoted by a star) out of 10 items on the rating scale. The 10 items are assessed are clearly defined beneath the table below. The total score of 5-6 means good, 7-8 very good and 9-10 portray excellent scores. Overall, the ratings for study quality of included studies ranged from good to excellent.

Table 1

Study	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Yoshitake *et al* 1995	★	★	★	★	★			★	★	★
Borenstein *et al* 2001	★	★	★	★	★		★	★	★	★
Gustafson *et al* 2003	★	★	★	★	★	★	★	★	★	★
Nourhashemi *et al* 2003	★	★		★	★		★			
Buchman *et al* 2005	★	★	★	★	★		★	★	★	★
Hayden *et al* 2006	★	★		★	★		★	★	★	★
Luchsinger *et al* 2007	★	★	★	★	★		★	★	★	★
Atti *et al* 2008	★	★	★	★	★		★	★	★	★
Dahl *et al* 2008	★	★	★	★	★	★	★	★	★	★
Hughes *et al* 2009	★	★	★	★	★	★	★	★	★	★
Fitzpatrick *et al* 2009	★	★	★	★		★	★	★	★	★
Scarmeas *et al* 2009	★	★	★	★	★	★	★	★	★	★
Power *et al* 2011	★	★	★	★		★	★	★	★	★
Lucca *et al* 2012	★	★		★	★	★	★	★		
Tolppanen *et al* 2014	★	★	★	★	★	★	★	★		★
Neergaard *et al* 2016	★	★	★	★		★	★	★	★	★

(**1**) Cohort truly representative (**2**) Controls from the same cohort (**3**) Clear measurement of obesity at baseline (**4**) Adequacy of Follow-up duration (≥24 months) (**5**) Reliable methods of dementia and AD diagnosis (i.e., Quality of outcome) (**6**) Data analysis controlled for smoking and medical co-morbidities (**7**) Data analysis controlled for any other three confounders (Age, social class/education, alcohol, ApoE4 carrier status, medical therapies and ethnicity etc.)(**8)** Findings interpreted well (**9**) Weakness mentioned and explained clearly (**10**) Paper written well.

3.3.2 Findings of the systematic review

The systematic review included sixteen studies all of cohort study design and conducted in high income countries with no eligible study from middle-and low-income countries. Notably, seven studies were conducted in the USA; two each were undertaken in Sweden and Finland while one study each was from France, Denmark, Italy, Australia, and Japan. The sample sizes ranged from 226 to 12,047 and included 38,219 participants and 4,479 dementia cases while the length of follow-up of the cohort ranged from 3 to 18 years. There were only three studies with long duration of follow-up of at least nine years (Gustafson *et al.,* 2003; Atti *et al.,* 2008; Tolppanem *et al.,* 2014) while all the remaining 13 studies had shorter follow-up periods.

The results showed inverse association of BMI with dementia in thirteen studies of which ten were statistically significant. In contrast, a significant positive association of BMI with dementia was only observed in two studies (Gustafson *et al.,* 2003; Hayden *et al.,* 2006) while a non-significant increased risk of dementia was observed in one other study (Nourhashémi *et al.,* 2003). The findings from the three studies that analysed WC as measure of central fat in relation to dementia, showed that one study had a positive significant association between AD risk and large WC but not dementia of all types (Luchsinger *et al.,* 2007); while the other two (Hughes *et al.,* 2009; Power *et al.,* 2011) show no significant association of large WC with incident dementia in the cohort. The review also extracted data on association of underweight BMI, Change of BMI, and WHR with dementia. However, there were limited numbers of these studies that also considered those parameters in their study, while the findings from the available data were not consistent. For instance, only one study (Luchsinger *et al.,* 2007) reported increased risk for weight gain and it was in participants with dementia associated with stroke while findings in those with loss of weight were mixed.

The characteristics of all 16 included studies are summarized in table 1a below while a more detailed table is provided in (Appendix 11).

Table 1a: Characteristics of studies in the systematic review of impacts of overweight and obesity in older adults on dementia risk

First Author (publication year): study place	**Participants / recruitment**	**Sample size and follow up**	**Baseline measure/End points**	**Main Findings and adjusted variables**	**Comments**
Yoshitake (1995): Japan.	Age≥65 years Japanese residing in the community within Hisayama town in	Sample size 828. The follow up was 7 years.	**Baseline:** Measured BMI used as continuous variable. **End points:** Incident AD and VaD	The age adjusted HR for AD and VaD were 0.75 (0.54-1.03) and 1.31 (0.98-1.74) respectively in relation to continuous BMI.	The study did not adjust for other confounding factors apart from age.
Borenstein Graves (2001): USA	Japanese Americans aged ≥ 65 years with mean age 72.6 (SD 6.1) were recruited in King	Sample size 1,869. Follow up of 3.8 years.	**Baseline:** Measured BMI as Continuous variable in the study**.** **End point:** AD	Fully adjusted HR was 1.06 (0.90-1.25) for continuous BMI and AD. After adjusting for age, sex, education, height, verbal IQ and head circumference.The HR in women was 1.06 (0.87-1.31) and in men it was 1.05 (0.82-1.34) with control for head circumference and APOE ε4 alleles.	The study stratified analysis by sex but duration of follow-up was too short (3.8 years) and there was no control for smoking and medical comorbidities.
Gustafson (2003): Sweden.	Age≥70 years. Recruited 392 individuals (166 men, and 226 women).	Sample size 382; Follow up≥ 18 years.	**Baseline:** BMI were measured at ages of 70, 75 and 79 years as Continuous variable in the study.**End point:** dementia, AD and VaD	The hazard ratio for dementia risk (95%CI) was 1.13 (1.04-1.24), 1.13 (1.04-1.24) and 1.15 (1.05-1.26) for BMI at ages of 70, 75 and 79 respectively. Similar harmful effects for AD and VaD, after Controlling for diastolic blood pressure, Cardiovascular diseases, Socioeconomic status, cigarette smoking and treatments for hypertension.	The study had very long follow-up of 18 years. However, it was unable to examine the effects in men owing to limited sample size. Therefore, it was unknown from the study if excess weights were

Nourhashemi (2003): France	Age ≥65 years as part of the longitudinal PAQUID study.	Sample size used was 3,557. Follow up was 8 years with different time point at 1, 3, 5 and 8 years. Loss in follow-up was 89 (2.4%).	**Baseline:** Self-reported weight and heights. Mini-Nutritional assessment cut offs for BMI were used; underweight BMI<21, normal BMI 21-22, overweight BMI 23-26 and Obese BMI ≥27 **End point:** incident dementia	The HR (95%CI) for dementia in those with BMI<21 compared to those with BMI 23-26 was 1.48 (1.08-2.04) and 1.19 (0.716-1.960) for model 1 and 2. The RR for BMI 21-22 was 1.07 (0.76-1.51 and 0.71 (0.40-1.25) for model 1 and 2. For BMI ≥27 they were 0.833 (0.59-1.18) and 0.716 (0.43-1.20), respectively after adjustments for sex, age and education.	The study used self-reported BMI which might have introduced bias while fewer covariates were used with no control for medical co-morbidities and smoking. It is likely that if they were considered the significance of the results would have tended towards the null or led to wider confidence intervals. The impact could remain even after the exclusion of early dementia cases.
Buchman (2005): USA	Data from the Religious Orders Study of older Catholic clergy (≥65 years; mean age 80.2) that	Sample size 820. The mean follows up was 5.6 years.	**Baseline:** Measured heights and weight were used. Continuous BMI was used. **End point:** AD	The HR was 0.94 (0.91-0.98) for baseline continuous BMI and AD; and for annual change in BMI it was 0.73 (0.63-0.85) after adjusting for sex, education and chronic diseases	Did not not account for smoking and reverse causality while follow-up was short in the study.
Hayden (2006): USA	5,092 aged ≥ 65 years were recruited (response rate 85.5%).	Sample size 3, 264. Follow up 3.2 years. Loss in follow up was 1,429 (30.2%).	**Baseline:** Self-reported height and weight were employed. BMI assessed as obese (BMI≥ 30) or not obese (BMI<30) **End points:** Dementia, AD and VaD.	The H.R and 95%CI, for dementia, AD and VaD risks for BMI≥30 as compared to BMI<30 was 1.76 (1.03-2.88), 1.93 (1.05-3.36) and 1.16 (0.37-3.12) respectively. The risks of AD for males and females was 1.48 (0.41-4.18) and 2.23 (1.09-4.30) respectively. For VaD, it was 0.71 (0.04-4.31) and 1.30 (0.32-4.29) for males and females, respectively. All models in the analysis adjusted for current age, sex, education, and number of APOE e4 alleles	The study examined dementia subtypes and stratified the analysis by sex. However, the use of self-reported BMI and CVRFs measures or informant must have biased the risk estimates. Duration of follow-up was too short.

Lunchsinger et al. (2007): US	Age ≥65 years (mean 77). 2,126 randomly selected Medicare participants were recruited study	Sample sizes for analysis of BMI 893, WC 907, and weight change 709. The lost to follow-up rate was 30.2% over a mean period of 5.1 years.	**Baseline:** Weight, height, and WC were measured. BMI and WC quartiles used. **Endpoints**: Dementia, AD, dementia- associated with stroke (DAS).	The fully adjusted model showed that the HR (95%CI) for continuous BMI and dementia, AD and DAS were 0.90 (0.90-1.00), 0.9 (0.90-1.00), and 1.10 (0.90-1.30), respectively. For the WC, the HR for the 3rd (91-97cm) and 4th WC quartile (>97cm) was 0.94 (0.60-1.40) and 1.10 (0.70-1.80) respectively; while in those of age<76 years it was 2.30 (0.90-5.80) and 5.10, 1.00-26.40) for dementia and AD but in those >76 years, it was 1.00 (0.60-1.70) and 0.80 (0.40-1.80).Adjusted for age, sex, education years, ethnic group, and APOE 4 status. Secondary analysis adjusted for diabetes mellitus, hypertension, low density lipoprotein level, heart disease, stroke, and current smoking	The study investigated weight change and dementia however some covariates were self-reported.
Atti et al (2008): Sweden	Age 75 years. 1,810 were recruited.	Sample size 1,255 (87.5%) with BMI data. The lost to follow-up rate was 12.5% over the 9 years period.	**Baseline:** Measured BMI cut-offs of ≥30 for obese, 25-29.9 for overweight and 20-24.9 for normal and but < 20 for underweight. BMI change was assessed as decrease (>10% or 5-10%), stable (±5%) or increase (5-10% or >10%). **End points:** Dementia	HR for dementia were 0.98 (0.94-1.00) for continuous BMI. It was 0.97 (0.71-1.34) and 0.75(0.59-0.96) for BMI<20 and ≥25 when compared to 20-24.9 after 9 years follow up. The findings for overweight males and females were 0.62 (0.36-1.08) and 0.73 (0.55-0.95). The risk of AD was reduced for overweight (RR 0.66, 0.50-0.88) while in the overweight APOE ε4 carriers and non-carriers they were 0.83 (0.54-1.30) and 0.66 (0.47-0.91) respectively. The study also reported risk of 1.58 (1.02-2.46) for BMI decrease of >10% after 6 years and 2.18 (1.27-3.74) after 3 years with no significant results for other BMI changes.Adjusted for age, sex, education, baseline MMSE, depressive symptoms, chronic disease, and impairment in activities of daily living.	The finding from sensitivity analysis was not taken into consideration of the overall conclusion of findings. For instance, BMI≥25 reduced dementia significantly after 9 years but after excluding first 3 years data the significant association varnished suggesting the earlier protective result was probably due to reverse causality.

Dahl et al 2008 (Finland)	Age 65-92 years. Recruited 1,196	Sample size used was 605. The loss to follow-up rate was about 17% over the 8 years period	**Baseline:** Measured weight and height. BMI categorized as ≥30 for obese, 25-29.9 for overweight and 18.5-24.9 for normal weight, <18.5 for underweight.**End points:** Dementia	Fully adjusted HR (95%CI) was 0.92 (0.87-0.97) while after excluding dementia within 4 years from baseline, the risk was 0.93 (0.86-0.99). The risk for women and men (with low BMI scores) was 0.90 (0.84-0.96) and 0.94 (0.84-1.07), respectively. The risk for continuous BMI in women was 0.90 (0.84-0.96) and men was 0.95 (0.84-1.07) while in older age at baseline (71-92 years) it was 0.92 (0.86-0.98), and the risk in younger age group (65-70) was 0.91 (0.82-1.03). Adjusted for age, sex, education, diabetes mellitus, CVD (stroke coronary heart disease, hypertension, and atrial fibrillation), smoking, and alcohol use.	The study captured nearly the whole adult population residing in the Lieto residential area. However, the dropped-out rate of participants was high 17%.
Hughes et al. (2009) USA	1,985 Japanese Americans (males and females) aged ≥65 years (mean 71.8 years) were recruited.	Sample size 1,478. Follow up of 8 years. The lost to follow-up rate was 19.5%.	**Baseline:** Height, weight, WC, and hip circumference were measured. After follow-up, only weight measured. Used Taskforce cut-offs for Asians; Obese≥25.0, Overweight 23.0-24.9, normal 18.5-22.9 and underweight <18.5 while WC (inches) and WHR used as secondary measures of adiposity**. End points:** Dementia, AD and VaD	The fully adjusted risk of dementia, AD and VaD for baseline BMI were 0.80 (0.38-1.68), 0.68 (0.31-1.51), and 0.40 (0.06-2.51), respectively. For BMI change, the risk of dementia, AD, and VaD were 0.31 (0.09-1.02), 0.21 (0.06-0.80), and 0.43 (0.02-10.60) respectively while no significant risk for WC and WHR. Adjusted for age, sex education, smoking, alcohol intake, regular exercise, hypertension, hypercholesterolemia, angina pectoris, diabetes, heart attack, TIA, stroke, ApoE genotype status	The study participants were mainly American Japanese population therefore the findings might not apply to most of the US population.
Fitzpatrick et al 2009 (USA)	Age 65 -97 years (mean age 74.7years). 3,602 were recruited for the Cardiovascular Health Cognition Study.	Sample size 2,798. Follow up 5.4 years.	**Baseline:** Measured weight, height (m) and waist/hip circumference (cm) at Late life. Weight for midlife was self-reported but height measured. The BMI was categorized into 4 groups using >30 for obese, >25-30 for overweight, 25-30 for normal weight, and <20 for underweight. **End points:** Dementia, AD and VaD	The fully adjusted risk for Late life Continuous BMI and dementia was 0.95 (0.92-0.98) while for categorical BMI<20, BMI>25-30 and BMI>30 the risks were 1.62 (1.02-2.64), 0.90 (0.70-1.16), and 0.63 (0.44-0.91) when compared to BMI 20-25. The risks of AD were 1.42 (0.74-2.70), 0.74 (0.52-1.05), and 0.58 (0.36-0.96); and for VaD they were 2.15 (1.11-4.19), 1.20 (0.83-1.76), and 0.72 (0.41-1.27), respectively, for BMI<20, BMI 25-30 and BMI>30 as compared to BMI 20-25. Adjusted for age, sex, race, education, CVD risk factors (smoking, diabetes mellitus, coronary heart disease, hypertension history, total cholesterol, ankle-arm blood pressure, C-reactive protein, Interleukin-6, kilocalories consumed /week, APOE genotype).	The study had short follow-up of 5.4 years.

Scarmeas (2009):USA	Participants aged ≥65 years were Medicare beneficiaries from 2 cohorts recruited via Washington Heights-Inwood Columbia Aging project (WHICAP).	Sample sizes 1,880. They were followed 5.4 years (SD 3.3).	**Baseline:** BMI from measured heights and weight were used as continuous variable**.** **End points:** Dementia, AD and VaD	Fully adjusted hazard ratio for AD risk was (0.96, 0.93-0.99).Controlled for age, sex, ethnicity, education, APOE status, Calorie intake, smoking, depression, leisure activities, comorbidity index, baseline clinical dementia rating score, time between first dietary score and physical activity assessment.	Though, continuous BMI was included as a covariate and part of the diet, it significantly showed AD risk. However,The duration of follow-up was short (5.4 years) making it difficult to discount reverse causality.
Power et al. (2011): Australia	12,203 of age 64-84 years (mean 72.1) were recruited by the aid of the copy of electoral roll for the Health in Men Study.	Sample size 12,047. Mean follow up 9.7 years.	**Baseline:** The study used measured data from weight, height, and WC to compute BMI and WHR. BMI according to WHO cut offs. **End points:** Dementia	The fully adjusted dementia risk for BMI 25-<30 and ≥30 was 0.82(0.70-0.95) and 0.82 (0.67-1.01) respectively as compared to BMI<25. The risk for WC 94-<102cm and ≥102 was 1.02 (0.87-1.20) and 0.88 (0.74-1.04) respectively as compared to WC<94; while it was 0.82 (0.69-0.98) for WHR≥9.0 compared to <9.0. After Sensitivity analysis the risk for overweight was 0.82 (0.70-0.95), and obesity was 0.84(0.69-1.03); while no change for WC, but for WHR≥9 it was 0.81 (0.68-0.98).Adjusted age, marital status, educational level, alcohol intake, physical activity, diabetes prevalent, dyslipidaemia, CHD, and fat intake from milk. Repeated analysis (sensitivity) excluded first 2 years dementia cases or deaths.	The study used large sample size which helped the statistical power of the analysis however it was limited to male participants, therefore it is difficult to generalize to Australian females who might present different risk.
Lucca (2012): Italy	Recruited 2,813 aged ≥80 years in the Monzino-80-plus study. Data available for 2,504 individuals (Lucca et al., 2015*****). For the study, 1,110 were involved.	Sample size 1,035. Total followed-up period was 5.5 years. Loss in follow up 6.8%.	**Baseline:** Self- or caregiver reported weight and heights used. BMI assessed as continuous or categorical. Underweight BMI<18.5kg/m², normal BMI 18.5-24.9 kg/m² and Overweight/ obesity ≥25kg/m².**End points:** dementia	The fully adjusted dementia risk for continuous BMI was 0.966 (0.934-0.997), p=0.0328. For BMI<18.5Kg/m² and BMI≥25Kg/m². They were 0.62 (0.41-0.97) and 0.73(0.55-0.97) respectively when compared to BMI18.5-24.9Kg/m². Adjustments for age, sex, education, current smoking, alcohol consumption, physical activity, depression, diabetes, hypertension, heart failure, atrial fibrillation, myocardial infarction, ictus, and COPD.	The study employed self- or caregiver reported weights and heights at baseline to calculate participants' BMI which may have biased the results.

Tolppanen (2014): Finland	Recruited 1,511 aged 65-79 years (Response rate75.6%). 1,304 (38.9% males, 61.1% females) had complete data for midlife (mean age 50.2 SD 6.0) and late life study (mean age 71.2 SD 4.0).	Sample sizes 1,262 and 1,256 for dementia and AD for late life study. Sample sizes 1,304 and 1,289 for dementia and AD midlife study. Follow-up duration was 10 years for late life and 26 years for midlife.	**Baseline:** Measured BMI were used as continuous and/or categorical BMI. Cut offs included <25 kg/m² for Normal BMI, 25-30kg/m² for overweight and 30kg/m² for obesity. Included change in BMI. **End points:** Dementia and AD	The fully adjusted dementia risk for late life continuous BMI was 0.94 (0.86-1.03). The risk was 0.51 (0.25-1.04) and 0.55 (0.23-1.34) for BMI<25-30 Kg/m² and ≥30Kg/m² respectively when compared to BMI<25Kg/m². The AD risk was 0.89(0.81-0.98) for continuous BMI, while it was 0.57 (0.27-1.19) and 0.40 (0.15-1.08) for BMI 25-29Kg/m² and BMI ≥30Kg/m² respectively. The dementia risk for Midlife continuous BMI was 1.07 (1.00-1.14); and it was 1.04 (0.58-1.87) and 1.81 (0.91-3.57) for BMI<25-30 Kg/m² and ≥30Kg/m². The AD risk was 0.89 (0.47-1.68) and 1.57 (0.75-3.29) for BMI<25-30 Kg/m² and ≥30Kg/m² respectively. The dementia and AD risks for change of BMI into late life were 1.14 (1.03-1.25) and 1.20 (1.09-1.33), respectively. Fully adjusted model includes age, gender, ApoE status and region of residence, smoking and socioeconomic factors, likely mediators, serum cholesterol levels, systolic blood pressures, cardio- and cerebrovascular diseases and diabetes	The study involved long follow-up. However, the study did not use other measures of adiposity such as WC or WHR to compare its findings since BMI could underestimate the risks in older age.
Neergaard (2016): Denmark	5,855 post-menopausal Danish women of mean age 70.1 were recruited.	Sample size 5,512. The follow-up was 15 years (Mean 11.9 ±3.9).	**Baseline:** Measured heights and weight were used. underweight BMI<18.5, Normal weight BMI≥18.5-<25, Overweight BMI ≥25-<30 and obese BMI≥30. **End point:** Dementia and AD	The fully adjusted dementia risk was 0.88 (0.45-1.72), 0.75 (0.62-0.89), and 0.79 (0.62-1.01) for BMI<18.5, BMI ≥25-<30 and BMI≥30, respectively, when compared to BMI≥18.5-<25. The AD risk was 0.92 (0.34-2.51), 0.72 (0.54-0.96), and 0.74 (0.51-1.09) for BMI<18.5, BMI ≥25-<30 and BMI≥30, respectively. The VaD risk was 0.68 (0.33-1.40) and 1.28 (0.57-2.86) for BMI ≥25-<30 and BMI≥30, respectively (no data for BMI<18.5). Adjusted for age, education, smoking, alcohol consumption, physical activity, history of depression, cerebral embolism/haemorrhage, systolic blood pressure, fasting glucose levels and cholesterol levels	The study focused on a cohort of Danish women only. It is thus difficult to generalise the findings to the men population within Demark. It is also difficult to rule out pre-existing dementia while dementia cases at endpoint might have been under reported from use of the registry record linkage system.

6.3.2 Meta-analysis results

The results of the meta-analysis of all 15 studies (Figure 5) included 17 studied populations and 37,396 participants with 4,189 dementia cases. The findings of incident dementia in relation to continuous BMI (or obesity where continuous BMI data was unavailable) in all studies showed a non-significant reduced risk of dementia, with a relative risk (RR) and 95%CI of 0.97 (0.94-1.00), p=0.055.

The findings of publication bias for the 15 studies are presented by the figure 4. From the funnel plot, there was no evidence of the publications bias which was further confirmed by the results of Egger's test p=0.564.

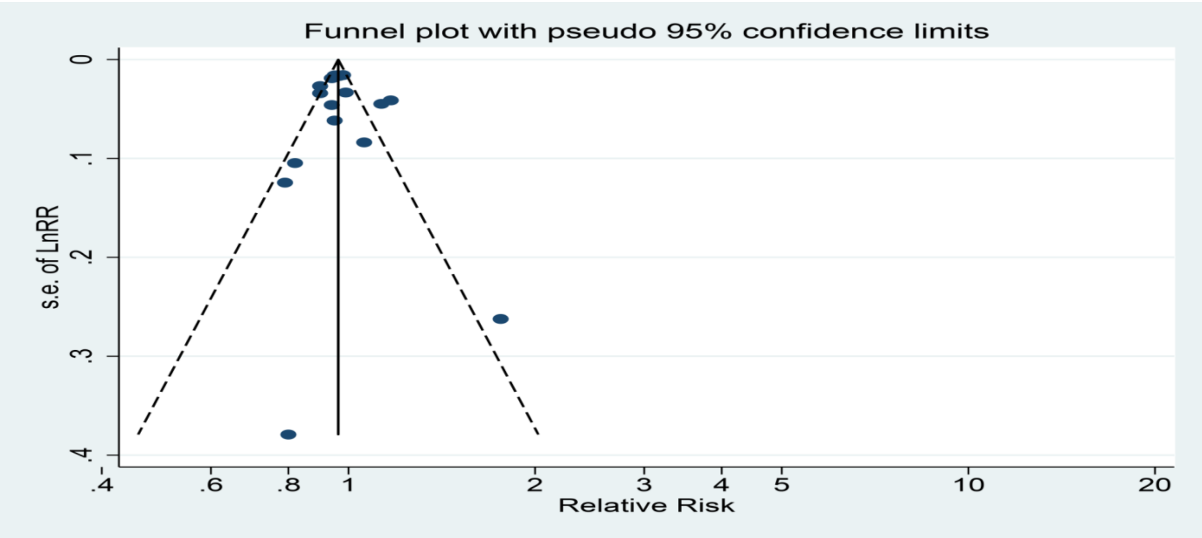


Figure 4 Funnel plot assessing publication bias

The data analysis after excluding the three studies that used self-reported data showed that the significance of the association between continuous BMI (or obesity where continuous BMI data was unavailable) and incident dementia was further reduced (0.97, 0.94-1.00, p=0.065). The analysis of continuous BMI associated with incident dementia, which included 14 studied populations with 2,373 dementia cases, also exhibited non-significant reduced risk (0.97, 0.95-1.00).

However, the stratified analysis using data from all 17 studied populations (Figure 6) by duration of study follow-up showed a significant inverse association with RR of dementia as 0.95 (0.92-0.97) for short term follow-up (<9 years) and no association was found for long term follow up (≥9 years) as indicated by RR of 1.00 (0.93-1.08). The matched figures based on findings using the data of AD as outcome only (figure 7), were 0.93 (0.88-0.99) and 0.99 (0.70-1.39) respectively, while the overall RR was 0.95 (0.89-1.02) for AD in relation to adiposity from all available studies (Appendix 8). Findings from the stratified analysis based on those 14 studied populations with continuous BMI data comprising of 16,576 participants with 2,372 dementia cases (in the top part of Figure 8), showed that the RRs for dementia in the short-term and long-term follow-up were 0.95 (0.93-0.96) and 1·03 (0·96-1·11) respectively.

The findings of categorised BMI meta-analyses in five studied population including data of the new study Anhui Cohort study (China) is presented in appendix 16. The findings showed that older people with overweight and obesity had a non-significant reduced risk of dementia when compared to their normal BMI counterparts, and the relative risk of dementia was 0.87 (0.66-1.14) and 0.86 (0.60-1.22) respectively. The matched RRs remained non-significant in overweight (0.98, 0.54-1.77) and obesity (1.17, 0.65-2.10) in comparison with combined normal and underweight BMI categories. The findings from further and separate analysis of AD (figure 9) showed no association with continuous BMI (RR 0.97, 0.91-1.03) or with obesity

(RR 0.78, 0.56-1.09). However, the risk of AD was significantly reduced in overweight (0.69, 0.57-0.88). There was no significant association of obesity with VaD (0.91, 0.60-1.39) and no association was observed for large WC (RR: 1·04, 0·90-1.20) and larger WC (RR: 0.94, 0.80-1.09) in relation to dementia (Figure 10).

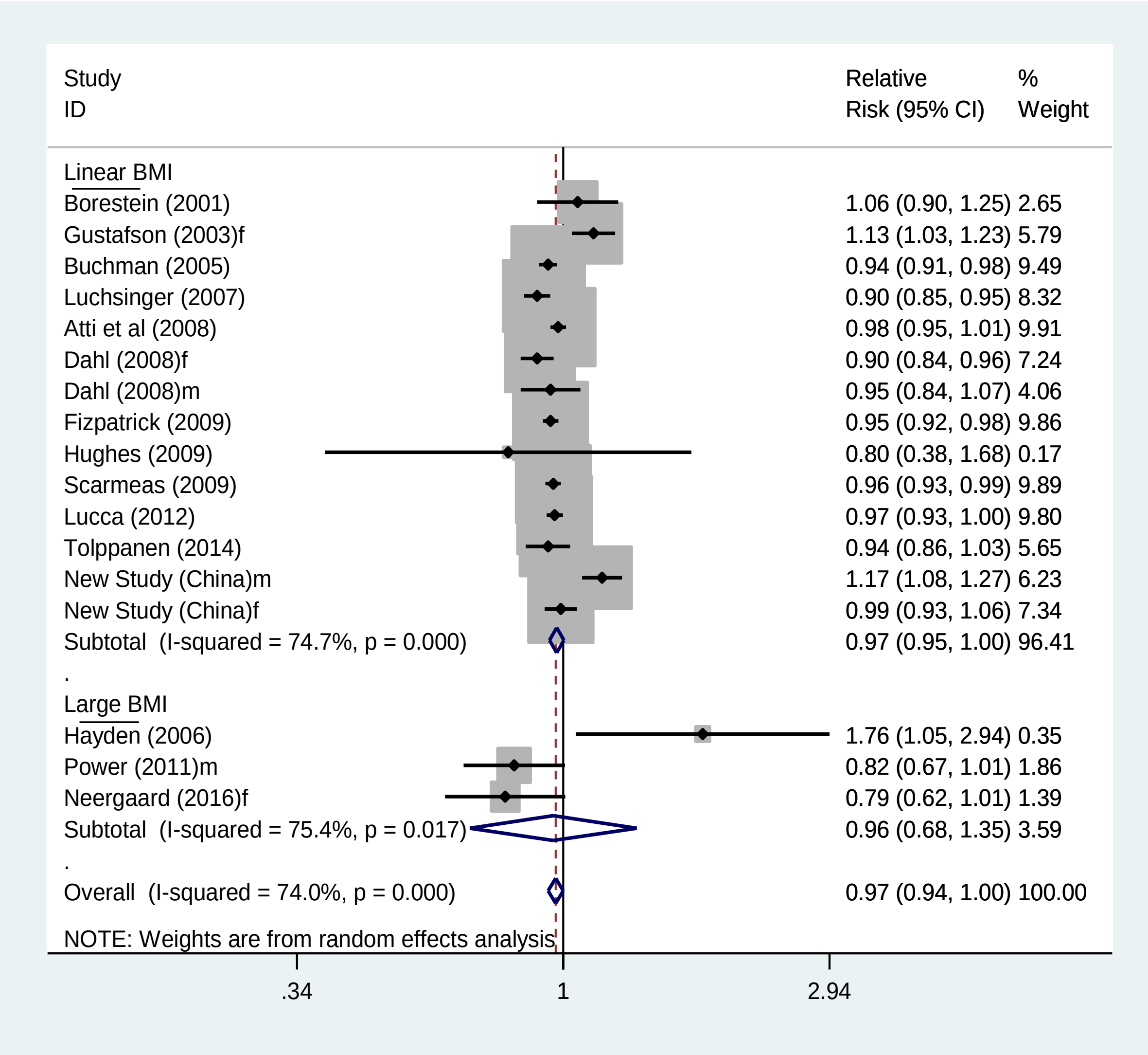


Figure 5 Forest plot showing pooled estimate of all included studies for BMI and dementia risk

(Three studies, in low part of above figure 5, did not examine the association of continuous BMI and dementia, and thus the overall meta-analysis took their data of categorised BMI in the highest group). Note: **f**=females, and **m**=males

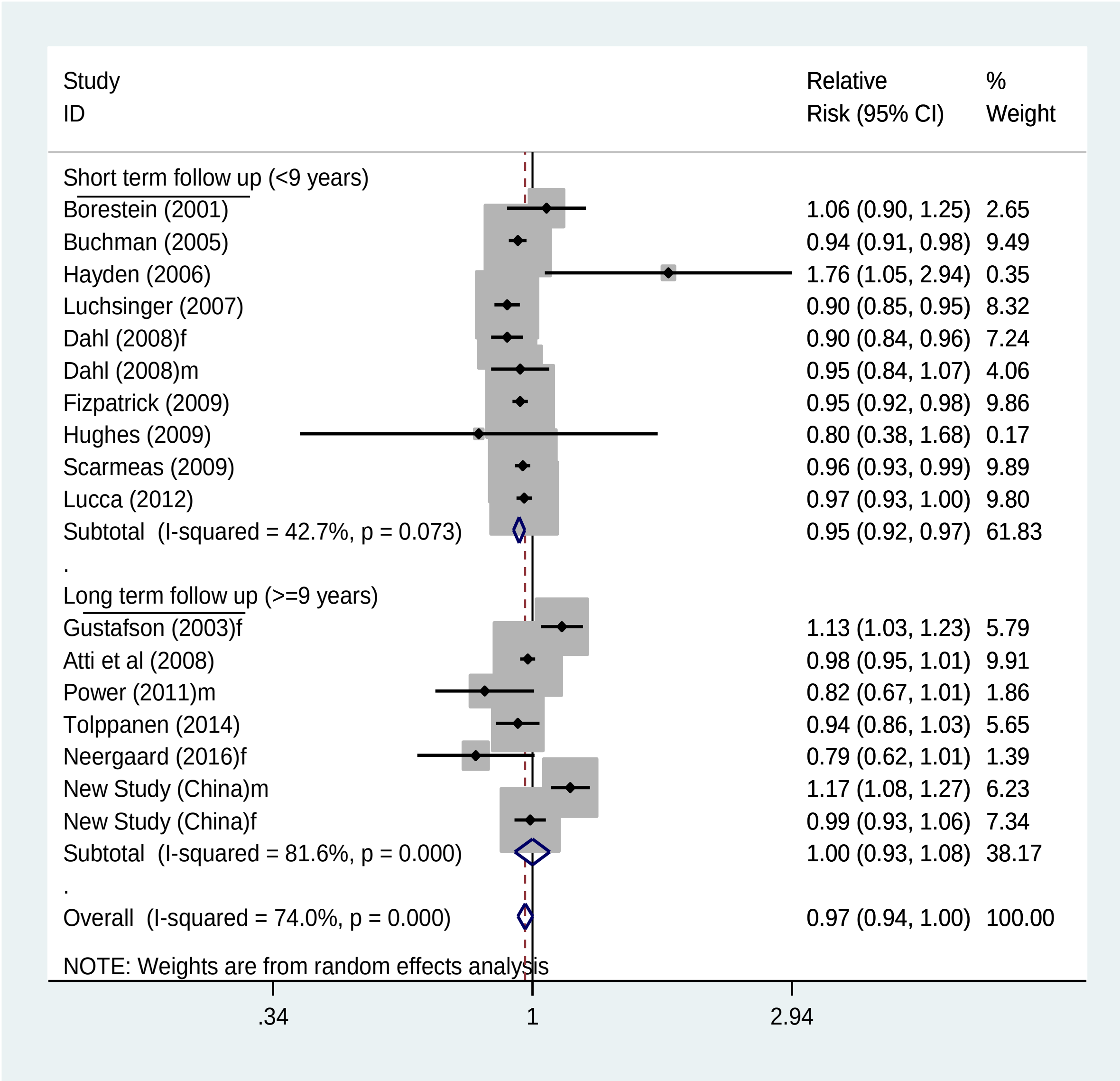


Figure 6 Linear/Large BMI and dementia risk (short term versus long term follows up)

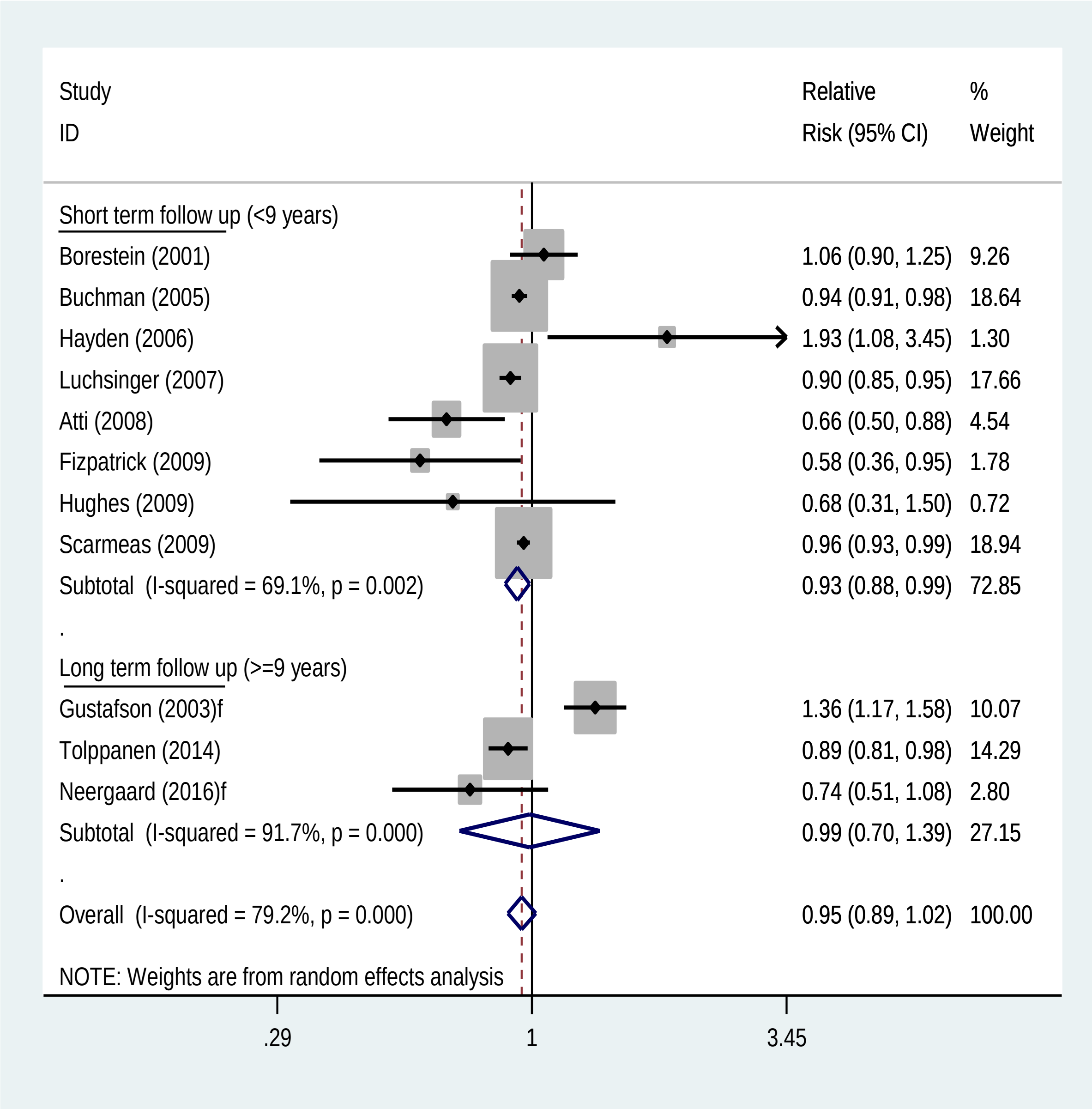


Figure 7 Linear/categorical BMI and Alzheimer's disease risk (short term versus long term follow up)

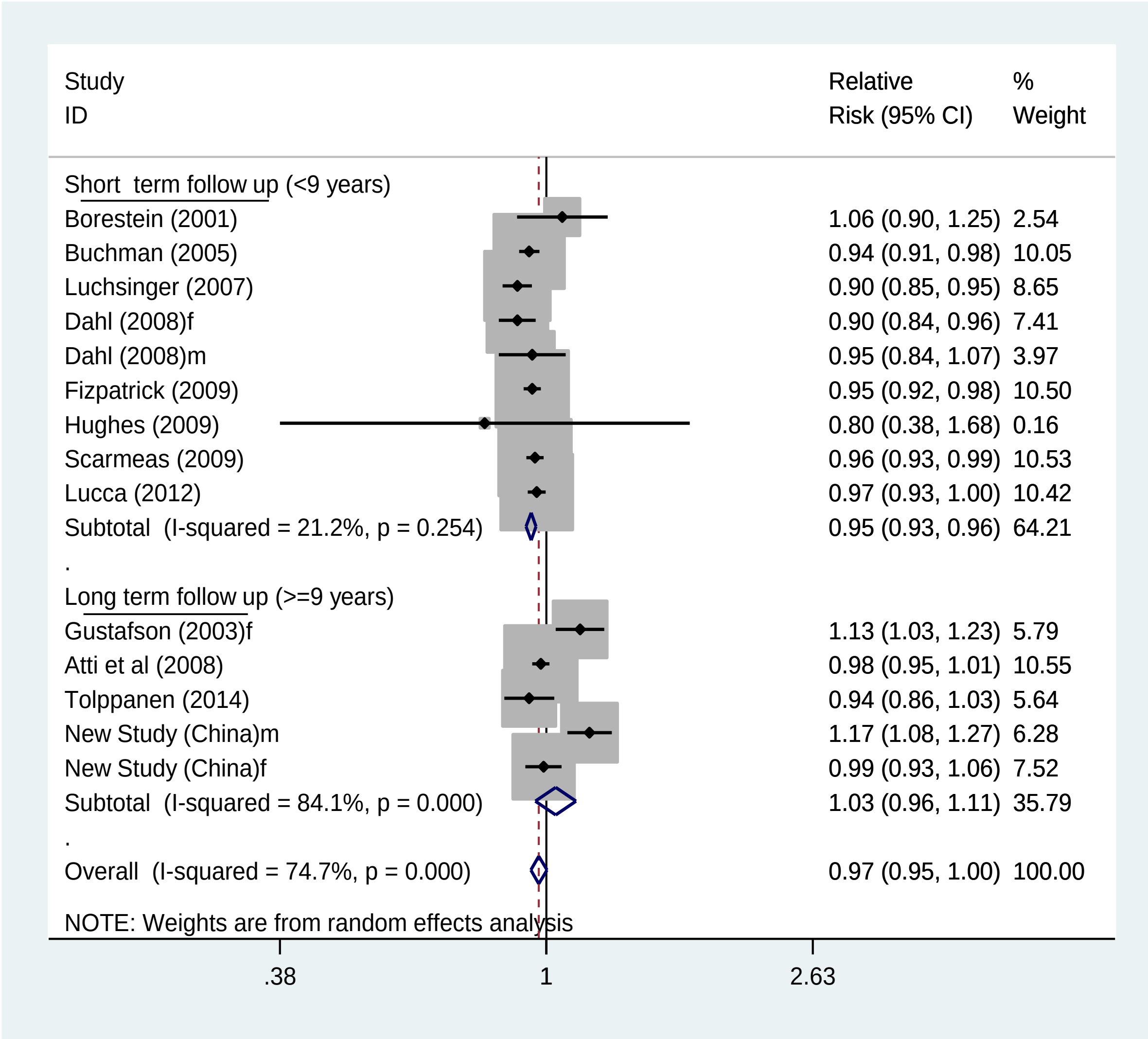


Figure 8 Continuous BMI and dementia risk (short term vs long term follow up)

(In total 11,378 participants with 1,741 dementia cases for short term and total 5,198

Participants with 631 dementia cases for long term studies).

Note: f=females, and m=males

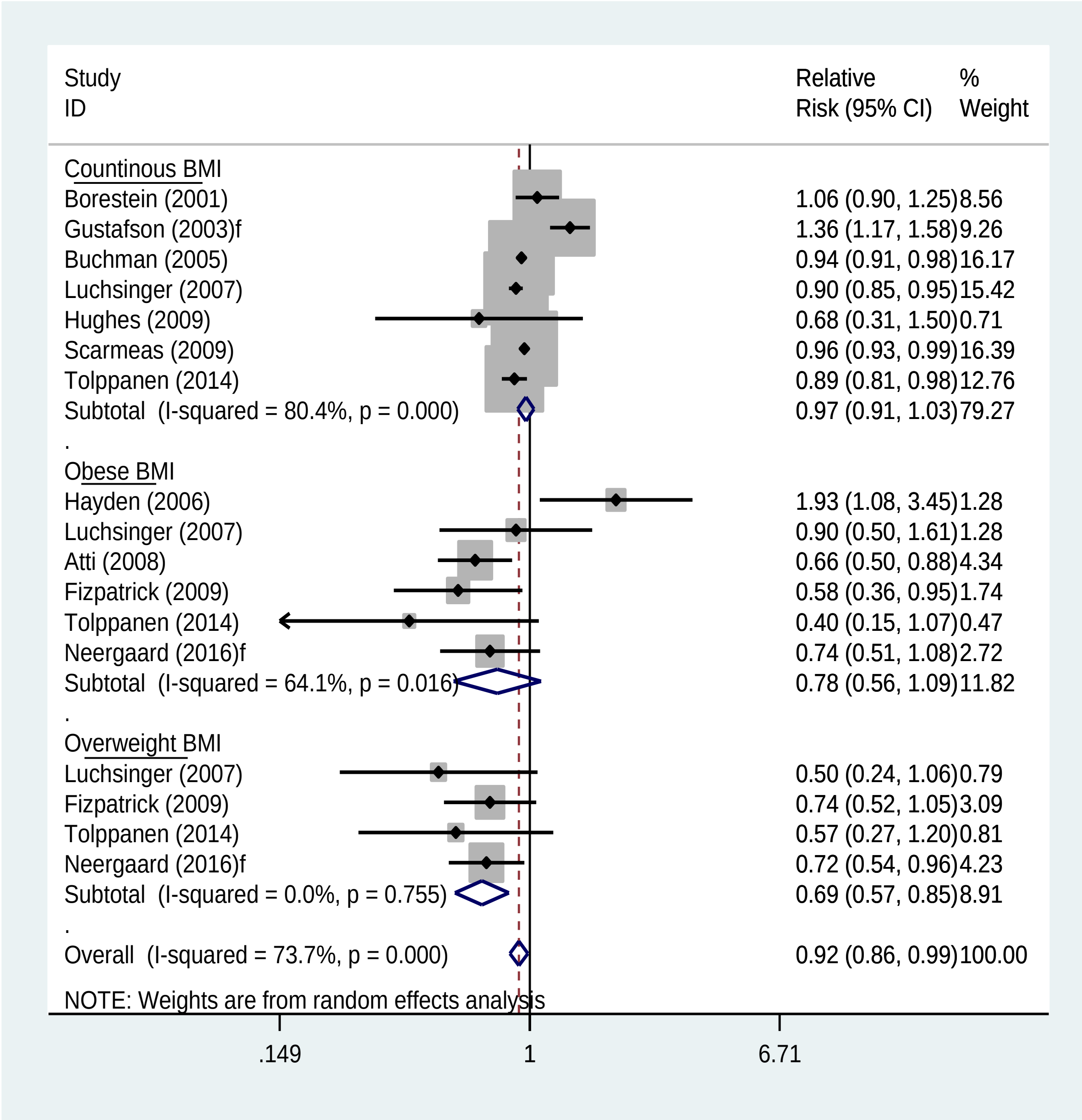


Figure 9 Alzheimer's disease risk in relation to continuous, obese and overweight BMI

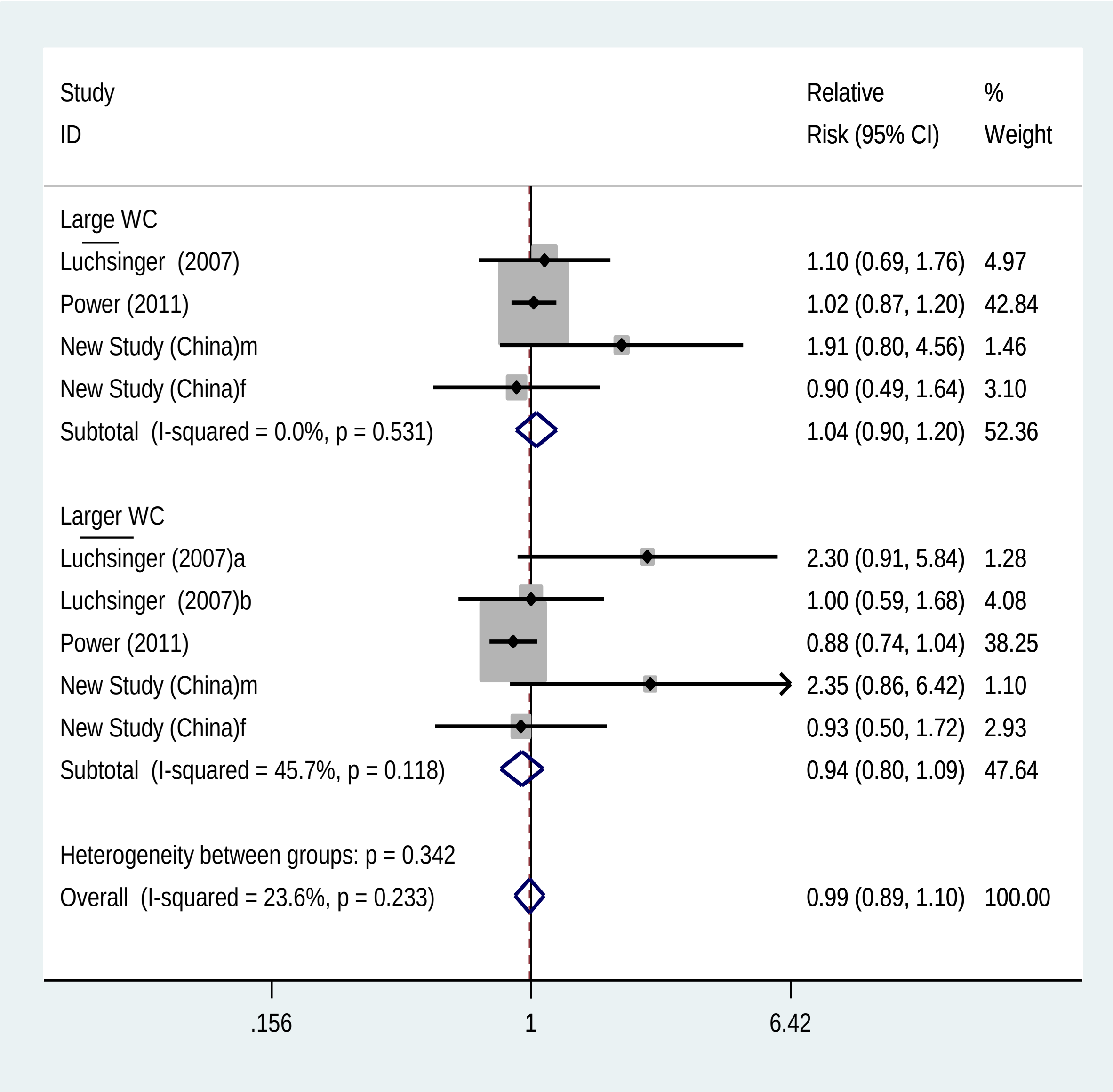


Figure 10 Forest Plots for Large and larger waist circumference and dementia risk

Note: f=females, and m=males

3.4 Discussion

This qualitative literature review showed that BMI in older age was inversely associated with dementia risk, while findings of WC as measure of central adiposity is mostly unrelated with dementia risk. A total of thirteen studies suggested inverse associations of BMI with dementia and ten of them reported significantly reduced risk. In contrast, only three studies suggested positive association of BMI and incident dementia with significantly increased risk found in two. Similar pattern of results was observed in studies that used continuous BMI data and in those that examined categorical BMI in relation to all dementia and subtypes while findings of underweight and change of BMI with dementia were inconsistent.

The meta-analysis of 17 studied populations including the new data from Anhui cohort (China) demonstrated that the consequences of overweight and obesity in older age on dementia risk is hard to observe in short-term follow-up cohort studies, whereas the inverse association could be found due to possible reverse causation. This was observed from the analysis of short-term studies (<9 years follow-up) which exhibited inverse association while in long term studies (≥9 years follow-up) the significant effect varnished. This finding was similar in the analysis of all-dementia and subgroup analysis of Alzheimer's disease in relation to categorical or continuous BMI (Figure 6-8). This, therefore, suggests that long duration, and not short term of follow-up, is required to detect incident dementia risk in overweight and obese older adults.

The findings from the review were suggestive of inverse association of adiposity with risk of dementia in short term studies but not long term. This decrease in dementia risk with higher BMI by 5% in studies with a short follow-up (< 9 years) and not in longer term studies (≥9 years) may be affected by attrition, survivor bias or the fact that change in BMI is more important in dementia risk development (Power et al., 2013; Tolppanem *et al.,* 2014; Howe *et al.,* 2016). The evidence from research (Powe et al., 2013; Tolppanem et al.,2014) suggests that change of weight is more related to dementia risk development and may explain the reduced risk of dementia for obesity and lack of association of overweight. This is important considering the findings from the meta-analyses showed that higher BMI in short term follow-up reduced the risk of dementia, and being overweight (but not obese) reduced risk of AD (figure 9) while WC had no significant association (figure 10). This role of change in weight in dementia risk is further buttressed by findings showing weight loss is associated with dementia pathology and precedes dementia diagnosis by a decade (Knopnan et al., 2007).

Furthermore, there are several notable variations among studies that springs from methodological issues with implications for more research. These include obesity assessment, length of follow-up, type of adiposity measure, analytical strategy and dementia types.

Type of adiposity assessment

The epidemiological literature on study of adiposity and health outcomes have always involved measured anthropometric or self-reported data (Flegal *et. al.,* 2013). It is well documented that self-reported anthropometric data are associated with bias (Spencer *et al.,* 2002; Merrill and Richardson, 2009: Preston *et al.,* 2015), while measured data are more likely to improve accuracy of height, weight and BMI estimates particularly when used as primary exposure in epidemiological research (Spencer *et al.,* 2002; Xu *et al.,* 2018). Impressively, most of the included studies (13 out of 16) in this systematic literature review used measured anthropometric data and only three studies (Nourhashemi *et al.,* 2003; Hayden *et al.,*2006; Luca *et al.,* 2012) used self-reported data. However, it was difficult to compare the findings of these studies that used measured data with those used self-reported data because of fewer studies. While this suggests better validity of findings from this review since most studies used measured data, there is need for epidemiological research using adiposity measures as primary exposure to avoid the use of self-reported anthropometric data. This is because in older age, recall bias is more likely compared to younger population (Devitt and Schacter, 2016). In addition, cognitively intact older adults may still erroneously report their weight and height since there is usually loss of height with aging as found from previous studies (Sorkin *et al.,* 1999; Solken, Muller and Andreas, 1999); and age-related co-morbidities may also impact on body weights (Guh *et al.,* 2009). While measured data is preferable, the age at adiposity assessment may impact differently on health outcomes.

Age at adiposity assessment

Finding from previous review, which summarized findings from 10 years of research (2003-2013), clearly suggested that the impacts of BMI on dementia risk varied with baseline age at which adiposity was assessed (Emmerzaal *et al.,* 2015), which showed harmful effects in younger/middle age (<65 years) but protective effects in older age (≥65 years). This is also reflected in the findings of recent systematic review and meta-analysis of BMI and dementia by Pedditizi *et al (* 2016). The study suggested that increased dementia risk for obesity measured at younger age (<65 years) and the opposite effect in older age (≥65 years). In addition, findings from studies using mixed sample of younger and older people would not be applicable to older population. This systematic review, therefore, focused on adiposity measured in older age (≥65 years) and the findings suggested inverse associations between adiposity and dementia risk, which is consistent with the findings by Pettiditizi et al (2016). However, the evidence of the impact in older adults remains uncertain since harmful effects were detected by two studies in older age, one of which had 18 years of follow-up. This suggests that length of follow-up is important.

Length of follow-up

The impact of adiposity on incident dementia require long time for the health effect to be evident (Zamboni *et al.,* 2005) and may vary according to the length of follow-up (Kivimaki *et al.,* 2017). This is regardless of the survival hypothesis (Brown and Kuk, 2014), suggesting a sub-population of resistant survivors may withstand health consequences of overweight and obesity in older age. The evidence from research (Johnson *et al.,* 2006) showed that on the average it takes seven to eight years for incident dementia to manifest in older adults with excess body weights and this period includes the prodromal stages of the disease. In addition, it could require longer follow-up of 10 years or more for younger/middle population to experience incident dementia (Knopman *et al.,* 2007). However, despite the importance of long follow-up for study of obesity and dementia there was only five studies with long follow-up duration of more than 8 years (Gustafson *et al.,* 2003; Atti *et al.,* 2008; Power *et al.,* 2011; Tolppanen *et al.,* 2014; Neergaard *et al.,* 2015), while all the remaining studies had shorter duration of follow-up.

The overall findings from this qualitative review suggested the inverse association of BMI with the risk of dementia. However, the meta-analysis from this study showed this is only true for short term studies (<9 years) and not long term (>9 years). Besides, the study by Gustafson *et al* (2003), which had the longest duration of follow-up (18 years), detected significantly increased risk of dementia and subtypes in relation to excess BMI. This suggests that perhaps the harmful effect of excess BMI on dementia risk is more observable from studies with long term follow-up. Recently a large scale study (Kivimaki *et al.,* 2017) of 1.3 million people (mean age 36.3-55.2 years) using unpublished individual participant data from 39 cohorts based on health records suggested increased dementia risk in association with midlife BMI in long term studies and not those with shorter follow-up. While evidence from prospective primary cohort studies with long follow-up are required, the type of adiposity measure used in cohort studies is also very important.

Type of adiposity measure

This systematic literature review showed that most research on adiposity in older age and dementia risk over the past two decades have relied more on use of BMI as exposure variable, with less focus on other adiposity measures like WC. For instance, out of the 16 studies that used BMI only three considered WC (Luchsinger et al., 2007; Hughes *et al.,* 2009; Power *et al.,* 2011). Even though these studies found no association of WC with all dementia, one of them (Luchsinger *et al.,* 2007) showed that WC increased AD risk significantly by fivefold in those of age 65-<76 years. This suggests that the impact of WC on dementia risk may be different. It is documented in the literature on aging and obesity (Zamboni *et al.,* 2005; Jura and Kozak *et al.,* 2016) that, while aging is associated with elevated body fat percentage, there is also redistribution and deposition of these fats in the abdominal regions. It is also well established that intra-abdominal central fat assessed by WC is clearly a significant risk factor for cardiovascular diseases (Reis *et al.,* 2015; Illiodromiti *et al.,* 2018) which are associated with incident dementia. Therefore, more research from primary cohort studies using both BMI and WC are needed.

Adjustments for confounders

One of the major challenges with longitudinal studies including those of adiposity and chronic diseases like dementia is the issue of confounding (Caruana *et al.,* 2015; Illiodromiti *et al.,* 2018). The quality assessments tool for the review clearly emphasized the importance of confounding with item six on the rating scale assigned to smoking and medical morbidities, while item seven required that cohort studies should have accounted for at least three additional important covariates including age, social class/education, ApoE4 status etc. However, four studies did not account for any of smoking or medical morbidities. One study excluded non-smokers in the analysis of change in weight and dementia associated with stroke, but without adjusting for medical comorbidities in study of BMI and dementia (Luchsinger *et al.,* 2007). In contrast, one other study adjusted for medical co-morbidities but not for smoking (Atti *et al.,* 2008). Therefore, considering these shortcomings, it is difficult to rule out confounding bias due to both smoking and pre-existing medical morbidities from these studies.

Smoking

It is well established from meta-analysis of prospective cohort studies that the risk of dementia is elevated by the effects of smoking in older adults (Anstey *et al.,* 2007), and evidence also showed that BMI and WC are influenced by smoking

(Winslow *et al.,* 2015). Therefore, dealing with confounding due to smoking in the study of the association of adiposity with dementia risk is important to minimize bias. While this is very vital there is the challenge of residual confounding which may not be completely addressed through adjustments of smoking in statistical models (Winslow *et al.,* 2015). The preferred approach to deal with residual confounding is the exclusion of smokers from analysis (Aune *et al.,* 2016; Di Angelatonio *et al.,* 2016; Xu *et al.,* 2018) though rarely considered in the study of dementia. Surprisingly, only one study (Luchsinger *et al.,* 2007) from the review considered residual confounding by exclusion of smokers from its analysis. This was however not applied in the main analysis of BMI and dementia, but for change of weight in relation to a subtype of dementia. The study by Luchsinger *et al* (2007) considered exclusion of current smokers and one and half year data as a sensitivity analysis to verify that the significantly increased risk of dementia (2.80, 1.00-7.90) associated with stroke caused by change of weight was not due to residual confounding and reverse causality and observed the results were unchanged. This approach is quite encouraging. Considering that none of the studies in the review have applied this in the main analysis of excess BMI or WC and all dementia types, it remain unclear whether the findings from cohort studies would have been different if residual effects of smoking was limited. Therefore, further research could consider residual confounding in analysis of adiposity and dementia risk.

Pre-existing morbidities

Research suggests several morbidities are associated with advancement of age (Guh *et al.,* 2009). Yet, ascertaining the complete baseline health status of older adults is cumbersome (Zamboni *et al.,* 2005). Therefore, it is hard to discount pre-existing illness in older age. In addition, the long-term effect of confounders on the association between adiposity in older age and health outcomes is yet to be completely unravelled. However, data of predominantly middle age population of 40-69 years (mean 55.2 years) suggests that the association of adiposity with chronic diseases are confounded by major pre-existing morbidities with the effect greater for use of BMI as exposure than other adiposity measures (Illiodromiti *et al.,* 2018). In older age, these effects may be greater considering that changes in body composition and fat distribution linked with aging may impact on adiposity measures (Jurah and Kozak, 2016) while the influence of chronic illness may also contribute to reverse causality through illness induced weight loss (Zamboni *et al.,* 2005; Flegal *et al.,* 2010). Therefore, accounting for pre-existing morbidities is very crucial to minimize biases from cohort studies of adiposity and dementia risk.

Reverse causation

One challenge for the study of adiposity and dementia risk is reverse causality, which describes a temporal bias. It is commonly encountered in cross-sectional studies but also observed in some prospective cohort studies, where instead of the exposure causing the disease, the assumed exposure (BMI) becomes the result of the undiagnosed outcome (dementia) (Szklo and Nieto, 2014, p.138-139). Evidence from dementia research revealed that weight loss tends to precede diagnosis or manifestation of dementia by 10 years (Knopman *et al.,* 2007). This suggests that the early dementia disease process impacts negatively on body weights or is accompanied by weight loss. The mechanism or causes of weight loss is yet to be fully understood in older adults. However, it suggests that at baseline of cohort studies, participants consist of heterogeneous mix of those with fairly stable weights and those who must have lost weight due to looming undetected dementia. Therefore, analysis of data close to baseline assessments or short follow-ups may generate false findings of adiposity and dementia relationship (Kivimaki *et al.,* 2017). Dealing with this inherent bias in the field of epidemiology involves exclusion of data of a specified period after baseline assessments or start of the study (Szklo and Nieto, 2014, p.138). The issue of whether the method resolves bias due to reverse causation completely has been debated in the literature (Flegal et al., 2010). However, recent large-scale studies including those by Global BMI Mortality Collaboration (Di Angelantonio *et al.,* 2016; Aune *et al.,* 2016) have argued based on available evidence in support of the validity of the method. In addition, recent studies based on data from primary healthcare or health records suggested that studies with shorter follow-up are prone to reverse causality (Bowman *et al.,* 2019), while the harmful effects of excess weights on dementia risk may be observed over a long term (Kivimaki *et al.,* 2017). However, evidence from prospective cohort studies of community dwelling older adults with long term follow-up that addressed reverse causality are lacking.

The findings from this review showed that most included studies were limited by short duration of follow-up and did not consider the sensitivity analysis of excluding data from early follow-up to limit reverse causality. Of the sixteen studies, only five studies did so (Nourhashemi *et al.,*2003; Luchsinger *et al.,*2007; Dahl *et al*.,2008; Atti *et al.,* 2008; Power *et al.,* 2011) while the purpose for some studies (Atti et al 2008; Power et al., 2011) seemed unrelated to reverse causality. The study by Atti *et al* (2008), for instance, excluded first three years data from its study with 9 years follow-up with the aim of testing if the impact on dementia risk differs by the period between baseline BMI assessment and diagnosis of dementia. However, the disappearance of the protective effect in the sensitivity analysis suggests lack of association of excess weight with dementia. However, the authours still concluded their finding based on the prior protective result that overweight was good for health. This highlights the need for consideration of possible bias from reverse causality.

Gender effect

The influence of gender on the association of overweight and obesity with dementia risk is grossly under-researched, while data from gender-specific associations of increased lipids with cognitive decline showed older men and women disparities in the risk of cognitive impairment (Ancelin *et al.,* 2014). In addition, the literature also suggests that in developed countries, women were more likely to be diagnosed of AD, while some studies (Petersen et al., 2010; Mielke *et al.,* 2014) suggested that men were more prone to risk of mild cognitive impairment compared to women. These suggest sex disparity in risk of developing dementia. However, there is lack of evidence to help clarify the relationship in men and women while data in older adults from developing countries are also lacking to contribute to understanding. This systematic review showed only four studies stratified their analysis by sex to examine gender differences in the association of BMI with dementia (or AD) while three out of all the sixteen studies focused on only one sex. However, the results from four studies (Borestein Graves *et al.,* 2001; Hayden et al., 2006; Dahl *et al.,* 2008; Atti *et al.,* 2008) that examined sex differences in the impact of adiposity on dementia risk within the same cohort data showed no significant associations in the male samples analysed for BMI and dementia of all types, while there were inconsistency in findings for the females. For instance, while previous finding from USA (Borestein Graves *et al* 2001) found no association of continuous BMI with AD risk in women (1.06, 0.87-1.31) and also in men. Another study of US population (Hayden *et al.,* 2006) reported significantly increased risk for AD in women with obesity (2.23, 1.09-4.30) but not in men. These suggest that findings are not consistent, and more research is required to clarify the sex-difference in association of adiposity in older age and dementia risk.

Dementia types

The systematic review investigated the association of adiposity with dementia of all types. It also included findings from dementia types like AD and VaD which may have different etiology and risk factors (Rantanen *et al.,* 2017). For instance, AD risk is increased by gene factors like APOEe4 and TOMM40 (Gustafson, 2012; Zade et al., 2013) while metabolic factors may be central to the etiology of vascular dementia (Mehlig *et al.,* 2018). The review showed that most of the studies (9 out of 12) that investigated BMI (as continuous or categorical data) supported an inverse association between BMI and AD risk with five of them reflecting significant effects, while no such an inverse association was observed in all five studies of BMI in relation to VaD. The findings of strictly continuous BMI and AD reflected similar inverse association. As a whole, the findings for VaD showed no significant association, while findings from for AD reflected similar results to the main findings of all types of dementia. Therefore, more research is needed from primary cohort studies to investigate if the association of adiposity and dementia vary by subtypes, such findings if confirmed could help understanding of the mechanism involved in each dementia type.

Strength and Limitation of this systematic literature review and meta-analysis

This systematic review is the most comprehensive review of the impacts of overweight and obesity on the risk of dementia and its subtypes by different adiposity measured in mainly older adult population of age ≥65 years. The review followed strict recommended protocols for conducting quality systematic review including extensive search using different databases and exploration of grey literature with successful communication with authors for additional information. The quality assessment was based on the recommended Newcastle Ottawa rating criteria. The systematic review included studies with moderate to excellent quality rating with most studies amassing points on important items on the rating scales such as measure of exposure, outcome and adjustments for confounders. It also included studies with relevant characteristics including those with long- and short-term follow-up, sub-group and sensitivity analysis, measured AD and VaD risks. These enhanced the quality of the in-depth review and identification of important gaps that needs to be addressed to advance knowledge of the impacts of adiposity on dementia risk.

Previous reviews (Goroscope *et al.,* 2007; Emmerzaal *et al.,* 2014), including those with meta-analysis (Anstey *et al.,* 2011; Pedditizi *et al.,* 2016) were limited by the number of studies in older age and lacked findings from use of different adiposity measures (Emmerzaal *et al.,* 2014; Pedditizi *et al.,* 2016). However, the associations of adiposity in this study were reviewed extensively in terms of the use of continuous, categorical and change of BMI by cohort studies associated with dementia and its subtypes, while the findings from studies that explored measures of central fats like the WC were also duly considered. In addition, the presentations of the systematic review findings in previous published studies in the literature were often not detailed enough to allow critical evaluation of the findings. However, this systematic review followed the PRISMA guidelines, is more detailed and included data of 38,219 participants from 16 cohort studies conducted in older adults from a wide range of countries across different continents.

The study has some limitations. While the systematic search of the literature was extensive and had no language limits, it identified and got all the included studies from high come countries, with none from developing countries. Therefore, it might be difficult to generalize the findings of this review to low- and middle-income countries. For instance, China is a middle income country from Asia with different population characteristics and has experienced epidemiological transition in chronic disease risk factors due to rapid economic developments, urbanization and nutritional transition over the past three to four decades (Yang et al., 2008; Popkin, 2010; 2014). In addition, it was documented that Asians have higher cardiovascular risk factors than Caucasians for the same BMI level (WHO, 2004; Chen et al., 2008). It is therefore possible that the impacts of adiposity on incident dementia might be different. This highlights the need for future original research of prospective design from developing countries.

3.5 Summary of knowledge gaps

1. Most of the studies from the review suggests that overweight and obesity in older age were associated with reduced risk of dementia, even though there were

inconsistency in the findings with some studies reporting no association while very few suggested harmful effects.

2. Most of the studies that reported inverse association between BMI and dementia risk were characterized by short duration of follow-up, as also confirmed by meta-analysis stratified by duration of follow-up, while one study with 18 years of follow-up showed a positive association. This suggest that the duration of follow-up is crucial in the study of obesity and dementia.

3. Findings of the impacts of overweight and obesity on incident dementia was mainly from use of BMI with little knowledge of the impact of waist circumference on the relationship

4. Evidence suggests there might be sex disparity in the impact of overweight and obesity on dementia risk. However, majority of studies (12 out of 16) did not examine sex differences. The findings from the few studies were inconsistent for females while excess weights in men seemed to have no association with dementia risk.

5. It was observed that all the included studies from the systematic literature review were all from developed countries with none from developing countries. It is therefore unknown if the impact of adiposity on dementia risk might differ from developed countries. Therefore, studies from developing countries are needed.

6. The literature suggests that the etiology of AD might be different from VaD if they could be purely discerned. However, findings of adiposity and these dementia subtypes were similar in prediction pattern with most findings of all types of

dementia supporting inverse associations. This highlights difficulty in distinguishing these dementia types clinically. However, more research is needed to examine their individual association with adiposity.

3.6 Recommendation for future research

There is need for more research from prospective cohort studies with long term follow-up, particularly from developing countries, to help examine the impacts of overweight and obesity on dementia risk. There is need to use both measured BMI and WC to investigate the association of adiposity and dementia risk and examine if the impact varies according to sex. Such research needs to account for relevant confounders including smoking and medical morbidities. Further sensitivity analysis should limit residual confounding due to smoking and pre-existing illness while limiting reverse causality.

3.7 Conclusion

The systematic literature review and meta-analyses showed that overall, there was an inverse association of body weight with dementia risk, which was mainly from the cohort with the short-term follow-up. Some long-term follow-up studies with more confounders adjusted showed no association between body weights and dementia risk or a positive association. Therefore, more research from well-designed cohort studies that address most, if not all the issues raised and discussed above, are needed to ascertain of overweight and obesity in older adults could reduce the risk of incident dementia.

CHAPTER FOUR: METHODOLOGY

This chapter covers the methodology employed for the thesis. It presents the mixed methodology which combined quantitative and qualitative approaches. The philosophical foundation behind the research approach, the justifications for the mixed method design and the strengths and limitations are presented. The quantitative and qualitative components of the overall design in terms of the prospective cohort and focus group studies employed and the rationales for the choices made are explained. The chapter concludes with how the findings from the separate study approaches in the mixed method design are integrated into the thesis.

4.1 Mixed methodology

The thesis used a mixed method to investigate the risk factors and health effects of overweight and obesity. Several definitions of mixed methods are documented in the literature (Tashakkori and Creswell, 2007; Onwuegbueze and Turner, 2007; Creswell, 2014) and they portray mixed methods as the mixing of quantitative and qualitative data in a study design to address research questions. However, one definition that mirrors current understanding of modern-day mixed method is the recent one by Creswell and Clark (2017 p. 5):

"In mixed methods, the researcher collects and analyses both qualitative and quantitative data vigorously in response to research questions and hypothesis, integrates (or mixes or combines) the two forms of data and their results, organises these procedures into specific research designs that provide the logic and

procedures for conducting the study, and frames these procedures within theory and philosophy". This definition emphasised the use of different data from different methodologies which are robust in themselves to help address the questions and hypothesis outlined for the same research; that is dictated by a philosophy and supported by theory. It is distinctly marked by the integration of data and findings in a manner that reflects the purpose of the design

4.1.1 Pragmatism

The pragmatism philosophy informs the study approach for this thesis which investigates the risk factors and health effects of overweight and obesity in older adults. It was argued by experts in mixed methods (Bryman, 2006; Denscombe, 2008; Onwuegbuzie, 2007; Creswell and Clark, 2017) that pragmatism philosophy not only serves as the foundation of most mixed methodology research but solidly rests on practicality. It also holds the belief that combining two different research approaches would yield better dividends in terms of achieving research goals and objectives. Ontologically, by this philosophy, the view of what constitutes knowledge of risk factors and health effects of obesity is not the only objective but also subjective. Epistemologically, how this knowledge may be known requires an approach which works, and this involves quantitative and qualitative strategies of inquiry (Bryman et al., 2006; Onwuegbueze, 2007). The combining of two different approaches in this research is guided by the thinking that no research paradigm or approach is superior to the other. The nature of the research problem and question is at the heart of how knowledge and truth may be known and what works is more important (Creswell and Clark, 2017). This pragmatism philosophy is cognisant of the obvious limitations inherent in the quantitative and qualitative strategies of inquiry while leveraging their strengths and underpinning philosophies.

4.1.2 The positivist research philosophy

Positivism is the underpinning philosophy behind quantitative research approaches which ontologically depicts the nature of reality as stable and observable, and epistemologically reality is measurable while what is viewed as true (axiology) represents proven knowledge (Bruce, Pope, and Stanstreet, 2008, p.3; Chilisa and Kawulich, 2012). By these assumptions, objective reality exists independent of human behaviour, and what is truth must be determined by accurate observations and verifiable measurements, and known within the confines of probability (Crotty, 1998, p.9; Chilisa, 2011; Creswell and Clark, 2017). The philosophical tradition of positivism is evident in health research and dictates most of the strategies of inquiry in the entire field of epidemiology (Bhopal, 2008; Bruce, Pope, and Stanstreet, 2008, p.3: Rothman, 2012).

4.1.3 Strengths and limitations of quantitative research approach

Quantitative research is one of the approaches for investigating a health problem and it is concerned with the testing of hypotheses and theories by examining relationships that exist between or amongst variables. It applies statistical methods to the analysis of numbers generated from measurements of variables using defined instruments (Yilmaz, 2013; Creswell, 2014, p.4).

One of the major strengths of the quantitative research approach is the generation of data that are highly consistent, precise and reliable due to the use of the scientific method which is known to be characterized by a rigorous and systematic process that is reproducible and repeatable (Nigel, 2008, p.3). Another main strength is the associated large sample sizes and the generalizability of the findings particularly with properly designed selection procedures and samples from the target population (Martin and Bridgmon, 2012). In addition, an advantage of the approach is the relatively easier analysis of data using statistical software packages compared to the alternative approach such as qualitative research (Queiros, Faria and Almeida, 2017). Despite these strengths, there are limitations of the quantitative research method. For instance, it is hard to understand the context of a phenomenon since objectivity is emphasized independently of human behaviour or experience (Crossan, 2003). Besides, there is sometimes the challenge of having data that is not large enough to explain complicated issues (Maher, Markey and Ebert-May 2013) while lack of secondary data to conduct large scale quantitative study presents another important limitation (Choy, 2014).

4.1.4 The constructivist research philosophy

Qualitative research is underpinned by interpretivism or constructivism philosophy which recognises knowledge as subjective, considers truth as context reliant and how the world may be studied requires strategies of inquiry including beliefs and value systems that lead to understanding of the meanings of phenomena (Kawulich, 2012). Constructivism emerged as an alternative to the positivist philosophy in the quest for comprehension of human experience and it is marked by multiple views and interpretations of reality (Appleton and King, 2002; Doyle, Brady and Byrne, 2009; Creswell 2016). This philosophy has informed numerous health research internationally and produce useful findings that contributed to knowledge, policy change and practice (Doyle, Brady and Byrne, 2009).

4.1.5 Strengths and limitations of qualitative research

Qualitative research is a strategy of inquiry associated with emerging questions and procedures that are focused on examining and understanding of the meanings assigned by groups or individuals to human or social issues (Creswell, 2014, p.4). It involves collection of data from multiple sources through observation, interviews, focus groups, written documents, cases studies etc. (Choy, 2014).

One of the major strengths of the qualitative research approach (Choy, 2014; Creswell, 2014, p.4) is that complex issues can be explained from the interpretation of data gathered through detailed information collected by open-ended inquiry and broad issues raised as part of the research procedure. It is also possible to achieve a better understanding of people's beliefs, assumptions, and behaviours of values since the research approach is rooted in subjectivity of reality (Choy, 2014). Also, qualitative research helps to complement, refine data or corroborate findings from quantitative studies particularly when triangulated (Bryman, 2006; Casey and Murphy, 2009). Also, data collection based on this approach is more cost-effective with multiple sources available to the researcher unlike in the quantitative research which demands higher resources with limited options. A major limitation of the qualitative research is inability to generalize findings to the study population or community due to very few participants and the use of non-probability samples (Crossan, 2003; Choy, 2014). Another concern about qualitative research is that it is time-consuming and the analysis difficult with issues of poor or lack of fitting of some data into standard categories. Besides, there is also the challenge of high skill requirements of the interviewer and that of the researcher in ensuring issues of truth worthiness, rigour and reliability are addressed in the entire process (Choy, 2014; Nowell, 2017).

4.1.6 Rationale for the mixed method approach

Mixed method is largely driven by pragmatism research philosophy and draws from the wisdom that no approach is self-sufficient and infallible. The purpose of mixed method in this thesis is to expand and strengthen its research findings, study conclusion and to significantly contribute to knowledge in the field of epidemiology on the risk factors and health effects of overweight and obesity in older adults. Therefore, using quantitative (cohort study) and qualitative (focus group) data in the research project will help to maximise the strengths of the study while limiting any weakness associated with either approach. One major rationale for integrating quantitative and qualitative methods in the same study is the context of the research problem and the question asked or aims of the study (Bryman, 2006; Creswell and Clark, 2017). In this PhD study, obesity is conceptualised as a complex health problem that is not only medically defined but also socially constructed. This view is supported by findings of social and cultural patterning of overweight and obesity within the society and internationally (Napier *et al.,* 2014; Fox, Fen and Asal, 2019). It means that the understanding of risk factors for excess body weight and their impacts on dementia risk and survival would require different types of data (from quantitative and qualitative data collection) which are numerical to test hypotheses and textual to provide meanings and understanding. Additionally, recommendations for policies and strategies that affect older adults would surface from this thesis. Therefore, including quantitative data to objectively investigate cause and effect relationships and qualitative data of focus group to examine the same research questions subjectively will support the findings from the thesis and produce useful recommendations from older adults that may be affected by proposed policies and strategies. In this research work, therefore, the mixed method approach is needed to help achieve a more complete or better understanding of risk factors and health effects of obesity in older adults and add new knowledge in the literature

4.1.7 Strengths and limitations of mixed method

The mixed method counterbalances the limitations associated with either quantitative or qualitative research alone (Johnson and Onwuegbueze, 2004). Therefore, using the mixed method helps the strengths of the study to be maximized while the weaknesses are reduced. Mixed method research offers the researcher the benefits of multiple data thereby helping to strengthen and provide more evidence or answers to questions that cannot be addressed by quantitative or qualitative method alone (Johnson and Onwuegbueze, 2004). One of the strengths of mixed method is that it supports the use of various research paradigms and their associated approaches. This could lead to new insights or findings that contribute to knowledge and understanding. Mixed method also presents an important opportunity to enhance the research skills of researchers and helps several publications from the work (Creswell and Clark, 2017, p.12-14).

On the side of weaknesses, conducting mixed method study could be demanding in terms of human resources including time, cost, research skills and experience. There is also the complexity associated with mixed method research designs making planning and implementation cumbersome. While there is also need for understanding of more than a single method, the technical know-how of integrating quantitative and qualitative study as well as resolving any disagreement in terms of findings from research approaches within the mixed method is a major challenge (Johnson and Onwuegbueze, 2004; Creswell and Clark, 2017, p.12-14).

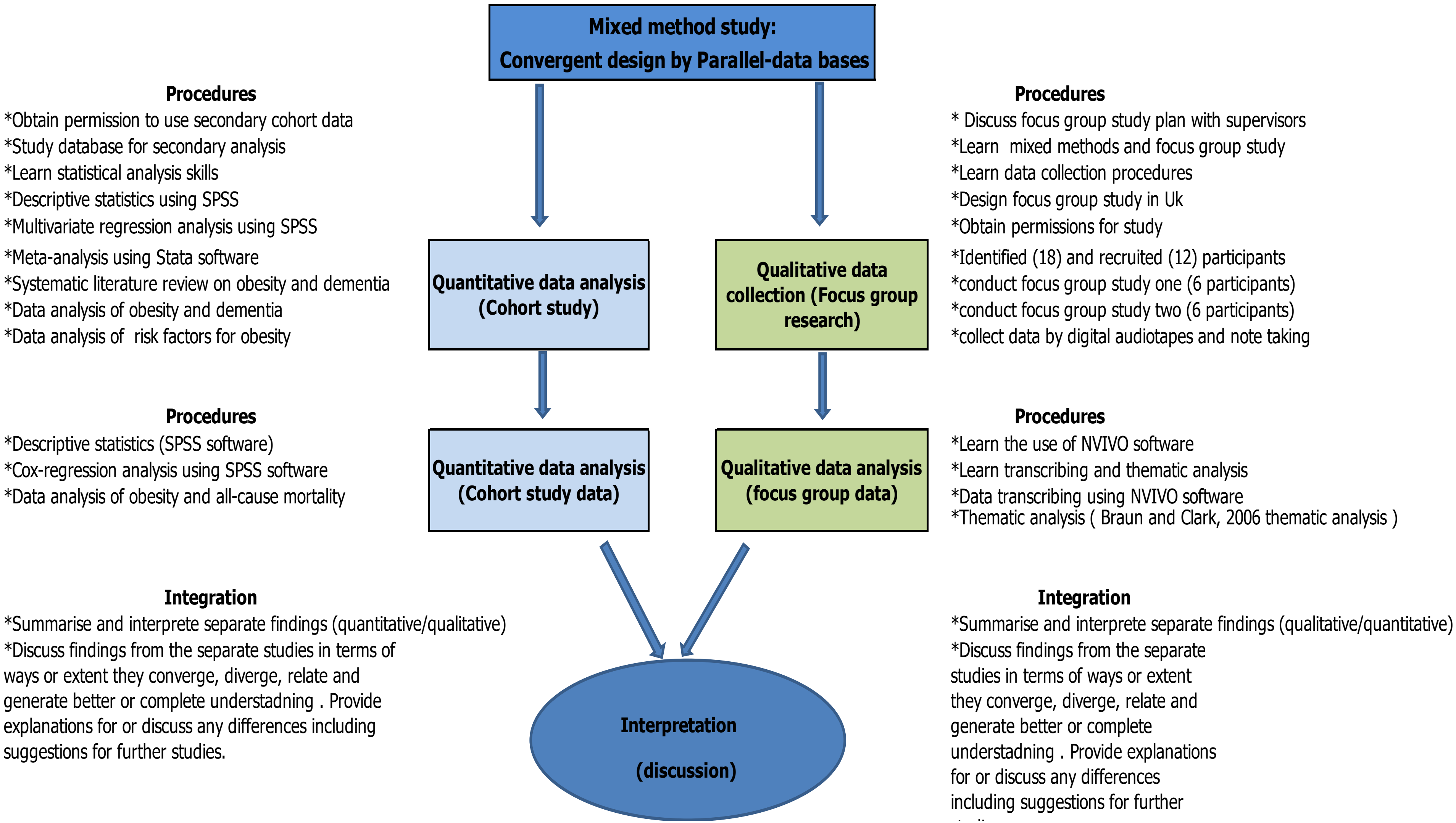
4.1.8 The mixed method design: The convergent design by parallel databases

This design is the most popular and oldest among the three core research designs in modern mixed methods which include explanatory sequential, exploratory sequential and convergent designs. The convergent design was referred to as triangulation as originally coined by Greene (1989) which emphasised complementarity and further expanded by Bryman (2006) to include offsetting weaknesses and drawing from strengths of quantitative and qualitative methods, completeness, credibility and enhancements. According to Creswell and Clark (2017, p.68), *"the convergent design is a mixed method design in which the researcher collects and analyses two separate databases— quantitative and qualitative— and then merges the two databases to compare or combine the results".*

The parallel database variant of the convergent design adopted in this thesis is a newer type of convergent design. Creswell and Clark (2017, p. 72) explained that the convergent design by parallel databases *"is the 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 synthesized or compared during the discussion"*.

This thesis involves the use of two parallel databases or independent studies based on the prospective cohort (China) and Focus group study (UK) to explore the risk factors of overweight and obesity. Figure 2 depicts the convergent design by parallel databases for the research work in this thesis. It shows the procedures for the quantitative and qualitative research approaches as components of the overall design and it included the point of integration of the findings at the interpretation stage (discussion). In the diagram (Figure 2), the quantitative research involves examining data of large-scale cohort of older people for incident dementia and all-cause mortality outcome in relation to overweight and obesity. The systematic review and meta-analysis as part of the quantitative research work are also identified in the design. The qualitative aspects involve focus group data and the key details including the chosen analysis strategy are stated

Figure 2 Mixed method convergent design by parallel databases



4.2 Quantitative research design: Cohort study

Quantitative study designs are the most crucial considerations in epidemiologic research of obesity (Hu, 2008, p.24). Several options are available including ecological, cross-sectional, case-control, cohort and experimental trial study designs (Nigel 2008; Bhopal, 2016). Whilst, experimental trials remain the goal standard in establishing causal relations, cohort studies offer the huge benefits of measuring incidence, causes and prognosis of disease and are considered the best non-randomized control study design for investigating causes and effects relationship, particularly in prospective cohort study design (Mann, 2004; Hu, 2008, p.35; Caruana *et al.,* 2015). This thesis, therefore, uses data from a prospective cohort study to examine risk factors for excess body weight and to examine the health effects of overweight and obesity in older age in terms of incident dementia and all-cause mortality risk.

4.2.1 The prospective cohort study design

Cohort studies are marked by the term 'follow-up', 'longitudinal' and 'perspective' to emphasize the following or tracking of a group of people with a defined characteristic (cohort) over time (Bhopal, 2016, p.338). The prospective cohort study design is a type of observational study which involves the assessment of exposure at baseline and outcome followed-up over a period. It involves the measurement of exposure as they occur in real-time (Bailey and Handu, 2013, p.42; Nigel, Daniel and Debbi, 2008, p.263).

4.2.1.1 Strengths of cohort studies

The prospective cohort study is the best non-randomized control study design for investigating causes and effects relationship (Hu, 2008, p.35; Caruana *et al.,* 2015). In this study design, temporal order or sequence of events can be demonstrated with the cause (exposure) preceding the disease (outcome) thereby providing necessary criteria to help ascertain causality (Hu, 2008, P.35; Caruana *et al.,* 2015). It is also a perfect fit for hypothesis testing and generation, while the incidence and natural disease history can be determined and described (Mann, 2004; Bhopal, 2016, p341-342). Besides, the design permits the use of the term relative risk or risk ratio (as well as hazard ratio or odds ratio) since incidence is measured (Bhopal, 2016, p341-342). This is different from case-control studies which are often confined to use of odd ratio only.

4.2.1.2 Limitations of cohort studies

Cohort studies are expensive in terms of financial and human resources and are often time-consuming since cases could take a long time to develop particularly for health problems like obesity (Bailey and Handu, 2013, p.43). This is aside from the challenges of attrition with loss of cohort members in follow-up (Caruana *et al.,* 2015) due to several reasons including the personal reason for withdrawing from a study, inability to trace members who perhaps must have relocated or due to death etc. There is also the challenge of confounding which demands a strong design that anticipates the limitation and puts in place sound statistical methods to deal with it (Caruana *et al.,* 2015).

4.2.2 Rationale for using prospective cohort study data in the thesis

The quantitative aspects of the research work for the PhD thesis is based on prospective cohort study design and data analysis. It was suggested by Mann (2003) that the choice of research design should be driven by the main objective of the study. The decision for using data from prospective cohort study was informed by the overall objective of the research work for the thesis which is concerned with investigating causes and effects relationship. The thesis is concerned with exploring the major factors associated with the risk of overweight and obesity in older adults and the health impacts of excess body weight on incident dementia and all-cause mortality. Therefore, drawing from recommendations of Hu (2008 p.35), the most reliable and strongest study design of all non-randomized studies to demonstrate cause and effect-relationship in obesity epidemiology research is the prospective cohort study.

It was argued that a major concerns in investigating "causes and effects" relationship is the challenge of demonstrating the sequence of events or that exposure preceded the outcome (Mann, 2003; Bailey and Handu, 2013, p.39; Caruana *et al.,* 2015) However, unlike cross-sectional studies, prospective cohort studies are capable of demonstrating temporality of order thereby supporting the criteria to help ascertain causality (Hu, 2008, P.35; Caruana *et al.,* 2015). Though the randomised control trial is a goal standard, it is highly expensive and beyond the reach of the researcher. It was argued that prospective cohort studies are also expensive and could be time-consuming (Bailey and Handu, 2013, p.43). While this is true, the research work in this thesis is based on analysis of secondary data from already completed prospective Anhui cohort and the 4-province cohort studies of older adults in China. The approval for using and access to cohort data was granted for the research project thereby taking off the burden in terms of cost and time in collecting fresh data.

One concern for the use of cohort data in the study of a health problem like obesity is that it could take time for the health effects to manifest thereby requiring longer follow-up (Zamboni *et al.,* 2005). However, the prospective cohort study data for the thesis is based on 10 years of follow-up which was considered adequate (Johnson, Wilkins and Morris, 2006) to detect the health effects of obesity in older adults. Another concern for the use of cohort study data is dealing with confounding factors (Zamboni et al., 2005; Caruana *et al.,* 2015). However, a lot of covariates as potential confounders were assessed at baseline assessment of the cohort study used in the thesis while appropriate and strict statistical methods were selected in the analysis to limit bias**.**

4.2.3 The Anhui Cohort study

The quantitative research for the thesis involves data from the Anhui prospective cohort study in China. The method for the cohort study is described in the following sections.

4.2.3.1 Study area

The Anhui cohort study was conducted in the Anhui province, China. Anhui is one of the 34 provinces in China and is located in the mid-eastern region with its capital at Hefei City. Anhui province is the 12th most densely populated; it is ranked the 22nd largest Chinese province and 8th in terms of population (62 million). The areas for the Anhui cohort study were Hefei City and Tangdian District of Yinshang County.

Figure 11 Map showing the location of Anhui Province, with Hefei City the capital

4.2.3.2 Study population and setting

The targeted population was those of age ≥65 years from urban areas (Yiming sub-district of Hefei City) and those of 60 years and above who had lived for at least 5 years in the rural (all 16 villages of Tangdian District of Yinshang County) of the Anhui province. The study population was 3,336 older adults residing in urban and rural communities. The Yiming district from Hefei City was used as the collaborative base for the teams facilitating the collection of data.

4.2.3.3 Sampling strategy and participants' recruitment

The study opted to investigate up to 2000 subjects in the community based on the sample sizes in the previous studies (Chen et al., 1999) and the practical resources and working experience at disposal (Chen et al., 2004). The required sample was selected by stratified random technique drawing six from 10 sub-district residency committee lists of older adults. The Anhui medical University, the district government and sub-district residency committees approved the study. After this, the public was informed through advertisement in local newspapers and Television of the proposed general health study of older people within the districts in Anhui province. Before recruiting into the study, permission was obtained from each elderly person or their closest responsible adult if it was difficult to do so directly. However, when refusals were encountered, they were respected. The older adults were recruited provided they had lived for at least 5 years within the district (This was to ensure their permanent address could be confirmed and they could be traced back to the community in the follow-up after baseline assessments). A total of 1,810 eligible older participants were invited, of which 1736 agreed to participate (95.9% response rate). Participants were interviewed and other baseline investigations done at their homes by a trained survey team from the School of Health Administration in the Anhui Medical University from 1st November 2001. Using the same approach in 2003, a rural sample of 1709 older people of age ≥60 years were selected from the 16 villages of Tangdian district (of Yinshang County in Anhui province) out of which 1,600 (754 men and 846 women) agreed to participate (93.6%). The data collection started on 1st April and was completed by 30th April 2003 (Chen *et al.,* 2005). As a whole, there were 3336 participants with a response rate of 94.8% in this study for baseline survey interview, comprising of 1736 from the urban and 1600 from rural areas.

4.2.3.4 Data collection and tool development for the cohort study

The data collection tools for the cohort study included the General Health and Risk factors Questionnaires, the Geriatric Mental State Questionnaires (GMS) and the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT). These are described below.

4.2.3.4.1 The General Health and Risk Factors Questionnaires

The materials for the interview of participants during baseline investigations were mainly from an already validated Chinese version of the general health and risk factors questionnaires (Wilson *et al.,* 1999; Chen and Tunstall-Pedoe, 2005), which were partly obtained from the MRC-ALPHA study and the Scottish MONICA surveys (Saunders *et al.,* 1991; Chen *et al.,* 2003). The questionnaire contained some risk factors from the MRC-ALPHA study (Copeland *et al.,* 1999) while most were from the Scottish MONICA surveys (Chen et al., 2003). It also involved the Geriatric Mental State Questionnaire. The General Health and Risk Factors Questionnaire and the Geriatric Mental Status (GMS) questionnaires captured the following: (1) socio-demographic information and lifestyles, (2) social support and relationships, (3) psychosocial aspects and diagnosis of depression, (4) doctor-diagnosed cardiovascular diseases and medications and self-assessed physical health, (5) adverse life events occurring in the last two years, (6) hobbies and activities of daily living (ADL). Weight, heights and waist circumference.

The participants' height, weight, waist circumference and blood pressure were measured while trained medical doctors diagnosed various diseases such as cardiovascular diseases. Height was measured without shoes to the nearest 0.5 cm by portable stadiometer, while weight was recorded to the nearest 0·1kg by digital scales with light clothing on. Waist circumference was measured to the nearest 0.1 centimetres using a plastic tape placed mid-way between the lowest rib and the iliac crest. According to standard methods the systolic and diastolic blood pressures were measured (Chen *et al.,* 2003). Blood pressure measurements were assessed twice at the first visit, seated after five minutes rest, by doctors subject to quality assessment who used a Hawksley random-zero sphygmomanometer and the first and fifth Korottkoff sounds. The mean of the two readings was used

4.2.3.4.2 The Geriatric Mental Status (GMS) questionnaires and Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT)

The GMS questionnaire is a comprehensive semi-structured mental state interview which is widely used globally in older people (Saunders *et al.,* 1991). The GMS is used with the AGEGAT for diagnosis of depression and dementia in older people in developed and developing countries. The Chinese version of the GMS used in the Anhui cohort study is popular in Asia and has been validated among older Chinese in Mainland China, Hong Kong, Beijing, Taiwan, and Singapore. Double blind methods were used for the validation of the GMS-AGECAT depression and dementia diagnosis. Two independent clinicians who were consultant psychiatrists from Hefei Psychiatric Hospital were used as gold standard for diagnosis. They re-examined the cases identified by GMS-AGECAT, and a similar number of controls who were at the GMS-AGECAT levels of 0–2 (i.e. not cases of mental illness) and randomly selected according to the case's closest home address. The validation of an agreement on depression diagnoses between the GMSAGECAT and the Chinese psychiatrists was examined by Kappa test (Chen et al., 2004). The psychiatrists successfully re-examined 30 cases and 31 controls (out of 39 cases of depression and their 40 controls), three subjects with AGECAT case depressions and two controls refused to be re-examined, which was not significantly different between the two groups. There was good agreement on depression diagnoses between the GMS-AGECAT and the psychiatrists. This was indicated by a total agreement of 83.6% and Kappa 0.67 ($p < 0.001$). The GMS-AGECAT depression diagnosis showed sensitivity of 85.7% and specificity of 81.8%, while positive predictive value was 80.0% and negative predictive value was 87.1% respectively (Chen et al., 2004). Similarly, the validation test of the GMSAGECAT dementia diagnoses in an urban community in Beijing (China) was on 120 Chinese who were aged 60 (60 normal, 30 with dementia and 30 depressive subjects diagnosed according to ICD-10). There was a total agreement of 88.3% for dementia and depression with a Kappa 0.78 (Liu et al., 2001).

The AGEGAT is a computer programme aided tool for diagnosis which works with the GMS to ascertain mental disorders such as depression and dementia by analysing the information collected from the GMS. A theoretical model was used in the development of the GMS-AGEGAT and was tested against its success at replicating diagnosis on samples diagnosed by psychiatrists which follows the process of accomplishing a syndromic diagnosis followed by a differential diagnosis (Chen *et al.,* 2008). Usually, the Geriatric Mental State symptoms are combined into a 150 'symptoms components. The symptom components are combined in groups at the first stage which reflects the symptom areas of each diagnostic syndrome. This is followed by the second stage where the various syndrome levels are compared to generate a final differential diagnosis (Copeland, Dewey and Griffiths-Jones, 1986; Copeland *et al.,* 2002).

The GMS-AGECAT dementia and depression diagnosis in the Anhui cohort showed a total agreement of 83.6% and Kappa 0.67 ($p < 0.001$) indicative of robost reliability as confirmed from the Kappa test (Chen *et al.,* 2004). The Anhui cohort study used the GMS-AGEGCAT described above for the diagnosis of dementia and depression at baseline. It is considered as the most popularly used community-based study method for investigations of dementia and depression in older adults internationally (Chen *et al.,* 2005). The differential diagnosis employs confidence level of diagnosis from 0–5 with the level of ≥3 indicative of dementia case level while level 1 and 2 represents sub-cases. Those of no confidence interval or level of 0 represents 'normal' or 'well'. The diagnostic tool and dementia 'case' has been likened in studies with psychiatrists' diagnoses using DSM–III and DSM–IV or ICD–10 criteria and found to achieve a good level of agreement in varied settings, including in Chinese older adults (Prince *et al.,* 2003; 2004). Therefore, the use of the GMS-AGEGAT in the Anhui study is internationally recognised and it supported the quality of the data from the prospective cohort study for the research project on dementia outcome. To ensure the research team had the technical know-how for the diagnosis, there was systematic training of the survey team in the use of the GMS prior to the interviews. In 2001, two research workers from the Anhui team were trained on use of the GMS at the Institute of Psychiatry, Beijing Medical University, Beijing, China and this training was cascaded by an investigator who had attended a GMS-AGECAT course in Liverpool, UK They then trained the eight members of the survey team in Anhui. There were 10 interview groups with each having a male and female charged with interviewing at least 200 subjects. The questionnaires from daily interviewing were returned and collated at the survey office in the school where they were checked for completeness by quality controllers. All surveys data collection was completed by 30th Nov 2001 (Copeland, Dewey, and Griffiths-Jones, 1986; Copeland *et al.,* 2002; Chen *et al.,* 2005).

4.2.3.5 Follow-up of the cohort

Their vital status has been followed up until 2011 for various diseases and mortality outcome. During the follow-up period, 3 waves of re-interview were conducted for surviving cohort members, Wave 2 followed the same protocol as the baseline and it involved the re-interview of 2,608 cohort members one year after baseline (i.e., in 2002 for the urban cohort, and 2004 for the rural cohort). After taking out those who died, moved to a new home without trace or left home for a long period the response rate was 86.9%. The wave 3 of follow-up occurred between 2007 and 2009 in the whole cohort. It involved 1757 surviving cohort members with the use of GMS and general risk factors questionnaires (response rate of survival cohort was 82.4%). Wave 4 was conducted in 2010-2011 using the 10/66 dementia algorithm package and the general health and risk factors questionnaire. It included 944 surviving cohort members. The 10/66 dementia algorithm which was used to diagnose dementia, has been widely used and validated in older adults with low educational levels in low and middle-income countries including China (Rodriguez *et al.,* 2008). The 10/66 dementia diagnosis requires four inputs from the interview: the GMS-AGECAT diagnostic output, the Cognitive score (COGSCORE) which is an item-weighted total score from the 32-item cognitive test administered to the participant , the informant score (RELSCORE) and Consortium to Establish Registry for Alzheimer's disease (CERAD) 10-word list learning task with delayed recall

(Prince *et al.,* 2008). A cut-off point of probability (≥0.25) derived from the full 10/66 algorithm was used to diagnose dementia. The mortality outcome was ascertained from causes of death through electronic registration databases from the local Centres for Disease Control and records from the local resident committees. There were six hundred and one deaths recorded in the cohort over the follow-up period. We used a standard Verbal autopsy questionnaire to explore further causes of death (Chen *et al.,* 2014).

4.2.3.6 lost to follow-up in the Anhui cohort study

The lost to follow up serve as a threat to the internal validity of estimates from cohort studies (Howe *et al.,* 2016). Though it is also known that loss to follow up is unavoidable in most studies of cohort study design (Kristman, Manno and Côté, 2004). The Anhui cohort had 3336 participants, after recording a high response rate of 94.8% from the baseline survey interview which consisted of 1736 from the urban and 1600 from rural areas. However, over the ten years follow-up period, there was a 10.5 % attrition. In the Anhui cohort study, 358 were lost to follow-up leaving a total of 2,978 participants. A detailed analysis has been previously reported on those lost to follow-up compared to the rest of the population in the Anhui cohort (Chen *et al.,* 2014). It showed no significant differences in the baseline characteristics of participants followed up and those lost to follow-up, aside from them being mostly women (61.2%), non-lifetime smokers (66.4%), married (65.6%) and widows (32.1%) who were less likely to be followed up (Chen *et al.,* 2014). In this thesis, these variables (gender, marital status, and smoking history) were included in the adjusted covariates in the main analyses, which limits any bias emanating from loss to follow-up.

4.2.4 Data management and data analysis

The research project used data of the prospective cohort studies from Anhui Province China and the 4-province study that were already completed as described above. The datasets were already cleaned by the research team in China and ready for statistical analysis to address the research questions. After access was granted, the datasets were carefully studied, using their data dictionaries to identify and explore the variables of interests. The dataset preparation stages involved the construction of categorical variables such as BMI categories, computing of quartiles of BMI and WC. Categorical BMI variables were created based on the BMI classification recommended for Asian Chinese population by the Chinese government (Chen *et al.,* 2008). This is because the Chinese people (The Asians), as compared with the Caucasians, have higher body fat percentage for same BMI (Kanazawa *et al.,* 2002; Chen *et al.,* 2008). Therefore, participants with baseline BMI of ≥28 Kg/m2 were classified as obesity, 24-27·9 Kg/m2 as overweight, 18·5-<24 Kg/m2 as normal and <18·5Kg/m2 considered as underweight. The WC cut-offs for Chinese men and women were also used apart from the WHO cut-offs. The WHO recommended WC classification groups includes no action<94cm, action level one 94-<102cm and action level two ≥102cm for men; while in women they are defined by no action <80cm, action level one 80-<88cm and action level two ≥88cm (Lean, Han, and Morrison, 1995; Chen *et al.,* 2008). The WC values for the Chinese people are <85, 85-95 and ≥95cm for men and they are <80, 80-90 and ≥90cm for women for no action, action level one and two (Chen *et al.,* 2008). There was also the merging of categories of some variables or modification of variables for further analysis such as data transformation. They were done by applying the transform and recode into different variable fuction in SPSS on a computer. Data linkages were also required for linking datasets in preparation for analysis.

Data were explored using descriptive statistics such as frequencies and Chi-square tests for categorical variables and one-way analysis of variance for continuous outcome variables. The numbers of deaths, person-years, and mortality rate were computed with the aid of SPSS version 24.0 (SPSS Inc, Chicago, USA). Using logistic regression and Cox-regression models I examine associations of exposures (e.g., BMI and WC) with outcomes (e.g., incident dementia, all-cause mortality). All analyses were performed using SPSS version 24.0 (SPSS Inc, Chicago, USA) while meta-analysis involved the use of Stata IC version 14.0 (Stata Corp, College Station, Texas, USA). Records of syntax for the completed analysis and tables of results constructed in excel spreadsheets and word documents were kept (Appendix 10).

4.2.4.1 Descriptive statistics

In the study of risk factors for adiposity (chapter four), the outcome variables were overweight and obesity. In the data analysis, they were merged as a single outcome for the presentation of the main findings, while overweight and obesity were also analyzed separately. Theoretically, it allows for comparison of the prevalence of and risk factors for overweight/obesity with those of previous studies. From a statistical point of view, it increases the number of participants in the outcome variable of interest for a robust analysis. Means with Standard Deviation and frequencies were used to explore and describe data of continuous and categorized variables while ANOVA and Chi-square test were used to investigate differences in baseline characteristics of participants in different groups of body weight in the follow-up.

Similarly, differences in BMI categories and other risk factors at baseline were explored in study of dementia risk (Chapter six). In the study of impacts of overweight and obesity on all-cause mortality, the numbers of deaths, person-years, and mortality rate were computed in different BM categories groups and their differences were investigated by Chi-square test.

4.2.4.2 Multivariate regression analysis

The analysis of cohort data for the studies in the thesis involved multivariate regression analysis. Multivariate analysis as described by Szklo and Nieto (2014, p.229), are sets of statistical methods in epidemiology that are guided by mathematical models. It adjusts for confounding variables on measuring the association between exposures and an outcome. The thesis used two types of regression model analysis, called as binary logistic regression and Cox regression analysis. The details of how these were employed, including strategies used in limiting the threats to validity, are explained below.

4.2.5.2.1 Logistic regression analysis

The binary logistic regression analysis was employed in the study of risk factors for overweight and obesity (Chapter four) and the study of the impacts of overweight and obesity on incident dementia risks (Chapter six). In these two chapters, the binary logistic regression analysis involved the computation of odds ratio (OR) for the association between exposure and a binary outcome variable with adjustments for covariates considered as confounders. The ORs were computed in SPSS with giving its 95% confidence interval (CI) and p-value (≤0.05 of which indicates a statistical significance).

The study of risk factors for overweight/obesity (chapter four) involved age-sex adjusted and multivariate analysis. The outcome analyzed included 'obesity versus normal', 'overweight versus normal weight' and 'underweight versus normal weight'. The multivariate analysis used overweight/obesity as a binary outcome variable with adjustments for more covariates. Theoretically, the approach takes into consideration that the risk factors for overweight/obesity do not act singly but in combination with multiple factors that may confound the association (Hruby and Hu, 2015). The findings from this analysis (ORs, 95%CI and p-values) provided a measure of association of each factor with overweight/obesity when more covariates were controlled in the model.

In chapter six, the ORs, 95%CI and p-values were computed from the multivariate logistic regression analysis which was accomplished in two statistical models. The above analyses were done using data for BMI and Waist circumference of older adults as predictor variables. Continuous and categorical adiposity data were employed including recommended Chinese cut-offs and quartiles and WC/√height. These analyses explored the impacts of overweight and obesity on incident dementia risk in comparison to other body weights and normal body weight as control.

4.2.5.2.2 Cox regression analysis

Cox regression analysis was the main inferential statistical test for the impacts of overweight and obesity on all-cause mortality (chapter seven). Cox regression models were used to calculate the risk of all-cause mortality with the main statistical output being the Hazard Ratio (HR), 95% confidence intervals and a p-value. It utilizes data of censored and uncensored cases and provides relationships between covariates and survival time. Therefore, the analysis required the status event (binary outcome variable) of death, a time variable and the covariates (BMI or WC and other variables). The time variable usually measures the duration to the occurrence of event as defined by the status event (death).

In chapter seven, the cox-regression analysis of the impacts of overweight and obesity on all-cause mortality involved data of older adults who were followed up for 10 years. The HR, 95%CI and p-values were computed for all-cause mortality in relation to baseline overweight and obesity in older adults. The multivariate analysis involved adjustment for several confounding factors in two models. Several approaches were employed in the analysis to enhance statistical validity as discussed below

4.2.4.3 Reducing the threats to validity

Epidemiological studies are often confronted with several issues that may impact on findings and their interpretation. Therefore, dealing with the main threats to validity is of uttermost importance. The main threats to statistical validity (Szklo and Nieto, 2014, p.227-296) includes confounding, incomplete adjustments (residual confounding), over-adjustments, lack of subgroup analysis, and reverse causation owing to pre-existing diseases

4.2.5.3.1 Confounding

Confounding is a common threat to validity in epidemiological studies. A confounder is a variable existing as a third factor that is not only associated with the outcome of interest but also independently is linked to the exposure (Merril, 2016 p.78). Szklo and Nieto (2014 p.156) summarized the nature of the association between confounder, exposure and outcome as a relationship marked by a confounder being causally associated with outcome and also causally associated or non-causally related with exposure yet not in the causal pathway between exposure and outcome as an intermediate factor. It may be argued that associations not attributed to causal effect could be strengthened or true associations attenuated or negated by some confounders (Szklo and Nieto, 2014, p.153). Therefore, identifying and selecting appropriate confounders for adjustments is crucial in establishing a statistically valid association between exposure and outcome. In this thesis, the selection of confounders for adjustment analysis involved a careful choice based on theory and understanding of the confounders from the literature before inclusion in the statistical models. For instance, age, education, and smoking were considered as strong confounders in the study of all-cause mortality risk. Evidence showed that these factors predict the risk of obesity (McLaren, 2007; Cohen et al., 2013), significantly impact on survival in older adults (Zajacoya and Hummer, 2009; Müezzinler *et al.,* 2015) and are not intermediates in the causal pathway between obesity and mortality. Therefore, adjusting for appropriate confounders informed by theory in statistical models improves the validity of the findings.

4.2.5.3.2 Incomplete adjustment

Another issue is incomplete adjustment or residual confounding where the confounding effects could not be eliminated through adjustments due to effects of a crop of variables or a given variable. Residual confounding could emanate from different sources as described by Szklo and Nieto (2014, p. 293-295). This includes improper definition of categories of the confounding variable, absence of important confounders in the model, misclassification of confounders and alternative or substitute for an actual confounder. To improve validity, these above source of bias due to residual confounding are important. For instance, age may be better off adjusted as continuous data if the association between exposure and outcome varies linearly with age, while several categories of age variable may provide a better outcome than fewer categories of age used in statistical models. Taking this into consideration help reduce incomplete adjustments due to an improper definition of the categories of the confounding (Szklo and Nieto, 2014, P. 296).

4.2.5.3.3. Over adjustment

In contrast to the incomplete adjustment, over adjustment in statistical models could occur when there is a strong relationship of the outcome or exposure with another variable such that their true association is distorted. It could also result from adjusting for variable located in the causal pathway between exposure and outcome. Such over-adjustment in the analysis could lead to false findings. Therefore, it was argued that the biological underpinnings of the exposure-outcome relationship are important to avoid over-adjustments (Szklo and Nieto, 2014, P. 296). In this thesis, the choice of covariates for the statistical models for the study of all-cause mortality (chapter 7) was carefully considered with variables such as heart diseases, diabetes, and hyperlipidemia not adjusted in the models because they are intermediate factors in the causal pathway as suggested by the conceptual model for the thesis.

4.2.6.4.4 Effect modification: applying subgroup analysis

Effect modification tends to overlap with explanations of interaction (Kamangar, 2012; Szklo and Nieto, 2014, Pg. 186) even though some argued that they are different and independent of each other (VanderWeele, 2009; Knol and VanderWeele, 2012). Without dragging into debates about effect modifications and interactions, the thesis tried to examine whether the magnitude of the impacts of overweight and obesity on incident dementia or all-cause mortality remained or change in subgroups of the population under study. To achieve this, subgroup or stratification of analysis by sex and smoking status were done. It was argued that the approach not only helps to detect effect modification but also disentangle the effects of confounding in the association of a predictor and health outcome (Szklo and Nieto, 2014, P. 229-296). Therefore, it was believed that employing sub-group analysis in the research work could enhance the statistical validity of the associations established from this thesis.

4.2.6.4.5 Reverse causation: applying sensitivity analysis

Another challenge in the study of adiposity and health outcome is the temporal bias of reverse causality. The literature suggests that sensitivity analysis may allow certain checks on findings to determine if they differ under different model or assumptions used in the analysis (Szklo and Nieto, 2014, p. 296). One of such approach is excluding data of first few years (s) in the follow up under the assumption that reverse causality must have resulted from outcome impacting on the exposure instead of the other way around (Di Angelantonio *et al.,* 2016). In this thesis, the statistical analysis for the impacts of overweight and obesity on incident dementia (chapter 6) and all-cause mortality (chapter 8) involved exclusion of the first year and first three years data respectively to limit the effect of reverse causality. The extent to which exclusion of a few years of data improves validity was debated in studies of all-cause mortality (Flegal *et al.,* 2010). However recent evidence from large studies (Di Angelantonio *et al.,* 2016; Aunne *et al.,* 2016) showed that the method enhances the validity of findings. Though in this thesis a more conservative approach to avoid over-exclusion was applied since not more than three years data was considered adequate unlike in several studies excluding up to 5 years data to limit reverse causality.

4.3 Systematic literature review and meta-analysis

The thesis method also included a systematic literature review and meta-analyses, which helped to assess the current state of knowledge and evidence on the impacts of overweight and obesity on health come. The details of the study is presented in chapter three, and a summary of the approach used in the systematic literature review and meta-analyses is below.

4.3.1 Systematic literature review

According to Liberati et al (2009) "a systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria to answer a specific research question. It uses explicit, systematic methods that are selected with a view to minimizing bias, thus providing reliable findings from which conclusions can be drawn and decisions made". The thesis research followed the recommended PRIMA Guidelines for systematic reviews (and meta-analysis) by Liberati et al (2009) as outlined in the entire process presented in chapter three. This process ensured the conduct of a comprehensive and high-quality systematic literature review (and meta-analyses) for the thesis. Briefly, this included a clear objective and rationale for the study, and the methods which involve a systematic search of the literature as outlined in the PRIMA flow chart (figure 3, chapter three) using a search strategy developed according to the Population, Exposure and Outcome framework (PEO) (Khan et al., 2003; Bettany-Saltikov et al., 2012). The standard protocol followed involved the use of three independent reviewers, and an assessment of the quality of included studies (Table 1) using the modified version of the Newcastle Ottawa scale (Wells et al., 2018). The data from included studies were extracted and presented (Table 1a and appendix 11, chapter three) while Egger test and the funnel plot (figure 4) were carried out in Stata statistical software on a computer to assess the risk of publication bias.

4.3.2 Meta-analyses

Meta-analyses provide a statistical combination of the results from included studies in a systematic literature review (Liberati et al., 2009). Before the meta-analyses, a database of included studies with extracted data was exported into SPSS, prepared, and saved as Stata file for analysis using Stata IC version 14.0 (Stata Corp, College Station, Texas, USA) on a computer. The detail of the various meta-analysis is in chapter three. The meta-analyses involved the random effect model, which considers both within-and between-study variability, and the fixed effect model that yields within-study variability. The choice of the statistical model depended on the outcome of the heterogeneity test performed in the analysis. The meta-analyses also included various subgroup analyses according to the duration of follow-up of cohort studies, continuous and categorical BM, studies with measured BMI, dementia subtypes. The report of the pooled effect estimates from the meta-analysis included their 95% confidence intervals.

4.4 Qualitative research: Focus group study

Focus group research, as a method of qualitative data collection, is popular in social research (Onwuegbuzie *et al.,* 2009) and is increasingly recognized and used in the field of health and medical research for studying health problems (Schulze and Angermeyer, 2003; Friedman and Shepheard, 2007; Wong, 2008; Krueger and Casey, 2014). A focus group research allows for information gathering from the dynamics of a group discussion through a non-directive interviewing with only a minimal role played by the interviewer or researcher (Hennink (2007). The typical focus group should be conducted with 5 to 10 participants and moderated by skilled interview (Krueger and Casey (2014, p.2). Focus group research is suitable for identifying and exploring community-level views or experiences on a given topic from a selected group of participants drawn from a target population.

4.4.1 Justification for the focus group study

The decision to use qualitative study by focus group research method for the doctoral research project was informed by the need to increase understanding of the risk and health effects of overweight and obesity. Recent literature of epidemiologic research methods considered focus groups as useful epidemiologic study designs (Merrill, 2016 p. 233). Therefore, incorporating focus group study in this PhD study provides a useful and recommended approach to help address the research aims of the thesis. The typical Focus group research provides an alternative qualitative study method which is different from the traditional one-on-one in-depth interview or observation. Unlike the traditional in-depth interview which relies solely on data from individuals, focus groups generate quality data from the power of group interactions (Hennink, 2007). It is also capable of deepening understanding and providing explanations for statistical data using the detailed and broader range of information gathered from personal and group experience, beliefs, feelings, perceptions and opinions about a subject or topic (Hennink, 2007; Onwuegbuzie *et al.,* 2009). Recent literature put together on the advance in mixed method research (Creswell and Clark, 2017) suggests that combing two different approaches could help strengthen study outcome which would not have been possible through either method. It was considered that by using this qualitative study focus group method it will help complement the quantitative research which was considered by the researcher as inadequate or lacked the view of older adults on health risk associated with overweight and obesity in older age. In addition, one of the aims of the doctoral research, apart from contributing to knowledge and understanding of the risk factors and health effects of overweight and obesity, is to also inform policy and practice on weight management in older adults. To support recommendations, focus group study is considered one of the preferred options since it can generate group-level data on decisions reached from interactions on a subject (Onwuegbuzie *et al.,* 2009). Therefore, focus group research will be conducted to support the overall research goal of the doctoral project.

4.4.2.1 Rationale for the focus group study in the UK population

The focus group research will be in the UK. The decision to conduct the focus group study in the UK, as part of the larger doctoral research project, is to generate new data and evidence from a different population that will support recommendations for policy and practice on the risk factors and health effects of overweight and obesity in older adults. Indeed, the research work in this thesis adopts a mixed-method design by the convergent parallel database (which uses different data sets). However, the research for the thesis is predominantly quantitative based on a large prospective cohort study conducted in China. Besides, it included a systematic review and meta-analysis that shed light on the knowledge gaps to be addressed by the findings from the Anhui cohort study. The Anhui cohort study could address all the research questions, but the findings may not be generalisable outside China to a place like the UK, where the evidence is also conflicting. Though qualitative studies are much more limited in generalisability of findings, it is unclear what the views of UK older adults would be, for instance, considering that the recent evidence from a study of two million UK adults which showed that overweight/obesity was beneficial to health by protecting people from developing dementia and reducing early mortality (Qizilbash *et al.,* 2016).

Furthermore, the research student resides in the UK for doctoral research and have considered using different population data apart from China for the research project. A key consideration is that, to the best of knowledge, no qualitative research is available on the subject in the UK, and the findings could contribute to new knowledge and understanding. It was documented by Krueger and Casey (2014 p.14) that "focus groups have been used after other research methods to help interpret or to develop recommendations for later action or study". Therefore, conducting a focus group study in the UK will explore the health effects of overweight/obesity and support recommendations. Besides, it will also highlight the need for a similar study in other settings to guide policymakers and researchers.

4.4.2 The Focus group design

The focus group research in the project is similar to the single-category design described by Krueger and Casey (2014 p.27-31) which casts its study lens on particular sub-population or population group of interests in line with the main objective of the research. The qualitative research for the project focused on a group of older adults from the community which represent the population segment of interest to the researcher. In line with recommendations for conducting focus group study (Bender and Ewbank, 1994; Onwuegbuzie *et al.,* 2009) the research project used two different focus groups (different participants) to explore the same topic with emphasis on the group interactions and bearing in mind the earlier chosen analysis plan (Braun and Clarke, 2006) which permits combining of data generated from the different focus groups into one large data set for thematic analysis. The issue of costs and time available for the research project were also considered by carefully planning and executing the two focus group studies in the best possible way to optimize the generation of quality data that could help address the research aims for the project. The steps taken in the conduct of the focus group study including data analysis and the proposed approach to interpretation and presentation of findings is briefly explained below.

4.4.2.1 Study Population and sampling

The target population for the study was older adults of the age 60 years and above residing within the community in Wolverhampton, UK. Wolverhampton is the most diverse city in the West Midlands and is marked by a heterogeneous mix of nationalities, religions and ethnic groups above the average for England. It also has an ageing population with 50,065 older adults (age ≥60 years) representing 21.7% of the general population (WPIS, 2014). A non-probability sample of 5 to 8 older adults (age≥60 years) was targeted and considered adequate for the research. This is because it was proposed that focus groups should have enough participants to help generate diverse information. However, it must not be too large or else it may create an uncomfortable environment with some participants unable to freely express their views, thoughts or experiences (Onwuegbuzie et al., 2009).

4.4.2.2 Recruitment and participants for the study

The participants for the study were recruited from older adults residing within the communities through their usual place of worship in Wolverhampton UK. Notification of the focus group research and request for interests from willing older adults was sent to the congregation at a selected place of worship (Appendix 3 and 4). Potential participants were also approached through face-to-face and provided a detailed explanation of the proposed research and requirements for recruitment into the study (Appendix 5). For inclusion into the focus group, study participants were required to be of the age of 60 years and above, not known to have any history or diagnosis of dementia and must have the capacity to provide consent by themselves to partake in the research. Those considered as unable to provide consent were neither approached nor included. The details of the recruitment are presented in chapter 8.

4.4.2.3 Setting

The focus group discussion was conducted within the Millennium City (MC) Building of the University of Wolverhampton, UK. This venue and location were selected because it was quite convenient and safe. It was close to participants' usual place of worship and easily accessible by walking or transport services and for those driving, car parking spaces were available.

4.4.2.4 Data collection procedure and tools

Prior to the focus group study, a very brief questionnaire was used to collect basic socio-demographic background information on the participants (Appendix 7). The two focus group discussion sessions were held three weeks apart and each lasted for approximately 1 hour. The focus group session involved a moderator and a note-taker. The data collection involved a digital audio recording device by Olympus Corporation (Tokyo, Japan). To facilitate the Focus group session a discussion guide that included semi-structured open-ended questions with a focus on the research questions were used to prompt participants to talk or discuss the topic (Appendix 8).

4.4.2.4 Data transcribing and data management

The data on the background information of participants were analysed using SPSS version 24.0 (SPSS Inc., Chicago, USA). The audio recorded data from focus group discussion sessions were transferred using the USB stick from the recorder to a personal laptop computer (that is pass-worded and had antivirus installed) and was uploaded unto an NVIVO software version 11.0. A verbatim transcribing of the data from each of the focus group discussion was done with the aid of the NVIVO software.

4.4.3 Focus group data analysis

There is no consensus on what may be regarded as a generally endorsed method of focus group data analysis (Plummer-D'Amato, 2008; Onwuegbuzie *et al.,* 2009). However, some methods of analysis have been documented in the literature and this includes thematic analysis (Boyatzis, 1998; Braun and Clarke (2006), classical content, constant comparison, key-words-in-context, discourse analysis (Leech and Onwuegbuzie, 2007) and micro-interlocutor analysis (Onwuegbuzie *et al.,* 2009). The focus group data in this thesis was analysed using thematic analysis method proposed by Braun and Clarke (2006) and this is described and applied in chapter eight. The units of analysis associated with focus groups generally are briefly discussed with a focus on the thematic analysis used for the research work in the thesis and its implications.

4.4.3.1 Units of focus group data analysis

Focus group study generates different types of data which include individual, group and group interaction data with implications for data analysis and interpretation (Duggleby, 2005; Onwuegbuzie *et al.,* 2009). Duggleby (2005) argued for analysis of the predominant interactions among the focus group members besides the individual or group data and integrating the findings when presenting the reports. Though there is no agreement on the preferred unit of analysis, it was reported that employing the group unit analysis is more common in the literature (Onwuegbuzie *et al.,* 2009). The group as the unit of analysis is often characterized by the reliance on emerging themes as evident from studies using thematic analysis (Cederval and Aberg, 2010; Choi et al., 2012). This also represents the focus group data analysis approach adopted for this thesis. It was argued that thematic analysis produces important and useful information and findings based on emergent themes (Braun and Clarke, 2006); however, there is the challenge of possibly missing out on information pertaining consensus reached during focus group discussion and the negative cases or dissenters. To enhance the validity of the focus group study as recommended by Maxwell (1992; 2005), the findings relating to the themes that emerged were carefully analysed, interpreted and information on negative or contrary views reported to help better understanding.

4.4.4 Rigor and trustworthiness of the focus group study

Qualitative studies are required to generate results that are both useful and meaningful and this can be achieved through rigour and trustworthiness of the research process (Braun and Clarke, 2006; Nowell *et al.,* 2017). The concepts of rigour and trustworthiness in qualitative research is akin to reliability and validity of the positivism driven quantitative research (Schwandt, Lincoln and Guba, 2007) and it helps to determine the extent to which confidence may be gained on the data, the interpretation and methods deployed for quality (Connelly, 2016). Trustworthiness is characterized by certain criteria as previously outlined by Lincoln and Guba (1985; 1994) for qualitative study which includes credibility, transferability, dependability, and confirmability. These criteria which also include audit trail and reflexivity were recommended for focus group study by Plummer-D'Amato (2008). They were also recently reflected in the work put together by Nowell *et al* (2017) on ensuring trustworthiness in qualitative research using thematic analysis. To help achieve this goal, the focus group study followed strictly the popular thematic analysis method by Braun and Clark (2006). This was also recommended by Nowell *et al* (2017) for meeting trustworthiness criteria in thematic analysis. The key aspects considered in the entire focus group study to enhance trustworthiness are summarized below.

4.4.4.1 Credibility

This criterion is met if the views of respondents or participants are accurately represented by the researcher such that it is recognizable by a reader or fellow researchers (Nowell *et al.,* 2017). This is akin to internal validity in quantitative research (Connelly, 2016). It implies confidence in the truth and findings of the qualitative study and is one of the most important criteria (Guba and Lincoln, 1985; Shenton, 2004).

To achieve credibility in the focus group study, there was constant engagement with participants during the recruitment process at their place of worship. I attended their Sunday service every week for a month and I had the opportunity of clarifying the purpose and nature of the study. This helped to build rapport with participants and assist them to freely express their views and experience during the study. There was also triangulation of the different data collection modes which included digital recording device and note-taking. There was also persistent observation including views of dissenters which were captured in the data analysis and reflected in the findings. There was also debriefing of the research process and findings to colleagues, and to supervisors who provided external verification of the data, the analysis and the results.

4.4.4.2 Transferability

Transferability is a criterion which is similar to external validity or generalizability in quantitative research and it reflects the degree to which findings may apply to closely related setting, group or context (Schwandt, Lincoln and Guba, 2007; Plummer-D'Amato, 2008). It was proposed that providing a rich description of data in terms of explanation of the context may guide decisions as to where such findings could be applied (Schwandt, Lincoln and Guba, 2007).

In the focus group study, the data produced was described in detail. The presentation of data involved the exact words they were used and interpretation 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 ensure clarity and understanding of the context. This approach allows judgement of the transferability to similar setting, group and context.

4.4.4.3 Dependability

This is akin to reliability in quantitative research and it emphasizes consistency in the interpretation of data from a qualitative study (Plummer-D'Amato, 2008) or the extent to which within the same conditions of the study, the data remains stable (Connelly, 2016). Nowell *et al* (2017) emphasized logicality and traceability in accordance with suggestions by Tobin and Begley (2004) for a well-documented research process. It was suggested that the dependability in a focus group study could be achieved when different researcher arrives at similar findings using the audit trail kept for the research process (Plummer-D'Amato, 2008). Audit trails entail keeping detailed, accurate and critical account of the researcher's decisions and selections relating to methodological and theoretical challenges faced in the course of the entire study (Nowell *et al.,* 2017).

The focus group study was carried out in detail and an audit trail of the entire process including challenges were kept. This also included note-taking during the study, raw data, transcripts and records of the thematic analysis steps executed. There was also external auditing of the research process including transcripts, data analysis and reporting through close and constant supervision from the supervisory team. These ensured there was consistency in the interpretation and presentation of the findings.

4.4.4.4 Confirmability

In qualitative research, the term confirmability is likened to objectivity or neutrality concept that typifies quantitative approach (Tobin and Begley, 2004; Polit and Beck, 2014). It implies that the findings that emerged from focus group study are based on the actual data captured or the context of discussions that occurred among group members and not due to biases from the researcher (Plummer-D'Amato, 2008). Confirmability may be enhanced via member checks depending on the study or through detailed and accurate records of the research process including data analysis for audits by other researchers (Plummer-D'Amato, 2008) or for review during debriefing to research colleagues (Connelly, 2016). Guba and Lincoln (1989) put it clearly that achieving confirmability entails meeting the three criteria of credibility, transferability and dependability as described above

4.4.4.5 Reflexivity

Reflexivity entails reflections by the researcher about personal values, interests and other relevant information about oneself that should be taken into consideration in the interpretation or viewing the findings by others (Creswell, 2014, p.186; Nowell *et al.,* 2017). This aspect of my values, interests, and key information was acknowledged in the thesis.

As a whole, the findings generated from thematic analysis of the qualitative focus group data using Braun and Clark (2006) approach were presented and discussed in Chapter eight of the thesis. The evidence from the qualitative focus group study was merged with those from the quantitative study in the discussion (chapter 9) to address the overall research aim and the objectives of the thesis.

4.5 Ethical considerations

The entire study was carried out in accordance with the approved research protocol. Ethical approval was granted by the Research Ethics Committee of Anhui Medical University in China, the Research Ethics Committee of the University College London, UK, and the Research Ethics Committee of the School of Health, UoW (Appendix 1). The access and permission to use the cohort study data were granted for the doctoral study after submitting an official request through the principal investigator in the Chinese cohort study. The place of worship in Wolverhampton granted permission for the recruitment of their members for the focus group study

(Appendix 2). The Research Ethics Committee of the Faculty of Education, Health and Wellbeing, University of Wolverhampton UK granted approvals for the study (Appendix 1)

The informed consent of participants was required for the focus group study. Therefore, a general consent and right to withdraw forms (Appendix 6) were signed and returned by participants. This was after reading the research information sheets sent to them which explained the nature of the study including the risks and benefits. Codes were used (not participant names) in all associated documents including questionnaires, transcripts and quotes from the research. Other recognizable information was changed to ensure anonymity. All the information collected from the study was kept confidential. The transcription of the discussion data was done and stored in a password-protected computer in a locked cupboard in a locked office. Only the researcher working on the project, supervisors or examiners had access to the information. The data is stored in a password-protected computer in the office and it will be kept for a maximum of 2 years after which it will be destroyed confidentially.

4.6 Conclusion

The chapter described the mixed methodology used in the thesis. One crucial aspect is the integration of the findings. As it was illustrated in figure 2 research design, the data from the quantitative and qualitative research would be analysed separately and the findings merged in the discussion (chapter 9) of the thesis. In interpreting and discussing these findings, the focus would be on comparing the findings and pointing out ways they converge, diverge or relate thereby leading to better or more complete understanding of risk factors and health effects of overweight and obesity in older adults. The subsequent chapters after this provide a detailed account of the studies conducted in the thesis including discussions of findings and implications.

CHAPTER FIVE: THE RISK FACTORS FOR OVERWEIGHT AND OBESITY IN OLDER ADULTS: A COHORT STUDY

5.1 Introduction

Globally, nearly 1.9 billion adults are either overweight or obese (WHO, 2018). Older adults contribute significantly to this figure, and with an ageing world population, there would be an increased prevalence of overweight, and obesity in the future. Evidence from recent research based on the Global burden of disease study data (Chooi, Ding and Magkos, 2019) showed that the age-adjusted prevalence of overweight in China has tripled between 1980 and 2015 (7.8% to 29.9%). Thus, overweight and obesity are problems of enormous concern not only in developed countries but also in LMICs like China.

The literature suggests that despite the population differences in adiposity by ethnicity and race, overweight and obesity may be related to the combination of multiple factors operating at different levels as upstream and downstream social determinants (WHO, 2008; Hu, 2008; Hruby and Hu, 2014). The is crucial considering the contributions of economic globalisation to the obesity epidemic (Fox, Fen and Asal, 2019) and how local environments may modify the risk factors (Swinburne et al., 2011). Besides, China is experiencing an epidemiological transition in nutrition and disease risk factors due to rapid economic developments and urbanisation in the past three decades (Yang et al., 2008; Popkin, 2010). Therefore, the risk factors for overweight/obesity may be different from developed countries. Also, there is little research on the impacts of the social determinants of health on overweight and obesity in older adults. Therefore, to increased knowledge and understanding of the risk factors for the prevention of excess body weight, this Chapter study investigates the risk factors for overweight and obesity in older adults using prospective cohort data from China with seven years follow-up.

5.2 Methods

5.2.1 The participants in the Anhui Cohort study

The studied population is from the Anhui cohort in China as described in the methodology (chapter three). Briefly, from those who had lived for a minimum of 5 years as at 2001 in Yiming sub-district of Hefei City, 1736 people aged ≥65 years were selected (urban sample) using stratified random technique, and other 1600 aged ≥60 years selected from all the 16 villages in Tangdian District of Yingshang County in 2003 (rural sample). The study participants totalled 3,336, giving an overall 94.8% response rate. Before each participant interview, permission and consent were first obtained. The consent to participate were sought and obtained from them or if they had difficulties in answering the question their closest relatives or carers were used; and refusals, when met, were respected.

5.2.2 Baseline assessment

Participants in the urban areas of the Anhui cohort study were interviewed and assessed for baseline information in 2001, and in the rural areas in 2003. A trained survey team, from the School of Health Administration at Anhui Medical University, interviewed the participants at their residence. The materials for the interview were mainly the general health and risk factors questionnaires, which were partly obtained from the MRC-ALPHA study and Scottish MONICA surveys, and the

Geriatric Mental Status (GMS) questionnaires. The GMS questionnaire is a comprehensive semi-structured mental state interview and widely used globally in the elderly population. The general health and risk factors questionnaire were used to captures the followings; (a) sociodemographic details and this included age, sex, smoking, alcohol drinking, Rural/urban location, educational level, main occupation, income satisfactory, financial difficulties, satisfy with life/current living, marriage, frequency of visiting children/relatives, contacting friends/relatives, contacting neighbours, help when needed. (b) Weight, height and waist circumferences were measured using standard measures (c) doctor-diagnosed cardiovascular diseases and self-assessed health included hypocholesteraemia, diabetes, heart diseases and stroke, while systolic and diastolic blood pressures were measured based on standard protocol (d) hobbies and activities of daily living (ADL) were documented (e). The GMS questionnaire data was read and analysed by the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT) every participant. Dementia/depression was diagnosed using the GMS-AGECAT.

Height was measured without shoes to the nearest 0.5 cm by portable stadiometer, while weight was recorded to the nearest 0·1kg by digital scales with participants putting on light clothing.

5.2.2.1 Measure of overweight and obesity

The overweight and obesity were assessed using Body Mass Index (BMI) in Kg/m^2 according to the Asian Chinese population cut offs as recommended by the Chinese government (Chen *et al.,* 2008). BMI of ≥28 Kg/m2 were classified as obesity, 24-

27·9 Kg/m2 as overweight, 18·5-<24 Kg/m2 as normal and <18·5Kg/m2 considered as underweight.

5.2.3 Follow-up of the cohort

Participants were followed up from baseline in 2001-2003 until 2007-2009 when 1462 surviving cohort members were re-interviewed with their body weight and height measured to calculate Body Mass Index (BMI). The average year of the cohort follow-up was 7.

5.2.4 Statistical analysis

In this study, participants of aged ≥65 years were included for analysis to examine the risk factors for overweight and obesity. Out of the 3,336 participants, those of age<65 years (419) at baseline were excluded leaving 2,917 of aged≥65 years in the cohort study. Out of this, 1462 cohort members were interviewed at wave 3 for the risk factors for overweight and obesity. The participants with complete data for both weight and height at the end of the 7 years follow-up in 2007-2009 were 1,313. This final number was used as the analytical sample for the study. The Chi-square test was used to investigate differences in baseline characteristics among the four groups of underweight (BMI <18.5), normal weight (18.5-<24) overweight (24-<28) and obesity (≥28) outcome in older people.

Binary logistic regression models were used to compute age-sex adjusted odds ratios (OR) and 95% confidence intervals for the risk factors for obesity, overweight and underweight versus normal weight respectively. The age-sex adjusted ORs of risk factors for overweight/obesity were also computed with entry criteria for the co-variables set at $p<0.1$. Then the multivariate logistic model was used to examine risk factors for overweight/obesity (BMI≥24) versus normal weight with adjustment for age, sex, smoking, urban/rural areas, and educational level. In all analysis for obesity, those who were overweight or underweight at baseline were excluded. Similarly, in the analysis for overweight, the obese or underweight were not included, while in the analysis for the underweight the obese or overweight were excluded. This approach was to reduce any bias from the analysis by focusing on the main outcome variable of interest in relation to the key exposures.

`5.3 Results

The findings are presented in three parts, the descriptive statistics, the age-sex adjusted and multivariate logistic regression results.

5.3.1 Descriptive statistics

The analysis of 1313 participants in the study showed 13.3% were underweight, 55.9% normal body weight, 24.4% overweight and 6.5% obese in the follow-up. The prevalence of overweight/obesity was 30.8% in the whole cohort; 34.5% in women and 26.7% in men ($p=0.005$). Most participants were females (53.4%) and only few (12.5%) were ≥80 years. The females were more underweight (54.6%), overweight (57.6%) and obese (67.1%) compared to males. Most participants were uneducated (56.6%), likely to come from the rural (58%) and underweight (71.3%) while the urban dwellers were more overweight (55.4%) and obese (52.9%). The details of participants' characteristics are provided in table two.

5.3.2 Findings from Age-sex adjusted logistic regression analysis for underweight, overweight and obesity (abnormal weight)

Table 3 shows the results of the adjusted odds ratios (OR) for abnormal weight. Findings regarding lifestyle factors showed that watch TV/read book or newspaper was associated with increased risk of overweight (OR: 1.84, 95%CI: 1.33-2.54) and marginally significantly related to obesity (1.71, 0.99-2.96). There was no significant association of watch TV/read book or newspaper with Underweight (1.22, 0.86-1.74). The data also showed an inverse association of smoking and underweight (0.59, 0.39-0.90) but no significant association with obesity and overweight. The drinking of alcohol was inversely related to obesity (0.35, 0.15-0.85) but not to overweight and underweight. There was a significant association of high socioeconomic status (SES) with obesity; the adjusted OR in urban versus rural living was 1.75 (1.10-2.79), highest educational level (≥higher 2nd School) compared with no education (illiterate) was 1.81 (1.01-3.24), and higher occupation (official/teacher) compared with the lowest occupation (peasant) was 1.96 (1.15-3.34). However, the results for income were not non-significant. The findings in the overweight showed similar pattern; the adjusted OR for Urban versus rural living was 1.92 (1.46-2.52), highest education (higher 2nd School/greater) vs no education (illiterate) was 1.66 (1.18-2.35), and higher occupation (Business/other) compared to the least occupation (peasant) was 1.79 (1.31-2.45). Surprisingly, underweight was also related to high SES. For instance, the adjusted OR was 1.49 (1.03-2.15) in the Urban, 1.73 (1.04-2.87) in the highest educational level (higher 2nd School/greater) and 1.46 (0.96-2.23) in the higher occupation (official/teacher). But it was not related to income satisfactory. The analysis also showed that Cardiovascular disease Risk Factors (CVDRFs) were associated with an increased risk of obesity. The adjusted ORs for uncontrolled hypertension and stroke were

2.55 (1.30-5.01) and 3.46 (1.20-10.00) respectively. Similarly, uncontrolled hypertension was associated with overweight (1.54, 1.05-2.27) but not related to stroke (OR: 0.84, 0.30-2.35). The findings in the underweight showed no significant relationship with uncontrolled hypertension (3.46, 0.80-14.91), and stroke (0.69, 0.25-1.93). However, underweight was inversely associated with baseline depression (0.57, 0.33-0.97) but it was non-significant for overweight and obesity.

5.3.2.2 Findings of Age-sex adjusted analysis for overweight/obesity

Table 4 shows the age-sex adjusted logistic regression results in older adults with excess body weight defined as those with either overweight or obesity (BMI≥24). The findings showed that watch TV/read book or newspaper was significantly associated with increased overweight/obesity (1.80, 1.34-2.43). While no significant association was found in those who smoke and drank alcohol in the past 2 years before baseline investigation. Findings of SES variables showed reduced odds of overweight/obesity in rural dwellers (0.53, 0.41-0.68) compared to their urban counterparts, in the illiterate (0.59, 0.41-0.68) compared to ≥high 2nd school (highest education), in the peasant (lowest) occupation (0.46, 0.28-0.75) compared to the Business/other (highest) occupation, in the poor (0.55, 0.30-0.999) and average income satisfactory (0.45, 0.29-0.72) compared to those of very satisfactory income. Also, those with financial difficulties in the past two years exhibited a reduced risk of overweight/obesity (0.62, 0.48-0.80) compared to those without such a challenge. All the social and community network factors showed no significant association with overweight/obesity except being unmarried/divorced which significantly reduced the risk of excess body weight (0.11, 0.03-0.46). The findings showed increased odds of overweight/obesity in those with baseline hypercholesterolemia (1.62, 1.01-2.58) and hypertension including controlled (2.26, 1.25-4.08), uncontrolled (1.70, 1.19-2.44) or untreated hypertension (1.96, 1.15-3.34) in comparison to no hypertension. The results also showed no association of frequency of contacting children or relatives, feeling lonely, and depression with overweight/obesity but there were reduced odds in those with dementia (0.56, 0.36-0.89) when compared to those without it.

5.3.3 Findings from multivariate logistic regression analysis for overweight/obesity

Table 5 shows the odds ratio, 95%CI and p-value for each of the co-variables associated with overweight/obesity. Men had significantly reduced risk of overweight/obesity (0.70, 0.52-0.94) when compared to women, while watching TV/listen to the radio, read book/newspaper significantly increased overweight/obesity (1.46, 1.05-2.02). The data also showed overweight/obesity was reduced (0.61, 0.41-0.92) in rural compared to urban living, while those with primary school (low education) had increased risk (1.66, 1.02-2.71) when compared to ≥high 2nd school (highest education). The risk of overweight/obesity was reduced in those of average income satisfactory (0.60, 0.36-0.99) when compared to very satisfactory income (highest). In addition, being never married/divorced was associated with reduced risk (0.14, 0.03-0.62) of overweight/obesity. The findings revealed a significantly elevated risk of overweight/obesity in those with hypertension (untreated 2.00, 1.16-3.43, uncontrolled 1.49, 1.03-2.16 and controlled 1.86, 1.02-3.40 hypertension). The results of all other remaining variables

(Table 5) in the multivariate-adjusted model were not significant. The remaining variables that did not contribute to the variance include age, smoking, drinking alcohol, occupation, financial difficulties, hypercholesteremia, stroke, depression, and dementia.

Table 2 Characteristics of participants in the study of risk factors for overweight and obesity

Characteristic	Total participants		Underweight (<18.5)		Normal BMI (18.5-<24)		Overweight (24-<27.9)		Obese (>=28)		p-value
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	
Age (years)											
65-69	463	35.3	53	30.5	248	33.8	128	40.0	34	40.0	0.054
70-74	418	31.8	52	29.9	228	31.1	112	35.0	26	30.6	
75-79	270	20.6	40	23.0	161	21.9	52	16.3	17	20.0	
>=80	162	12.3	29	16.7	97	13.2	28	8.8	8	9.4	
Sex											
Female	702	53.5	95	54.6	365	49.7	185	57.8	57	67.1	0.005
Male	611	46.5	79	45.4	369	50.3	135	42.2	28	32.9	
Smoking over the last 2 years											
No	924	70.4	109	62.6	502	68.4	244	76.3	69	81.2	0.001
Yes	389	29.6	65	37.4	232	31.6	76	23.8	16	18.8	
Drinking alcohol over the 2 years											
No	1053	80.2	143	82.2	579	78.9	252	78.8	79	92.9	0.016
Yes	260	19.8	31	17.8	155	21.1	68	21.3	6	7.1	
Watch TV, Listen to the radio, read book/newspaper											
No	375	28.6	64	36.8	228	31.1	64	20.0	19	22.4	0.000
Yes	938	71.4	110	63.2	506	68.9	256	80.0	66	77.6	
Combination of hobies											
None	95	7.2	17	9.8	57	7.8	16	5.0	5	5.9	0.053

Any 1	252	19.2	43	24.7	146	19.9	48	15.0	15	17.6	
Any 2	389	29.6	52	29.9	218	29.7	94	29.4	25	29.4	
≥3	577	43.9	62	35.6	313	42.6	162	50.6	40	47.1	
Activity of daily living(score)											
0	1247	95	165	94.8	702	95.6	301	94.1	79	92.9	0.576
≥1	66	5	9	5.2	32	4.4	19	5.9	6	7.1	
Urban/rurality											
Urban	552	42	50	28.7	280	38.1	177	55.3	45	52.9	0.000
Rural	761	58	124	71.3	454	61.9	143	44.7	40	47.1	
Educational level											
Illiterate	743	56.6	117	67.1	441	60.1	145	45.3	40	47.1	0.000
Primary Sch.	132	10.1	20	11.5	59	8.0	44	13.8	9	10.6	
Secondary Sch.	161	12.3	15	8.6	82	11.2	50	15.6	14	16.5	
>=High 2nd Scho	277	21.1	22	12.6	152	20.7	81	25.3	22	25.9	
Main occupation											
Peasant	736	56.1	121	69.5	439	59.8	139	43.3	37	43.3	0.000
Manual labourer	121	9.2	11	6.3	58	7.9	40	12.5	12	14.1	
Official/teacher	372	28.3	35	20.1	197	26.8	110	34.4	30	35.3	
Business/other	84	6.4	7	4.0	40	5.4	31	9.7	6	7.1	
Income satisfactory											
Very satisfactory	107	8.1	8	4.6	54	7.4	35	10.9	10	11.8	0.001
Satisfactory	628	47.8	77	44.3	329	44.8	174	54.4	48	56.5	
Average	469	35.7	73	42	287	39.1	88	27.5	21	24.7	
Poor	109	8.3	16	9.2	64	8.7	23	7.2	6	7.1	

Financial difficulties over the last years											
no	596	45.4	59	33.9	312	42.5	180	56.3	45	52.9	0.000
yes	717	54.6	115	66.1	422	57.5	140	43.8	40	47.1	
Satisfied with life/ current living											
Very satisfactory	483	36.8	62	35.6	281	38.3	111	34.7	29	34.1	0.630
Satisfactory	700	53.3	91	52.3	384	52.3	179	55.9	46	54.1	
Average	121	9.2	21	12.1	65	8.9	26	8.1	9	10.6	
Poor	9	0.7	0	0.0	4	0.5	4	1.3	1	1.2	
Marriage											
Married	984	74.9	125	71.8	544	74.1	249	77.8	66	77.6	0.007
Never married/divorced	43	3.3	5	2.9	36	4.9	2	0.6	0	0.0	
Widow	286	21.8	44	25.3	154	21	69	21.6	19	22.4	
Frequency of visiting children or other relatives											
<Yearly or Never	36	2.7	2	1.1	26	3.5	3	0.9	5	5.9	0.074
At least Monthly or less often	147	11.2	16	9.2	76	10.4	47	14.7	8	9.4	
At least weekly	332	25.3	48	27.6	182	24.8	80	25.0	22	25.9	
Everyday	798	60.8	108	62.1	450	61.3	190	59.4	50	58.8	
Contacting friends in the community											
<Yearly or Never	63	4.8	11	6.3	39	5.3	9	2.8	4	4.7	0.608
At least Monthly or less often	312	23.8	41	23.4	181	24.7	76	23.8	14	16.5	
At least weekly	523	39.8	66	37.9	288	39.2	132	41.3	37	43.5	
Everyday	415	31.6	56	32.2	226	30.8	103	32.2	30	35.3	
Contacting neighbours											

<Yearly or Never	26	2	4	2.3	15	2	5	1.6	2	2.4	0.583
At least Monthly or less often	361	27.5	47	27.0	209	28.5	89	27.8	16	18.8	
At least weekly	482	36.7	58	33.3	271	36.9	123	38.4	30	35.3	
Everyday	444	33.8	65	37.4	239	32.6	103	32.2	37	43.3	
Help available when needed											
No	95	7.2	14	8.0	59	8.0	20	6.3	2	2.4	0.225
Yes	1218	92.8	160	92	675	92.0	300	93.8	83	97.6	
Feeling lonely											
No	1228	93.5	152	87.4	694	94.6	301	94.1	81	95.3	0.005
Yes	85	6.5	22	12.6	40	5.4	19	5.9	4	4.7	
Hypertension status											
No hypertension (<140*90)	539	41.1	89	51.1	307	41.8	122	38.1	21	24.7	0.000
Undetected	457	34.8	60	34.5	271	36.9	96	30.0	30	35.3	
Untreated	70	5.3	6	3.4	33	4.5	22	6.9	9	10.6	
Uncontrolled	194	14.8	17	9.8	98	13.4	61	19.1	18	21.2	
Controlled	53	4.0	2	1.1	25	3.4	19	5.9	7	8.2	
Hypercholesterolemia											
No	1222	93.6	169	97.7	688	94.1	285	90.2	80	94.1	0.010
Yes	83	6.4	4	2.3	43	5.9	31	9.8	5	5.9	
Angina											
No	1278	97.5	167	96.0	718	97.8	310	97.6	83	97.6	0.581
Yes	33	2.5	7	4.0	16	2.2	2	2.4	2	2.4	
Diabetes											
No	1255	95.8	169	97.1	702	95.8	303	95.3	81	95.3	0.794
Yes	55	4.2	5	2.9	31	4.2	15	4.7	4	4.7	

Heart diseases (ischaemic, valve disease/ others)											
No	1143	87.3	150	86.2	648	88.4	268	84.5	77	90.6	0.261
Yes	166	12.7	24	13.8	85	11.6	49	15.5	8	9.4	
Stroke											
No	1281	97.7	169	97.1	719	98.0	313	98.4	80	94.1	0.107
Yes	30	2.3	5	2.9	15	2.0	5	1.6	5	5.9	
Depression GMS_level											
Non-depression	1215	92.5	153	87.9	682	92.9	300	93.8	80	94.1	0.091
depress 1 or 2 (subcase)	44	3.4	7	4.0	24	3.3	12	3.8	1	1.2	
depress>=3 (cases)	54	4.1	14	8.0	28	3.8	8	2.5	4	4.7	
Dementia											
No dementia	1230	93.7	162	93.1	679	92.5	308	96.3	81	95.3	0.125
dementia cases	83	6.3	12	6.9	55	7.5	12	3.8	4	4.7	

Table 3 Age-sex adjusted logistic regression analysis of risk factors for obesity

	Obese BMI (≥28)				Overweight BMI (24-27.9)				Underweight BMI (<18.5)			
	N=819				N=1054				N=908			
Variable	**Age-sex adjusted OR**	**95%CI**		**p-value**	**Age-sex adjusted OR**	**95%CI**		**p-value**	**Age-sex adjusted OR**	**95%CI**		**p-value**
Age (years)												
65-69	1.20	0.70	2.07	0.505	1.05	0.77	1.43	0.755	1.07	0.70	1.63	0.763
70-74	Ref				Ref				Ref			
75-79	0.93	0.49	1.76	0.815	0.66	0.45	0.97	0.033	0.92	0.58	1.45	0.715
>=80	0.72	0.32	1.65	0.443	0.59	0.36	0.95	0.029	0.76	0.46	1.27	0.301
Sex												
Female	Ref				Ref				Ref			
Male	0.49	0.31	0.79	0.004	0.72	0.55	0.94	0.015	1.22	0.88	1.70	0.239
Smoking over the last 2 years												
No	Ref				Ref				Ref			
Yes	0.69	0.36	1.33	0.267	0.75	0.53	1.06	0.104	0.59	0.39	0.90	0.014
Drinking alcohol over the 2 years												
No	Ref				Ref				Ref			
Yes	0.35	0.15	0.85	0.020	1.19	0.84	1.68	0.337	1.14	0.72	1.81	0.569
Watch TV, listen to radio, read book/ newspaper												
No	Ref				Ref				Ref			

Yes	1.71	0.99	2.96	0.054	1.84	1.33	2.54	0.000	1.22	0.86	1.74	0.270
Urban/rurality												
Urban	1.75	1.10	2.79	0.018	1.92	1.46	2.52	0.000	1.49	1.03	2.15	0.034
Rural	Ref				Ref				Ref			
Educational level												
Illiterate	Ref				Ref				Ref			
Primary Sch.	1.76	0.81	3.84	0.156	2.35	1.51	3.65	0.000	0.76	0.44	1.32	0.337
Secondary Sch.	1.99	1.01	3.92	0.047	1.87	1.24	2.81	0.003	1.38	0.76	2.51	0.287
>=High 2^{nd} Scho	1.81	1.01	3.24	0.047	1.66	1.18	2.35	0.004	1.73	1.04	2.87	0.033
Main occupation												
Peasant	Ref				Ref				Ref			
Manual labourer	2.11	1.03	4.33	0.043	1.96	1.24	3.09	0.004	1.46	0.74	2.90	0.275
Official/teacher	1.96	1.15	3.34	0.014	1.79	1.31	2.45	0.000	1.46	0.96	2.23	0.078
Business/other	1.63	0.64	4.14	0.302	2.30	1.38	3.84	0.001	1.59	0.69	3.65	0.276
Income satisfactory												
Very satisfactory	1.97	0.67	5.85	0.220	1.81	0.95	3.46	0.071	1.66	0.66	4.18	0.284
Satisfactory	1.53	0.62	3.78	0.351	1.46	0.87	2.44	0.153	1.06	0.58	1.93	0.861
Average	0.75	0.29	1.96	0.562	0.85	0.50	1.46	0.555	1.00	0.55	1.83	1.000
Poor	Ref				Ref				Ref			
Financial difficulties over the past 2 years												
No	Ref				Ref				Ref			
Yes	0.68	0.43	1.09	0.109	0.60	0.46	0.78	0.000	0.72	0.50	1.02	0.065
Marital status												
Married	1.06	0.60	1.86	0.837	0.98	0.71	1.38	0.939	1.16	0.77	1.73	0.480
Never married/divorced	na				0.13	0.03	0.56	0.006	1.79	0.65	4.98	0.263
Widowed	Ref				Ref				Ref			

Frequency of visiting children or other relatives												
Never	Ref				Ref				Ref			
At least monthly or less	0.51	0,15	0.74	0.285	0.51	1.47	18.00	0.011	0.34	0.73	1.60	0.174
At least weekly	0.59	0.20	1.71	0.320	3.61	1.06	12.33	0.041	0.29	0.64	1.22	0.091
Daily	0.54	0.20	1.50	0.238	3.56	11.06	11.93	0.040	0.31	0.73	1.35	0.119
Feeling lonely												
No	Ref											
Yes	0.84	0.29	2.41	0.742	1.09	0.62	1.93	0.757	0.41	0.23	0.70	0.001
Hypertension status												
No hypertension (<140*90)	Ref				Ref				Ref			
Undetected	1.75	0.97	3.15	0.062	0.95	0.69	1.31	0.765	1.30	0.90	1.88	0.160
Untreated	3.80	1.60	9.05	0.003	1.63	0.91	2.91	0.102	1.62	0.66	4.00	0.296
Uncontrolled	2.55	1.30	5.01	0.007	1.54	1.05	2.27	0.027	1.67	0.95	2.95	0.077
Controlled	4.35	1.66	11.38	0.003	1.93	1.02	3.65	0.043	3.46	0.80	14.91	0.096
Hypocholesteraemia												
No	Ref											
Yes	1.09	0.42	2.87	0.860	1.77	1.08	2.89	0.023	2.49	0.88	7.06	0.086
Stroke												
No	Ref				Ref				Ref			
Yes	3.46	1.20	10.00	0.022	0.84	0.30	2.35	0.738	0.69	0.25	1.93	0.481
Depression GMS_level												
Non-depression	Ref				Ref				Ref			
depress>=1 (subcases/cases)	0.76	0.29	1.98	0.578	0.86	0.50	1.48	0.585	0.57	0.33	0.97	0.040
Dementia												

No dementia	Ref				Ref				Ref			
Dementia cases	0.60	0.21	1.71	0.338	0.49	0.26	0.94	0.0.31	1.12	0.6	2.15	0.732

Table 4 Age-sex adjusted logistic regression analysis of risk factors for overweight/obesity

	Obesity/Overweight (BMI≥24)			
	N=1139			
Variable	**Age-sex adjusted OR**	**95%CI**		**p-value**
Age (years)				
65-69	1.08	0.81	1.44	0.606
70-74	Ref			
75-79	0.71	0.50	1.01	0.055
>=80	0.61	0.40	0.95	0.028
Sex				
Female	Ref			
Male	0.67	0.52	0.85	0.001
Smoking over the last 2 years				
No	Ref			
Yes	0.74	0.54	1.02	0.065
Drinking alcohol over the 2 years				
No	Ref			
Yes	0.99	0.71	1.38	0.960
Watch TV, Listen to the radio, read book/ newspaper				

No	Ref			
Yes	1.80	1.34	2.43	0.000
Urban-rural areas				
Urban	Ref			
Rural	0.53	0.41	0.68	0.000
Educational level				
Illiterate	0.59	0.43	0.82	0.001
Primary Sch.	1.33	0.84	2.10	0.225
Secondary Sch.	1.13	0.74	1.71	0.575
>=High 2nd School	Ref			
Main occupation				
Peasant	0.46	0.28	0.75	0.002
Manual labourer	0.93	0.52	1.67	0.806
Official/teacher	0.84	0.51	1.38	0.486
Business/other	Ref			
Income satisfactory				
Very satisfactory	Ref			
Satisfactory	0.81	0.52	1.25	0.335
Average	0.45	0.29	0.72	0.001
Poor	0.55	0.30	1.00	0.050
Financial difficulties over the past 2 years				
No	Ref			
Yes	0.62	0.48	0.80	0.000
Marital status				
Married	0.99	0.73	1.36	0.970
Never married/divorced	0.11	0.03	0.46	0.003
widowed	Ref			

Frequency of visiting children or other relatives				
Never	Ref			
At least monthly or less	2.27	0.95	5.42	0.066
At least Weekly	1.73	0.75	3.98	0.198
Daily	1.68	0.75	3.79	0.210
Feeling lonely				
No	Ref			
Yes	0.86	0.62	1.79	0.863
Hypercholesterolemia				
No	Ref			
Yes	1.62	1.01	2.58	0.044
Stroke				
No	Ref			
Yes	1.32	0.58	3.00	0.505
Hypertension status				
No hypertension (<140*90)	Ref			
Undetected	1.07	0.80	1.43	0.661
Untreated	1.96	1.15	3.34	0.013
Uncontrolled	1.70	1.19	2.44	0.004
Controlled	2.26	1.25	4.08	0.007
Depression GMS_level				
Non-depression	Ref			
depress>=1 (subcases/cases)	1.01	0.502	2.016	0.987
Dementia	0.71	0.354	1.427	0.337
No dementia	Ref			
dementia cases	0.52	0.30	0.92	0.023

Table 5 Multivariate logistic regression analysis of risk factors for overweight/obesity

	Obesity/Overweight (BMI≥24)			
	N=1139			
Variable	**OR**	**95%CI**		**p-value**
Age (years)				
65-69	0.97	0.72	1.31	0.857
70-74	Ref			
75-79	0.73	0.51	1.04	0.083
>=80	0.68	0.43	1.06	0.090
Sex				
Female	Ref			
Male	0.70	0.52	0.94	0.019
Smoking over the last 2 years				
No	Ref			
Yes	0.82	0.59	1.14	0.232
Drinking alcohol over the 2 years				
No	Ref			
Yes	1.06	0.75	1.49	0.762
Watch TV, Listen to the radio, read book/ newspaper				
No	Ref			
Yes	1.46	1.05	2.02	0.023
Urban-rural areas				
Urban	Ref			
Rural	0.61	0.41	0.92	0.019
Educational level				

Illiterate	0.94	0.58	1.52	0.794
Primary Sch.	1.66	1.02	2.71	0.041
Secondary Sch.	1.18	0.78	1.80	0.436
>=High 2nd School	Ref			
Main occupation				
Peasant	0.60	0.27	1.31	0.200
Manual labourer	0.84	0.46	1.54	0.570
Official/teacher	0.83	0.49	1.43	0.506
Business/other	Ref			
Income satisfactory				
Very satisfactory	Ref			
Satisfactory	0.85	0.55	1.32	0.473
Average	0.60	0.36	0.99	0.046
Poor	0.73	0.39	1.39	0.337
Financial difficulties over the past 2 years				
No	Ref			
Yes	1.62	0.86	3.06	0.138
Marital status				
Married	0.97	0.71	1.33	0.853
Never married/divorced	0.14	0.03	0.62	0.009
widowed	Ref			
Frequency of visiting children or other relatives				
Never	Ref			
At least monthly or less	2.12	0.87	5.15	0.971
At least Weekly	1.54	0.66	3.59	0.142
Daily	2.06	0.90	4.74	0.089
Feeling lonely				

No	Ref			
Yes	1.13	0.66	1.94	0.651
Hypercholesterolemia				
No	Ref			
Yes	1.21	0.74	1.98	0.446
Stroke				
No	Ref			
Yes	1.40	0.61	3.21	0.432
Hypertension status				
No hypertension (<140*90)	Ref			
Undetected	1.17	0.87	1.59	0.299
Untreated	2.00	1.16	3.43	0.012
Uncontrolled	1.49	1.03	2.16	0.036
Controlled	1.86	1.02	3.40	0.042
Depression_GMS_level	_	_	_	_
Non-depression	Ref			
depress>=1 (subcases/cases)	1.06	0.523	2.141	0.875
Dementia	0.87	0.432	1.767	0.707
No dementia	Ref			
dementia cases	0.61	0.34	1.09	0.096

Adjusted variables: Age, Sex, Smoking, Urban-rural areas and educational level

5.4 Discussion

The Anhui cohort study showed a high prevalence of abnormal weight in older Chinese, with 13.3% underweight, 24.4% overweight, and 6.5% obesity. The prevalence of overweight/obesity was 30.8% in the whole cohort; 34.5% in women and 26.7% in men. The study found that older people with primary school education (low education) versus >=high 2nd school (highest) had a significantly elevated risk of overweight/obesity. The risk of overweight/obesity was not significantly related to occupational class but reduced for income satisfactory that was average. The lifestyle factor of watching TV/listening to the radio, reading newspapers and also hypertension was associated with an elevated risk of overweight/obesity. The findings showed that rural living, being male and unmarried or divorced were associated with reduced risk of overweight/obesity in older age.

5.4.1 Prevalence of underweight, overweight and obesity

The data on the prevalence of underweight, overweight and obesity in older adults in China, as compared to reports in the other population groups, are relatively scarce and most data is often merged with those of middle age adults. For instance, the study by Mi and colleagues (2015) used the data from China Health and Nutrition Survey based on Chinese BMI offs for Asians to investigate the prevalence and secular trends in overweight and obesity spanning from 1991-2011. They found overweight and obesity have increased across all age brackets, and in those ≥60 years, the prevalence of obesity was 14.1% in women and 8.38% in men while for overweight and obesity combined, they were 46.5% and 42.1% respectively. The findings from the Anhui cohort of older age ≥65 years showed 30.8%

overweight/obesity with higher prevalence in women (34.5%) compared to men (26.7%). The findings from the Anhui cohort were lower compared to the national ones for overweight/obesity (30.8% versus 46.5% for women and 26.7% versus 42.1% for men). This could be explained by the age differences of the sample analysed, the disparity in the period the survey data was collected and variation between areas included in the different studies. For instance, the Anhui cohort study used BMI data collected between 2007 and 2009 while the study by Mi et al (2015) used national data from China Health and Nutrition Survey (CHNS) from 1991 to 2011. The inclusion of recent years' data in the study by Mi and Colleges must have contributed to higher prevalence estimates since there has been a continuous increase in overweight/obesity annually within China. It could also be ascribed to differences in the age of participants in the sample analysed for the Anhui cohort study (≥65 years) and study by Mi et al (≥60 years). In addition, the Anhui cohort data was based on the Anhui province while the CHNS study data was from nine provinces including the three largest municipalities (Beijing, Shanghai and Chongqing). Despite the differences, the findings from the Anhui cohort and the CHNS study data suggest a high prevalence of overweight/obesity in Chinese older adults. The finding supports the view that China is experiencing an overweight and obesity epidemic. This could be a huge challenge and may increase the future burden of chronic diseases for China if overweight/obesity is not controlled.

5.4.2 Socioeconomic factors

The findings from this study reinforced the theory that poor socioeconomic position increases the risk of overweight and obesity as observed in developed countries

(Sobal *et al.,* 1989; Wang *et al.,* 2007; McLaren, 2007). This is contrary to the previous finding that in developing countries low socioeconomic status is associated with reduced risk of overweight/obesity (Dinsa *et al.,* 2012). The evidence from the Anhui cohort study (China) with seven years follow-up suggests that low SEP measured by education is associated with increased risk of overweight/obesity. However, a significant association was not detected for occupation. Also, it was found that having an income that was considered satisfactory (on the average) significantly reduced the risk of overweight/obesity while having financial difficulties showed increased risk that was not significant. The finding that satisfactory income reduces the risk of overweight/obesity in China is consistent with the reports of studies from developed countries like the USA, Canada, Germany and UK (Dugravot *et al.,* 2010; Loman *et al.,* 2013; Hajek **et al.,** 2015). It could be because of epidemiological transition in nutritional factors, and lifestyle changes in China due to increased economic development in the past three decades and urbanisation. It is also possible that the differences in the stages of epidemiological transition among Low-and Middle-Income countries (LMIC) may explain some of the opposite findings of increased overweight/obesity due to high SES reported in other studies (McLaren, 2007; Dinsa *et al.,* 2012). In addition, it is difficult to rule out methodological issues of confounding or difficulty in ascertaining temporal order since most findings from studies conducted in LMICs are based on cross-sectional designs.

The Anhui cohort study suggests that urban living is related to increased risk of overweight/obesity while rural living reduced the risk. This finding highlights the effect of the rapid urbanisation in China which is accompanied by nutrition and lifestyle changes that support overweight and obesity (Gong *et al.,* 2012). The reduced risk of overweight/obesity in rural areas could be due to contextual issues relating to the local environments. This could be in terms of differences in social norms relating to dietary choices between the rural areas and urban areas and across different regions. For instance, one recent study in China by Zhang *et al* (2015) showed that the traditional south diets (staple rice, pork and vegetables) was associated with reduced risk of overweight and obesity compared with the diet for those in the north (for instance higher snack, high protein and cereals) Research also showed that physical activity and eating behaviours may be determined by social norms independently of social supports (Ball *et al.,* 2010) while cultural patterning of overweight and obesity is becoming more evident in different settings (Brewis, 2010). Therefore, it is more likely that older adults from rural areas would experience a lower risk of overweight/obesity compared to their urban counterparts depending on prevailing neighbourhood factors including social and cultural norms.

5.4.3 Social and community network factors

It is well documented from the literature that dietary behaviours and physical activity may be culturally and socially patterned (Brewis, 2010; Biddle *et al.,* 2010; Ball *et al.,* 2010) while overweight and obesity could be transmitted via social network (Christakis et al., 2007; Fowler and Christakis 2008: 2013). For instance, previous evidence from the study by Christakis *et al* (2007) found that obesity may be spread through social networks in a measurable and noticeable Pattern depending on the type of social ties such as peer groups, spouse and families. However, the findings from this study using the Anhui cohort data showed no significant association of most social network factors with overweight or obesity in older adults except for the unmarried/divorced that showed reduced risk.

The lack of association for most social network factors and overweight/obesity in the Anhui cohort study seems to support the view that the impact of social network factors such as friends/peers, spouse, families and neighbours is not a straight forward relationship as it was previously argued by Cohen-Cole and Fletcher (2008). It is also likely that such effects in older adults may be diluted by environments, personal characteristics, and individual choices. This is important since it was argued that environmental factors often outweigh the social network effects (Cole and Fletcher, 2008). Therefore, it is unclear whether social network factors significantly impact on the overweight and obesity in older age considering lack of evidence from the literature. A recent finding based on prospective data from a developed country (Switzerland) suggests that living in a couple reduces weight gain after 5.5 years of follow-up (Guerra *et al.,* 2015). However, the Anhui cohort study found that were never married or divorced significantly reduced excess body weight. This is consistent with some studies in developed countries that reported higher calorie intake may be enhanced by the influence of spouse while being unmarried reduces it (Sobal *et al.,* 2009; Scherr, Brenchley and Gorin, 2013).

5.4.4 Lifestyle/ behavioural factors

A previous cross-sectional study (Zhang et al., 2008) of rural Chinese elderly suggest that alcohol drinking is associated with increased risk of overweight/obesity while smoking conferred protection. The Anhui cohort study found a significant association of smoking, and alcohol drinking with overweight/obesity in the age-sex adjusted analysis but the effects were attenuated in the multivariate analysis. The findings are contrary to previous studies in high-income country like Canada (Kaplan *et al.,* 2003) which reported an inverse association of obesity in relation to alcohol drinking in the elderly. The findings from US older adults (Kruger *et al.,* 2009) found a 28% increase in obesity in moderate drinkers compared to non-drinkers. The study also reported that while older men who were former smokers were 43% more likely to be obese, they were also found to be 29% more likely to be overweight than never smokers. These differences in the impact on obesity by lifestyle behaviour in different settings may reflect prevailing social norms relating to dietary behaviour involving alcohol drinking and smoking (Ball et al., 2010) or the complex nature of overweight and obesity in older adults with contextual issues confounding the association in this population (Kruger *et al.,* 2009; Cohen-Cole and Fletcher, 2010).

There has been a lack of evidence from research in middle-income countries on watching TV as a possible risk factor for overweight/obesity. As a result, knowledge of the association in older age has been sparse. For instance, a recent study by Xie *et al* (2014) investigated the impact of TV viewing time on obesity in the adult population from Hong Kong, China and found a positive association but the study sample used was limited to those between 18-34 years. However, evidence in older adults are lacking and there is a possible notion that exposure to media at an older age is inconsequential compared to the impact on the behaviour of the younger population.

The findings from developed countries (Gómez-Cabello *et al.,* 2012) suggest that at an older age the impact of watching TV may be unrelated to the influences of the media such as advertising, but the sedentary behaviour accompanied with the lifestyle such as sitting for several hours. Consistent with this hypothesis and likely impact on body weight, the findings from the Anhui cohort of Chinese older adults demonstrated a significant positive association of watching TV with overweight/ obesity in all the analysis. This finding may be due to increased sedentary behaviour associated with watching TV and perhaps increased calories consumed in the process. This may be true since previous study found more calories are consumed while watching TV (Williams *et al.,* 2008).

5.4.5 Cardiovascular disease and related individual factors

There has been less attention to chronic diseases such as cardiovascular diseases and related risk factors (CVDRF) that affects body weight in older age. Older adults are prone to multiple morbidities associated with ageing (Marengoni *et al.,* 2011) which impacts on body weight and contributes to the risk of mortality (Aunne *et al.,* 2016). In the Anhui cohort study, data from the age-sex adjusted analysis showed that CVDRFs of hypercholesterolemia and hypertension were significantly associated with increased risk of overweight or obesity, and the findings from the multivariate analysis confirmed hypertension as a significant risk factor in the Chinese older adults. The multivariate analysis further demonstrated that the risk of excess weight was greater in those with untreated hypertension than those with controlled or uncontrolled hypertension when compared with those with no hypertension. The reduced risk of overweight/obesity in those with controlled hypertension could be attributed to medical advice received regarding body weight control as opposed to those with untreated hypertension who may not be visiting health care provider as required. One explanation is that hypertension could reflect a wider context within which persistent high blood pressure tends to manifest. This could be independent of an underlying disease including work stress, unfavourable condition of living, poor diets and reduced physical activity.

5.4.6 Strengths and Limitations of the Study

5.4.6.1 *Strengths*

The strength of the study is in terms of the cohort study design, detailed analytical strategy employed, use of measured weight and height and use of data for only older adults.

Cohort study design

The strength of the study is the use of cohort design with 7 years follow-up of older adults who were recruited from the community. The use of prospective cohort data ensured that temporal order of the exposure and outcome relationship was established (Hu, 2008, P.35; Caruana et al., 2015); the exposure variables were measured and documented from the baseline of the study while the outcome (BMI) was ascertained at the end of 7 years follow-up. A longer follow-up allowed adequate time for the impact of the exposures on the outcome to manifest thereby avoiding the challenge with short duration that is prone to reverse causality and confounding (Caruana et al., 2015).

The detailed analytical strategy deployed

The strength of the study also comes from the detailed statistical analysis deployed that helped in ascertaining the major risk factors associated with overweight/obesity in older age. First, in the analysis for obesity, those that were overweight or underweight at baseline were excluded. Similarly, in the analysis for overweight, the obese or underweight were not included. This approach helped to reduce any bias from the prevalent obesity or overweight and focus on the "incident obesity or overweight" outcome variables of interest. Secondly, age-sex adjusted, and multivariate logistic regression analysis was carried out. The differences in the findings suggest that apart from issues of temporal order and reverse causality with cross-sectional studies, incomplete adjustments (residual confounding) may account for the disparity in outcomes. For instance, high socio-economic positions measured by education, income and occupation were reported to be positively associated with overweight/obesity in developing countries. However, in the China cohort study, it was only true in the age-sex adjusted analysis for overweight, obesity or combined overweight/obesity. In the multivariate analysis, the association was inversed with the risk of overweight/obesity significantly increased by low SES (primary education) while satisfactory income conferred protection. Similarly, the significant associations of smoking or alcohol with overweight/obesity from the age-sex adjusted analysis were attenuated in the multivariate analysis when more covariates came into the equation. In contrast, findings on watching TV and hypertension remained significant risk factors for overweight/obesity in all analysis. Therefore, the approach helped to confirm the findings of the risk factors for overweight and obesity from this study.

Use of measured weight and height

One other strength of this study is the use of anthropometric data based on measured weight and height which helped to avoid bias associated with self-reported data. Older adults are more likely to manifest recall bias than younger and middle age adults and they experience loss of height with ageing (Zamboni et al., 2005). Therefore, using measured data in the study might have helped the validity of the reported findings.

Use of data for only older adults

The data on the determinants of overweight/obesity in older adults is very scarce internationally. Therefore, it is common for studies even in developed settings to use data from a mixed population consisting of middle age and older adults to maximise sample sizes. However, findings from such studies may not reflect the evidence is strictly older adults who may require public health strategies well-tailored to them. This study ensured that strictly older adults sample (≥65 years) was used to investigate the risk factors for overweight/obesity in older age. Therefore, the findings could be generalised to older adults within China and compared with those of western countries like the UK and USA, where older adults are considered as those of the age of 65 years and above.

5.4.6.2 *Limitations*

Lack of variables on social norms

The study investigated a range of risk factors for overweight and obesity. However, the array of variables considered as risk factors could not capture social norms or cultures even though lifestyle and social network factors were considered. This is important since the literature suggests that prevailing culture or social norms tend to impact on behaviour relating to diet and physical activity (Brewis, 2010; Ball *et al.,* 2010). Considering this shortcoming and less research in these aspects, it represents an important area for future study.

Gender effect

One previous report from the UK (Johnson and Wardle, 2011) suggested that in terms of behaviours concerning body weight, women were more likely to conform to social norms than their men counterpart. The Anhui cohort study suggest higher prevalence of overweight/obesity in women (34.5%) compared to men (26.7%). The men also showed lower risk for overweight/obesity compared to women. The reasons behind this sex disparity was not explored in this study. It is also unknown if sex differences in conformation to social norms around diet and physical activity play a significant role. Therefore, further research is needed to help understand the sex-differences in risk factors for overweight/obesity in older Chinese adults.

Lack of data on dietary intake, detailed physical activities and genetics

It is known from the literature of obesity epidemiology (Hu, 2008 pg. 275) that dietary intake, dietary type and pattern of eating are crucial to the understanding of the determinants of overweight/obesity. Also, detailed physical activity may impact on body weight while the role of genetics in overweight/obesity is postulated in the literature. However, the Anhui cohort study lack data on dietary intake neither were data on detailed physical activities or genetics available to examine these relationships in older adults. This highlights the need for further study.

5.5 Implications and Conclusion

The findings of the major risk factors for overweight and obesity have several implications in terms of policymaking and public health practice. The findings suggest that abnormal body weight, including underweight, overweight and obesity are common in the Chinese older adult population. It therefore supports or confirms the reports of growing excess weight in China particularly in the ageing population (Wang *et al.,* 2008; Ying-Jun *et al.,*2015; Chooi, Ding and Magkos, 2019) and the concerns over current and future burden of morbidity and increased mortality (Mai and Chen, 2013).

The high prevalence of overweight and obesity, as confirmed by 30.8% in the Anhui cohort of older adults, buttressed the recent finding that the age-adjusted prevalence of overweight in China has tripled (from 7.8% in 1980 to 29.9% in 2015). This is often related in the literature to epidemiological transition due to global trade liberalization which fueled rapid economic growth and urbanization in the country for several decades (Yang *et al.,* 2008; Swinburn *et al.,* 2011; Popkin, 2014). However, local environments tend to shape these global drivers of excess body weight (Swinburn *et al.,* 2011), and this could affect the extent and pattern of nutritional transition and changes in disease risk factors witnessed in the Chinese population. The study showed several factors contribute to increased overweight and obesity in Chinese older adults. Notably, it was found that lower socioeconomic position measured by education and living in the urban compared to rural areas increased the risk of overweight/obesity. Therefore, wider policies and specific strategies to change obesogenic behaviours at population and individual level are required. Strategies on improving the level of education in the Chinese population and changing nutritional and lifestyle behaviours particularly in urban areas will reduce the prevalence of overweight/obesity. Also, older population often represent those who have transitioned from active work life to retirement and this is often accompanied by changes in lifestyle as reflected in the findings from the study which showed significantly increased risks of overweight or obesity in those watching TV. This finding implies that sedentary life is common and is a huge challenge in the Chinese older population. Therefore, policies and strategies that will promote a better active lifestyle and curtail overweight/obesity in older age are needed.

In addition, there is a need for increased prevention strategies in the Chinese women considering that male gender was associated with reduced risk of excess weight while higher prevalence was observed in females. Though, research is still needed from prospective cohort studies to explore gender differences in risk factors for overweight and obesity in older adults and the mechanisms involved to help guide appropriate interventions. Furthermore, since a significant positive association exists between hypertension and excess weight, it calls for early screening for detection of hypertension in older adults showing excess body weight or screening for overweight/obesity in those presenting with high blood pressure. Also, the wider context within which such high blood pressure tends to persist in older age should be considered because it is more crucial to public health prevention.

CHAPTER SIX: IMPACT OF OVERWEIGHT AND OBESITY ON DEMENTIA RISK: A COHORT STUDY

6.1 Introduction

Dementia is a significant public health problem affecting older adults which needs urgent action to reduce the growing epidemic in developed and developing countries (WHO, 2018). Since there is currently no cure for dementia, this has led to an increased interest in detecting the modifiable risk factors to guide prevention approaches (Shah *et al.,* 2016). Overweight and obesity are also important public health problems that are becoming increasingly prevalent in older adults internationally (Fakhouri *et al.,* 2012; Mathus-Vliegen *et al.,* 2012; Ng *et al.,* 2014). They contribute significantly to various chronic illnesses in older age (Guh et al., 2009), and of importance is their impact on cardiovascular diseases which accounts for 30.3% of morbidity, disability, and premature mortality in the older population. It may be hypothesised that since dementia often arises from cardiovascular complications and other vascular factors (Lunchsinger *et al.,* 2005; Meng *et al.,* 2014), overweight and obesity in older age may have significant positive association with dementia. However, many studies suggested that excess body weight measured in older age may instead delay incident dementia risk (Fitzpatrick *et al.,* 2009; Power *et al.,* 2010; Neergaard *et al.,* 2016; Peddittzi *et al.,* 2016). This is despite the findings of midlife obesity and dementia risk indicating deleterious effects (Whitmer *et al.,* 2005; Beydoun *et al.,* 2008; Albanese *et al.,* 2017).

One of the earlier studies in US older adults (65-97 years) by Fitzpatrick *et al* (2009) investigated the association of midlife and late-life obesity with incident dementia risk using prospective cohort data of 2,798 participants that were followed up for 5.4 years. They found that, while midlife obesity predicted the risk, there was an inverse association of late-life continuous BMI and incident dementia risk (RR 0.95, 95%CI: 0.92-0.98). They also reported that obesity significantly reduced dementia risk by 37% (0.63, 0.44-0.91). However, there was no association of overweight (BMI 25-30Kg/m²) with incident dementia (0.92, 0.72-1.18). Similar findings were also found elsewhere (Buchman *et al.,* 2005; Atti *et al.,* 2008; Power *et al.,* 2010) while some studies reported no effects at all (Borenstein *et al.,* 2001; Hughes *et al.,* 2009) and only a few studies suggesting an increased risk (Gustafson *et al.,* 2003; Hayden *et al.,* 2006). Furthermore, a previous meta-analysis of prospective cohort studies (≥65 years) supported the paradoxical findings of an inverse association between obesity and incident dementia (Peddittzi *et al.,* 2016). It found that while obesity in midlife increased the risk of dementia (1.41,1.20-1.65), in late life it significantly reduced dementia risk (0.83, 0.74-0.94) with no effect observed for the overweight (0.88, 0.76-1.02). Though the review did miss the data for some studies (Buchman *et al.,* 2005; Lucca *et al.,* 2012; Tolppanem *et al.,* 2014; Neergaard *et al.,* 2016), it reported that obesity confers protection against incident dementia risk.

The evidence from research suggests that change of weight is more related to dementia risk development, with possible explanation for the reduced risk of dementia for obesity and lack of association of overweight (Powe et al., 2013; Tolppanem et al.,2014). The study by Tolppanem et al (2014) found that midlife obesity significantly predicted dementia, and every decrease in BMI from midlife to late life elevated the risk of dementia (1.14, 1.03-1.25) and Alzheimer's disease (1.20, 1.09-1.33). Besides, the highest BMI decline had the greatest dementia risk when compared to more stable BMI (Power et al (2013). This suggests that dementia risk depends on the magnitude of BMI change. Therefore, it is possible that the lack of association of overweight with dementia risk in some studies (Borenstein *et al.,* 2001; Hughes *et al.,* 2009; Fitzpatrick et al., 2009), may reflect the extent of change of BMI from baseline after years of follow-up, while further weight loss may significantly predict dementia risk. This is true since decrease in body weight is an early marker of dementia pathology with evidence showing that weight loss precedes dementia diagnosis by ten years or more (Stewart et al., 2005; Knopman *et al.,* 2007; Gustafson *et al.,* 2012).

It was also observed that several issues relating to the duration of follow-up, type of adiposity measure, adjustments of confounding factors, pre-existing morbidities and reverse causation may explain differences in the unclear findings from cohort studies (as reported in chapter three). Besides, there is a lack of research on the effect modification by gender in the association of adiposity with incident dementia in most studies. Furthermore, all included studies for the meta-analysis in chapter three on obesity and dementia risk were from high-income countries and none was from the low and middle-income countries where the risk factors might be different from those observed in the Caucasians. For instance, it was documented that in western populations obesity/overweight, low socio-economic status (SES), high cardiovascular disease risk factors (CVDRFs) (e.g. smoking) and depression are highly interconnected, making it difficult to distinguish causal factors for obesity from confounding factors (Chen *et al.,* 2008; 2011). One important way of addressing this problem is to study the impact of obesity/overweight in older age on dementia in markedly different populations. Therefore, China has provided an important opportunity to do this since older Chinese tend to be more socio-economically deprived and have a higher risk of dementia yet have higher levels of social support than western populations; moreover, levels of depression and CVDRFs and obesity/overweight are much lower. This study, therefore, investigates the impact of obesity and overweight measured in older age on dementia risk using data from a Chinese cohort study with ten years of follow-up.

6.2 Methods

6.2.1 Participants from the Anhui Cohort Study

The studied population was derived from the Anhui cohort in China. The methods of the Anhui study have been fully described in the methodology chapter. Briefly, from those who had lived for a minimum of 5 years as of 2001 in Yiming sub-district of Hefei City, 1736 people aged ≥65 years were randomly selected, and another 1600 aged ≥60 years were selected at random from all 16 villages in Tangdian District of Yingshang County in 2003. The study participants totalled 3,336. They were interviewed and assessed for baseline information. Before each participant interview, permission and consent were first obtained. The consent to participate was sought and granted by their closest relatives or carers; and refusals, when met, were respected. Informed consent was impossible among only 5% of the participants. A trained survey team, from the School of Health Administration at Anhui Medical University, interviewed the participants at their residence. The materials for the interview were mainly the general health and risk factors questionnaires, which were partly obtained from the MRC-ALPHA study, the Scottish MONICA surveys, and the Geriatric Mental Status (GMS) questionnaires. The GMS questionnaire is a comprehensive semi-structured mental state interview and widely used globally in the elderly population (Saunders *et al.,* 1991).

6.2.2 Baseline assessments

The general health and risk factors questionnaire captures the followings; (a) sociodemographic details including; educational levels, occupation and annual income, (b) doctor-diagnosed cardiovascular diseases, medications, and self-assessed health, (c) adverse life effects in the last 2 years, (d) hobbies and activities of daily living (ADL). The systolic and diastolic blood pressures were measured based on a standard protocol.

6.2.2.1 Body Mass Index (BMI)

BMI of participants (in Kg/m^2) were calculated based on measured weight and height. Height was measured without shoes to the nearest 0.5 cm by portable stadiometer, while weight was recorded to the nearest 0·1kg by digital scales with light clothing on. The WHO (2008) defined overweight and obesity by BMI values of 25-<30 Kg/m^2 and ≥30 kg/m^2 whilst underweight and normal weights are classified by BMI of <18.5 Kg/m^2 and 18.5-<25 Kg/m^2 respectively. However, for this research work, categorical BMIs were created based on the classification recommended for the Asian Chinese population by the Chinese government (Chen *et al.,* 2008). This is because the Chinese people (The Asians), as compared with Caucasians, have higher body fat percentage for same BMI; and thus, have an increased risk of cardiovascular disease (Chan et al., 2009; Huxley et al., 2010).The categorical BMI included; underweight (<18·5kg/m^2), normal weight (18·5 to <24kg/m^2), overweight (24 to <27·9kg/m^2) and Obese BMI (≥28 kg/m).

6.2.2.2 Waist Circumference (WC)

Waist circumference was measured to the nearest 0.1 centimetres using a plastic tape placed mid-way between the lowest rib and the iliac crest. The WHO (2011) defined high body fats by WC 94-<102cm for men and 80-<88cm for women (action levels one); whilst higher body fats are defined by WC ≥102cm for men and ≥88cm for women (action level two). In this research, the recommended WC classification groups defining central fat distributions based on waist circumference action levels 1 and 2 with 94 and 102cm for men, 80 and 88cm for women were used (Chen *et al.,* 2008; Huxley *et al.,* 2010).

6.2.2.3 Dementia diagnosis at baseline

To diagnose dementia in the participants, a computer program-aided diagnosis called Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT), was used to analyse the interview data from a Geriatric Mental State (GMS) questionnaire. The instrument identifies dementia cases and subcases. This method of diagnosis has been likened with psychiatrists' diagnoses and the DSM-III criteria, and it has demonstrated high levels of consistency across different settings including older Chinese populations. The PhD research work for the thesis focused on cohort data of strictly older adults of the age of 65 years and above. Therefore, those of below the age of 65 years, who happened to be from the rural cohort and of no education were excluded. Also, considering that the GMS-AGECAT was initially developed for the literate elderly in the West, excluding the rural cohort of those <65 years (325 participants), who were not literate may have removed bias from the overdiagnosis of dementia cases, and also ensure comparability within the urban and rural sample and with the findings from the West. The total baseline dementia cases diagnosed and excluded from the study was 257. The details of this GMS-AGECAT and its use for dementia 'case' diagnoses have been described in Chapter three (methodology chapter).

6.2.3 Follow-up of the cohort

In the follow-up, vital status was monitored until 2011. This involved three waves of re-interviews after baseline assessments were completed (wave 1). Based on the same protocol and using the GMS-AGECAT to diagnose dementia, 2608 cohort members were re-examined in wave 2, a year after the baseline investigation. After taking out those who died, relocated to new homes for a long time or who were no longer traceable, around 87% response rate was recorded. The Wave 3 re-interviews were completed from 2007-2009 with 82·4% response rate; it involved 1,757 participants and the use of the 10/66 dementia algorithm package for dementia diagnosis. The final re-interviews (wave 4), which involved 944 cohort members, was completed from 2010-2011 with the 10/66 dementia algorithm also used. Apart from the vital status of cohort members that was assessed, causes of death were identified through electronic registration databases from the local Centers for Disease Control and records from the local resident committees. To explore further causes of death a standard Verbal Autopsy questionnaire was used and a total of six hundred and one deaths were identified. The total number lost in follow-up over the 10 years was 324 (10.5%).

6.2.4 Cohort data analysis

The data of 2,430 participants who were aged >=65 years, and free of dementia as diagnosed by the GMS-AGECAT at baseline and not lost to the follow up (Figure 6.1), were analysed. Distributions of risk factors among individuals with different groups of BMIs were examined using Chi-square test for categorical variables. Binary logistic regressions were employed to calculate Odds ratio (OR) and 95% confidence interval (95%CI) of incident dementia in relation to baseline BMI categories using combined underweight/normal weight (BMI<24kKg/m^2), and also normal weight (18.5-<24Kg/m^2) as controls. In the models, adjustments were made for age, sex, smoking status, alcohol consumption, urban-rural areas, education level, income satisfactory, marital status, contacting friends in the community, hypertension status, stroke, activity of daily living, and depression. To reduce the inverse association between dementia and overweight/obesity, a sensitivity analysis was conducted by excluding dementia wave 2 data. Also, central fat distributions were defined based on waist circumference action levels 1 and 2 with 94 and 102cm for men, 80 and 88cm for women (Chen *et al.,* 2008); and the risk of incident dementia in relation to WC was examined using these cut-offs. To also examine gender differences in the impact of obesity/overweight on dementia, the analysis was further separated for men and women. Also, a separate analysis in non-smokers was conducted for BMI and WC since it may be difficult to eliminate residual confounding due to smoking through adjustments in the statistical models. The analyses were also replicated using quartiles of BMI, WC and WC/ √ height as well as their continuous data. All analyses were performed using SPSS (Windows version 24·0; SPSS Inc., Chicago, Illinois).

6.3 Results

The results in this section are divided into two parts. The first is the findings from the Anhui cohort study and the second is from the meta-analysis conducted which included the findings of the Anhui cohort study.

6.3.1 Anhui cohort study results

The descriptive and inferential statistics (multivariate logistic regression) from the analysis are presented separately below.

6.3.1.1 Descriptive statistics

In 2430 participants, the mean age was 71·7 years (SD ±6·7) and 48.9 % of the sample were male. Table 6 shows the details of the characteristics of participants in 4 groups of BMIs. The majority of the participants (61.7%) were from the urban areas and were more likely to be overweight and obese compared to their rural counterparts. Although 43.8% had no education, there were 27.9% and 15.3% who had higher education and secondary education respectively while the rest were of primary school level. The overweight (23.4%) and the obese (18%) older adults were less likely to be smokers compared to those of normal weight (38.5% %) and underweight (31.2%). Conversely, there were more obese (18·5%) and overweight (18·4%) people with heart diseases compared to those classified as normal (14·8%) and underweight (15·4%).

Over the 10 years follow up, there were 271 incident dementia cases; 131 were documented from wave two, 57 from wave three, 96 from wave four (of which two were from the causes of death).

6.3.1.2 Multivariate logistic regression analysis

The findings from the multivariate logistic regression analysis are presented according to the adiposity indices investigated in relation to incident dementia. This includes incident dementia in relation to continuous BMI and WC.

6.3.1.2.1 BMI and incident dementia

Table 7 shows number, risk and adjusted ORs of incident dementia among 3 BMI categories (obesity, overweight and normal/underweight). In the whole cohort, there was no significant association of obesity and overweight with dementia risk from the categorical BMI data analysis no matter which co-variables were adjusted for. However, in sex-stratified data analysis it was found that there was about 2-3 times higher risk of dementia in men with overweight and obesity compared to their counterparts of normal or underweight weight, although further adjustment for hypertensive status, stroke, ADL and depression attenuated these ORs to 2.16 (1.33-3.51) for overweight and 2.63 (1.28-5.42) for obesity. This suggest that these factors mediate the association. In women, adjusted ORs were significantly reduced in those classed as overweight (0.66, 0.45-0.98) and obese (0.52, 0.28-0.97) compared to normal weight/underweight (Table 2). After excluding 131 incident dementia cases from wave 2 (Table 8), it was found that the predictive effects were stronger in men for overweight (3.09, 1.65-5.77) and obesity (4.19, 1.75-10.03), and not significant in women for both overweight (0.74, 0.43-1.27) and obesity (0.72, 0.32-1.64). Using the normal BMI of 18.5<24 as a reference, adjusted ORs of dementia in participants with obesity and overweight were reduced but still significantly high for men but no association in women (Appendix 12), and the patterns for their associations with incident dementia were not substantially changed in comparisons to those in Table 8. The findings from the quartiles of BMI data analysis were similar to those in Table 8 as well, but less significant (Appendix Table 12). Additionally, the results from further analysis limited to non-smokers for BMI and incident dementia risk (Table 9) also reflected similar predictive effects in men for obesity (4.28, 1.46-12.53) and overweight (2.33, 0.98-5.53) but not in women.

6.3.1.2.2 WC and Incident dementia

Table 10 shows numbers, risk and adjusted ORs of incident dementia in relation to three levels of waist circumference. The results did not show any significant ORs, except for increased OR of dementia in men having action level 2 approaching significance (2.35, 0.86-6.42, p=0.097). However, a further analysis of incident dementia risk in strictly non-smokers (Table 11) showed significantly increased risk for action level 2 by over three-fold (3.19, 1.04-9.77) while that of action level 1 was almost significant (2.52, 0.90-7.06, p=0.078). The findings from the quartiles of WC data analysis (Appendix 13) were similar to those in Table 5 but increased OR of dementia in men having 4^{th} quartile versus 2^{nd} quartile was significant (2.71, 1.06-6.95). Data of the WC/√heights quartiles (Appendix table 14) also showed significantly increased OR in men for both 3^{rd} quartile (3.07, 1.27-7.39) and 4^{th} quartile (3.64, 1.42-9.35) versus 2^{nd} quartile.

6.3.1.2.3 Continuous data of adiposity and incident dementia

Findings from continuous BMI data (appendix 3c) for the entire cohort showed that excess body weights significantly increased incident dementia risk (OR 1.06, 95%CI:

1.06-1.11). Analysing continuous data of BMI, WC and WC/√heights according to sex it was found that while none of these 3 measurements in women had a liner relation to dementia, in men they positively predicted the risk of dementia and WC/√heights had a better prediction (Appendix 15). Whilst incident dementia risk in men was significantly increased by 17% for continuous BMI (1.17, 1.27) and 3% for WC (1.00-1.06), the dementia risk for WC/√heights was raised by 44% (1.44, 1.00-2.06).

Table 6 Characteristics of participants within each Body Mass Index (BMI) category

Characteristics	**Total participants**		**Obese (>=28)**		**Overweight (24-<27.9)**		**Normal BMI (18.5-<24)**		**Underweight (<18.5)**		**p-value**
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	
Age (years)											
65-69	863	35.5	90	37.7	325	39.3	416	33.5	32	25.6	0.000
70-74	733	30.2	71	29.7	256	31.0	367	29.6	39	31.2	
75-79	485	20.0	53	22.2	163	19.7	248	20.0	21	16.8	
>=80	349	14.4	25	10.5	82	9.9	209	16.9	33	26.4	
Sex											
Men	1188	48.9	104	43.5	398	48.2	625	50.4	61	48.8	0.255
Women	1242	51.1	135	56.5	428	51.8	615	49.6	64	51.2	
Waist Circumference (cm)†											
No Action	1323	54.4	48	20.1	312	37.8	854	68.9	109	87.3	0.000
Action Level 1	518	21.3	43	18.0	239	28.9	227	18.3	9	7.2	
Action Level 2	589	24.2	148	61.9	275	33.3	159	12.8	7	5.6	
Smoking over the last 2 years											
No	1802	74.2	196	82.0	633	76.6	887	71.5	86	68.8	0.001
Yes	628	25.8	43	18.0	193	23.4	353	28.5	39	31.2	
Drinking alcohol over the 2 years											
No	1963	80.8	203	84.9	677	82.0	970	78.2	113	90.4	0.001
Yes	467	19.2	36	15.1	149	18.0	270	21.8	12	9.6	
Socioeconomic factor											
Urban/rurality											

Urban	1500	61.7		154	64.4		550	66.6		716	57.7		80	64.0		0.001
Rural	930	38.3		85	35.6		276	33.4		524	42.3		45	36.0		
Educational level																
>=High 2nd School	677	27.9		56	23.4		253	30.6		339	27.3		29	23.2		0.006
Secondary Sch.	372	15.3		39	16.3		149	18.0		168	13.5		16	12.8		
Primary Sch.	316	13.0		40	16.7		99	12.0		158	12.7		19	15.2		
Illiterate	1065	43.8		104	43.5		325	39.3		575	46.4		61	48.8		
Main occupation																
Business/other	226	9.3		15	12.0		111	9.0		79	9.6		21	8.8		0.006
Official/teacher	898	37.0		44	35.2		427	34.4		343	41.5		84	35.1		
Manual labourer	382	15.7		22	17.6		184	14.8		126	15.3		50	20.9		
Peasant	924	38.0		84	35.1		278	33.7		518	41.8		44	35.2		
Income satisfactory																
Business/other	226	9.3		21	8.8		79	9.6		111	9.0		15	12.0		0.006
Official/teacher	898	37.0		84	35.1		343	41.5		427	34.4		44	35.2		
Manual labourer	382	15.7		50	20.9		126	15.3		184	14.8		22	17.6		
Peasant	924	38.0		84	35.1		278	33.7		518	41.8		44	35.2		
Financial difficulties over the last years																
no	1521	62.6		153	64.0		555	67.2		735	59.3		78	62.4		0.004
yes	909	37.4		86	36.0		271	32.8		505	40.7		47	37.6		
Satisfied with life/ current living																
Very satisfactory	737	30.3		78	32.6		234	28.3		393	31.7		32	25.6		0.032
Satisfactory	1388	57.1		134	56.1		500	60.5		686	55.3		68	54.4		
Average	272	11.2		21	8.8		84	10.2		146	11.8		21	16.8		
Poor	33	1.4		6	2.5		8	1.0		15	1.2		4	3.2		

Social network and psychosocial factors																
Marriage																
Married	1792	74.0		177	74.4		631	76.7		903	73.0		81	65.3		0.073
Never married	68	2.8		4	1.7		20	2.4		37	3.0		7	5.6		
Divorced																
Widow	562	23.2		57	23.9		172	20.9		297	24.0		36	29.0		
Frequency of visiting children or other relatives																
Everyday	1321	54.4		134	56.1		451	54.6		677	54.6		59	47.2		0.541
At least weekly	718	29.5		69	28.9		252	30.5		350	28.2		47	37.6		
At least Monthly or less often	304	12.5		28	11.7		96	11.6		167	13.5		13	10.4		
<Yearly or Never	87	3.6		8	3.3		27	3.3		46	3.7		6	4.8		
Contacting friends in the community																
Everyday	817	33.6		98	41.0		289	35.0		392	31.6		38	30.4		0.001
At least weekly	889	36.6		93	38.9		303	36.7		454	36.6		39	31.2		
At least Monthly or less often	603	24.8		44	18.4		197	23.8		327	26.4		35	28.0		
<Yearly or Never	121	5.0		4	1.7		37	4.5		67	5.4		13	10.4		
Contacting neighbours																
Everyday	799	32.9		101	42.3		262	31.7		394	31.8		42	33.6		0.009
At least weekly	826	34.0		82	34.3		279	33.8		429	34.6		36	28.8		
At least Monthly or less often	718	29.5		51	21.3		263	31.8		364	29.4		40	32.0		
<Yearly or Never	87	3.6		5	2.1		22	2.7		53	4.3		7	5.6		
Help available when needed																
No	130	5.3		9	3.8		36	4.4		73	5.9		12	9.6		0.047
Yes	2300	94.7		230	96.2		790	95.6		1167	94.1		113	90.4		

Cardiovascular disease and risk factors																
Hypertension status																
No hypertension (<140*90)	1003	41.3		61	25.5		289	35.0		576	46.5		77	61.6		0.000
Undetected	740	30.5		72	30.1		248	30.0		390	31.5		30	24.0		
Untreated	133	5.5		12	5.0		55	6.7		61	4.9		5	4.0		
Uncontrolled	417	17.2		68	28.5		178	21.5		160	12.9		11	8.8		
Controlled	137	5.6		26	10.9		56	6.8		53	4.3		2	1.6		
Hypercholesterolemia																
No	2207	91.6		209	88.9		729	88.7		1151	93.7		118	95.9		0.000
Yes	202	8.4		26	11.1		93	11.3		78	6.3		5	4.1		
Diabetes																
No	2265	93.5		218	92.4		769	93.1		1161	93.8		117	95.1		0.706
Yes	158	6.5		18	7.6		57	6.9		77	6.2		6	4.9		
Heart diseases (ischaemic, valve disease/others)																
No	2020	83.6		194	81.5		673	81.6		1049	85.2		104	84.6		0.131
Yes	397	16.4		44	18.5		152	18.4		182	14.8		19	15.4		
Stroke																
No	2329	96.0		225	94.9		785	95.0		1198	96.8		121	97.6		0.142
Yes	96	4.0		12	5.1		41	5.0		40	3.2		3	2.4		
Activity of daily living (score)																
0	2207	90.8		219	91.6		763	92.4		1119	90.2		106	84.8		0.005
01-Apr	120	4.9		13	5.4		29	3.5		72	5.8		6	4.8		
≥5	103	4.2		7	2.9		34	4.1		49	4.0		13	10.4		
Depression (GMS_level)																
Non-depression	2231	91.8		225	94.1		761	92.1		1131	91.2		114	91.2		0.021

depress 1 or 2 (subcase)	88	3.6		4	1.7		38	4.6		45	3.6		1	0.8		
depress>=3 (cases)	111	4.6		10	4.2		27	3.3		64	5.2		10	8		

Table 7 Multivariate analysis of incident dementia in relation to BMI

				Multivariate-adjusted analysis							
Body mass index	Dementia			Model 1				Model 2			
(kg/m²)	n	(%)	*P**	OR†	95%CI		*P*	OR‡	95%CI		*P*
All											
Underweight/ Normal (<24)	154/1365	11.3	0.9	Ref				Ref			
Overweight (24-<27.9)	89/826	10.8		1.08	0.81	1.45	0.591	1.06	0.79	1.42	0.693
Obese (>=28)	28/239	11.7		1.06	0.68	1.65	0.814	1.00	0.63	1.57	0.994
Total	271/2430	11.2									
(Men)											
Underweight/ Normal (<24)	43/686	6.3	0.01	Ref				Ref			
Overweight (24-<27.9)	42/398	10.6		2.20	1.37	3.54	0.001	2.16	1.33	3.51	0.002
Obese (>=28)	14/104	13.5		2.97	1.47	6.00	0.002	2.63	1.28	5.42	0.009
Total	99/1188	8.3									
											Women
Underweight/ Normal (<24)	111/679	16.3	0.020	Ref				Ref			
Overweight (24-<27.9)	47/428	11.0		0.67	0.45	0.98	0.039	0.66	0.45	0.98	0.038
Obese (>=28)	14/135	10.4		0.55	0.30	1.01	0.054	0.52	0.28	0.97	0.040
Total	172/1242	13.8									

Model 1: OR adjusted for age, sex, smoking status, alcohol drinking, urban-rural areas, education level, income satisfactory, marital status, contacting friends in the community. **Model 2:** OR adjusted for age, sex, smoking status, alcohol drinking, urban-rural areas, education level, income satisfactory, marital status, contacting friends in the community, hypertension status, stroke, activity of daily living, and depression

Table 8 Multivariate analysis of BMI and dementia risk (excluding dementia wave 2 data)

Multivariate-adjusted analysis							
Body mass index	Dementia			Model 2			
(kg/m²)	n	(%)	*P**	OR‡	95%CI		*P*
All							
Underweight/ Normal (<24)	70/1281	5.5	0.290	Ref			
Overweight (24-<27.9)	52/789	6.6		1.34	0.91	1.98	0.140
Obese (>=28)	18/229	7.9		1.52	0.86	2.70	0.149
Total	140/2299	6.1					
Men							
Underweight/ Normal (<24)	21/664	3.2	0.001	Ref			
Overweight (24-<27.9)	28/384	7.3		3.09	1.65	5.77	0.000
Obese (>=28)	10/100	10.0		4.19	1.75	10.03	0.001
Total	59/1148	5.1					
Women							
Underweight/ Normal (<24)	49/617	7.9	0.433	Ref			
Overweight (24-<27.9)	24/405	5.9		0.74	0.43	1.27	0.274
Obese (>=28)	8/129	6.2		0.72	0.32	1.64	0.436
Total	81/1151	7.0					

Table 9 Multivariate analysis of BMI and dementia risk in non-smokers

	cases					**Dementia risk**				**Dementia risk (excluding wave 2)**			
Body mass index	No		Yes			Model 2				Model 2			
(kg/m²)	n	(%)	n	(%)	*P**	OR‡	95%CI		*P*	OR‡	95%CI		*P*
All													
Underweight/Normal (<24)	860	88.4	113	11.6	0.199	Ref				Ref			
Overweight (24-<27.9)	574	90.7	59	9.3		0.86	0.60	1.22	0.399	1.09	0.70	1.72	0.699
Obese (>=28)	170	86.7	26	13.3		1.14	0.70	1.86	0.610	1.56	0.83	2.90	0.166
Total	1604	89.0	198	11.0									
(Men)													
Underweight/ Normal (<24)	339	95.0	18	5.0	0.003	Ref				Ref			
Overweight (24-<27.9)	218	91.6	20	8.4		2.37	1.12	5.02	0.024	2.33	0.98	5.53	0.056
Obese (>=28)	61	83.6	12	16.4		4.36	1.72	11.05	0.002	4.28	1.46	12.53	0.008
Total	618	92.5	50	7.5									
Women													
Underweight/ Normal (<24)	521	84.6	95	15.4	0.032	Ref				Ref			
Overweight (24-<27.9)	356	90.1	39	9.9		0.62	0.40	0.94	0.024	0.80	0.45	1.39	0.420
Obese (>=28)	109	88.6	14	11.4		0.62	0.33	1.17	0.137	0.81	0.35	1.89	0.630
Total	986	86.9	148	13.1									

Table 10 Multivariate analysis of Waist Circumference and dementia risk

Waist Circumference group	cases n	(%)	*P**	Dementia risk Model 2 OR‡	95%CI		*P*	Dementia risk (excluding wave 2 Model 2 OR‡	95%CI		*P*
(All)											
No action	148/1323	11.2	0.993	Ref				Ref			
Action level 1	57/518	11.0		1.07	0.74	1.54	0.739	1.17	0.72	1.90	0.536
Action level 2	66/589	11.2		1.08	0.73	1.58	0.706	1.18	0.70	2.00	0.533
Total	271/2430	11.2									
(Men only)											
No action	79/862	9.2	0.234	Ref				Ref			
Action level 1	11/189	5.8		1.10	0.53	2.31	0.797	1.91	0.80	4.57	0.147
Action level 2	9/137	6.6		1.37	0.59	3.18	0.461	2.35	0.86	6.42	0.097
Total	99/1188	8.3									
(Women only)											
No action	69/461	15.0	0.586	Ref				Ref			
Action level 1	46/329	14.0		1.03	0.66	1.59	0.904	0.90	0.49	1.62	0.719
Action level 2	57/452	12.6		1.01	0.66	1.57	0.951	0.93	0.50	1.71	0.815
Total	172/1242	13.8									

Table 11 Multivariate analysis of Waist Circumference and dementia risk in non-smokers

	Dementia					**Dementia risk**				**Dementia risk (excluding wave 2)**			
Waist circumference	No		Yes			Model 2				Model 2			
Group	n	(%)	n	(%)	*P**	OR‡	95%CI		*P*	OR‡	95%CI		*P*
All													
No action	756	89.3	91	10.7	0.872	Ref				Ref			
Action level 1	394	88.3	52	11.7		1.29	0.87	1.94	0.210	1.40	0.83	2.36	0.213
Action level 2	454	89.2	55	10.8		1.23	0.81	1.87	0.341	1.49	0.85	2.60	0.168
Total	1604	89.0	198	11.0									
(Men)													
No action	397	92.5	32	7.5	0.973	Ref				Ref			
Action level 1	129	92.8	10	7.2		1.78	0.73	4.32	0.204	2.52	0.90	7.06	0.078
Action level 2	92	92.0	8	8.0		1.83	0.69	4.85	0.227	3.19	1.04	9.77	0.042
Total	618	92.0	50	7.5									
Women													
No action	359	85.9	59	14.1	0.496	Ref				Ref			
Action level 1	265	86.3	42	13.7		1.14	0.71	1.80	0.592	1.01	0.54	1.88	0.982
Action level 2	362	88.5	47	11.5		1.05	0.66	1.68	0.834	1.05	0.55	2.01	0.885
Total	986	86.9	148	13.1									

6.4 Discussion

The long-term follow-up prospective cohort study of older people in Anhui, China showed that overweight and obesity in older age were associated with increased risk of late-life dementia in men. The association was dose-dependent and independent of other factors such as age, educational level, lifestyles, CVDRFs, ADL and depressive status. The effects of overweight and obesity measured in older age on increased risk of dementia were more obviously seen in the long-term follow-up. Positive predictions of older age overweight and obesity to incident dementia risk in men were consistently observed in different data analyses for BMI, WC and WC/ √ height with their continuous and different cutting-point groups including separate analysis for non-smokers. However, the study did not observe such positive association in women from categorical BMI or WC even though the continuous BMI data for all cohort members regardless of sex significantly predicted incident dementia. Therefore, contrary to suggestions that overweight and obesity confer protection against morbidities. This study has demonstrated that excess body weight is harmful to health as confirmed by the increased incident dementia risk associated with overweight and obesity in older age.

This study is the first to examine the association of incident dementia with overweight and obesity measured in older age in Low- and Middle-Income Countries (LMICs) and to find a significant positive association in men. Around 60% of the world's dementia cases occur in LMICs (Prince *et al.,* 2015; 16) which coincides with an increasingly older population with overweight and obesity. The data of unique patterns of risk factors (different from western populations) contributes new knowledge of the impact of overweight and obesity in older age on late-life dementia. The Anhui cohort study, unlike most studies, used multiple indicators of older age overweight and obesity including BMI, WC, and WC/√height, with different cut-off points to examine their associations with late-life dementia. The cohort was meticulously followed up for a long period of 10 years which allowed the impact of overweight and obesity on the development of dementia to be detected. The three-wave surveys data allowed for the exclusion of first-year data to limit the effects of reverse causality which was rarely considered in previous studies.

The systematic literature review (chapter three) included 16 studies which examined the association of overweight and obesity in older age (≥65 years) with late-life dementia. Most of them suggested either no association or an inverse relationship. Even in studies that separated data analysis for men and women, there were no positive associations of incident dementia with overweight and obesity. In Denmark, Neergaard et al (2016) followed up 5512 postmenopausal women with mean age >70 years for 15 years and found that overweight (BMI 25-<30) was associated with a decreased risk of dementia (0·75, 0·62-0·81) (6). In Australia, the Health in Men Study (Power et al., 2011) followed up 12047 participants of age 65-84 years for 9·7 years and found that obesity (BMI ≥30) was not associated with dementia (0·82, 0·67-1·01), but overweight (BMI 25-<30) reduced the risk (0·82, 0·70-0·95). These two studies had some limitations. For instance, the study by Neergaard et al lacked standard diagnostic dementia screening at baseline which is likely to have influenced the dementia cases and thus the cause and effect relationship in the study. Besides, the study did not consider a sensitivity analysis such as the exclusion of short term follow up dementia cases. Similarly, the study by Power et al only established the dementia diagnosis of participants from the administrative records information and thus the uncertainty of the validity of specific diagnoses might have affected the detection of dementia cases in their study. In addition, the current health condition of participants at the time of study was self-reported which might have also introduced bias since there was no means of confirmation.

In contrast, the findings from this study are based on data of older Chinese with patterns of CVDRFs and depression different from western populations (Chen *et al.,* 2011). It showed that excess body weight in older age significantly increased the risk of incident dementia in men. The prediction pattern was consistent, irrespective of the different cut-off points of the measures of overweight and obesity from BMI, WC and WC/√height that were used. Interestingly, even when residual confounding was taken into consideration by limiting the analysis to only non-smokers, obesity still significantly predicted incident dementia by more than four folds in men but not in women. Though the confidence intervals were a bit wide which in part may be due to reduced sample size, but the significant effect was retained and the prediction pattern similar. The finding of harmful effect of excess body weights on dementia risk development in old age is consistent with two previous studies that use community-based data in Sweden and USA (Gustafson *et al.,* 2003; Hayden *et al.,* 2006). However, unlike previous studies, a significant positive effect in men which was not previously reported was demonstrated. The findings of a Swedish cohort study of 166 men and 226 women aged ≥70 years did not provide adjusted OR for the whole cohort neither was a male sample used in the multivariate analysis (even though a T-test suggests no difference in dementia risk in the male sample when compared to the control) but a significantly increased risk in the Women with BMI at baseline age 70 years was found (adjusted 1.13, 1.04-1.24) (Gustafson *et al.,* 2003). The findings from the study by Gustafson *et al* (2003) may however be due to the under sampling of men, with the effects related to increased sedentary life of men. This appeared likely considering there more men (58.1%) at the age of 70 years who were overweight (BMI≥25.5± SD).

The data from a USA cohort of 3,264 older people aged ≥65 years showed an increased risk of Alzheimer's disease due to obesity; the sex-stratified analysis revealed significantly increased risk for women but not men (adjusted HR for AD was 1.93, 1.05-3.36 in the cohort and 2.23, 1.09-4.30 for females and 1.48, 0.41-4.18 for males) (Hayden *et al.,* 2016). The study, however, there was also evidence of undersampling of men which showed they comprised only 42.8% of the sample used for analysis. It therefore it is difficult to rule out the effect of sampling bias. However, our data of women in the Anhui cohort did not show such an association probably because of other important prevailing dementia risk factors (e.g., they had much lower levels of education, and other socioeconomic indicators). This requires further investigation.

Furthermore, the evidence from the meta-analysis (Chapter three) supported the findings from the Anhui cohort study in terms of the effect of long term (10 years) follow-up, which made the significant incident dementia risk detectable in the entire cohort for continuous BMI and overweight and obese men. This is because the meta-analysis of the 17 studied populations (Figure 6) stratified by duration of follow-up showed an inverse association of excess body weight in short term studies

(<9 years follow-up) but not over a long follow-up (≥9 years). This was also replicated in studies that investigated AD as outcome (Figure 7) and in those that examined continuous BMI and dementia risk (Figure 9). Also, recent data from a large study (Kivimaki *et al.,* 2017) supported the hypothesis that the length of follow-up impact on BMI and dementia risk relationship. The study by Kivimaki *et al* (2017) examined unpublished individual-participant data from health records of 1.3 million people in Europe, USA, and Asia (mean baseline age of 36.3–55.2 years) and found that the harmful effect of higher BMI on dementia risk was from studies with long term but not short-term follow-up. Similarly, Bowman *et al* (2019) examined the association of obesity with longer-term risks of dementia using primary care data of 257,523 older adults from the UK and found inverse associations of overweight and obesity with dementia in short term follow-Up (<10 years). However, after a longer follow-up between 10-14.9 years, there was 17% increased risk (1.03–1.32) for obesity while the inverse effect for overweight varnished (1.01, 0.90-1.13). Though the study was based on data from a patient population, it still supported the hypothesis that excess body weight in older age is harmful to health through an increased risk of dementia.

This study showed that underweight measured in older age was associated with reduced risk of late-life dementia compared to normal weight (appendix 2). This is inconsistent with the findings of increased risk from studies undertaken in western populations (Nourhashemi *et al.,* 2003; Fitzpatrick *et al.,* 2009). However, we should bear in mind that it may be due to the inverse relationship effect from those dementias identified in a short time after baseline. This is because after excluding year 1 followed-up dementia data, the association was not significant (appendix 12) which may be from reduced dementia cases. Similarly, the association of obesity with reduced risk of dementia in women (Table 7) could be explained by such an inverse association (Table 8 in the second column).

6.4.1 Strengths and Limitations of the study

This study is the first to examine the association of incident dementia with overweight and obesity measured in older age in LMICs and to find a significant positive association in men. Around 60% of world dementia cases occur in LMICs (Prince *et al.,* 2015) and these areas also have higher population figures for those with overweight and obesity and in older age. The data of unique patterns of risk factors (different from the western population) in this thesis contributes new knowledge of the impact of overweight and obesity in older age on late-life dementia. As far as we know, the Anhui cohort data is the first study to measure multiple indicators of older age overweight and obesity by BMI, WC, WC/√height, within different cut-off points to examine their associations with late-life dementia. The cohort has been meticulously followed up for a longer time of 10 years, with a higher response rate. Its three-wave surveys data allowed for the exclusion of the effects of reverse causality while examining the association of dementia with overweight and obesity, which most of the published papers did not consider (Atti *et al.,* 2008; Fitzpatrick *et al.,* 2009; Neergaard *et al.*, 2015).

This study has a few limitations. Firstly, the sample size for the Anhui cohort was large, however, there were wider confidence intervals of dementia risk in different groups of abnormal weights, and particularly, after excluding the wave 2 dementia cases, the reduced OR of dementia in underweight became non-significant. It was therefore unclear whether a larger sample size would have resulted in significant results. Secondly, dementia was diagnosed in the 1st and 2nd wave surveys by the GMS-AGECAT and in the 3rd and 4th wave surveys by the 10/66 dementia research algorithms. The GMS-AGECAT is a part of the 10/66 algorithms. The GMS-AGECAT dementia diagnosis has been validated in western populations and could principally diagnose dementia in middle-income countries but may make over-diagnosis due to educational bias. Over-diagnosed dementia is mainly due to the low educational level. Excluding them from the baseline for incident dementia analysis would reduce the associations of overweight and obesity with incident dementia. Thus, the findings would be more conservative. Thirdly, the study did not stratify data analysis by dementia subtypes since at baseline the variants were not considered separately. Therefore, the comparison of results was made only with those of major studies that investigated excess body weight in relation to dementia in general and not specific subtypes like Alzheimer's disease and vascular dementia. However, the findings of the harmful effects of excessive body weights were consistent with previous studies (Gustafson et al., 2003; Hayden et al., 2006), which showed significant association of both AD and VaD with overweight and obesity.

6.5 Implications and conclusion

The finding of the causal relation of overweight and obesity in older age with increased risk of late-life dementia is of importance for policymaking and practice. This has provided evidence against a paradox that excess body weight in older age could prevent dementia. Even our data of older Chinese women did not show that overweight and obesity significantly reduced the risk of late-life dementia, which was different from those in previous studies. Besides, the combined continuous BMI data for men and women reflected significantly increased risk. This suggests that maintaining normal body weight would reduce dementia within China and internationally.

CHAPTER SEVEN: IMPACTS OF OVERWEIGHT AND OBESITY ON ALL-CAUSE MORTALITY RISK: THE COHORT STUDY

7.1 Introduction

Overweight and obesity are global health issues that affect older adults in both developed and developing Countries (Ng *et al.,* 2014; WHO, 2018). It is well documented that obesity and overweight in middle age increases the risk of all-cause mortality (Adams *et al.,* 2006; Aunne *et al.,* 2016). For instance, the meta-analysis study by (Aunne et al., 2016) found that obesity in midlife (<65 years) was harmful, and that for every 5 unit increase in BMI the relative risk of all-cause mortality was elevated by 21% (1.18-1.25) in never smokers. However, in older age, their impacts are poorly understood and debatable, with most reported findings from cohort studies exhibiting inverse associations of all-cause mortality risk with overweight and obesity (Tamakoshi *et al.,* 2010; Flegal *et al.,* 2013; Baleigoli *et al.,* 2012; Wang *et al.,* 2016). These paradoxical findings have generated several debates on the relationship and possible explanations (Flegal *et al.,* 2010; Keith *et al.,* 2016), including whether they captured true effects or reflected methodological biases (Wang *et al.,* 2016; Di Angelantonio *et al.,* 2016). The debated issues included the use of BMI, confounding particularly by smoking and pre-existing diseases, duration of follow-up, and reverse causality.

Substantial evidence of the inverse association of overweight and obesity with mortality comes from epidemiological studies of midlife and late life using BMI as sole adiposity measure (Tamakoshi *et al.,* 2010; Flegal *et al.,* 2013; Wang *et al.,* 2016). However, the association of BMI in older age with increased mortality may be underestimated since it is limited in detecting accrued abdominal fats (Zamboni *et al.,* 2005). This is true because central adiposity predicts cardiovascular diseases (De Koning *et al.,* 2007) and other morbidities that are strongly associated with elevated mortality risk (Canoy *et al.,* 2004; Abdullah *et al.,* 2010; Huxley *et al.,* 2013). Despite central adiposity increasing the risk of morbidities that shortens survival, the inverse association of waist circumference and adiposity with mortality is also reported (Saito *et al.,* 2012). This suggests that other factors may be involved. Smoking can reduce body weight, and chronic morbidities may lead to reverse causality (Winslow *et al.,* 2015; Aune *et al.,* 2016). Smoking is a major confounder and capable of promoting weight loss (Winslow *et al.,* 2015) and failure to adequately address it, including the residual effects, may lead to falsified association of adiposity with all-cause mortality (Aune *et al.,* 2016). Similarly, pre-existing chronic diseases may involve weight loss and affect the relative risk estimates for all-cause mortality, while shorter follow-up of the participants would not allow sufficient time for deleterious effects of excess body weights to be detected. The issue of reverse causality in studies of BMI and all-cause mortality has been debated (Flegal et al., 2010). However, the reverse causality is increasingly identified as an issue to be addressed if the statistical validity of findings must be improved (Aune *et al.,* 2016; Di Angelantonio *et al.,* 2016). Furthermore, current knowledge on the association of adiposity with all-cause mortality are predominantly from studies in western countries, where health risks associated with adiposity may be different from the non-Caucasians due to ethnic and racial disparities (WHO, 2004; Lim *et al.,* 2011; Haldar *et al.,* 2015). In addition, gender differences in the BMI and all-cause mortality risk is rarely detected from prospective cohort studies (Winter *et al.,* 2014).

Aside from addressing the above issues, one way of testing the hypothesis that overweight and obesity in older age reduces all-cause mortality risk is to study a different population. Therefore, this study investigates the impacts of overweight and obesity in older age (≥65 years) on all-cause mortality by analysing a prospective cohort data from China, which was followed up for 10 years. The study examines sex-disparity in the association, including subgroup of smokers and never-smokers. It also examines all-cause mortality risks in overweight and obese older adults with and without major morbidities, and in those with baseline dementia.

7.2 Methods

7.2.1 The participants in the Anhui cohort study

The studied population which involved 3,336 participants was derived from the Anhui cohort in China. The methods of the Anhui cohort study have been fully reported (chapter four on methodology, and chapter six).

7.2.2 Baseline assessment

Recruited participants for the Anhui cohort study were interviewed and assessed for baseline information as reported in the methodology chapter four (section 4.2.3) and chapter six (section 6.2.2). The Body Mass Index (BMI) of participants (in Kg/m^2) was calculated based on measured weight and height. The recommended Waist circumference (WC) classification groups defining central fat distributions based on waist circumference action levels 1 and 2 for WHO and the Chinese cut-offs for men and women were used (Lean, Han, and Morrison,1995; Chen *et al.,* 2008)

7.2.3 Follow-up of the cohort for mortality

In the follow-up, vital status and death were monitored in the cohort until 2011. The mortality outcome was ascertained from causes of death through electronic registration databases from the local Centres for Disease Control and records from the local resident committees. To explore further causes of death a standard Verbal Autopsy questionnaire were used and six hundred and one death recorded.

7.2.4 Statistical analysis

Out of the 3,336 participants, those of age <65 years (n=419 from the rural sample) were excluded because similar age of populations between urban and rural was needed for comparison. Thus 2,917 of aged ≥65 years were left for analysis. Categorical BMI variables were created according to the BMI classification recommended for Asian Chinese population by the Chinese government (Chen *et al.,* 2008). This is because the Chinese people (the Asians), as compared with the Caucasians, have higher body fat percentage for the same BMI, with increased cardiovascular disease risks (Kanazawa *et al.,* 2002; Chen *et al.,* 2008). Therefore, according to the BMI classification participants with baseline BMI of ≥28 Kg/m2 were classified as obesity, 24-27·9 Kg/m2 as overweight, 18·5-<24 Kg/m2 as normal and <18·5Kg/m2 considered as underweight. Similarly, WC cut-offs for Chinese men and women were also used apart from the WHO cut-offs. The WHO recommended WC classification groups includes no action<94cm, action level one 94-<102cm and action level two ≥102cm for men; while in women they are defined by no action <80cm, action level one 80-<88cm and action level two ≥88cm (Lean, Han, and Morrison, 1995; Chen *et al.,* 2008). The corresponding WC values for the

Chinese people are <85, 85-95 and ≥95cm for men and they are <80, 80-90 and ≥90cm for women for no action, action level one and two (Chen *et al.,* 2008).

The distributions of risk factors among individuals with different groups of BMI classifications were examined using Chi-square test for categorical variables while one-way analysis of variance was used for continuous outcome variables. Mortality rates within cohort over 10 years of follow-up according to BMI and WC categories were calculated in all participants and in men and women separately.

Cox regression models were employed to calculate Hazard ratio (HR) and 95% confidence intervals (95%CIs) of all-cause mortality in relation to baseline BMI categories and WC. All analyses were done in two models. In Model 1, adjustments were made for age, sex, smoking status, alcohol drinking, urban-rural areas. Model 2 adjusted for all covariates in model 1 and additional variables including educational level, activity of daily living and dementia/depression. Covariates that are considered as an intermediate variable between BMI and all-cause mortality base on theory were not included in the models. This included cardiovascular diseases and their risk factors such as heart disease, diabetes, hyperlipidaemia, and stroke. The Cox-regression analyses were performed in stages. The first Cox-regression analysis examined in all participants, the association between categorical BMI and all-cause mortality using normal body weight (18·5-<24 Kg/m2) as reference category with the analysis further stratified by sex (male or female). The second analysis was the same as the first except that participants with pre-existing diseases (baseline diseases) were excluded. These diseases are heart diseases, stroke, diabetes, and depression/dementia. In the third analysis, pre-existing diseases and first three years of follow-up data were excluded. The fourth and fifth analyses were the same as the third (previous one) but in never-smokers and smokers separately. The above Cox regression analyses were replicated using WC based on WHO and the Chinese cut-offs instead of BMI with the first group 'no action' as the reference category. All analyses were performed using SPSS (Windows version 24·0; SPSS Inc., Chicago, Illinois).

7.3 Results

7.3.1 Descriptive statistics

The mean age of the 2,917 included participants was 73.3 years (SD 6.1) and 52.9 % were women. According to the BMI category, there were 5.6% underweight, 33.4% overweight and 9.3% obese participants. The distribution of adiposity by WC action levels (WHO) showed 21.4% and 23.6% of all participants were action level 1 and 2 respectively. Using the Chinese WC cut-offs, 26.9% of males had WC action level 1 and 21.6% had action level 2. The corresponding values for females were 33.1% and 31.8% respectively. The distributions of baseline characteristics of participants with different levels of BMI are shown in Table 12. Participants classified as overweight and obese were more likely to be younger age 65-69 years (38.3% overweight, 36% obese), females (52.4% overweight, 57.7% obese), living in urban areas (65.1% overweight, 63.2% obese), having no education (40.7% overweight, 45.6% obese), smokers (23.3% overweight, 19.1% obese) and alcohol drinkers (17.4% overweight, 15.2% obese).

Participants with underweight were less likely to have cardiovascular diseases and related risk factors compared to the overweight and obese. For instance, 14.7% of underweight older adults had heart disease compared to 17.3% overweight and 16.7% obese. Similarly, the prevalence of diabetes was 4.3% in participants with underweight, 6.9% in overweight and 8.2% in the obese, respectively. The cohort had 588 deaths occurred over the 10 years of follow-up.

7.3.2 Findings of the impact of BMI on mortality from Cox-regression analysis

Table 13 (column 2) shows the number of deaths, person-years, and mortality in all participants and separately in men and women according to the different BMI categories. The mortality rate was the highest (83.9 per 1000 person-years) in the underweight BMI compared to other BMI categories (normal weight 37.5, overweight 25.5, and obesity 29.9 per 1000 person-years). Such patterns of mortality in the BMI groups were similar for the underweight men and women as compared to other BMI categories. The table 13 (columns 3 and 4) showed the adjusted Hazard ratio and 95% CIs for all-cause mortality in relation to four BMI categories. In the whole cohort, obesity (BMI ≥24) was not associated with all-cause mortality after adjusting for covariates in the initial model (0.87, 0.65-1.18) and final model (0.93, 0.69-1.25) when compared with normal weight (BMI 18.5-<24). The findings were similar in men and women. However, in the overweight, the findings were different, as it showed significantly reduced all-cause mortality risk in the Model 1 (0.77, 0.64-0.94) and Model 2 (0.79, 0.65-0.97). Data from the sex-stratified analysis showed no statistical significance for reduced risk of mortality in the overweight, probably due to the small numbers of men and women. Interestingly, underweight was significantly associated with increased risk of all-cause mortality compared to normal weight when the entire cohort was examined in the Model 1 (2.14, 1.63-2.82) and the Model 2 (1.98, 1.50-2.61). The increased risk remained significant after stratifying the analysis by sex.

7.3.2.1 Data analysis after excluding pre-existing diseases and the first 3 years follow-up data

The findings after excluding pre-existing diseases (heart disease, diabetes, stroke and depression/dementia) were similar to the ones for obesity and overweight reported above, (Table 14). While obesity showed no significant association with all-cause mortality, overweight was only significant in the entire cohort and not in men and women. The underweight still significantly increased the risk of all-cause mortality (1.73, 1.20-2.49) when compared to normal weight after adjusting for all covariates. However, the sex-stratified analysis showed that underweight have no significant risk in women (1.26, 0.68-2.33) while the risk remained significantly increased in men (2.09, 1.31-3.35). The results from analysis that excluded pre-existing diseases and first three years data (Table 15) were similar to those in Table 14 but the risk of all-cause mortality in the underweight increased further as evident in results of the analysis in the whole cohort (2.04, 1.25-3.33) and men (2.31, 1.21-4.42) (Table 15).

7.3.2.2 Data analysis in never-smokers versus smokers

Table 16 showed shows the numbers of deaths, person-years, and mortality incidence rates in all never-smokers, and in men and women separately according to the different BMI categories. The mortality rate was 66.2 per 1000 person-years in all underweight never smokers which is highest among all BMI categories, and similar between men and women. The findings from the cox-regression analysis after excluding pre-existing diseases and first three years of data and full adjustments showed no association of obesity or overweight with risk of all-mortality. However, similar to the above findings, the underweight was significantly associated with increased risk of mortality (2.31, 1.25-4.26) in the whole cohort analysed, and also in men (2.82, 1.00-7.99) but not women. The findings in smokers (Appendix 17) showed that while obesity and underweight had no association with mortality, overweight was significantly associated with reduced risk of all-cause mortality (0.49, 0.26-0.92). In sex-stratified data analysis, the findings in men showed a non-significant reduced risk of mortality (probably due to reduced sample size) in obesity (0.80, 0.24-2.68) and overweight (0.55, 0.28-1.09), and non-significant increased risk of mortality in the underweight (2.35, 0.98-5.60). There was no result for women due to the very limited sample of female smokers

7.3.3. Findings of the impact of Waist circumference on mortality from Cox-regression analysis

Tables 17-19 show the results from the analysis of WC (WHO action levels) and all-cause mortality using no action group as the reference category in the whole cohort and those excluding pre-existing diseases and first three years data. In the whole cohort data analysis, while crude mortality rate was highest in the no action group compared to action level 1 and 2, the findings from the cox-regression analysis exhibited non-significant results in all the analysis (Table 17-18) except for women having significantly reduced risk for action level 2 (0.68, 0.50-0.94) in table 17 and after excluding pre-existing diseases (0.61, 0.40-0.94) in table 18. In the data analysis by excluding pre-existing diseases and the first three years, the association of WC with mortality was no longer significant (0.74, 0.43-1.27). The findings in never smokers and smokers (Appendix 18 and 19) both produced non-significant results.

Using the Chinese WC cutting-off action levels for analysis (Table 20), the result showed inverse association (0.74, 0.56-0.98) for men with action level one (WC 85-<95cm) but no association (0.83, 0.59-1.15) for action level 2 (WC≥95cm) when compared to the no action group (WC<85 cm). In women, there was no association (0.95, 0.71-1.26) for action level 1 (WC 80-<90 cm) but the association was inverse (0.65, 0.46-0.92) for action level 2 (WC ≥90cm) when compared to no action group (WC<80) after adjusting for all covariates model 2. These inverse associations remained after excluding pre-existing morbidities (Table 21). However, after excluding pre-existing diseases and first three years data the associations were no longer significant for men (0.82, 0.50-1.32) and women (0.57, 0.31-1.05) with the action level 1 and action level 2 respectively (Table 22)

7.3.4. Findings of BMI and WC and mortality in people with dementia at baseline

Table 23 and 24 shows the result for analysis of BMI, WC and All-cause mortality in people with baseline dementia. There was a total of 210 participants of age ≥65 years who were diagnosed with dementia at baseline out of which 75 died over the 10 years of follow-up. The second columns of Table 23 and 24 show the incidence rate per 1000 person-years according to BMI and WC categories. The Cox regression results from Table 23 based on BMI as the predictor variable showed that underweight was significantly associated with increased risk of all-cause mortality by over two and a half fold after adjustments for covariates in model one (2.64, 1.21-5.75) and in Model 2 (2.51,1.05-6.00). However, there were no significant association of overweight (0.95, 0.48-1.90) and obesity (1.72, 0.64-4.62) with the risk of all-cause mortality after adjusting for all covariates in model 2. The sex-stratified analysis did not yield significant results for any BMI category perhaps due to the small number of participants. The results in appendix 20 based on Waist circumference as the predictor variable (no action as reference) showed no significant association for action level one in both models. The results for action level two showed significantly reduced all-cause mortality risk (0.34, 0.13-0.89) model 1. However, the risk became attenuated and was no longer significant (0.40, 0.15-1.11) in the fully adjusted model two, while the stratification of analysis by sex also did not produce significant findings.

Table 12 Characteristics of participants with different categories of Body Mass Index (BMI): the Anhui cohort study

Body Mass Index (BMI) category											
Variable	**Total participants**		**Underweight (<18.5)**		**Normal BMI (18.5-<24)**		**Overweight (24-<27.9)**		**Obese (>=28)**		**p-value**
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	
Age (years)											
65-69	990	33.9	38	23.3	481	31.9	373	38.3	98	36.0	0.000
70-74	876	30.0	47	28.8	446	29.6	302	31.0	81	29.8	
75-79	598	20.5	33	20.2	309	20.5	196	20.1	60	22.1	
>=80	453	15.5	45	27.6	272	18.0	103	10.6	33	12.1	
Sex											
Women	1542	52.9	92	56.4	783	51.9	510	52.4	157	57.7	0.256
Men	1375	47.1	71	43.6	725	48.1	464	47.6	115	42.3	
Waist Circumference (cm)†											
No Action	1604	55.0	137	84.0	1039	68.9	370	38.0	58	21.3	0.000
Action Level 1	625	21.4	16	9.8	279	18.5	281	28.9	49	18.0	
Action Level 2	688	23.3	10	6.1	190	12.6	323	33.2	165	60.7	
Smoking over the last 2 years											
No	2172	74.5	117	71.8	1088	72.1	747	76.7	220	80.9	0.004
Yes	745	25.5	46	28.2	420	27.9	227	23.3	52	19.1	
Drinking alcohol over the 2 years											
No	2371	81.3	144	88.3	1192	79.0	805	82.6	230	84.6	0.004
Yes	546	18.7	19	11.7	316	21.0	169	17.4	42	15.4	
Urban/rurality											
Urban	1736	59.5	106	65.0	824	54.6	634	65.1	172	63.2	0.000
Rural	1181	40.5	57	35.0	684	45.4	340	34.9	100	36.8	
Educational level											
Illiterate	1350	46.3	82	50.3	748	49.6	396	40.7	124	45.6	0.000

Primary Sch.	361	12.4	25	15.3	183	12.1	112	11.5	41	15.1	
Secondary Sch.	437	15.0	22	13.5	201	13.3	171	17.6	43	15.8	
>=High 2nd Scho	769	26.4	34	20.9	376	24.9	295	30.3	64	23.5	
Main occupation											
Peasant	1180	40.5	59	36.2	679	45.0	342	35.1	100	36.8	0.000
Manual labourer	432	14.8	27	16.6	212	14.1	142	14.6	51	18.8	
Official/teacher	1036	35.5	53	32.5	485	32.2	402	41.3	96	35.3	
No formal job (including business/other/housewife)	269	9.2	24	14.7	132	8.8	88	9.0	25	9.2	
Income satisfactory											
Very satisfactory	325	11.1	14	8.6	147	9.7	128	13.1	36	13.2	0.000
Satisfactory	1487	51.0	85	52.1	734	48.7	513	52.7	155	57.0	
Average	870	29.8	47	28.8	480	31.8	274	28.1	69	25.4	
Poor	235	8.1	17	10.4	147	9.7	59	6.1	12	4.4	
Financial difficulties over the last years											
no	1775	60.9	105	64.4	852	56.5	645	66.2	173	63.6	0.000
yes	1142	39.1	58	35.6	656	43.5	329	33.8	99	36.4	
Satisfied with life/ current living											
Very satisfactory	903	31.0	42	25.8	485	32.2	290	29.8	86	31.6	0.015
Satisfactory	1643	56.3	88	54.0	822	54.5	577	59.2	156	57.4	
Average	328	11.2	27	16.6	180	11.9	97	10.0	24	8.8	
Poor	43	1.5	6	3.7	21	1.4	10	1.0	6	2.2	
Marriage											
Married	2088	71.6	101	62.0	1059	70.2	735	75.5	193	71.0	0.031
Never married	82	2.8	7	4.3	45	3.0	24	2.5	6	2.2	
Divorced	13	0.4	2	1.2	5	0.3	4	0.4	2	0.7	
Widow	734	25.2	53	32.5	399	26.5	211	21.7	71	26.1	
Frequency of visiting children or other relatives											

<Yearly or Never	102	3.5	7	4.3	57	3.8	29	3.0	9	3.3	0.699
At least Monthly or less often	365	12.5	21	12.9	194	12.9	121	12.4	29	10.7	
At least weekly	859	29.4	56	34.4	426	28.2	298	30.6	79	29.9	
Everyday	1591	54.5	79	48.5	831	55.1	526	54.0	155	57.0	
Contacting friends in the community											
<Yearly or Never	150	5.1	16	9.8	84	5.6	43	4.4	7	2.6	0.002
At least Monthly or less often	730	25.0	49	30.1	393	26.1	236	24.4	52	19.1	
At least weekly	1027	35.2	47	28.8	533	35.3	344	35.3	103	37.9	
Everyday	1010	34.6	51	31.3	498	33.0	351	36.0	110	40.4	
Contacting neighbours											
<Yearly or Never	113	3.9	12	7.4	64	4.2	29	3.0	8	2.9	0.007
At least Monthly or less often	859	29.4	50	30.7	439	29.1	309	31.7	61	22.4	
At least weekly	971	33.3	47	28.8	512	34.0	323	33.2	89	32.7	
Everyday	974	33.4	54	33.1	493	32.7	313	32.1	114	41.9	
Help available when needed											
No	158	5.4	12	7.4	93	6.2	43	4.4	10	3.7	0.095
Yes	2759	94.6	151	92.6	1415	93.8	931	95.6	262	96.3	
Hypertension status											
No hypertension (<140*90)	1209	41.4	97	59.5	705	46.8	340	34.9	67	24.6	0.000
Undetected	883	30.3	40	24.5	464	30.8	294	30.2	85	31.3	
Untreated	160	5.5	9	5.5	75	5.0	63	6.5	13	4.8	
Uncontrolled	499	17.1	13	8.0	200	13.3	209	21.5	77	28.3	
Controlled	166	5.7	4	2.5	64	4.2	68	7.0	30	11.0	
Hypercholesterolemia											
No	2651	90.9	155	95.1	1405	93.2	854	87.7	237	87.1	0.000
Yes	239	8.2	5	3.1	91	6.0	114	11.7	29	10.7	
Unknown	27	0.9	3	1.8	12	0.8	6	0.6	6	2.2	
Diabetes											
No	2719	93.6	154	95.7	1414	94.0	906	93.1	245	91.8	0.346

Yes	187	6.4	7	4.3	91	6.0	67	6.9	22	8.2	
Heart diseases											
No	2830	85.2	151	85.3	1506	87.1	914	82.7	259	83.3	0.01
Yes	492	14.8	26	14.7	223	12.9	191	17.3	52	16.7	
Stroke											
No	3189	95.8	172	96.6	1672	96.3	1048	94.8	297	95.8	0.222
Yes	141	4.2	6	3.4	64	3.7	58	5.2	13	4.2	
Activity of daily living (score)											
0	2619	89.8	131	80.4	1336	88.6	902	92.6	250	91.9	0.000
1-.4	150	5.1	8	4.9	92	6.1	35	3.6	15	5.5	
≥5	148	5.1	24	14.7	80	5.3	37	3.8	7	2.6	
Dementia/Depression											
Non-depression/dementia (0.00)	2180	74.6	108	5	1105	50.7	752	34.5	215	9.9	0.000
depress (subcase) 3.12	105	3.6	2	1.9	55	52.4	43	41.0	5	4.8	
depress (case) 3.35	116	4.0	10	8.6	68	5.6	27	23.3	11	9.5	
dementia (subcases) 12.12	306	10.5	21	6.9	156	51.0	103	33.7	26	8.5	
dementia (cases) 12.35	210	7.2	22	10.5	124	59.0	49	23.3	15	7.1	

Table 13 Multivariate-adjusted analysis of BMI and All-cause Mortality (using normal BMI as reference category)

BMI, Kg/m²	Nos.of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1				Model 2			
				HR	95CI		p-value	HR	95CI		p-value
(All)											
Underweight (<18.5)	64/163	762.96	83.9	2.14	1.63	2.82	0.000	1.98	1.50	2.61	0.000
Normal (18.5-<24)	325/1508	8668.61	37.5	Ref				Ref			
Overweight (24-<27.9)	149/974	5847.91	25.5	0.77	0.64	0.94	0.010	0.79	0.65	0.97	0.021
Obese (>=28)	50/272	1688.48	29.6	0.87	0.65	1.178	0.376	0.93	0.69	1.25	0.617
(Men)											
Underweight (<18.5)	35/71	338.54	103.4	2.33	1.61	3.37	0.000	2.06	1.41	3.00	0.000
Normal (18.5-<24)	184/725	4172.82	44.1	Ref				Ref			
Overweight (24-<27.9)	86/464	2753.5	31.2	0.79	0.61	1.02	0.068	0.81	0.62	1.05	0.108
Obese (>=28)	24/115	700.58	34.3	0.83	0.54	1.268	0.384	0.91	0.59	1.40	0.657
(Women)											
Underweight (<18.5)	29/92	424.42	68.33	1.93	1.289	2.901	0.001	1.82	1.21	2.76	0.004
Normal (18.5-<24)	141/783	4495.79	31.36	Ref				Ref			
Overweight (24-<27.9)	63/510	3094.41	20.36	0.75	0.55	1.01	0.058	0.76	0.56	1.02	0.071
Obese (>=28)	26/157	987.9	26.32	0.92	0.60	1.394	0.682	0.91	0.59	1.386	0.648

Model 1 Adjusted for age, sex, smoking status, alcohol drinking and urban areas

Model 2 Adjusted for age, sex, smoking status, alcohol drinking, urban areas, income level educational level Activity of daily living and dementia/depression

Table 14 Associations of BMI with all-cause mortality: the Anhui cohort study (Excluding heart disease, stroke, diabetes and depression/dementia)

BMI, Kg/m²	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 HR	Model 1 95CI		Model 1 p-value	Model 2 HR	Model 2 95CI		Model 2 p-value
All participants											
Underweight (<18.5)	35/106	528.4	66.2	1.86	1.29	2.68	0.001	1.73	1.20	2.49	0.004
Normal(18.5-<24)	196/1038	6078.47	32.2	Ref				Ref			
Overweight(24-7.9)	87/650	4012	21.7	0.75	0.58	0.96	0.025	0.74	0.57	0.95	0.018
Obese (>=28)	26/184	1174.33	22.1	0.74	0.49	1.12	0.157	0.70	0.46	1.05	0.087
(Men)											
Underweight (<18.5)	23/53	265.18	86.7	2.35	1.48	3.72	0.000	2.09	1.31	3.35	0.002
Normal (18.5-<24)	112/517	3048.75	36.7	Ref				Ref			
Overweight (24-<27.9)	51/310	1915.62	26.6	0.77	0.55	1.08	0.125	0.75	0.54	1.05	0.094
Obese (>=28)	16/83	506.74	31.6	0.89	0.53	1.51	0.669	0.87	0.51	1.49	0.619
(Women)											
Underweight (<18.5)	12/53.	263.23	45.59	1.31	0.71	2.42	0.389	1.26	0.68	2.33	0.469
Normal (18.5-<24)	84/521	3029.72	27.73					Ref			
Overweight (24-<27.9)	36/340	2096.38	17.17	0.70	0.47	1.03	0.073	0.69	0.46	1.03	0.068
Obese (>=28)	10/101	667.59	14.98	0.56	0.29	1.086	0.086	0.51	0.26	0.991	0.047

Table 15 Associations of BMI with all-cause mortality: the Anhui cohort study (Excluding pre-existing diseases and first 3 years data)

BMI, Kg/m²	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 HR	95CI		p-value	Model 2 HR	95CI		p-value
All participants											
Underweight (<18.5)	20/77	499.41	40.0	2.16	1.32	3.51	0.002	2.04	1.25	3.33	0.004
Normal (18.5-<24)	106/836	5914.59	17.9	Ref				Ref			
Overweight (24-<27.9)	52/551	3953.14	13.2	0.79	0.57	1.10	0.163	0.78	0.56	1.08	0.137
Obese (>=28)	17/162	1157.66	14.7	0.87	0.52	1.45	0.596	0.79	0.47	1.33	0.378
(Men)											
Underweight (<18.5)	12./38	245	49.0	2.66	1.40	5.05	0.003	2.31	1.21	4.42	0.012
Normal (18.5-<24)	56/417	2947.76	19.0	Ref				Ref			
Overweight (24-<27.9)	31/262	1878.64	16.5	0.88	0.56	1.36	0.559	0.86	0.55	1.34	0.502
Obese (>=28)	9./71	491.71	18.3	0.98	0.48	1.99	0.958	0.92	0.45	1.90	0.830
(Women)											
Underweight (<18.5)	8./39	254.41	31.45	1.59	0.75	3.40	0.230	1.59	0.73	3.44	0.242
Normal (18.5-<24)	50/419	2966.83	16.85	Ref				Ref			
Overweight (24-<27.9)	21/289	2074.49	10.12	0.66	0.40	1.11	0.118	0.64	0.38	1.08	0.095
Obese (>=28)	8./91	665.95	12.01	0.72	0.34	1.52	0.387	0.63	0.30	1.343	0.232

Pre-existing diseases: heart disease, stroke, diabetes, and depression/dementia

Table 16 Associations of BMI with all-cause mortality in non-smokers: (Excluding pre-existing diseases, first 3 years data)

BMI, Kg/m²	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 † (Non-smokers) HR	95CI		p-value	Model 2 ‡ (Non-smokers) HR	95CI		p-value
All participants											
Underweight (<18.5)	35/106	528.4	66.2	2.35	1.28	4.32	0.006	2.31	1.25	4.26	0.007
Normal (18.5-<24)	196/1038	6078.5	32.2	Ref				Ref			
Overweight (24-<27.9)	87/650	4012	21.7	0.96	0.64	1.43	0.827	0.94	0.63	1.41	0.773
Obese (>=28)	26/184	1174.3	22.1	0.88	0.48	1.63	0.687	0.79	0.42	1.48	0.462
(Men)											
Underweight (<18.5)	23/53	265.18	86.7	2.82	1.05	7.61	0.041	2.82	1.00	7.99	0.051
Normal (18.5-<24)	112/517	3048.8	36.7	Ref				Ref			
Overweight (24-<27.9)	51/310	1915.6	26.6	1.27	0.69	2.37	0.444	1.30	0.70	2.44	0.408
Obese (>=28)	16/83	506.74	31.6	1.20	0.49	2.96	0.694	1.12	0.44	2.85	0.814
(Women)											
Underweight (<18.5)	12/53.	263.23	45.59	1.99	0.92	4.31	0.080	1.95	0.88	4.30	0.099
Normal (18.5-<24)	84/521	3029.7	27.73	Ref				Ref			
Overweight (24-<27.9)	36/340	2096.4	17.17	0.77	0.45	1.30	0.328	0.74	0.43	1.26	0.263
Obese (>=28)	10/101	667.59	14.98	0.66	0.28	1.552	0.338	0.58	0.25	1.39	0.221

Table 17 Multivariate analysis of WC and All-cause mortality (no action as reference category)

WC (cm)	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 HR	95CI		p-value	Model 2 HR	95CI		p-value
All participants											
No action	383/1604	8948.85	42.8	Ref				Ref			
Action level one	110/625	3680.72	29.9	0.89	0.71	1.11	0.307	0.93	0.74	1.16	0.492
Action level two	95/688	4338.39	21.9	0.72	0.56	0.93	0.010	0.79	0.61	1.02	0.067
(Men)											
No action	261/1005	5660.88	46.1	Ref				Ref			
Action level one	39/217	1317.51	29.6	0.84	0.59	1.20	0.348	0.88	0.62	1.25	0.471
Action level two	29/153	987.05	29.4	0.91	0.61	1.37	0.656	1.01	0.66	1.52	0.982
(Women)											
No action	122/599	3287.97	37.10	Ref				Ref			
Action level one	71/408	2363.21	30.04	0.94	0.70	1.27	0.700	0.98	0.73	1.32	0.895
Action level two	66/535	3351.34	19.69	0.64	0.46	0.87	0.004	0.68	0.50	0.94	0.020

Model 1: age, sex, smoking status, alcohol drinking and urban areas; **Model 2**: age, sex, smoking status, alcohol drinking, urban areas, income level educational level Activity of daily living and dementia_dep

Table 18 Multivariate-adjusted analysis of WC and All-cause Mortality (excluding heart disease, stroke, diabetes and depression/dementia)

WC (cm)	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 †				Model 2 ‡			
				HR	95CI		p-value	HR	95CI		p-value
All participants											
No action	235/1133	6565.71	35.8	Ref				Ref			
Action level one	52/407	2425.06	21.4	0.76	0.55	1.04	0.086	0.77	0.56	1.07	0.115
Action level two	57/438	2802.44	20.3	0.76	0.55	1.05	0.100	0.80	0.57	1.11	0.186
(Men)											
No action	163/733	4281.92	38.1	Ref				Ref			
Action level one	18/127	797.34	22.6	0.71	0.43	1.19	0.192	0.76	0.46	1.26	0.286
Action level two	21/103	657.03	32.0	1.08	0.67	1.76	0.749	1.15	0.70	1.89	0.576
(Women)											
No action	72/400	2283.79	31.53	Ref				Ref			
Action level one	34/280	1627.72	20.89	0.78	0.51	1.18	0.233	0.74	0.49	1.13	0.164
Action level two	36/235	2145.42	16.78	0.60	0.39	0.91	0.016	0.61	0.40	0.94	0.025

Model 1: age, sex, smoking status, alcohol drinking and urban areas; **Model 2**: age, sex, smoking status, alcohol drinking, urban areas, income level educational level Activity of daily living

Table 19 Multivariate-adjusted analysis of WC and All-cause Mortality (excluding pre-existing diseases and first 3 years data)

WC (cm)	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 †				Model 2 ‡			
				HR	95CI		p-value	HR	95CI		p-value
All participants											
No action	125/915	6365.57	19.6	Ref				Ref			
Action level one	33/37	2396.35	13.8	0.84	0.56	1.26	0.389	0.85	0.57	1.28	0.442
Action level two	37/195	2762.88	13.4	0.83	0.55	1.26	0.388	0.87	0.57	1.33	0.517
(Men)											
No action	84/594	4138.52	20.3	Ref				Ref			
Action level one	12/108	787.5	15.2	0.79	0.42	1.49	0.466	0.88	0.47	1.66	0.686
Action level two	12./1986	637.08	18.8	1.00	0.53	1.9	0.997	1.04	0.54	2.01	0.897
(Women)											
No action	41/321	2227.04	18.41	Ref				Ref			
Action level one	21/229	1608.84	13.05	0.84	0.49	1.43	0.512	0.79	0.46	1.35	0.380
Action level two	25/288	2125.08	11.76	0.74	0.44	1.26	0.269	0.74	0.43	1.27	0.278

Pre-existing diseases: heart disease, stroke, diabetes and depression/dementia

Table 20 Multivariate analysis of WC (Chinese cut-offs) and All-cause mortality

WC (cm)	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 †				Model 2 ‡			
				HR	95CI		p-value	HR	95CI		p-value
(Men)											
WC<85	187/631	3408.88	54.9	Ref				Ref			
WC85-<95	79/397	2404.26	32.9	0.73	0.55	0.96	0.026	0.74	0.56	0.98	0.035
WC >=95	63/347	2156.3	29.2	0.75	0.54	1.05	0.090	0.83	0.59	1.15	0.264
(Women)											
WC <80	122/599	3287.97	37.10	Ref				Ref			
WC 80-<90	86/514	3025.49	28.43	0.91	0.69	1.20	0.497	0.95	0.71	1.26	0.706
WC >=90	51/429	2689.06	18.97	0.61	0.43	0.85	0.004	0.65	0.46	0.92	0.016

Model 1 †Adjusted for age, smoking status, alcohol drinking and urban areas

Model 2 ‡Adjusted for age, smoking status, alcohol drinking, urban areas, income level educational level Activity of daily living and dementia_dep

Table 21 Multivariate analysis of WC (Chinese cut-offs) and All-cause mortality (excluding heart disease, stroke, diabetes and depression/dementia)

WC (cm)	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 †				Model 2 ‡			
				HR	95CI		p-value	HR	95CI		p-value
(Men)											
WC<85	118/466	2283.79	51.7	Ref				Ref			
WC85-<95	48/281	1761	27.3	0.64	0.45	0.92	0.017	0.65	0.45	0.94	0.021
WC >=95	36/216	1367.61	26.3	0.70	0.45	1.07	0.096	0.77	0.50	1.19	0.240
(Women)											
WC <80	72/400	2283.79	31.53	Ref				Ref			
WC 80-<90	45/356	2122.48	21.20	0.80	0.54	1.16	0.239	0.78	0.53	1.14	0.201
WC >=90	25/259	1659.65	15.06	0.53	0.33	0.85	0.008	0.53	0.33	0.86	0.010

Model 1 †Adjusted for age, sex, smoking status, alcohol drinking and urban areas

Model 2 ‡Adjusted for age, sex, smoking status, alcohol drinking, urban areas, income level educational level Activity of daily living

Table 22 Multivariate analysis of WC (Chinese cut-offs) and All-cause mortality (excluding pre-existing diseases and first 3 years data)

WC (cm)	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 †				Model 2 ‡			
				HR	95CI		p-value	HR	95CI		p-value
(Men)											
WC<85	56/361	2491.02	22.5	Ref				Ref			
WC85-<95	31/246	1734.26	17.9	0.78	0.48	1.26	0.307	0.82	0.50	1.32	0.405
WC >=95	21/181	1337.83	15.7	0.71	0.40	1.25	0.233	0.80	0.45	1.43	0.452
(Women)											
WC <80	41/321	2227.04	18.41	Ref				Ref			
WC 80-<90	30/296	2099.1	14.29	0.93	0.57	1.50	0.758	0.91	0.56	1.47	0.688
WC >=90	16/288	1635.54	9.78	0.60	0.33	1.09	0.095	0.57	0.31	1.05	0.073

Model 1 †Adjusted for age, sex, smoking status, alcohol drinking and urban areas

Model 2 ‡Adjusted for age, sex, smoking status, alcohol drinking, urban areas, income level educational level Activity of daily living

Table 23 Multivariate-adjusted analysis of BMI and All-cause Mortality in those with dementia

BMI, Kg/m²	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 †				Model 2 ‡			
				HR	95CI		p-value	HR	95CI		p-value
(All)											
Underweight (<18.5)	11/22	845.66	13.0	2.64	1.21	5.75	0.015	2.51	1.05	6.00	0.039
Normal (18.5-<24)	47/124	9995.66	4.7	Ref				Ref			
Overweight (24-<27.9)	12/49	6599.84	1.8	0.69	0.36	1.31	0.258	0.95	0.48	1.90	0.892
Obese (>=28)	5/15	1887.93	2.6	1.10	0.42	2.87	0.840	1.72	0.64	4.62	0.279
Total	75/210	19329.11	3.9								
(Men)											
Underweight (<18.5)	4./16	358.15	11.2	2.37	0.62	9.11	0.210	2.96	0.58	15.04	0.191
Normal (18.5-<24)	23/46	4863.40	4.7	Ref				Ref			
Overweight (24-<27.9)	7/19	3069.49	2.3	0.84	0.35	2.01	0.692	1.25	0.48	3.27	0.644
Obese (>=28)	2/14	768.43	2.6	1.79	0.38	8.38	0.462	3.36	0.64	17.61	0.151
(Women)											
Underweight (<18.5)	7/16	487.51	14.4	2.98	1.10	8.08	0.032	2.49	0.60	10.30	0.208
Normal (18.5-<24)	24/78	5132.26	4.7	Ref				Ref			
Overweight (24-<27.9)	5/30	3530.35	1.4	0.58	0.22	1.56	0.278	0.79	0.27	2.32	0.667
Obese (>=28)	3/11	1119.51	2.7	0.88	0.26	2.99	0.840	1.56	0.43	5.733	0.500

Table 24 Multivariate-adjusted analysis of WC and All-cause Mortality in those with dementia (no action as reference)

Waist circumference Group (cm^2)	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 †				Model 2 ‡			
				HR	95CI		p-value	HR	95CI		p-value
(All)											
No action	54/134	573.69	94.1	Ref				Ref			
Action level 1	16/41	181.27	88.3	1.27	0.70	2.31	0.428	1.28	0.69	2.35	0.431
Action level 2	5/35	193.42	25.9	0.34	0.13	0.89	0.027	0.40	0.15	1.11	0.078
(Men only)											
No action	31/66	264.23	117.3	Ref				Ref			
Action level 1	5/6	25.35	197.2	1.97	0.69	5.59	0.203	1.33	0.39	4.56	0.654
Action level 2	0/3	23.37	0.0	No	data			No	data		
(Women only)											
No action	23/68	309.46	74.3	Ref				Ref			
Action level 1	11/55	155.92	70.5	1.22	0.55	2.68	0.624	1.40	0.59	3.30	0.443
Action level 2	5/32	170.03	29.4	0.40	0.15	1.05	0.064	0.56	0.17	1.81	0.334

7.4 Discussion

This Anhui cohort study which assessed the impacts of overweight and obesity on all-cause mortality did not find significant protective effects in older adults over the 10 years of follow-up, except a significantly reduced risk in smokers who were overweight when compared to normal weight. It appeared initially that overweight, and not obesity could confer protection against the risk of death when the whole cohort data was examined. However, after accounting for the effects of reverse causality, pre-existing morbidities and smoking status, overweight was no longer significantly related to a reduced risk of all-cause mortality. The study also comprehensively demonstrated that underweight older adults have significantly increased risk of all-cause mortality when compared to their normal weight counterparts. The sex-stratified analysis showed that this harmful effect was stronger in men and not in women, thereby contributing to the finding of effect modification by gender that is rarely reported in the literature.

7.4.1 Strengths and Limitations of the study

One of the strengths of the study is the use of data from a prospective cohort study design with long term follow-up of 10 years. There are limited long-term studies to investigate obesity consequences in older age since it takes a long time for the effects to manifest. The Anhui cohort study had a 10-year follow-up of the older people, which made it suitable for investigating all-mortality outcome in overweight and obesity.

This study adds new data from LMICs. The literature on the impact of obesity in older adults on all-cause mortality is predominated by evidence from HICs (Winter *et al.,* 2014). Therefore considering the lack of evidence from prospective cohort studies in developing countries, this finding from the Chinese population in this thesis has added new evidence and expanded the knowledge on all-cause mortality in relation to overweight and obesity as well as underweight in older population.

In this Anhui cohort study, the BMI and WC were measured, rather than self-reported, thereby helping to limit bias. Moreover, this study used the recommended cut-off BMI for the Chinese (Chen, 2008) to classify overweight and obesity since Asians have higher cardiovascular diseases risks per unit BMI compared with the Caucasians. The study also used WC which is hardly used in most studies of obesity and all-cause mortality in older adults. Research using computed tomography to compare body fats of older adults with middle-age adults showed higher abdominal fats, including in those with lower body weights (Zamboni *et al.,* 2005). In addition, BMI may not accurately distinguish between general body fats and ectopic fats, while findings suggest WC or waist-to-hip circumference may help overcome such limitation (Srikanthan *et al.,* 2009). Previous findings from a meta-analysis of 10 studies showed that WC was a better index of abdominal adiposity and discriminator of health risks than BMI (Lee *et al.,* 2008). Therefore, the use of measured WC in addition to BMI strengthened the evidence from this study.

This study followed stringent analytical strategy in limiting the threats to the validity of the findings. One of the major challenges for epidemiological studies of obesity in older adults is choosing the appropriate analytical strategy and executing it in a manner that will limit the common threats to validity in the findings. The main threats to validity from the statistical perspectives (Szklo and Nieto, 2014, p.227-

296) include over-adjustments, choice of covariates for statistical model, issue of confounding including residual effect due to smoking, absence of stratified analysis, and reverse causation owing to pre-existing diseases. All these potential threats to validity where considered in the study to ensure reliable findings. For instance, it was considered that at baseline older adults entered the Anhui cohort study with some illnesses and 25% of the cohort was smokers which had the potential to contribute to the risk of all-cause mortality. Therefore, such pre-existing morbidities were excluded in some of the analysis while data in never-smokers and smokers were analysed separately to limit bias. This is in addition to the exclusion of the first few years of data to remove the effects of reverse causation. Analyses were also stratified by gender to examine the effect of obesity on all-cause mortality in men and women. These were in addition to the use of two regression models for analysis, with carefully chosen covariates based on literature and practice. All these contributed to useful findings with minimal bias.

There were notable limitations of the study**.** There was a smaller sample size in the study of BMI, WC and all-cause mortality in people with dementia which limited further analysis. For instance, only data of 210 older adults with dementia was used in the analysis due to fewer cases at baseline, which gave a larger 95%CI range. Considering this small sample size, it was difficult to further exclude other pre-existing morbidities that could compete for mortality with dementia while stratification could only yield non-significant results.

Another limitation of the study is that it focused on only all-cause mortality without examining the impacts of overweight and obesity on disease-specific mortality such as cardiovascular disease mortality. This was because the Anhui cohort lacked data on disease-specific mortality to help explore the relationship and possibly add to its evidence.

The Anhui cohort study had no previous weight history of participants before baseline and there were no repeated measurements in the follow-up to help ascertain the impact of change in weight on all-cause mortality. The use of a single baseline measure of BMI to investigate all-cause mortality risk is popular, even in large scale epidemiological studies (Flegal *et al.,* 2013; Di Angelantino *et al.,* 2016). However, if the Anhui cohort had the weight history of participants, it would have been possible to examined weight change over time and all-cause mortality risk. Further study with data on weight change could help examine the impact on all-cause mortality.

7.4.2 All-cause mortality in those with major morbidities

The overall findings from the analysis of Anhui cohort data with 10 years follow-up did not support the protective effects of excess weight on all-cause mortality risk after accounting for pre-existing chronic illnesses and reverse causality. However, the initial findings in older adults with major morbidities including heart disease, stroke, diabetes and depression/dementia were consistent with those in several studies that reported inverse associations in older adults (Beligoli *et al.,* 2012; Dahl *et al.,* 2013; Takata et al., 2013; Yamazaki et al., 2017). For instance, a Swedish cohort study of older adults (age 70-95 years) by Dahl *et al* (2013) showed that all-cause mortality risk was significantly reduced by 20% for overweight (RR 0.80, 0.67-0.95) in over a period of 18 years when compared to normal/underweight group.

However, they found no significant all-cause mortality risk for obesity (RR 0.93, 0.71-1.22) after adjustments for age, sex, education, and multi-morbidity. The findings of the Swedish cohort study were similar to those in the Anhui cohort of older adults in China (≥65 years), over 10 years of follow-up (overweight, 0.79, 0.65-0.97, and obesity 0.93, 0.69-1.25) which adjusted for age, sex, smoking status, alcohol drinking, urban areas, income level educational level, Activity of daily living and dementia/depression (Table 13). However, the stratified analysis by sex did not produce significant association of overweight with all-cause mortality (perhaps due to small size), except for the inverse effect of obesity in women and increased mortality risk in underweight older adults.

If conclusions on impacts of adiposity on all-cause mortality were made solely on findings from the Anhui cohort data analysis of those with major morbidities, then it would suggest that overweight and obesity prolong survival as reported by several studies (Beligoli *et al.,* 2012; Dahl *et al.,* 2013; Yamazaki *et al.,* 2017). However, in addition to the issue of pre-existing morbidities, there is possible bias from lack of stratified analysis for smokers versus non-smokers and reverse causality that disguise findings of overweight, obesity and all-cause mortality (Di Angelatonio *et al.,* 2016). To address these issues the Anhui cohort study carried further analysis which excluded pre-existing diseases and reverse causality and stratified the findings by smoking status.

7.4.3 All-cause mortality in those without major morbidities

Some investigators who examined the association between adiposity and all-cause mortality (Zamboni *et al.,* 2005; Mazza *et al.,* 2008; Joshy *et al.,* 2014; Di

Angelantonio *et al.,* 2016) suggested that the inverse associations of excess weight and all-cause mortality could be due to methodological bias from smoking and pre-existing morbidities. However, it was argued from studies reporting inverse associations of obesity and all-cause mortality (Flegal *et al.,* 2010; Beleigoli *et al.,* 2012; Wang *et al.,* 2016) that they make no differences in the findings between general population (Wang *et al.,* 2016) and older adults (Beleigoli *et al.,* 2012; Flegal et al., 2013). Indeed, the findings of inverse effect remained significant from the Anhui cohort study (China) after adjusting for smoking and excluding pre-morbidities. However, when residual effects of smoking and reverse causality were addressed in the further analysis that excluded pre-existing morbidities and first three years data, the inverse association of excess weights with all-cause mortality become not significant for overweight (0.78, 0.56-1.08) and obesity (0.79, 0.47-1.33). The findings were similar in subgroup analysis for never smokers with overweight (0.94, 0.63-1.41) and obesity (0.79, 0.42-1.48) whilst underweight men remained significantly associated with all-cause mortality risk (2.82, 1.00-7.99) and not women (1.95, 0.88-4.30). This, therefore, refuted the hypothesis that excess body weights prolong survival in older adults. It also supported increased all-cause mortality risk in underweight older adults even though it was observed only in men over the 10 years of follow-up.

The validity of excluding the first three years data to address reverse causality was previously challenged by Flegal *et al* (2010). However, recent evidence from large scale studies including that by Global BMI Mortality collaboration in four contents (Aunne *et al.,* 2016; Di Angelantonio *et al.,* 2016) demonstrated that the residual effects of smoking are better addressed by limiting analysis to never smokers, whilst reverse causality should be curtailed by excluding 3-5 years data. The authours also concluded that such a statistical approach improves the validity of findings of the association between adiposity and all-cause mortality. The findings from the Anhui cohort is congruent with some cohort studies that shared similar results (Berrho *et al.,* 2010; Clack *et al.,* 2014), but contrary to others, for instance, a previous study by De Hollander *et al* (2012) that suggested increased risk of mortality in relation to continuous BMI and concluded that excess weights were protective since minimum BMI for survival was within the overweight range. Further studies will, however, be required to examine the lack of significant association in older Chinese population and why underweight men and not women had increased all-cause mortality risk.

7.4.3.1 All-cause mortality risk in underweight without major morbidities

The Anhui cohort study comprehensively demonstrated that underweight was significantly associated with all-cause mortality. The evidence of significantly increased all-cause mortality risk in Chinese men and not women is an important addition to knowledge on effect modification by gender which is rarely reported in the literature. Similar findings were previously reported but this was in underweight middle age European Dutch men and women (aged 30-54 years), where the elevated risk in men was ascribed to early mortality particularly in smokers with chronic lung cancer (Seidell *et al.,* 1997). The study in middle-aged Asian Korean men and women (35-59 years) reported no association of underweight with all-cause mortality in never-smokers after 14 years follow-up. However, the Anhui cohort study demonstrated a significantly increased risk in underweight older men which was independent of baseline smoking and pre-existing chronic morbidities even after limiting the effects of reverse causality and adjustment for several confounding factors.

It was previously postulated that lean body mass, and not low-fat mass, was responsible for the high mortality detected in underweight older adults (Allison *et al.,* 1997). The plausible explanation for the association of underweight with all-cause mortality, which is consistent with this hypothesis, is embedded in the interesting work by Morley and several other researchers on sarcopenia and all-cause mortality (Morley, 1996; Omran and Morley, 2000; Thomas *et al.,* 2000; Morley *et al.,* 2010; Morley *et al.,* 2011; Morley, 2012; Morley and Anker, 2014). Underweight measured by low BMI (<18.5 Kg/m^2) is one of the indicators, aside the data on food intake, serum protein analysis and delayed hypersensitivity tests, for diagnosis of malnutrition which predicts poor health outcomes and high mortality risk in older adults (Larsson *et al.,* 1990; Omran and Morley, 2000 ;Thomas *et al.,* 2000). Malnourished elderly subjects are prone to sarcopenia which is characterised by reduced muscle mass that affects their mobility and clinical outcome (Morley *et al.,* 2011). Sarcopenia is strongly associated with physical inactivity and aging particularly where there is physiological anorexia leading to decline in food intake and reduced nutrients to maintain muscle mass and strength (Morley, 1996; Morley *et al.,* 2010; Morley, 2012).

Sarcopenia is associated with several health consequences such as frailty, disability, poor health and all-cause mortality risks (Morley and Anker, 2014). The recent evidence from systematic reviews and meta-analysis of health outcomes of sarcopenia in middle age and elderly men and women by Beaudart *et al* (2017) showed that it was significantly associated with increased functional decline (3.03, 1.80-5.12) and all-cause mortality (3.60, 2.96-4.37) with higher effects observed in those ≥79 years compared to ≤79 years. Furthermore, the meta-analysis on Sarcopenia as a predictor of all-cause mortality among community-dwelling older people (≥65 years) by Liu *et al* (2017) found increased all-cause mortality is those with sarcopenia (1.60, 1.24-2.06) compared to those without sarcopenia. The risk increased in subgroup analyses for studies that used anthropometric measures (2.26, 1.30-3.92) versus dual energy x-ray (1.82, 1.04-3.18, and for short (<5 years) follow-up (2.26, 1.30-3.92) versus long (≥5 years) follow-up (1.52, 1.14-2.01). These findings clearly showed that sarcopenia, which may be considered as an umbrella term for underweight in the elderly due to weight loss associated with loss of body mass, is a significant risk factor for all-cause mortality. This provides a possible explanation for the observed association of underweight with all-cause mortality risk in older adults, particularly where the effects of smoking and pre-existing morbidities as well as reverse causality have been discounted.

7.4.4 All-cause mortality in people conditioned to a major morbidity

The findings from the study of all-cause mortality in a population of patients by Garcia-Ptacek *et al* (2014) suggested that overweight and obesity confer protection against all-cause mortality in those with dementia, thereby supporting the obesity paradox hypothesis on beneficial effects of adiposity. The Anhui cohort study with long follow-up was analysed to examine the impacts of body weights in those with dementia in order to test the obesity paradox hypothesis which posit that overweight and obese older adults conditioned to a major morbidity such as dementia are associated with reduced risk of mortality or may live longer than their normal weight counterparts. This study found that while underweight significantly increased the risk of mortality by two and a half fold in people with dementia, there was no evidence for obesity paradox as suggested by the lack of significant results after adjusting for all covariates in the final model for both obesity (1.72, 0.64-4.62) and overweight (0.95, 0.48-1.90) as defined by BMI. Similar outcome was observed using WC. However, the limited sample size due to fewer dementia cases at baseline could not allow for comprehensive analysis for more robust findings. Therefore, reverse causality, residual smoking and co-existing chronic diseases were not addressed in the data analysis for mortality in participants with dementia. If this was done, the findings would have been different. These shortcomings highlight the need for further study using a large sample with dementia cases.

7.5 Implications and Conclusion

The findings from this Chapter study have several implications for policymaking, practice and further research. The study found no evidence in support of the beneficial impact of overweight and obesity on all-cause mortality in healthy older adults or those without major morbidities after discounting the effects of reverse causality. The study supported the view (Di Angelantonio *et al.,* 2016; Xu *et al.,* 2018) that the observed inverse association between adiposity and mortality in older adults could be a product of methodological bias. It remains to be further tested if overweight and obese older people with dementia may live longer than their normal weight counterparts after a prolonged follow-up from studies with large sample sizes of the cohort. However, this appears unlikely since reverse causality tends to disguise findings on the impacts of excess weights on all-cause mortality in those with major morbidities. Although the harmful consequences of excess weights could not be detected from this study, the findings suggest that there is need for increased focus on the underweight population, particularly the Chinese older men who showed stronger risk of increased all-cause mortality as evident in most of the analyses. In addition, while the lack of association in women warrants further study, there is need for understanding of the mechanism involved in the increased risk of all-cause mortality in underweight older Chinese men to guide public health intervention and prevention for prolonged survival. Additionally, the study showed a reduced risk of all-cause mortality in overweight smokers compared to their normal weight counterparts, thereby suggesting caution in considering weight loss in this population group. However, since it is unclear if this association is causal or represents a true biological effect, more research would be needed to clarify this relationship. Furthermore, further cohort studies which are followed for similar or even longer duration with tracked measured weight history from midlife to late life may provide useful data to explore the impacts of excess weights on all-cause mortality. This is important since recent findings (Yu et al., 2017; Xu et al., 2018) using such data has shown some promising outcome of limiting reverse casualty and detecting the harmful effects of excess BMI on all-cause mortality.

CHAPTER EIGHT: THE IMPACTS OF OVERWEIGHT AND OBESITY ON DEMENTIA AND SURVIVAL: FOCUS GROUP STUDY

8.1 Introduction

The findings of the effects of overweight and obesity in younger and middle age population support increased dementia risk (Albanese *et al.,* 2017) and all-cause mortality risk (Whitmer *et al.,* 2005; Aune *et al.,* 2016). However, the contrary is observed for overweight and obesity in older age. Recent studies have shown that older people with overweight and even obesity may have a reduced risk of dementia in future (Fitzpatrick *et al.,* 2009; Neergaard *et al.,* 2016) and prolonged survival (Dahl *et al.,* 2013; Wang *et al.,* 2016). In addition, while data of positive association between overweight/obesity and health outcome such as dementia and mortality are rare, some studies (De Hollander *et al*., 2012; Aune *et al.,* 2016) have detected increased risk of death for people with obesity while others (Tamakoshi *et al.,* 2010; Winter *et al.,* 2014)) have concluded that overweight was not associated with all-cause mortality.

This follows an existing debate on whether older adults with overweight had a lower mortality than their normal weight counterparts (Flegal *et al.,* 2013; Wang *et al.,* 2016). If overweight and obesity at older age protects against early deaths and the risk of developing dementia, it would be of public health importance in guiding strategies to curb the problems. However, findings so far on the impact of obesity at older age on late-life dementia (Fizpatrick *et al.,* 2009; Hughes *et al.,* 2009; Neergaard *et al.,* 2016) and survival (De Hollander *et al.,* 2012; Dahl *et al.,* 2013; Wang et al., 2016) have remained controversial with prevention and clinical management of adiposity in older adults still debatable (Walters *et al.,* 2013; Starr and Bales, 2015). Besides, existing knowledge emanates from quantitative research and the findings from qualitative studies are lacking. Thus, the views of older adults on the impact of overweight and obesity in older age on dementia risk and survival are unknown.

Therefore, as part of a larger ongoing doctoral project on the risk factors and health effects of overweight and obesity in older adults, this study will explore the views of older adults on effects of overweight and obesity on dementia risk and all-cause mortality. It will also investigate the perspectives of older adults on the body weight associated with better survival, and how body weight may be managed. The findings could help advance knowledge and understanding of obesity and health risks and guide public health strategies on reducing dementia and extending survival in older age.

8.2 Methods

8.2.1 Study design

The rationale for the focus group was explained in chapter four (methodology). The design is like the single-category focus group design described by Krueger and Casey (2014, p.27-31) which targets a group or sub-population of interest in line with the main objective of the research. The target group for this focus group study is older adults residing within the community. However, unlike a typical single category design which uses 3-4 focus groups of the same participants to achieve theoretical saturation, this research uses two different focus groups of different participants to generate quality data from group interactions on the same topic and combine into a single data set for thematic analysis to determine the emerging themes on the impacts of overweight and obesity on dementia and survival. The detail of the proposed design and rationale is reported in the methodology chapter (Chapter Three).

8.2.2 Study population and sampling

The target population for the study was older adults of the age 60 years and above residing within the community in Wolverhampton, UK. Wolverhampton is the most diverse city in the West Midlands and is marked by a heterogeneous mix of nationalities, religions and ethnic groups above the average for England (SEPHO 2011). It also has an ageing population with 50,065 older adults (age ≥60 years) representing 21.7% of the general population (WPIS 2014). A non-probability sample of 5 to 8 older adults (age≥60 years) was targeted and considered adequate for the research. This is because it was proposed that focus groups should have enough participants to help generate diverse information. However, they must not be too large or else they may create an uncomfortable environment with some participants unable to freely express their views, thoughts or experiences (Onwuegbuzie *et al.,* 2009).

8.2.3 Recruitment

The participants for the study were recruited from older adults residing within the communities through their usual place of worship in Wolverhampton UK. Before contacting or recruiting participants for the study, approval was received from the University of Wolverhampton research ethics committee (Appendix 1) and a Church in Wolverhampton after submitting full research proposal and protocols (Appendix 2). An initial notification of the focus group research and request for interest from willing older adults was put out in the weekly Sunday printed bulletin with the help of the leader of the place of worship (Appendix 3). Potential participants were also approached face-to-face by the researcher after each Sunday service and were provided with a detailed explanation of the proposed research and requirements for recruitment into the study (Appendix 4). For inclusion into the focus group, study participants were required to be of the age of 60 years and above, not known to have any history or diagnosis of dementia and must have the capacity to provide consent by themselves to partake in the research. Those considered as unable to provide consent were neither approached nor included. Interested and potential participants for the study were given the research information sheets and consent forms (Appendix 5 and 6) and adequate time allowed to confirm interest and return the signed consent forms which ranged between 1-2 weeks.

8.2.4 Participants for the study

A total of 18 people was identified for the focus group study, out of which 12 confirmed their interest in participating. These 12 participants were divided into two groups, each consisting of 6 focus group members. Though the second focus group was reduced to 5 members as one participant left the venue to attend to urgent family needs. There were no defined criteria for selection into any of the two focus groups except interest confirmation and availability of members to participate in any of the sessions arranged for separate dates and times. Once the 6 spaces for the first focus group discussion session were filled the other participants were automatically allocated into the spaces for the second focus group session which took place about three weeks later. Therefore, the focus group members for each focus group session were different but the topic for discussion was the same.

8.2.5 Data collection Procedure and tools

The focus group discussion was conducted in a quiet room suitable for 6 to 9 participants within the Millennium City (MC) Building of the University of Wolverhampton. The participants found this venue and location quite convenient and safe since it was close to their usual place of worship and easily accessible by walking or transport services with car parking spaces available.

Prior to the focus group study, a very brief questionnaire was used to collect basic socio-demographic background information on the participants (Appendix 7). It was also confirmed again that each participant had signed and returned the consent form before the commencement of the focus group activity for each day. The two focus group discussion sessions were held three weeks apart and each lasted for approximately 1 hour. Each session was facilitated by the researcher while a research colleague was present to assist with arrangements at the venue and note-taking. A project supervisor was only present before the activity for one-minute introduction and welcoming of participants before leaving the venue for the researcher to continue with the focus group discussion. The data were collected using a digital audio recording device by Olympus Corporation (Tokyo, Japan). To facilitate the focus group session a discussion guide that included semi-structured open-ended questions with a focus on the research questions was used to prompt participants to discuss the topic (appendix 8). During the focus group discussion, however, a few more questions were also used to clarify responses from participants or to ensure speakers remained focused on the main subject of deliberation.

8.2.6 Ethical Consideration

The entire study was carried out strictly in accordance with the research protocol approved for the study by the University of Wolverhampton Research Ethics Committee and the Church in Wolverhampton (Appendix 1 and 2). Before the commencement of the study, participants provided their consent by signing provided consent forms after reading the research information sheets (Appendix 5 and 6).

8.2.7 Transcribing of data

The audio recorded data from focus group discussion sessions was transferred using the USB stick from the recorder to a personal laptop computer (that is pass-worded and had antivirus installed) and uploaded unto an NVIVO software version 11.0. A verbatim transcribing of the data from each of the focus group discussion was done with the aid of the NVIVO software. Care was taken to ensure data were transcribed in enough detail and to also ensure accuracy the transcripts were checked against the audio-recordings. The total transcribed data consisted of 11,612 words (Appendix 9).

8.2.8 Data analysis

The data on the background information of participants was analysed using SPSS version 24.0 (SPSS Inc., Chicago, USA. The data from the focus group research was analyzed by thematic analysis using the approach described by Braun and Clarke

(2006). This approach is widely used in similar qualitative research and considered very useful in exploring participants' perspectives on an issue raised. It helps to also highlight differences and similarities in the participants' views on a topic as well as uncover unexpected insights produced from the study (Braun and Clark. 2006; Nowell *et al.,* 2017). It is accessible, quick to understand and permits key features of large data sets to be generated and summarized in a well-structured manner (Nowell *et al.,* 2017). The thematic analysis used for the analysis of the focus group data on overweight and obesity associated with dementia and survival involves 6 steps as described by Braun and Clark (2006). These includes getting acquainted with the data, producing the initial codes, identifying themes, reviewing themes, defining and naming themes and generating the report of the analysis.

8.2.8.1 Acquaintance with focus group data

The analysis of the focus group data started with an initial acquaintance with the data which happened while collecting the data during the interactive discussions among focus group members and while doing a verbatim transcribing of the data itself. When the transcribing was completed, the data was read four times to gain further acquaintance with it before commencement of coding; and while doing so, the initial ideas that could be relevant to the subsequent stages of the analysis were carefully noted.

8.2.8.2 Producing initial codes

The key features of the transcribed data or basic expressions from each focus group member regarding overweight and obesity associated with dementia and survival were coded. These codes, as described by Boyatzis (1998) and re-emphasized by

Braun and Clarke (2006) represented the 'the most basic segment, or element, of the raw data or information that can be assessed in a meaningful way regarding the phenomenon'. These codes served as the bedrock from which the subthemes emerged. Although specific questions were asked during the focus group discussion which would have allowed for coding around those key questions for theory-driven themes, a more general approach to coding was preferred to support data-driven themes. This was necessary considering the complex nature of the topic and various overlaps of the responses and discussions among the focus group members. To allow for numerous potential themes emerging from the data, as many codes as possible were generated and the coding included surrounding extracts of data to avoid the context of each code being lost, as advised by Bryman (2001).

8.2.8.3 Looking for themes

All the data at this stage were already coded and a total 154 codes were generated across the entire data set. The codes were then sorted into different subthemes with the thoughts of these codes coming together to form the major themes. An excel spreadsheet was used to organize the coded data extracts within the identified subthemes. To help visual presentation the codes were coloured according to the subthemes. Thematic maps were used to help show the relationships between different codes or subthemes at various levels and possible major themes above them. Although most codes did fit into one subtheme or the other, not all of them were involved and few had to be discarded. A total of 28 subthemes with coded data extracts for each subtheme collated under them were completed.

8.2.8.4 Reviewing themes

Although the subthemes appeared finalized in the previous stage, some had to be reviewed and even combined, separated into two different themes or discarded leaving a refined total of 26 subthemes from the initial 28. This stage of the analysis of reviewing the themes led to revisiting coded data and some re-coding of data was done while also ensuring that the subthemes reflected the codes they represented. This phase concluded with a clearer view of the themes merging from the data and how they could fit to make sense or tell a story.

8.2.8.5 Defining and naming themes

The completed thematic map was carefully viewed while identifying what each theme portrayed as well as the story behind them. This involved naming, redefining and refining the themes for the final presentation of the completed analysis. An account of what each theme represents, and their analysis was considered in detail to ensure they fit well with the subthemes and their related coded data extracts. As a whole, the initial 26 subthemes went on to form fewer subthemes of 16 and these were further refined to 8 subthemes and finally 4 major themes. Each of these four themes was represented by thematic maps as pyramids (Figure 13-16). The final stage of the analysis ends with presentation of the findings.

8.2.8.6 Producing the reports

This represents the last stage of the thematic analysis steps by Braun and Clarke (2006) after all themes have emerged from the entire process. It emphasized the write up of the reports including the use of data extracts or 'direct quotes' that gave rise to the emerged themes to support the presentation of the findings (King, 2004; Braun and Clarke, 2006). This stage of the analysis as recently described by Norwell

(2017) could include member or category checking, sufficient detail of description of the process of coding and analysis, description of the context and audit trail as well as explanations where applicable of the choices made regarding theory, method and analysis in the study. The details of this report are presented in the subsequent sections.

8.3 Results

The mean age of the eleven participants in the study was 69.4 years (SD ±9·4), and 63.6 % of them were male. The majority of the participants (81.8%) were White British, and the remaining were of Black African descent (18.2%). All the participants were educated to at least a secondary school level. There were 81.8% with higher education and 18.2% attained a secondary school level.

The findings from the thematic analysis revealed four themes for the impact of overweight and obesity in older age on dementia and survival. These include the themes harm, impairment, mortality, and moderation as depicted by Figure 12 below. The first three themes (in purple colour) portray the impact of body weight on dementia risk and survival while the fourth theme (in green) suggests a way forward in curtailing the consequences of abnormal body weight. Each of these themes is presented in detail below.

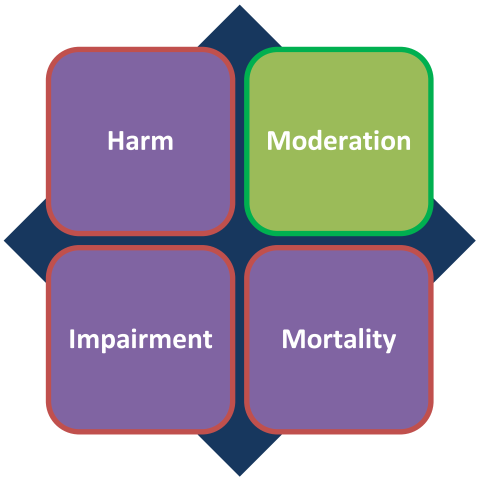


Figure 12 the four themes on study of the impact of overweight and obesity on dementia and survival in older adults

8.3.1 Theme-Harm

A major theme that emerged from the focus group discussion is the theme 'harm'. In the context of the study, harm refers to a negative health outcome which indicates damage or injury caused by an illness or a disease state. The participants believed that overweight and obesity are harmful and two subthemes "damages brain" and "dementia risk" describes how overweight and obesity suggest a type of body harm known as dementia. These subthemes are derived from four other subthemes namely increases body problems, affects brain function, increases brain illness, and link to dementia, as represented by Figure 12.1 below.

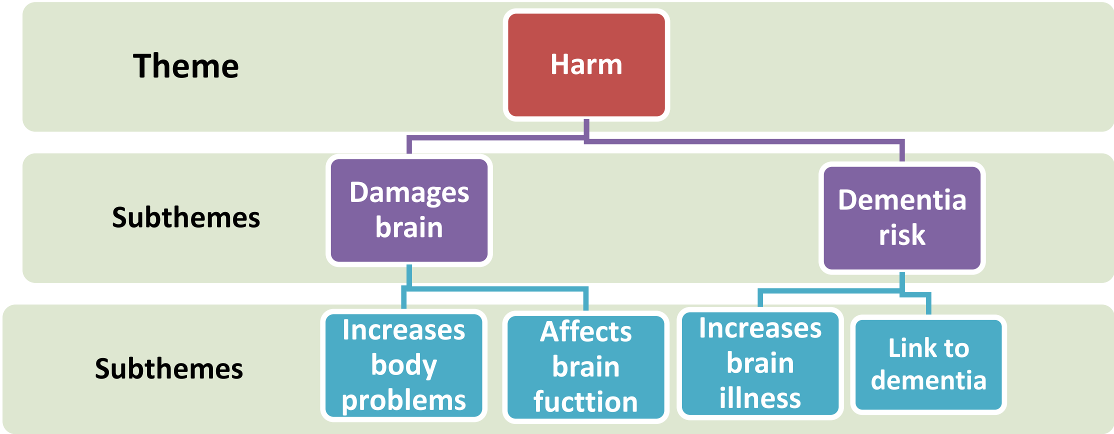


Figure 13 Theme-Harm

8.3.1.1 The Subtheme- damages brain

The subtheme-'damages brain' results from two subthemes-'increases body problems' and 'affects brain function'. The participants were of the view that overweight and obesity impact negatively on health or constitute harm by increasing body problems and interfering with the normal functioning of the brain which culminates in brain damage. It is this brain damage that might contribute to harm viewed as dementia.

8.3.1.1.1 Subtheme-Increases body problems

This is a subtheme under the main subtheme- 'damages brain'. According to participants, 'increased body problems' results from the effects of overweight and obesity on the body system which could manifest as poor physical ability, lack of fitness or poor body function: *"I am getting overweight and it is a real concern to me. It affects all my body, all my system".* A similar view was *"I am aware from all* *my studies, the theories and my athletic life that overweight wasn't good for the functioning, the best functioning of my body to run, to jump".* These expressions by participants suggest that overweight and obesity are associated with increased body problems.

8.3.1.1.2 Subtheme-affects brain function

This is another subtheme under the main subtheme-'damages brain'. Participants believed that overweight and obesity also affect the functioning of the brain. They considered that there might be a link between poor body fitness and brain function. For instance, there was a view from participants that *"There is a probable link between not being appropriately fit and mental health"*. This was also expressed as *"If you are overweight obviously it affects your physical ability, doesn't it? You are not as active, so presumably, your muscles are not working as well as they could be if you're not overweight; so, does it affect the brain as well? It may well do I suppose*". These suggest a possible link between poor physical ability or lack of fitness and poor functioning of the brain: This was further supported by similar view *"So, I think I go down if you are not active and you are obese then your brain I think isn't working well"*. These suggest that overweight and obesity impact negatively on body function which interferes with normal brain functioning. This interference with function might result in brain damage and constitute harm known as dementia.

8.3.1.2 The subtheme- dementia risk

One of the two main subthemes under the theme-'harm' is the subtheme-'dementia risk'. Participants identified 'dementia risk' as one of the consequences of overweight and obesity. There were two different views on the impacts of overweight and obesity on dementia risk. Some participants believed that overweight and obesity increase brain illness or dementia directly while others believe they may be linked to dementia indirectly through several other mechanisms. Therefore, the subtheme-dementia risk results from two subthemes-'increases brain illness/dementia' and 'link to dementia' as explained below.

8.3.1.2.1 subtheme-Increases brain illness/dementia

There was a strong view by some participants that overweight and obesity contribute to brain illness/dementia: *"I definitely think overweight and obesity increases dementia". "I believe I strongly believe that obesity is a sign, it has a correlation with dementia": "Dementia is something that is clearly defined, and it is not something that is automatic, something that has a lot of links; and I believe from my experience that one of the links is obesity*". In fact, it was proposed that dementia increases with increasing body weight: *"The more your body mass is increasing the more the chances of dementia coming to existence"*. All these views suggest that overweight and obesity might increase dementia in older people.

8.3.1.2.2 Subtheme-link to dementia

The 'link to dementia' is a subtheme under the main subtheme- 'dementia risk' and it suggests that overweight and obesity might be related to dementia via indirect or several links. It was argued that since overweight and obesity are not good for the body the harmful effects could well extend to dementia: *"Obesity isn't good in any respect. So, it could well affect dementia, but I don't just know". "So, I certainly won't discount it and I will certainly say it has an impact on one's health and I am* *putting dementia as part of ill health". "Yea, but for me, my experience I believe they have a correlation, they have a link".* These emphasized the link with dementia and suggest that the harmful effect of overweight and obesity may be an indirect one. Focus group members were also of the view that dementia have several other links apart from overweight and obesity and these include hereditary, living in a polluted area and carrying grief for years. According to the Focus group members, hereditary may be huge and important factor: *"I think hereditary factors seem to be huge".* While genetics is thought to be an important link that cannot be discounted, living in a polluted environment could increase vulnerability*: "If you live in a polluted area you are more likely to get dementia"*. The polluted area could mean a crowded place of living, noisy places, unhealthy or contaminated atmosphere with chemical substances and excessive heat or light. One interesting factor raised was 'carrying grief for years': *"Sometimes it is grief that people have inside them that they carry it inside for years and is a way of coping with that as they get older that they forget it"*. This means that prolonged grief experienced by people for several years may precipitate dementia in older age and this was viewed as a sort of coping mechanisms by the body or a way of ending or forgetting the grief (since dementia is accompanied by loss of memory).

Therefore, findings based on the theme-harm suggest that overweight and obesity is harmful, with dementia being one of the harmful health consequences of obesity in older age. This results from the negative impact on body function particularly through damage to the brain. However, other important links to dementia were also identified which suggest that dementia is a complex health problem involving several predisposing factors or mechanisms.

8.3.2 Theme-Impairment

Another major theme that emerged from the focus group study is the theme-'impairment'. The theme highlighted the consequences of both overweight and obesity and also underweight unlike the previous theme (harm) which depicted the consequences of excess weight only. The term impairment in the context of the study describes loss, deterioration or abnormality of brain function or structure including dementia. Dementia was considered as an impairment of the brain and is used interchangeably with impairment in the explanation of the subthemes. The theme –'impairment' consists of two main subthemes called 'Stress-related' and 'brain affected'. These two main subthemes emerged from four subthemes including 'stress harms brain', 'leanness has some effects', 'obesity affects brain' and 'complicated obesity link' as shown in Figure 13 below.

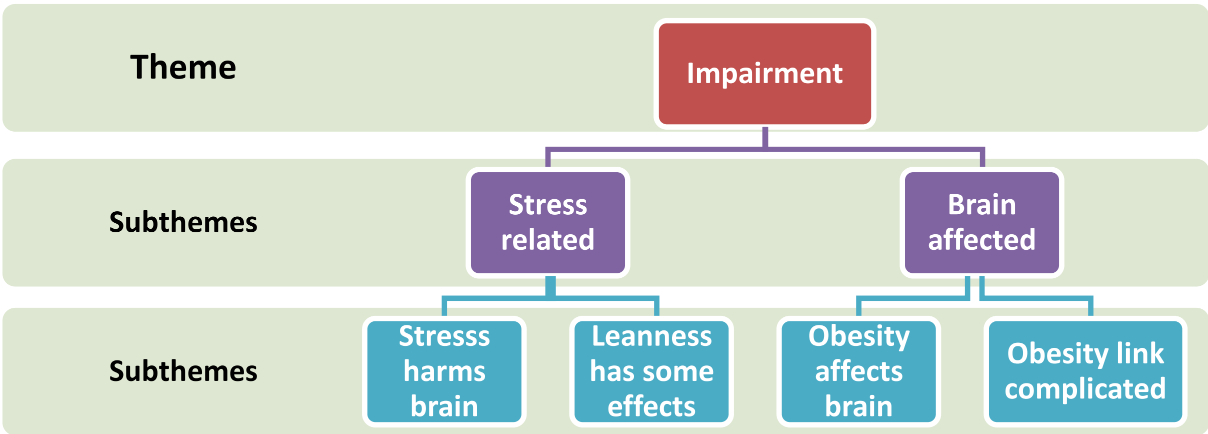


Figure 14 Theme-Impairment

8.3.2.1 The subtheme- Stress related

The subtheme-'Stress related' is one of the two main subthemes under theme-'impairment'. The subtheme suggests that impairment may be linked with stress. The main subtheme-'stress related' emerged from two subthemes 'Stress harms the brain' and 'Leanness has some effects' which are presented below.

8.3.2.1.1 subtheme-Stress harms brain

The focus group members considered that stress harms the brain. For instance, impairment was described as a harm on the brain that is stress-related : *"Sometimes it is grief that people have inside them that they carry it inside for years and is a way of coping with that as they get older that they forget it"*. This suggests a link through depression and prolonged stress on the brain. The view of stress constituting harm was also expressed in terms of people 'using their brain more' even though it was slightly confused with keeping the brain active: *"In my own mind it seems fairly almost obvious to me that someone who is very fit, very active and correct bodyweight and everything is probably more likely, in theory, should be using their brain more but often we hear the less likely"*. This suggests that contrary to popular view, using the brain more despite having the normal weight could impact negatively on the brain and result in dementia. This phrase '*using the brain more'* emphasized 'stress on the brain' as a major problem rather than keeping the brain or body active. Therefore, from the view of participants stress could increase the risk of impairment of the brain.

8.3.2.1.2 subtheme-Leanness has some effects

Focus group members also considered that people who are thin, lean or underweight tend to experience an impairment of the brain which manifests as dementia: *"People that are slim they can also suffer from dementia"*. This suggests that dementia is not only a problem of excess weight but also underweight: *"The only one person that I know at the moment who suffers seriously from dementia, he has got it for maybe 20 years ago, but he is a very active person, he is a very thin person, very fit person, very active person"*. This again highlights dementia as a problem that is related to being underweight and it happens in people who appear fit and active as well: *"It is people who are (you know) fit, athletic and thin who are more likely to get dementia".* This view of underweight and active people being associated with dementia risk is perhaps linked through stress since participants believed that stress harms the brain and lean people are perceived as those passing through stressful events. The view that underweight impacts negatively on health, and perhaps through stress, were reflected in the thoughts of participants about perceived benefits of overweight*: 'Some others who are a bit overweight might feel a lot happier though because of that (you know) of their happiness might live longer'*. While this view did not justify overweight and obesity, it emphasized underweight as a disadvantage while being slightly overweight could be more beneficial than leanness.

It was however observed that some of the data that supported underweight and dementia link were influenced by participants' experience of the life of people who already have dementia without consideration of their history of body weight before dementia diagnosis: For instance*, "How is it that a lot of people with dementia are very active? They wana walk, and they want to walk miles. They want to be active?"*

This showed obviously that the views were based on those already with dementia and there was no information on bodyweight history before dementia in those people. Therefore, participants maintained their view that underweight causes impairment of the brain manifesting as dementia. Though, one participant argued that perhaps, if underweight truly predisposes people to dementia then overweight might be protective: *"Being overweight seems to preserve you from possibly the dementia"* or it might be that the optimal weight associated with the lowest risk varies from one person to the other: *"The optimal weight for each person is different isn't it? It depends on the makeup of the body, the proportion and everything".* These suggests that if underweight is related to risk of dementia then the body weight that could be safe or help reduce risk is that which is above underweight. This could be normal weight or slightly overweight.

8.3.2.2 The Subtheme-Brain affected

This is another main subtheme under theme- 'Impairment'. The subtheme emerged from two other subthemes called 'obesity affects brain' and 'obesity link complicated'. These two subthemes suggests that overweight and obesity affects the brain and results in impairment but the obesity link is complicated by the fact that people who are underweight or with no history of overweight and obesity also experience impairment (or dementia).

8.3.2.2.1 subtheme-obesity affects brain

Participants viewed that impairment might result from overweight and obesity due to the negative effects on the brain*. "And I know my weight goes up every time and it affects me when I am reading". "So, I think I go down if you are not active and if* *you are obese then your brain I think isn't working as well". "He can run, I cannot run. He can do a lot of things I cannot do even though he says he is underweight, my tummy and everything. It affects even my understanding"*. These suggest obesity is a problem that affects the brain and its function. Overweight and obesity were also described in terms of one of their causes (excess calories from sugary diet) or what they represent (excess fats) and the negative effect on the brain*: "If peoples' diet is very sugary or very fatty is not going to be good for any part of them including the brain"*. All these showed that overweight and obesity are health problems that affect the brain, and these could result in an impairment of the brain.

8.3.2.2.2 subtheme-complicated obesity link

The link between obesity and dementia was viewed as a complicated one. The complexity surrounding the obesity link was reflected in the view of participants that people who had dementia were underweight and those who were overweight or obese tend to lose weight once they have dementia: *"Her husband was a cricketer and never had an inch of weight on in his life but got dementia". "I know several people who are either a bit overweight or more than a bit overweight and there is no sign of mental problems"*. This suggests that overweight have no relationship with dementia but underweight has an effect. *"My mother got dementia she wasn't overweight, my husband had dementia he was a rugby player and he was big and everything and when he got dementia, he started to lose his muscle and things like that"*. However, this last statement indicates that while the case of the mother suggested overweight had no relationship, the case of the husband who played rugby suggested that excess weight could be related to dementia since he was *"big* *and everything"* before dementia cropped in. The subsequent loss of weight when he developed dementia "*he started to lose his muscle and things like that"* suggest that the brain illness might have impacted on his body weight by causing weight loss in what is often described in epidemiology as reverse causality. While this suggests reverse causality the obesity and dementia link was viewed as confusing and complicated: *"I am still confused, I am on the fence a bit": "I think the very matter we are discussing is a hugely complex matter": "This is so difficult to handle! It seems whatever they said it seems to be exactly opposite of the subject".* The theme-impairment showed that impairment might be stress-related and may affects the brain. It might not only be related with overweight and obesity but underweight.

8.3.3 Theme-Mortality

One major theme that emerged from the focus group study was the theme-'mortality'. Mortality simply refers to death regardless of what cause (or all-cause mortality) and it emerged from two main subthemes-'poor health' and 'reduced lifespan'. These main subthemes resulted from four other subthemes namely, 'mobility-related disability', 'increases chronic diseases', 'damages body organs' and 'decreases survival chances. These are depicted in figure 15 below.

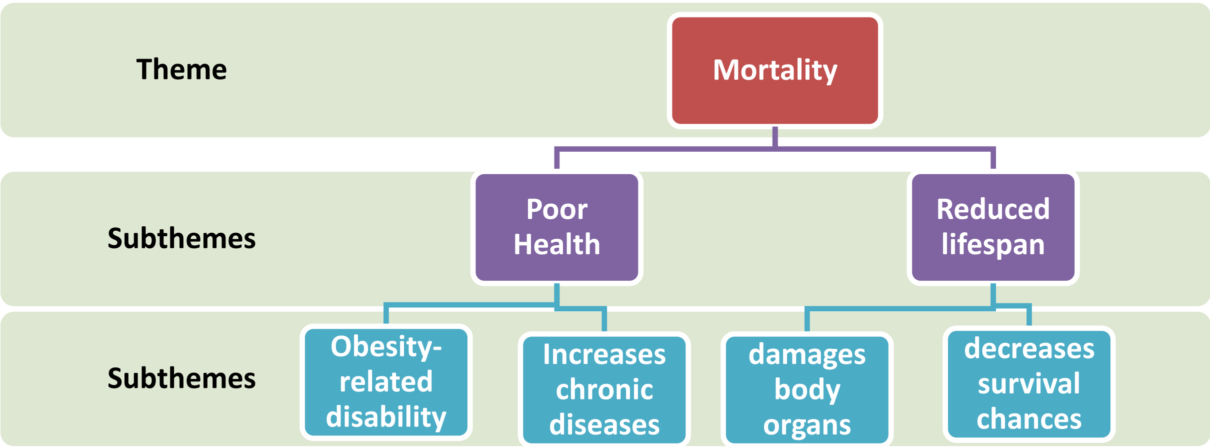


Figure 15 Theme-Mortality

8.3.3.1 The-subtheme-Poor Health

The subtheme- 'Poor health' is a main subtheme under theme-'mortality' which emerged from two subthemes "mobility-related disability" and "increases chronic diseases". The subtheme-poor health describes an intermediate outcome between the overall outcome-mortality and mobility-related disability and increased chronic diseases which are associated with overweight and obesity.

8.3.3.1.1 subtheme-mobility-related disability

Participants believed that overweight and obesity results in disability because they tend to reduce mobility and increase the risk of arthritis: For instance, they considered that *"Is a restriction in so many ways if you are obese" and viewed "other problem of overweight and obesity is Arthritis"*. The mobility challenge and risk of climbing up and possibly falling down the stairs was also raised: "*But one point that comes to me of being way overweight is being so breathless that you* *might not be able to go upstairs to get to your normal bed. Or indeed if you do get to bed upstairs there will be a higher risk of falling downstairs and which could be disastrous obviously. I think the mobility side could lead to not good things"*. While the mobility challenge and associated risk was raised, it was also thought that it could be an early marker of arthritis which may further compound mobility and cause inactivity: *"You can be overweight, and you start getting arthritis early because you are overweight. Arthritis can stop you from being active".* All these suggest that overweight and obesity could increase the risk of disability which in turn contributes to poor health in older adults.

8.3.3.1.2 subtheme-increases chronic diseases

The participants considered that overweight and obesity 'increases chronic diseases. These chronic diseases included cardiovascular diseases (CVDs) and their related risk factors: For instance, in their view *"Obesity causes cardiovascular diseases"* and felt that "*Being overweight affects so many things. One reason there has been a rise in diabetes and other things like heart problem"* and it was considered that *"There is diabetes; there are other things that through being overweight you may be at risk"*. Besides, the participants also mentioned other diseases or health problems associated with overweight and obesity which included high blood pressure (B.P) and cancers risk which could be reduced by having a good body weight: *"obesity not good for B.P". "I think having a good body weight would help a thousand. I think it will reduce the risk of cancer"*. All these reflected participants view that overweight and obesity are not beneficial but harmful and they are associated with chronic diseases which contribute to poor health and mortality.

8.3.3.2 The Subtheme-Reduced lifespan

Reduced lifespan is a major subtheme under the theme-mortality. It is derived from two subthemes "damages body organs" and "decreases survival chances". The main subtheme-'Reduces life span' describes the impacts of the damage to body organs and 'decreases survival chances' implied the consequences of being overweight and obese.

8.3.3.2.1 subtheme-damages body organs

Participants were of the view that one of the effects of overweight and obesity is damage to the body organs which contributes to reduced lifespan in older adults: *"if you are way overweight your chances are not very good. It affects all your organs"*. One of the body organs affected by obesity is the heart: *"Obesity causes heart problems"*. The brain is one complex organ also affected by overweight and obesity: *"If you are obese then your brain I think isn't working".* Dementia is one health problem linked with damage to the brain that was mentioned: *"Big body mass increases the risk of dementia"*. These shows that overweight and obesity are associated with organ damage. Also, the damaging effects on body organs like the heart and brain could result in diseases that reduce lifespan.

8.3.3.2.2 subtheme-decreases survival chances

Participants viewed overweight and obesity as health problems associated with the deleterious effect of decreased survival chances: *"Obesity isn't good in any respect":*

"if you are very obese your life expectancy might be less": "If you are way overweight your chances are not very good". Participants were also of the view that obesity is so harmful that people may not even survive long enough to experience age-related chronic disease like dementia. *"I will say that if you are way overweight it could contribute to the problems of health that could possibly kill them off before dementia". "If you are grossly obese then your life expectancy will be less anyway, so you might not get to the stage when you are going to be suffering from dementia"*. Participants also came to a consensus that overweight and obesity does not increase survival but rather reduces it; and even if it does then except perhaps in a very rare famine situation: *"If we were in a famine situation, there is no food available and you had resources, yes you will probably live longer than somebody lean but that is just obviously in an extreme condition"* That notwithstanding, the general view of participants was that overweight and obesity are associated with reduction in chances of living regardless of any possible thoughts of beneficial effects. Therefore, the findings based on the theme-mortality showed that overweight and obesity in older adults does not confer protection on health but causes ill- health, shortened lifespan and resulting in death.

8.3.4 Theme-Moderation

The final theme from the focus group discussion was theme-'moderation'. The theme-moderation highlights the importance of normal weight and the need for weight control. It draws from participants' view that "Anything is good for you in moderation". It emphasized the striking of a balance between energy intake and expenditure through dietary and exercise measures to help achieve and maintain normal body weight.

The main subthemes that made up the theme-moderation are subthemes-'normal weight beneficial' and 'weight control useful'. These emanated from four other subthemes as shown in Figure 16 below and they include subthemes-'normal weight reduces risks', 'normal weight supports life', 'diet control is important' and 'exercise should be encouraged'. The term 'normal weight' which appeared in some subthemes suggests a body weight that is associated with the lowest risk of illness or death. This is often expressed in terms of body weight in relation to the height of an individual. It is commonly defined by a body mass index which ranged from 18.5 Kg/m^2 to any value less than 25 Kg/m^2.

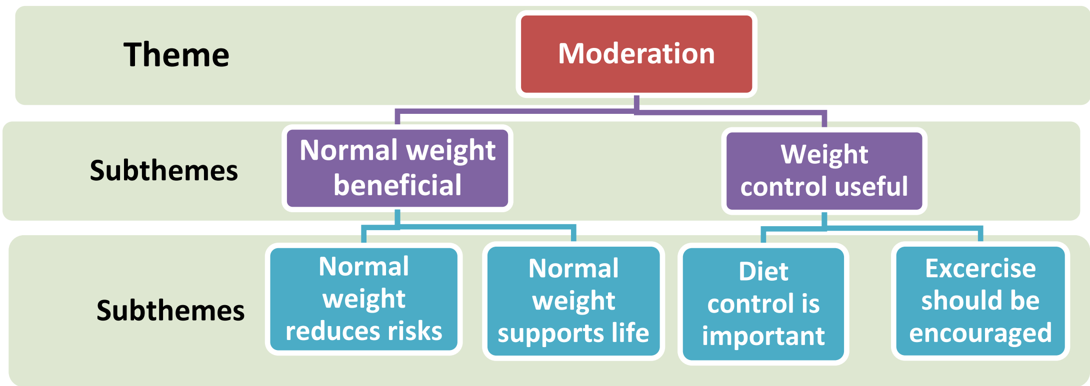


Figure 16 Theme-Moderation

8.3.4.1 The Subtheme-Normal weight beneficial

This is a subtheme of moderation and it is derived from "Normal weight reduces risks" and Normal weight supports life". The main subtheme-'normal weight beneficial' emphasizes the importance of normal weight in terms of limiting the risks of diseases and supporting life. The related subthemes are described below.

8.3.4.1.1 Subtheme-normal weight reduces risks

Participants were of the view that normal weight reduces health risks and that reducing excess weight or staying within normal weight could help prevent dementia: *"We need to reduce weight to prevent dementia". "In terms of dementia and overweight, I think striving to be normal weight is ideal"*. It was also considered that normal weight helps the normal functioning of the brain: "*when you have a normal weight, you are normal in every sense, even your brain everything works normal"*. It was clear from the focus group discussion that reducing excess weight is not limited *to dementia risk reduction but also helps to prevent many diseases including cancer: "I would say that if you are overweight you need to decrease it not only for dementia but for cancer, for other many things. I don't think that overweight, and for your mobility and for perhaps the other things, in the end, would be up against dementia". "Normal weight, it reduces your chances of heart attack, accident and so many things".* There was also the view that achieving normal weight is not only applicable to those with excess weight but the underweight people: *"I think it is the idea of everybody, is that people who are too thin, you know, bone density and your heart doesn't work as well, you are not as well fed. So, I think is trying to be normal. That is the ideal for everyone to aspire to"*. The findings based on this subtheme shows that risk reduction is desirable for older adults with overweight and obesity and underweight. Therefore, the common goal is to achieve and maintain normal weight.

8.3.4.1.2 Normal weight supports life

Participants were of the view that normal weight is a way to achieving health and better survival: *"If you are of normal weight usually you are feeling healthy so normal weight I will say probably is the path for achieving health". "To stay healthy, I suppose the normal weight should be ideal". "Yes, normal weight is better for survival"*. Although participants were of the view that normal weight is required for better health and survival, some also felt that perhaps a slightly expanded range from slightly below normal to slightly above normal range could be appropriate for health and survival: *"Normal weight, with a little bit of either side, is better for survival"*. This view which is also supportive of slight underweight and normal weight seemed to be based on the thinking that underweight might be safer than being obese: *"Normal or may be underweight. When you are underweight, you stand less chances of being attacked by diseases".* The suggestions of slightly above normal weight were based on the thoughts of circumstances where for health reasons weight reduction is not advisable*. "Normal weight I should say will be the weight to be as long as you can and you don't pick up any problem on the way."* The findings from this subtheme show that normal weight supports good health and life. It also suggests that normal or slightly below normal weight could be encouraged for good health and it is important to consider that certain circumstances in older adults might not support might reduction and in such cases achieving strictly normal weight could be difficult.

8.3.4.2 Subtheme-Weight control useful

The subtheme highlights the importance of moderation in body weight by achieving normal weight through appropriate weight management measures of diet and exercise. This main subtheme emerged from two subthemes "diet control is important" and "Exercise should be encouraged".

8.3.4.2.1 Diet control is important

Focus group members believed that paying attention to the diet could help achieve and maintain normal weight: *"diet is required to stay of normal weight". "Diet in the sense of eating the right food and the right quantity particular in terms of calories is important"*. Snacking after meals was viewed as being contributory to calorie and weight gain while some people could do with some advice from dieticians*: "I will say make sure that if you eat your meals your lunch or dinner whatever you can, avoid snacking". "Seek for advice. Go and see a dietician"*. Participants also viewed self-discipline and the will-power to change dietary behaviour as more critical for success in controlling body weight: *"Train your brain to do certain things that would also help. If you don't train yourself, you may start a diet today and break it the next two days". "We can add the will power to change something. If you train yourself to do certain things you do it"*. However, it was argued that the issue of diet is beyond the control of individuals. The supermarkets, food industries and government were seen as having some role in the overweight and obesity epidemic: "*When I go to supermarkets and you are out to check out and you see all the sweet things that are there all nearest. These fats that big industries are creating like I really think the government has a role to play. The government and the supermarket, if there is obesity, I would lay a lot of blame on them"*. This point suggests that the root causes of obesity could be the wider determinants which involve different stakeholders and policies that support obesity. It also shows that while approaches which directly apply to individual such as diet and exercise should be encouraged, it is very important to look at the distal factors such as policies, industries and supermarkets which impacts on individual behaviours.

8.3.4.2.2 Exercise should be encouraged

Participants believed that diet alone is not enough, exercise should be encouraged for older adults: For instance, they considered that achieving and maintaining normal body weight could be *"By exercising and being careful of what you eat"*. However, their view of exercise did not mean vigorous physical activity but being busy or active: *"Keep busy. Keeping active not in necessary going to play football. Be busy even when you don't want to be busy. Be busy doing something".* This encouraged the avoidance of a sedentary lifestyle by engaging in any possible form of physical activity to stay active. One form of exercise stressed was walking: *"Walking is also very good. Have a walk"*. It was clear from the participants' view that exercise should be encouraged for older adults even though it should not be vigorous.

The findings based on the main-subtheme "weight control useful" show that to maintain body weight dietary control measures which take into consideration the right type of food, food portions, seeking for advice from dieticians, self-discipline and willingness to change dietary behaviour is crucial. It also showed that exercise is necessary and should be encouraged in older adults and the goal should be on preventing sedentary life and keeping active. Findings base on the main theme-moderation showed that normal weight is beneficial for preventing or reducing the risk of diseases and enhance survival. Normal body weight can be attained and controlled through dietary and exercise measures that are appropriate for older adults

In summary, the findings from the focus group study revealed that overweight and obesity damages health and are associated with impairments, harm, and mortality in older adults. Moderation emerged as a preferred approach to limiting consequences of abnormal body weight and achieving normal weight was encouraged for people with overweight and obesity or underweight.

8.4 Discussion

The study, to the best of knowledge, is the first qualitative focus group study that examined the impacts of overweight and obesity in older adults on dementia and survival. Contrary to several reports in the literature of beneficial health effects of overweight and obesity in terms of dementia risk and all-cause mortality, the findings of the focus group study showed that the participants were aware that overweight and obesity may be harmful by contributing to chronic diseases such as cardiovascular diseases and other health problems that lead to mortality. Though it was difficult for the focus group to ascertain a link between body weight and dementia risk, the older adults were aware that normal body weight may reduce the risk of mortality and other obesity-related chronic diseases.

8.4.1 The impacts of overweight and obesity on dementia

The evidence from the focus group study suggested that overweight and obesity may be harmful particularly in terms of the risks of cardiovascular diseases which have been implicated in dementia from observational studies. However, it is difficult to infer any causal relation between overweight, obesity and dementia risk considering the limitation of using qualitative study design and focus group of few participants. Notwithstanding, the findings suggest that excess body weight was not beneficial but harmful to health. The findings that suggested the deleterious consequences of overweight and obesity emerged from the two main themes "Harm" and "impairment".

Though it is difficult to assume association of overweight and obesity with dementia risk from the focus group research, the harmful effects of excess body weight align with the views of some observational studies on health effects of overweight/obesity (Gustafson *et al.,* 2003; Hayden *et al.,* 2006; Bowman *et al* (2019). For instance, the previous study by Gustafson *et al* (2003) based on Swedish cohort data from the Gerontological and Geriatric Population Studies showed that higher BMI (overweight and obesity) was harmful and that it increased the risk of dementia after 18 years of follow-up. Similarly, the recent finding in the UK (Bowman *et al.,* 2019) based on analysis of health records data from 674 UK primary care practices reported increased dementia risk for older people (65–74 year) with obesity. Although the study by Bowman *et al* (2019) relied on patient health record linkage, the finding supported the hypothesis that obesity in older adults was detrimental to health by increasing the risk of dementia.

8.4.2 The impact of underweight on dementia risk

The literature suggests that the relationship between underweight and dementia risk is far from clear (Dahl *et al.,* 2008; Fizpatrick *et al.,*2009; Neergaard *et al.,*2016) even though weight loss which often leads to leanness may serve as a preclinical marker of incident dementia (Knopman *et al.,* 2007). Findings from observational research of older adults in Finland and Italy (Dahl *et al.,* 2008; Lucca *et al.,* 2012) showed that being underweight confers protection against dementia while similar studies conducted in Sweden, Finland and Denmark (Atti *et al.,* 2008; Dahl *et al.,* 2008; Neergaard *et al.,* 2016) reported that there was no association between underweight and dementia. Contrary to these findings, underweight was associated with increased dementia risk in older adults in France and the USA (Nourhashemi *et al.,* 2003; Fitzpatrick *et al.,* 2009). Consistent with the report of harmful effects, the findings from this focus group study of UK older adults suggested that being underweight might be related health risks in older adults.

The findings based on the focus group data suggested that stress might contribute to the harm of the brain. It suggested that underweight people might be overburdened by stress, and this might contribute to impairment of the brain leading to dementia. Indeed, the evidence from research supports the link of underweight and depression (Leonore *et al.,* 2009) with depression increasing oxidative stress as revealed from a meta-analysis (Palta *et al.,* 2014). It is, therefore, possible that underweight might impact on dementia through pathways involving both depression (Byers and Yaffe, 2011) and oxidative stress (Chen *et al.,* 2011b). This needs further research from observation studies to help explain the possible mechanism.

8.4.3 The impacts of overweight and obesity on survival

The findings from epidemiological studies on the effects of overweight and obesity on survival has been conflicting. For instance, older adults who were obese or overweight had reduced risk of mortality (Flegal *et al.,* 2013: Wang *et al.,* 2016) thereby standing greater chances of survival than their normal weight and underweight counterparts. However, a summary of evidence (Winter *et al.,* 2014) from different studies that examined the same relationship concluded that no significant association was found.

Contrary to the paradox of beneficial effects, the findings based on theme-mortality from the qualitative focus group study showed that participants were aware that overweight and obesity do not support survival in older adults but constitute health risks. While the theme-mortality emerged as the main outcome from the views of older adults on the impact of overweight and obesity on survival, it showed that overweight and obesity may increase chronic diseases such as cardiovascular diseases and mobility-related disability in older adults and that this could combine to worsen health and increase mortality risk. Furthermore, it suggested that overweight and obesity might contribute to mortality risk through body organ damage and shortened lifespan of older adults.

The focus group research also contributed to the understanding of how overweight and obesity might reduce survival in older adults. The findings based on this focus group study suggests that overweight and obesity is a restriction on its own and poses a mobility challenge for older adults such as the risk of falls when climbing staircase. It also suggests that overweight and obesity might lay a foundation for arthritis to set in and this could combine with other chronic diseases in older age to trigger poor health and result in increased mortality. Therefore, the findings of the focus group study suggest that overweight and obesity leads to diseases and contributes to poor health thereby shortening survival in older adults.

8.4.4 Reducing morbidity and mortality by the management of body weights in older adults

This part is discussed under two sections, the lowest body weight for survival, and the management of body weight in older adults.

8.4.4.1 The lowest body weight associated with survival

The goal of weight management in older age is to achieve and maintain a healthy weight or bodyweight with the least mortality risk in the safest possible way (Starr and Bales, 2015). However, there has been controversy on whether weight reduction in older adults was necessary since evidence from research in older adults supported beneficial effects of excess weight (Flicker *et al.,* 2010; Flegal *et al.,* 2013; Wang et al., 2016) or lack of association with mortality risk (Dahl *et al.,*2013; Winter *et al.,* 2014). For instance, the study of an Australian cohort by Flicker *et al* (2010) concluded that the risk of mortality was 13% less for the overweight compared to normal weight after 10 years followed up. A study of a Swedish cohort reported 20% less mortality risk for the overweight compared to both normal/underweight people and concluded that obesity was not harmful (Dahl *et al.,* 2013). These findings tend to weaken the evidence base for interventions aimed at curtailing overweight and obesity in older age (Starr and Bales, 2015).

The findings from this focus group study showed that older adults were aware that overweight and obesity, and even underweight might increase health risks. It suggested that moderation of body weight to achieve and maintain the official recommended normal weight range could help reduce morbidity and mortality in older age. This was because older adults viewed normal weight as beneficial in limiting health risks. Therefore, weight control should be encouraged. The findings that suggested reduced health risks for normal weight are consistent with evidence from large population base studies which reported lowest all-cause mortality in older adults with normal weight category (Aune et al., 2016; Di Angelantonio et al., 2016). For instance, the findings from the study by Di Angelantonio et al (2016) found that the lowest all-cause mortality was related to normal BMI of 20-<25Kg/m^2. Their study also showed that regardless of age at obesity assessment, the BMI associated with the least risk lies with the normal weight range.

8.4.4.2 Management of body weight in older adults

The management of body weight in older adults has been controversial with concerns over the safety of interventions involving weight loss (Waters, Ward and Villareal, 2013; Jahangier, De Shutter and Lavie, 2014; Brown and Kuk, 2015; Starr and Bales, 2015). For instance, there were concerns over loss of bone and lean mass leading to risk of falls and deaths while the difficulty in regaining of entire lean mass in older adults after it is lost remains a challenge (Shar et al., 2011; Waters, Ward and Villareal, 2013). Therefore, it was argued (Brown and Kuk, 2015; Star and Bales, 2015) that the goal of weight management involving exercise and dietary control in the elderly should be aimed at improving physical function through preserved or increased muscle mass and strength while reducing excess fat mass associated with health risk. Besides, the study by Loef and Walach (2012) showed that a combination of a healthy lifestyle including diet and physical activity could reduce all-cause mortality.

Consistent with the above views, the findings from the focus group emphasized moderation and supported the use of weight control such as exercise and dietary measures in older adults to reduce excess weight and maintain normal body weight. The emphasis from the findings in terms of exercise, however, was on avoiding sedentary life and staying active. The findings from the focus group data also supported the dietary measure for underweight older adults to increase body weight to normal range to avoid health risk associated with leanness or frailty. Furthermore, strategies on prevention and management of overweight and obesity in older age often focused on individual or lifestyle factors (Star and Bales, 2015). This may be due to less focus on the wider determinants. However, the findings from the focus group study recognize factors beyond the control of individuals such as the influence of the supermarkets, food industry and government policies in modifying behaviour and highlights the need for policies that could encourage healthy food environment.

8.4.5 Strengths and Limitations

8.4.5.1 Strengths

The focus group study contributed to the understanding of how body weight might impact on dementia and survival. The study identified four important themes; three of them including harm, impairment and mortality reflected the consequences of underweight, overweight and obesity while the fourth theme-moderation suggested normal weight as the optimum weight to support survival in older adults. To the best of knowledge, this is the first qualitative research based on focus group study that investigated the impacts of overweight and obesity on dementia and survival in older adults.

The study used two separate focus group discussion sessions of 5-6 different older adults including males and females and varied ethnic backgrounds to generate data on the same topic. This helped the richness of the data generated from the dynamics of the group discussion. The use of moderate number of participants as recommended from the literature (Hennink, 2007; Onwuegbuzie *et al.,* 2009) ensured that diverse information was gathered from the group members who felt comfortable, actively participated and were able to freely express their views, thoughts or experiences on the topic.

The study considered rigour and trustworthiness in terms of credibility, transferability, dependability, confirmability as well as research audit trail and reflexivity. To achieve this goal, the study followed strictly the popular and recommended thematic analysis method by Braun and Clark (2006) that helps to achieve trustworthiness criteria in thematic analysis (Nowell *et al.,* 2017). For instance, to help establish trustworthiness, while carrying out the first of the six steps of the thematic analysis outlined by Braun and Clark (2006) on familiarizing yourself with your data, there was constant engagement with the data and triangulation of the different data collection modes which included digital recording device and note-taking.

8.4.5.2 Limitations

The study used the group as the unit of analysis which involved emerging themes while it was possible to have considered other recommended units of analysis (Duggleby, 2005) such as the individual data or group interaction data. It was argued (Onwuegbuzie *et al.,* 2009) that even though majority of researchers use the group as the unit of analysis, the reliance on major emergent themes may obscure information of the degree of agreement or disagreement, leaving the voices of the minority unheard or sidelined. There was also concern that this could limit the robustness of the data. However, to address these limitations full transcripts of the audiotaped focus group discussion was produced and the entire data coded as far as possible to incorporate the views of all participants. Also, the presentation of results drew from the data, codes and actual texts of participants including dissenters while the manner of interpretation of the findings help in reflecting the voices of the minority where applicable. For instance, while most participants were of the view that diet and exercise was useful for weight control one participant did not believe in diet. This contradictory view was highlighted in the results. Besides, where consensus was reached it was clearly stated and the views of dissenters were presented to help assess the degree to which the data that supported the main themes reached saturation during the focus group discussion. An example of this is reflected in the result section on the subtheme-decreases survival chances under findings of theme-mortality. It is believed that addressing this limitation by ensuring the voices of dissenters reflected in the presentation and interpretation of the findings from this study must have enhanced the validity of the themes that emerged such the descriptive, interpretive and theoretical validities previously emphasized by Maxwell (2005) for focus group studies.

The main limitation of the study was the fewer number of focus group discussion on the complex obesity topic. Perhaps the study should have involved several focus groups sessions to provide a more detailed exploration of the topic and themes that emerged for better understanding. However, due to limited time for the study which was part of a larger research project for the thesis, it was difficult to have more than two sessions from the two focus groups. Nonetheless, with adequate trainings received by the researcher on facilitating focus group sessions, the two focus group discussions which lasted an hour each was well coordinated and executed using a moderator team (moderator and note-taker). This contributed to sufficient data of reliable quality that led to useful findings.

One major limitation of the focus group study is the inability to establish or infer any causal link between body weight and dementia. For instance, it was clear from the focus group study that overweight/obesity may be related to chronic diseases such as cardiovascular diseases. However, the link between obesity and dementia was too complex for the understanding of the participants even though they were a clearly educated focus group. Besides, while qualitative studies involving focus group helps understanding of a given phenomenon, it is uncapable of establishing causal relation between variables. This also suggest that observational studies such as prospective cohort studies are better suited for establishing a causal relation. Therefore, despite the views of some participants that bodyweight and dementia might be related, it was difficult to draw a conclusion that overweight and obesity or underweight conveys the risk of dementia.

Another major limitation is the number of participants and composition of the focus group which comprised of entirely educated people. The focus group used the recommended sample size for a typical focus group but in the context of explaining a complex health problem such as health effects of body weight, it is limited and remains a small number from a non-probability sampling and cannot be generalized to a large population. In addition, the sampling of participants resulted in a clearly educated focus group which portray selection bias with the views of the uneducated people not represented. Perhaps a focus group with a heterogenous mix of educated and uneducated people would have led to different findings. Therefore, future focus group may want to consider the views of people with little or no education. Also, this is because they are more likely to be overweight/obese due to their lower socioeconomic status and could contribute with knowledge of their personal experience.

8.4.5.4 Reflexibility

The focus group study typically involved a group interaction and some level of power dynamics that ensured the active involvement of participants. This led to a generation of quality data from the discussion among group members with minimal influence of the moderator. Reflecting on the entire process, however, it is difficult to downplay how my beliefs, personal and professional identity may have impacted on the research process and interpretation of the findings. Having worked previously as a pharmacist and in public health practice (as a senior analysist) may have influenced how the focus group data was interpreted. However, it brought into the research the previous experience of engaging with older adults in the community on a health issue. This was vital to the focus group study that yielded useful findings with implications for further research.

8.4.6 Suggestions for future study

The focus group study showed that the participants were aware that overweight and obesity may contribute to chronic diseases such as cardiovascular diseases, which have been linked with dementia from prospective cohort studies. Therefore, observational studies could examine the association of excess body weight and dementia to establish if they are causally linked. The focus group focused on the UK population and have led to interesting findings. This highlight the need for focus group study to be conducted in the Chinese population. Such focus group should consider heterogeneous mix of uneducated and educated participants. The focus group would be vital in guiding recommendations to policy makers and researchers on curtailing excess body weight and managing body weight in older age.

8.5 Implications and conclusion

The findings from the study have several implications in terms of theory, policy, and practice. The aetiology of dementia is complex and is yet to be unraveled. The focus group could not tell if bodyweight was related to dementia risk, but it was clearer from the focus group that overweight and obesity in older age may be harmful by contributing to cardiovascular diseases. It contributes to the understanding that sedentary lifestyles, poor physical activity, or lack of fitness which relates to overweight and obesity might impact negatively on health. Furthermore, overweight and obesity in older adults do not prolong survival but may increase the risk of death as revealed from the findings. It was understood by the participants that overweight and obesity in older adults contributes to poor health and reduced lifespan of older adults which heightens mortality risk. The study findings emphasized moderation by reducing excess weight and attaining and maintaining normal body weight for survival. Weight control measures involving diet and appropriate exercise that supports active lifestyles are recommended for older adults to reduce the health risk and extend survival.

CHAPTER NINE: GENERAL DISCUSSION

In this chapter, the findings from the quantitative study in the Chinese older population and the qualitative study in the UK older adults are integrated and discussed, while the various contributions to knowledge from both aspects of the research project are underlined to support the conclusions to be drawn for the thesis. The chapter commences with a summary of key findings from each of the main chapters of the thesis. It then progresses into the integration of the findings from the quantitative and qualitative research and this includes interpretations, the implications of the findings and contributions to knowledge. The discussions consider the discipline's broader context in terms of theory, policy, and practice. The chapter includes the recommendations for policy and practice, study strengths, limitations, suggestions for future research and general conclusion of the thesis.

9.1 The key findings from each chapter of the thesis

The thesis employed a mixed method approach to investigate the major risk factors for overweight and obesity in older adults and the health effects in terms of incident dementia and all-cause mortality risk. The key findings from each chapter of the thesis are presented below.

Chapter One: This provided an overview of the health issue addressed by the thesis, the research background, the study focus, the conceptual model and how the thesis was set out to address its research question and aims. This thesis adopted a modified version of a multilevel pathway model for obesity originally proposed by

Kim and Popkin (2006) to show the hypothesised causal thinking in the project whilst also serving as a testing framework.

Chapter Two: The literature on risk factors and the health effects of obesity in older adults was critically reviewed while highlighting the main gaps. The literature showed that the knowledge of the risk factors for overweight/obesity in older people was mostly derived from studies conducted in high-income countries with few studies undertaken in developing settings. Besides, prospective cohort studies to help investigate the long-term risk factors for overweight and obesity in older age are scarce. In addition, most findings were from studies of the general population, and this may not apply to older adults who could present with different risk factors from the rest of the population due to different body characteristics and lifestyle changes associated with both ageing and retirement. The literature also suggested that several risk factors may combine to predict overweight/obesity in older age, and these may include socioeconomic, social network, lifestyle, or individual factors. However, the magnitude and direction of the association in older adults are poorly understood.

The evidence that the risk of incident dementia was increased with obesity and probably overweight is derived from studies of younger/middle-age populations (<65 years). Most of the studies in older people showed that overweight and obesity reduced the risk of incident dementia, and a few studies suggested that they had no significant association with incident dementia. The findings, therefore, supported the beneficial health effects of adiposity in older age.

Most evidence of the association of overweight and obesity with all-cause mortality in older adults supported the medical hypothesis of beneficial health effects of overweight and obesity. This was contrary to findings of increased all-cause mortality observed in younger/middle age (<65 years). In addition, most findings of the studies in population of patients suggested that older people with excess body weight, and with major morbidities like CVDs and dementia, live longer than their normal weight counterparts. This suggests that overweight and obesity in older adults reduces all-cause mortality risk. Therefore, the impacts of overweight and obesity on incident dementia and all-cause mortality needed investigation to contribute to knowledge and understanding of these important topics.

Chapter Three: This chapter summarised the recent evidence through a systematic literature review and meta-analyses on the impact of overweight and obesity in older age on dementia risk. The findings aligned with the obesity paradox hypothesis which supported the beneficial impacts of obesity in older adults since many cohort studies (13 out of 16) suggested protective effects compared to very few (3) that detected harmful effects of overweight and obesity on incident dementia risk. All these studies were from developed countries, with no eligible cohort study from developing countries.

The meta-analysis of 17 studied populations, from 15 studies which included the new data from Anhui cohort study, showed that the protective effects of overweight and obesity on incident dementia were only observable in short term cohort studies (<9 years) and not in those with longer follow-up (≥9 years). This suggests that the long-term follow-up cohort studies would be required to detect any effect of excess weight on the increased risk of dementia, removing the inverse effects due to short term follow-up studies.

Several methodological issues in those studies reporting inverse association were identified including the type of adiposity measure and assessment, shorter length of follow-up, inadequate adjustments for confounders, not accounting for smoking, pre-existing morbidities, reverse causality and lack of sex-stratified analysis. These issues were well addressed in the Anhui cohort study (in Chapter six) with ten years follow-up.

Chapter Four: A mixed methodology approach based on a convergent design involving a parallel database was used for the project. The details of the research design and justifications were clarified. The components of the research work within the study design included the quantitative research on examining the data of large-scale prospective cohort study of Chinese older adults with 10 years follow-up and the qualitative study based on focus group research involving UK older adults. This is in addition to the systematic review and meta-analysis. The purpose of using the data from the two parallel databases of Chinese and UK older adults in a mixed method approach was to complement the findings to help clarify and advance understanding of the risk factors and health effects of obesity in older adults.

Chapter Five: The risk factors for overweight and obesity in older people were investigated using the prospective cohort data of 1,462 older adults (≥65 years). The findings showed a high prevalence of abnormal weight in older Chinese according to the Chinese government defined BMI criteria (Chen et al., 2008): 13.3% of them were underweight (BMI<18.5), 24.4% overweight (BMI 18.5-<24) and 6.5% obese (BMI≥24). The overall prevalence of overweight and obesity was 30.8%, with 34.5% in women and 26.7% in men (p=0.005). The risk factors for overweight/obesity in older adults were low education, watching TV/reading newspapers and hypertension. But older people who were male and lived in rural areas had satisfactory income and were divorced or never married had reduced risk of overweight/obesity.

Chapter Six: The findings from the Anhui cohort study showed that excess body weight in older age was associated with increased risk of dementia, with gender differences. In the whole cohort examined, continuous BMI was significantly associated with increased risk of incident dementia over 10 years of follow-up in older adults. When sex-stratified data analysis was conducted, the impact of overweight and obesity on increased risk of incident dementia was detected only in men but not women. This sex-difference was observed with the different adiposity indicators used and in a subgroup of non-smokers. The study clearly revealed gender differences in dementia risk in relation to adiposity in older age, which is different from the Caucasians.

Chapter Seven: When all-cause mortality was examined in relation to overweight and obesity from the prospective cohort study with 10 years follow-up, there was no significant protective effect from the analysis after accounting for pre-existing morbidities and reverse causality. Evidence from the impact of overweight and obesity on all-cause mortality including those with major morbidities (heart diseases, diabetes, stroke, depression/dementia) showed that obesity was not associated with all-cause mortality risk, while overweight significantly reduced the risk after adjustments for all covariates. However, the findings in those without major morbidities and excluding the first three years data showed that while the harmful effects of underweight remained, no significant association was detected for overweight and obesity. Being underweight in older age was significantly associated with increased risk of all-cause mortality in men, but not women. The findings using WC were similar in pattern to those of BMI.

Chapter Eight:

The impacts of overweight and obesity on health in terms of incident dementia and survival were further explored from the perspectives of older adults in focus group study in the UK. The findings revealed four themes, out of which three suggested deleterious effects of abnormal body weight (underweight, overweight and obesity) on health while the fourth theme emphasised moderation of body weight to stay within normal range as the optimum weight to prevent health risks and prolong survival in older adults. Findings based on the theme-harm suggest brain damage may result from increased body problems and alteration of normal brain function initiated by excess body weight. In addition, the finding from the theme-impairment suggested that impairment of the brain may result from stress-induced by excess weight. While these findings based on theme-harm and theme-impairment suggest health risks that might relate to dementia, it was difficult to conclude based on the focus group that bodyweight was associated with dementia risk. The study from the perspectives of older adults suggests that the participants were aware that overweight and obesity may increase the risk of all-cause mortality. According to the study, increased risk of mortality may result from poor health and reduced lifespan due to overweight and obesity increasing the risks of chronic diseases, mobility-related disability, damage to body organs and decreased survival chances. The study findings supported the moderation of body weight by reducing excess weight and attaining and maintaining normal body weight for survival.

9.2 Discussion of findings

The findings from the two aspects of the research work for the thesis are discussed to see how they contributed to or extended the boundary of knowledge of the risk factors for and of health effects of overweight and obesity in older adults. These included findings from the meta-analysis, and the original findings from the prospective cohort study in China and the focus group research in the UK. The health effects of overweight and obesity are discussed first and the risk factors for overweight and obesity are presented next.

9.2.1 The health effects of overweight and obesity in older adults

The discussions of the health effects are subdivided into two main sections: the impact on incident dementia risk and impacts on all-cause mortality risk. The discussion of these would involve those with and without major morbidities.

9.2.1.1 The impacts on incident dementia risk

This thesis is the first to comprehensively examine the harmful effects of overweight and obesity in terms of incident dementia risk using different adiposity measures within the entire cohort of older adults (≥65 years), including subgroup of smoking status at baseline and sex which showed a stronger effect in men and not women over the 10 years of follow-up. The finding is important since most previous epidemiological studies have reported protective effects against dementia risk. Even when sex-differences in the impact were explored in previous studies, they were strongly detected in women, not men. The data from the Anhui cohort study demonstrated the stronger harmful effects in men regardless of adiposity measures used. Importantly, the findings in women after sensitivity analysis did not support the protective effects of overweight and obesity against the risk of developing dementia. Instead, the evidence from continuous data for the whole cohort of men and women significantly increased the risk of incident dementia.

The findings of increased incident dementia risk in relation to overweight and obesity in older men in this thesis are contrary to the growing evidence of inverse associations reported by many cohort studies including recent systematic literature reviews and meta-analysis (Emmerzaal *et al.,* 2015; Pedditizi *et al.,* 2016). It is consistent with a few cohort studies that reported the harmful effects of adiposity on dementia (Gustafson *et al.,* 2003; Hayden *et al.,* 2006). The study by Gustafson *et al* (2003) reported 13% increased risk of incident dementia in older Swedish women with excess baseline BMI at 70 years after 18 years follow-up. In the same vein, the evidence from the Anhui cohort study in China for the thesis with 10 years of follow-up of older adults (≥65 years) found significantly increased dementia risk from continuous data for men and women. However, the evidence from the sex-stratified analysis confirmed a stronger effect in men but not women. Notably, the incident dementia risk was higher by three and fourfold in older people with overweight and obesity, thereby supporting a dose-dependent association that is independent of other factors such as age, educational level, lifestyles, CVDRFs, ADL and depressive status. The findings reflected similar prediction pattern using BMI, WC and WC/√ height with their continuous and different cutting-point groups and in separate analysis for non-smokers.

It makes sense from theory, as depicted by the conceptual model for the thesis (figure 1 in chapter 1), that since there is substantial body of evidence of a causal link of obesity with related morbidities (such as CVDs, diabetes, hypertension, and depression) with incident dementia (Newman *et al.,* 2005; Kloppenborg *et al.,* 2008; Saczynski *et al.,* 2010; Sharp *et al.,* 2011; Samieri *et al.,* 2018), there may be a positive association of older age overweight and obesity with risk of developing dementia. However, most epidemiological studies could not confirm this hypothesis in older adults except for midlife obesity. In older population studies, most of them reporting inverse associations were based on data from developed countries, where disease risk factors associated with adiposity may vary from different populations such as China. Importantly, most previous studies had several unaddressed methodological issues relating to adiposity measures and types, shorter duration of follow-up, adjustments of confounders including residual effects of smoking, no sex-stratified analysis, pre-existing morbidities, and reverse causation. However, using data from the well-designed and meticulously followed Anhui cohort with the 10 years follow-up, this thesis research has addressed those issues, with detailed statistical analysis. The impacts of overweight and obesity on incident dementia were detected from LMICs, i.e. China.

The findings from this thesis, therefore, have demonstrated new evidence that continuous BMI predicts dementia in all older adults, while overweight and obesity in men (and not women) significantly increased incident dementia risk regardless of the adiposity measure used. Even the findings from the qualitative focus group study of the UK older adults suggested that overweight and obesity may constitute health risks, particularly in terms of chronic diseases such as cardiovascular diseases that have been linked with dementia from cohort studies. The evidence from the focus group supported the damaging effects of excess body weight as suggested by the two main themes "Harm" and "impairment". Therefore, the findings from China and UK studies both supported harmful health effects of excess body weights in older people. As far as we know, the qualitative study of the UK older adults on the impacts of overweight and obesity on dementia risk is the first report in terms of focus group research, while the findings from the Anhui cohort study, China is a new addition to knowledge. The evidence generated from this thesis extends the boundary of knowledge on the health effects of overweight and obesity in older age in terms of incident dementia risk.

9.2.1.2 The impacts of overweight and obesity in older age on all-cause mortality

The prospective cohort study of the Chinese older population (≥65 years) with ten years follow-up of all-cause mortality risk found no evidence in support of the so-called obesity paradox hypothesis that older adults with overweight and obesity could be protected against the risk of death or have a survival advantage over their normal weight counterpart. The Anhui cohort study did not support harmful effects of overweight and obesity in terms of all-cause mortality, and neither was there support for their beneficial impacts as reported in the literature (Dahl et al., 2013; Flegal et al., 2013; Wang et al., 2016). However, increased risk of all-cause mortality was detected in older adults with underweight at baseline, which was seen in most of the previous studies. However, the effect was stronger in men and not women. This gender difference in all-cause mortality risk in relation to underweight is rarely detected by previous studies, and it is an important contribution to knowledge.

Several studies have reported that older age underweight predicted all-cause mortality (Winter et al., 2014; Di Angelantonio *et al.,* 2016; Aunne *et al.,* 2016). However, most of these studies found no gender differences in terms of impact (Winter *et al.,* 2014; Aunne *et al.,* 206). The findings from the Chinese cohort in this thesis showed significantly increased risk by two-fold in men but no effect in women which is contrary to findings in developed countries (Winter *et al.,* 2014). In addition, some recent studies including large scale studies (Di Angelantonio *et al.,* 2016) have doubted if the relationship of underweight and all-cause mortality was completely causal owing to possible illness-related weight loss prior to baseline assessment. However, after excluding prevalent morbidities at baseline and first three years data to limit such bias and stratifying the data by smoking status for analysis, the findings of the Chinese cohort study still retained increased risk for underweight. Nevertheless, considering the lack of data on weight history prior to baseline, further studies would still be needed to examine the extent of the causal relation between underweight and all-cause mortality in the older Chinese adults, particularly in men.

Furthermore, the evidence from the qualitative study conducted in the UK older adults in this thesis also refuted the hypothesis of better survival in those with excess body weight compared with their normal weight counterparts. The finding from a major theme that emerged after analysis of the focus group data was the theme-mortality. The theme-mortality emerged as a health consequence of excess body weight in older adults. Findings based on this theme suggested that overweight and obesity may increase chronic diseases like CVD and mobility-related disability in older adults which could combine to worsen health and increase mortality risk. In addition, overweight and obesity may heighten mortality risk by contributing to body organ damage, reducing survival chances and shorten the lifespan of older adults.

The findings from the UK study suggested that normal weight is the preferred weight for survival. The focus group study adds to the evidence from the views of older adults that normal body weight as recommended by official guidelines are the optimum for survival. In addition, the findings from the UK study did not only highlight normal weight for lowest mortality risk but emphasized moderation of body weight to maintain a normal weight. It supported weight control such as exercise and dietary measures in older adults to reduce excess weight and maintain normal body weight. The emphasis from the findings concerning exercise in older age, however, was on avoiding sedentary life and staying active. The findings from the focus group data also supported the dietary measure for underweight older adults to increase body weight to the normal range to avoid untoward health risks associated with leanness or underweight.

9.2.2 The risk factors for overweight and obesity in older adults

The findings from this thesis suggested a high prevalence of overweight/obesity (30.8%) and underweight (13.3%) in older Chinese, adding in the literature on the magnitude of the problem in China, where the population is ageing. These findings buttress the view that overweight and obesity are a fast-growing issue and a huge challenge for China (Tong et al., 2019). The findings of the major risk factors for overweight/obesity in older adults included rural living, low education, and satisfactory income. The study also found downstream factors were associated with overweight/obesity in the older adult, and these include being never/married, watching TV/reading newspapers, male gender, and hypertension. These factors are discussed in the next sections.

9.2.2.1 Neighbourhood factor (Rural versus urban living)

The findings from the China Study showed that living in rural areas significantly conferred protection against the risk of overweight and obesity compared to urban dwelling. This contradicts findings in developed countries that often link poor neighbourhoods with a high prevalence of overweight/obesity (Sheehan *et al.,* 2017). In China, living in the urban areas may be associated with higher risk of adiposity and this could be due to rapid urbanisation and lifestyle changes including the nutritional transitions brought about by rapid economic development witnessed by the country in the past three to four decades (Yang *et al.,* 2008; Popkin, 2010; 2014; Fox, Fen and Asal, 2019). In contrast, those from rural China are less likely to be affected significantly and immediately by these changes, particularly where socio-cultural norms within the local environment may be stronger and prevail to delay dietary and physical activity behaviour change supportive of increased body weight. This is likely since evidence from research (Zhang *et al.,* 2015) supports disparity in social norms relating to dietary choices between different regions in

China. Research also showed that physical activity and eating behaviours may be determined by social norms independently of social supports (Ball *et al.,* 2010) while cultural patterning of overweight and obesity is becoming more evident in different settings (Brewis, 2010). This, therefore, explains and supports the findings of lower risk of overweight/obesity among Chinese rural dwellers compared to their urban counterparts.

9.2.2.2 Low education

One major upstream social determinant is socioeconomic position measured by education. It was found from the China study that low SEP (primary school education) was a major risk factor for overweight/obesity in older adults when compared with High SEP (secondary/higher education). The findings from recent research in developing countries tend to be the opposite thereby suggesting protective effect of low education against overweight/obesity (Cohen *et al.,* 2013). Contrary to these reported findings, this study showed that low SES measured by education significantly heightened the risk of excess body weight in China. It is consistent with a previous study that reported that higher education was associated with lower abdominal obesity in older women in China (Altsi-Selmi *et al.,* 2013). This finding is also consistent with the evidence of low SEP measured by education as a risk factor for overweight and obesity in the UK and other developed countries (Mclaren, 2007; Cohen *et al.,* 2013).

The literature suggests that educational attainment is a strong social determinant of health (Dahlgren and Whitehead, 2007) with multiple pathways linking it to health outcomes (Braveman, Egerter and Williams, 2011). Therefore, it is possible that one of the pathways linking low education to increased risk of overweight/obesity in China might be through poor health knowledge and reduced self-control resulting in damaging health behaviours relating to diet and physical activity (Johnson and Wardle, 2011). Alternatively, it might be related to fewer opportunities for employment and decent work condition with less access to economic resources to support healthy living and maintain normal body weight.

9.2.2.3 Male gender

The findings of sex differences in risk factors for overweight/obesity from the Anhui cohort suggested that the male gender was associated with reduced risk of excess body weight. This also reflected in the higher prevalence of overweight/obesity observed for females (34.5%) compared to males (26.7%). The mechanisms of sex-disparity in risk factors for overweight/obesity are still poorly understood. However, there are several explanations for why men may be at lower risk compared to women. For instance, it was hypothesised that the physiological demands of extra energy for reproduction and lactation exposes women to the evolutionary pressure of excess body fat storage (Lovejoy *et al.,* 2008). Research also showed that in the same Body Mass Index (BMI), men have higher metabolic rates by about 20% more than women (Arciero *et al.,* 1993; Sharma and Padwal, 2010), thereby suggesting sex disparity in fat-free mass

9.2.2.4 Marital status

Marital status is considered in some literature as a social and community network or more of a mid-stream factor (Sobal *et al.,* 2009; Brenchley and Gorin, 2013). Social network factors such as peer effect, family and marital union are considered as possible mechanisms through which health risks such as obesity in older adults may be spread (Dahlgren and Whitehead, 2007; Christakis *et al.,* 2007). Evidence from developed countries (Switzerland) suggests that living in a couple reduces weight gain after 5.5 years of follow-up (Guerra et al., 2015). However, the findings from the Anhui cohort after 7 years follow-up suggest the opposite and aligns with the view of some studies that higher calorie intake may be enhanced by the influence of spouse (Sobal *et al.,* 2009; Scherr, Brenchley, and Gorin, 2013). It showed from this study that being never married/divorced was significantly associated with a reduction in excess body weight in Chinese older adults. Whilst the reasons for the reduced risk in these older adults is unclear, a previous study in the US by Sobal et al (2009) suggested that it may be related to the broader trends of involvement of the society in marriage including commitment to family, the norms and expectations regarding body weight which may differ between married and unmarried/divorced older people. However, considering that societal norms vary from one setting to the other depending on prevailing cultures, further research will be required to investigate the mechanism involved in Chinese older adults.

9.2.2.5 Watching TV/reading newspapers

The exposure variable 'watching TV/reading newspapers' in the older age of ≥65 years was considered in the Anhui cohort study as a lifestyle/behavioural factor that supports limited physical activity and increases calorie intake resulting in negative energy balance stored as excess body weight and fats in the elderly. While upstream determinants may modify lifestyle behaviours in the elderly, watching TV/reading newspapers represents a transitioning from active to sedentary lifestyle ushered by retirement from active service and age-related changes. This possibly explains the significant association of watching TV/reading papers with overweight/obesity in all the analyses. Surprisingly, research in older adults rarely capture or include this variable. Perhaps due to the assumption that watching TV represents media exposure of advertising which could be more impactful in the younger population. However, this study found that Watching TV/reading newspaper is a major risk factor for overweight/obesity in older age of ≥65 years and suggest it may be due to lifestyle change associated with both ageing and retirement from active service.

9.2.2.6 Hypertension

The findings showed that hypertension was significantly associated with increased risk of overweight/obesity. It was unclear how hypertension which is also considered as an individual risk factor may impact on the risk of overweight/obesity even though studies of health consequences of obesity showed that hypertension is a significant negative outcome (Rahmouni *et al.,* 2005; Chrostowska *et al.,* 2011). However, from a public health perspective, it is important to consider the immediate and wider context within which high blood pressures (hypertension) may build up in older adults. These could reflect a lack of social support, stress, unhealthy diets and inability to cope with the demands of independent living, etc. These have implications in terms of prevention and intervention.

9.3 Recommendations for policy and practice

The findings from the thesis research showed that underweight, overweight and obesity have huge health consequences in terms of increased morbidities and mortality in older people. These calls for public health initiatives on prevention and control of underweight, overweight and obesity associated with related morbidities including incident dementia risk in older adults. It was clear from the evidence in the thesis that the major social determinants of body weight cut across the upstream and downstream factors. This suggests that public health strategies to curb the epidemic of overweight and obesity in the older population and other age populations and the associated co-morbidities would require population-based strategies involving comprehensive approaches at different levels.

9.3.1 Population-based strategies (Upstream and midstream strategies)

The WHO considered the Population-based strategies as a combination of the upstream and midstream strategies while individual strategies are referred to as the downstream strategies. The framework for Obesity Policy Action (OPA) proposed by Sacks, Swinburn and Lawrence (2009) which was developed as a further advancement of the WHO framework for implementation of Global Strategy on Diet, Physical Activity and Health (DPAS), considered several policy options within upstream (socio-ecological), midstream (behavioural) and downstream (health services) targets to reduce overweight and obesity. It was contended that combining from the various public health approaches could offer better prospects of reducing the overweight and obesity epidemic (Sacks, Swinburn and Lawrence, 2009).

9.3.1.1 The upstream policies

The upstream policies are the topmost priority for obesity policy action in order to curtail the overweight and obesity epidemic and reduce the prevalence in older adults. According to the framework by Sacks, Swinburn and Lawrence (2009), policy actions to change behaviour in terms of diet and physical activity in countries like China and the UK population would require an upstream approach which is also called the socio-ecological approach. This is important since the root causes of overweight and obesity are mostly located upstream within the macro-policy environment (Dahlgren and Whitehead, 2007) as demonstrated from recent evidence that economic growth in GDP per capita (Fox, Feng and Asal, 2019) and economic growth strategies of economic globalisation backed by policies (Vogli et al., 2014) have significant impacts on increased prevalence of overweight and obesity internationally. Findings from the thesis showed major upstream and downstream social determinants including policies, SEP (education) and urban and rural areas living, lifestyle behaviour (watching TV), etc. as major risk factors for overweight/obesity. According to the OPA framework, therefore, upstream policies for China and UK could target three crucial aspects to indirectly elicit behaviour change and this includes; policy actions on determinants of health (e.g. education and income), policy action to modify the prevailing food system to support healthy nutrition, and policy action that is impactful on the physical activity environment. This population-based approach targets all population groups including older adults and it could involve increased taxation for the production, sales, and distribution of unhealthy food and drinks, subsidies on some agricultural products, increasing employment opportunities, improved education system, provisions of decent housing and welfare and ensuring environment supportive of increased physical activity and healthy living, etc. The success of the approach depends on cooperation from both the private sector and government in terms of responsibility for action.

9.3.1.2 Mid-stream policies

The mid-stream policies are a more direct approach that targets mainly behaviour change of a given population or sub-population such as older adults residing in the communities in China or the UK. Public health programmes and social marketing are the common policy instruments involved in the mid-stream strategy which helps to change behaviour by promoting healthy diets and physical activity. For instance, the findings from the China study showed a higher prevalence of overweight and obesity in women while the risks of excess weight in men were less. Therefore, mid-stream strategies may want to target sub-population consisting of women for such intervention apart from strategies for the entire population. In addition, watching TV/reading newspapers is sedentary and lifestyle behaviour in older age due to ageing and retirements. Policies could target older adults to encourage more active life or it may target middle age adults with strategies on planning for less sedentary life after retirement. Achieving success for the mid-stream policy strategies requires the involvement of the private sector, civil society, and the government.

9.3.2 Individual strategies (The downstream strategies)

This approach targets individual behaviours and is concerned with the reduction and management of body weight in those facing bodyweight challenges including overweight, obesity and underweight. The policy aspects are aimed at the provision of appropriate resources including health services and clinical intervention support and this requires health professionals, non-government and government services. It is documented that the goal of the approach (Sacks, Swinburn and Lawrence, 2009; Starr and Bales, 2015), also includes identifying and applying the most appropriate measures of adiposity to estimate body weight and fats while also ensuring diseases risk factors are minimised in older adults through body weight management.

The data and evidence of risk factors and health effects of obesity in older adults were limited, with a lot of studies suggesting beneficial effects of excess body weight and fats in older age. This challenged the official recommendations of the same cut-offs for indices of adiposity for all adult populations regardless of their age. In addition, it raised a very important question, which was addressed in this thesis, of whether weight management and even the prevention of overweight and obesity is necessary for older adults. However, evidence from this thesis supports weight reduction in overweight and obese older adults and encourages management of body weight to stay within normal weight range while the use of anthropometric indices as officially recommended by the WHO for the UK and by the Chinese government for the China population is also supported.

This thesis recommends appropriate control and management of body weight through dietary control and moderate exercise in older adults. A review of evidence on weight loss in older adults of age ≥65 years (Waters, Ward and Villareal, 2013) found that lifestyle interventions involving exercise and calorie restriction over 12 months were effective in achieving healthy weight loss and improved muscle quality and physical function. In addition, recent evidence in older adults based on data from English longitudinal study of ageing by Soni *et al* (2019) showed that the risk for cognitive decline and dementia can be reduced by 34%-50% by moderate to vigorous physical activity of at least once per week over an 8 to10 year follow-up. Therefore, the approach should be used for older adults with overweight and obesity. Furthermore, while weight loss interventions are necessary, underweight older adults need to be carefully monitored and supported with dietary measures to attain and maintain normal body weight in other to prevent health risks associated with leanness. It was however argued that nutritional strategies might be better if started early before late life and onset of dementia (Hogervorst, 2017). This emphasised the need for early interventions. The roles of nutritionists or dieticians in such interventions would be very crucial to success. Regular screenings and monitoring of body weight in older age by health professionals are necessary to maintain normal weight and identify those with underweight or excess body weight for appropriate interventions. Such screenings should involve the use of BMI to assess general adiposity and WC to measure central adiposity as recommended in the official guidelines. This is important since there is a lot of controversy concerning the effectiveness and safety of obesity treatments in older age (Waters, Ward and Villareal, 2013), and from a public health perspective it is much more cost-effective to prevent abnormal body weight in this population.

9.4 Summary of the contributions to knowledge

These are summarized under two sections for the contributions to the knowledge of the health effects of overweight and obesity and the risk factors for overweight/obesity.

9.4.1 Knowledge of health effects of overweight and obesity in older adults

- The mixed method approach led to findings that increased the knowledge and understanding of the health effects of overweight and obesity in older adults. The evidence from the different studies in China and the UK showed that overweight and obesity, and even underweight, are associated with health consequences in terms of increased morbidity and all-cause mortality risk.

- ❖ The thesis generated new evidence that adds to the body of knowledge of the impacts of overweight and obesity in older adults on incident dementia risk. It comprehensively explored and demonstrated the harmful effects of overweight and obesity in terms of incident dementia risk using different adiposity measures within the entire cohort of older adults (≥65 years) who were followed up for 10 years including a subgroup of never-smokers and found a stronger effect in men and not women. The effects were dose-dependent reflecting an increase by three and fourfold for men with overweight and obesity, respectively. This evidence from an LMIC country (China) has not been previously reported. This, therefore, extended the boundary of knowledge on the health effects of overweight and obesity in older age in terms of incident dementia risk.
- ❖ There was no evidence in support of the so-called obesity paradox hypothesis that older adults with overweight and obesity have reduced all-cause mortality risk than their normal weight counterparts. The all-cause mortality risk was increased in the underweight, but the effect was stronger in men and not women thereby revealing a gender difference that is rarely detected by most studies.
- ❖ The qualitative study of the UK older adults on the impacts of overweight and obesity on dementia risk and survival using focus group data is a new

addition to the knowledge which was not reported before. It generated further evidence from the views of older people and contributed to the knowledge base with findings that supported the harmful effects of overweight and obesity in older age.

- ❖ The findings from the qualitative study also added to the body of evidence on optimal weight for survival. Most previous evidence from epidemiological studies has located the optimal BMI for survival to be within the overweight and obese BMI range using quantitative data thereby supporting the beneficial effects of overweight and obesity in older age. However, the findings from the UK study older adults suggest that normal bodyweight is more appropriate for reduced health risks and survival in older age. In addition, the findings emphasized the moderation of body weight to maintain normal body weight.

9.4.2 Knowledge of risk factors for overweight/obesity

- ❖ This thesis supports the limited evidence in the literature on major risk factors for overweight/obesity in strictly older adults. It revealed upstream social determinants including neighbourhood SEP (rural versus urban living) and socioeconomic factors (education and income). Contrary to previous evidence that low education is negatively associated with overweight/obesity in LMIC, the findings from this thesis suggest a positive association that is consistent with evidence documented in developed countries. In addition, high income and living in rural compared to urban were protective in older adults. The study also found that the downstream factors including watching

TV/reading newspapers and hypertension increased overweight/obesity while being of male gender and never married/divorced reduced the risk.

9.5 Study strengths, limitations, and suggestions for future research

9.5.1 Strengths of the study

- The doctoral research involved quantitative (prospective cohort study) and qualitative (focus group study) approaches with each having its strengths and limitations as outlined in the methodology (Chapter four). The evidence base for the thesis was strengthened by using a mixed method convergent design by different datasets which involved prospective cohort study in China and focus group study in the UK. This mixed method approach has some advantages in the field of epidemiology and the findings contributed to the knowledge of risk factors and health effects of overweight and obesity in older adults. Although the studies from China and the UK were different, did not validate each other since they were conducted in different populations with varied race, ethnicity and culture, and were only integrated in the discussion stage, the separate findings added to knowledge. The China cohort study provided more evidence and a better understanding of the risk factors and health effects of overweight and obesity in older age. The findings refuted the obesity paradox hypothesis that overweight and obesity were beneficial to health in term of reducing the risk of incident dementia or that they could prolong survival in older adults. This was confirmed by their association with increased risk of dementia in all older adults, and with a stronger effect in Chinese men. The UK study suggested harmful health consequences of overweight and obesity and led to recommendations for prevention of excess body weight in older adults.

- One major strength is the use of prospective cohort study data with 10 years of follow-up in the study of dementia, and all-cause mortality in relation to overweight and obesity in older adults. It was argued from obesity epidemiology research perspective (Hu, 2008, Pg. 45) that prospective cohort study is the strongest non-randomised study design. This is because the temporal order of the exposure and outcome relation can be established and when compared with cross-sectional or case-control studies it is less susceptible to bias. Evidence from the literature suggests that the consequences of overweight and obesity on health outcomes takes a long time to manifest. For instance, it takes up to 7-8 years on average for dementia risk after exposure to excess BMI to be detected in older age, and in the younger population (<65 years) it requires at least 10 years or more. Therefore the 10 years follow-up of the Chinese cohort of older adults strengthened the findings from the thesis which showed that overweight and obesity are associated with harmful health effects in terms of incident dementia, which is in contrast with short term studies showing inverse associations.
- Cohort studies on risk factors for overweight/obesity are scarce internationally and frequently of fewer years of follow-up while most evidence has come from cross-sectional studies which are prone to bias due to issues with temporal order and reverse causality. However, the study of risk factors for overweight/obesity in the thesis was based on data from

prospective cohort design with long follow-up of 7 years. This strengthened the findings which have implications for policy and practice on combating overweight and obesity in older adults.

- The study of the health effects of overweight and obesity in the thesis employed multiple indicators of adiposity including measured BMI, WC and WC/√heights including their continuous data, categorical measures, and quartiles in the analysis. These are important considering limitations of BMI in estimating regional body fats while it still provides a very good measure of general adiposity. Besides, body fat redistribution to the abdominal region with ageing makes the use of WC a much better surrogate for quantifying abdominal fats. In addition, loss of height with the advancement in ageing for men and women makes the use of WC/√heights more relevant apart from BMI which accounts for height. The use of these indicators in the thesis helped to confirm the findings of the health effects of overweight and obesity. For instance, the prediction of incident dementia risk by overweight and obesity showed a similar pattern across the various indicators of adiposity used which showed their harmful health effects regardless of the adiposity measure considered. In addition, unlike most studies that relied solely on the use of BMI, both the BMI and WC were used as predictors of all-cause mortality risks in this thesis and the findings did not support a paradox of beneficial effects of excess weight on survival in older age.
- The quantitative research for the thesis involved a comprehensive analysis of the prospective cohort data. The statistical analysis considered several major confounders including socio-demographic covariates, smoking and

medical co-morbidities in the statistical models deployed. The influence of pre-existing illness at baseline and reverse causality were addressed through the statistical analysis which enhanced the validity of the findings. In addition, subgroup analysis was used to examine gender differences in the impacts of overweight and obesity on the health outcomes and to test if residual confounding owing to smoking could explain the findings of health effects detected. In doing so, the harmful effects of overweight and obesity on incident dementia risk were detected in Chinese men and not women, and when the sample of non-smokers was analysed, the dementia risk significantly increased by more than fourfold for obese BMI and threefold for large waist circumference. These statistical approaches were rarely exploited in most studies, especially those reporting inverse or no association of adiposity in older adults and incident dementia.

- The PhD thesis contributed evidence in Low and Middle-Income Countries (LMICs) where the data was lacking. It has found a positive association of excess weight in older age with incident dementia risk. Before now, findings from cohort studies in LMICs on the impacts of overweight and obesity in older age on dementia risk were very limited. This was confirmed from the comprehensive systematic literature review (Chapter five) that found no single eligible cohort study from the LMICs although 60% of dementia comes from these countries. However, using data from a different population like China with unique patterns of risk factors (different from western populations), the thesis contributed to new knowledge of the impact of overweight and obesity in older age on the development of late-life dementia.

- ❖ Another strength of the doctoral research work was drawn from the focus group study conducted in the UK. It supported the harmful effects of overweight/obesity in terms of cardiovascular diseases, and mortality and highlighted the recommended normal body weight as the optimum for lowest health risks and survival. As far as I know, there has not been a focus group study in the UK that investigated the impacts of overweight and obesity on dementia risk and survival. These findings from the focus group study based on the views and experience of older adults in the UK, strengthen the evidence base for the thesis and add to the knowledge of risk factors and health effects of overweight and obesity. The focus group study considered rigour and trustworthiness which was crucial for meaningful and useful findings by using suggestions from Nowell *et al* (2017) who emphasized credibility, transferability, dependability, confirmability as well as research audit trail and reflexivity. To help achieve this goal, the study followed strictly the popular and recommended thematic analysis method by Braun and Clark (2006) and drew from the further insight provided by Nowell *et al* (2017) for meeting trustworthiness criteria in thematic analysis. For instance, to help establish trustworthiness, while carrying out the first of the six steps of the thematic analysis outlined by Braun and Clark (2006) on familiarizing oneself with the data, there was constant engagement with the data and triangulation of the different data collection modes which included digital recording device and note-taking. The reflective thoughts about the process included proper documentation of the steps taken and the key experience. I also acknowledged and declared in the study of how my previous background and experience might have influenced interpretations of the qualitative study findings.

9.5.2 Limitations of the study

- One limitation is that, even though the sample size for the prospective cohort study was large, there were wider confidence intervals of dementia risk in different groups of abnormal weight, and particularly, after excluding the wave two dementia cases, reduced OR of dementia in underweight became non-significant. Therefore, it was unclear whether using a larger sample size would have confirmed a lack of association or protective effect of underweight on dementia risk.
- In the study of body weight and dementia risk (Chapter, six dementia diagnosis in the 1st and 2nd wave surveys was by the GMS-AGECAT and in the 3rd and 4th wave surveys by the 10/66 dementia research algorithms. The GMS-AGECAT is a part of the 10/66 algorithms. The GMS-AGECAT dementia diagnosis has been validated in western populations and could principally diagnose dementia in middle-income countries. The Chinese version used in the Anhui cohort study has been validated among older Chinese in Mainland China, Hong Kong, Beijing, Taiwan, and Singapore. Double blind methods were used for the validation of the GMS-AGECAT with two independent consultant psychiatrists used as gold standard for diagnosis. It showed good total agreement of 83.6% and Kappa 0.67 ($p < 0.001$). The GMS-AGECAT depression diagnosis showed sensitivity of 85.7% and specificity of 81.8%, while positive predictive value was 80.0% and negative predictive value was

87.1% respectively (Chen et al., 2004). Similarly, the validation test of the GMSAGECAT dementia diagnoses in an urban community in Beijing (China) a total agreement of 88.3% for dementia and depression with a Kappa 0.78 (Liu et al., 2001). However, it may make over-diagnosis due to educational bias. Those over-diagnosed dementias in the Anhui cohort are mainly due to low educational level. Excluding them from the baseline for incident dementia analysis might have reduced the associations of overweight and obesity with incident dementia. Thus, the increased dementia risk estimates would be more conservative.

- The Anhui cohort study recorded a 10.5 % loss to follow-up which is quite low and could be considered impressive as suggested by the literature (Kristman, Manno and Côté, 2004; Fewtrell *et al.,* 2008). However, it is difficult to discount the impact it would have had if there was lower or no loss to follow-up. This is because lost to follow up serve as a threat to the internal validity of estimates from cohort studies (Howe *et al.,* 2016). It was also argued that loss to follow up is unavoidable in most studies of cohort study design (Kristman, Manno and Côté, 2004). While this is true, the Anhui cohort study had a high follow-up rate of 89.5% which exceeds the minimum recommended rates for cohort studies (Kristman, Manno and Côté, 2004; Fewtrell *et al.,* 2008). Besides, those lost to follow-up were not significantly different from the baseline characteristics of participants followed up (Chen *et al.,* 2014). Therefore, it could be argued that the Anhui cohort was meticulously followed up in the study and led to robust data that supported the validity of the findings in this thesis.

- ❖ In the study of the impacts of overweight and obesity on all-cause mortality (Chapter seven), there was the challenge of a limited sample size in some sub-group analysis. For instance, the analysis for non-smokers produced wide confidence intervals including subgroup analysis by gender with results showing non-significant increased mortality risk for overweight and obesity in men who were never-smokers and the opposite in women. Similarly, the analysis of all-cause mortality in older adults with established baseline dementia produced non-significant findings with wide confidence intervals reflective of the reduced sample sizes of people with dementia at baseline. Having larger sample sizes of people with dementia at baseline would have allowed in-depth analysis with robust findings of impacts of overweight/obesity on all-cause mortality risk in that dementia; this is because some recent studies suggested paradox of beneficial effects in dementia patient samples.
- ❖ One limitation of the focus group study was the low number of focus group discussions on the complex obesity topic. Perhaps the study should have involved a greater number of focus groups sessions to provide a more detailed exploration of the interesting themes that emerged for more understanding. However, due to the limited time for the PhD study, it was difficult to have more than two sessions from the focus group discussions. Nonetheless, with adequate training received by the researcher on facilitating focus group sessions, the two focus group discussions which lasted about an hour each were well-coordinated and executed using a moderator team

(moderator and note-taker). This contributed to enough data of reliable quality that led to findings which added to knowledge.

- The focus group study used the group as the unit of thematic analysis which is popular and recommended. However, some researchers have argued for individual data or group interaction data as a unit of analysis. It is contended that the reliance on major emergent themes may obscure information of the degree of agreement or disagreement and leaves the voices of the minority unheard or side-lined with implications for the robustness of the data. However, to address these limitations full transcripts of the audiotaped focus group discussion were produced and the entire data coded as far as possible to incorporate the views of all participants. Besides, the presentation of results drew from the data, codes and actual texts of participants including dissenters while the manner of interpretation of the findings reflected voices of the minority where applicable. Also, where consensus was reached it was stated and the views of dissenters were presented to help show how the data supported the main themes that emerged from the focus group discussion. Therefore considering, these steps taken, and that the voices of dissenters reflected in the presentation and interpretation of the findings from this study, it would be appropriate to claim that the validity of the themes that emerged including the descriptive, interpretive and theoretical validities were enhanced for the focus group study.
- One major limitation is the inability of the focus group study to determine or infer any causal link between body weight and dementia. For instance, it was clear from the focus group study that overweight/obesity is associated with

chronic diseases such as cardiovascular diseases. However, the link between obesity and dementia was confusing for the participants, even though they were an educated focus group. Besides, while qualitative studies involving focus group helps to understand a given phenomenon, it is difficult to infer any causal relationship between variables. This also suggests that observational studies such as prospective cohort studies are better suited for determining a possible causal relationship. Therefore, despite the views of some participants that bodyweight might be associated with dementia, it was difficult to conclude that overweight and obesity or underweight conveys the risk of dementia.

- Another major limitation is the number of participants and the composition of the focus group, which comprised of entirely educated people. The focus group used the recommended sample size for a focus group, but in the context of explaining a complex health problem such as health effects of body weight, it is limited and remains a small number from a non-probability sampling and cannot be generalized to a large population. Also, the sampling of participants resulted in an educated focus group which portray selection bias with the views of the uneducated people not represented. Perhaps a focus group with a heterogeneous mix of educated and uneducated people would have led to different findings. Therefore, a future focus group study may want to consider the views of people with little or no education. Also, this is because they are more likely to be overweight/obese due to their lower socioeconomic status and could contribute with knowledge of their personal experience.

9.5.3 Suggestions for future study

- The thesis found major risk factors associated with overweight/obesity in older adults which cut across upstream social determinants (e.g. education, income, urban/rural living) and downstream (e.g. marital status, watching TV, gender) factors in line with the scope of the doctoral work. However, more studies would be required in future to examine the mechanisms through which the upstream determinants may impact on the downstream factors or how these factors combine or interact to increase overweight and obesity in older adults.
- The array of variables considered in the study of risk factors for overweight and obesity could not capture social norms or cultures even though lifestyle and social network factors were considered. Since the literature suggests that prevailing culture or social norms tends to impact on behaviour relating to diet and physical activity there is need for further research to help understand the role of social norms or culture in the epidemiology of overweight and obesity in older adults.
- Dietary intake, dietary type and pattern of eating are crucial to the understanding of the determinants of overweight/obesity. Besides, detailed physical activity may impact on body weight while the role of genetics in overweight/obesity is postulated in the literature. However, the Anhui cohort study lack data on dietary intake neither were data available on detailed physical activities or genetics to examine these relationships in older adults. This highlights the need for further study.

- ❖ Future research will be needed to understand the mechanisms through which overweight and obesity impacts on dementia risk in older Chinese men and why women with overweight and obesity reflected no association.
- ❖ The thesis found that underweight is associated with increased health risks China. More research in older Chinese adults would be needed to understand the sex differences in all-cause mortality risks in those with underweight.
- ❖ The evidence from the UK study suggests that both underweight and overweight/obesity might be associated with health risks. However, it was not possible to infer any causal association with dementia, considering the study design used, and the complex nature of the topic which was difficult for the small number of the educated participants. Therefore, research from observational studies in the UK would be needed to ascertain if bodyweight in older age impacts on dementia risk.
- ❖ The focus group in the UK led to interesting findings and recommendations, and similar study would be needed in China considering ethnic/cultural differences. Such focus group should consider heterogeneous mix of educated and uneducated participants. The findings could be vital in guiding recommendations to policy makers and researchers on curtailing excess body weight and managing body weight in the Chinese people.
- ❖ Underweight in older age has been linked with sarcopenia, a condition associated with physical inactivity and aging with difficulty in maintaining muscle mass and strength (Morley, 1996; Morley *et al.,* 2010; Morley, 2012). Therefore, research would be needed on increasing muscle mass to prevent frailty and improve brain health via physical activity.

- ❖ Future research using prospective cohort designs and data of weight history could examine the impacts of weight change on incident dementia risk.
- ❖ It is clear from this thesis that future epidemiological studies need to consider the long duration of follow-up to allow the health effects of chronic diseases such as overweight and obesity to manifest. There is a need for more attention to the effects of confounding, including smoking and pre-existing morbidities, while accounting for the effects of reverse causality is necessary. Subgroup analysis should be encouraged as such approach could reveal important findings as observed for sex disparity in health risks using different indicators of adiposity in this thesis.

9.6 General conclusions

This PhD thesis research investigated the risk factors and health effects of overweight and obesity in older adults using data from the 10 years follow-up prospective cohort study of older population in China. The evidence from the thesis extended the boundary of knowledge and increased the understanding of the risk factors and health effects of overweight and obesity in older adults.

It is clear from the doctoral thesis that, contrary to previous suggestions by some authours that excess body weight in older age confer beneficial or protective health effects, it was found that overweight and obesity were associated with harmful consequences. These were revealed from the harmful effects on health in terms of increased incident dementia risk, and no evidence in support of reduced all-mortality risk in those with overweight and obesity in older age. Over the 10 years follow-up of the cohort, a significant increase in incident dementia risk was found in the older population who had overweight and obesity and the harmful effects were stronger in men and not women regardless of the measures of adiposity used including BMI, WC and WC/√heights. The gender differences in incident dementia risk due to excess body weight in older Chinese adults needs to be researched in future to understand the mechanisms involved.

In terms of increased mortality risk, the evidence from the study of the Chinese population did not support the paradox of beneficial effects of overweight and obesity in older age which was observed in many previous studies. This was after accounting for confounders including smoking and pre-existing morbidities and reverse causality. However, harmful effects were not observed except for subgroup analysis of never-smokers for men where it suggested increased risk, but the confidence interval was too wide, and the results remained non-significant. Furthermore, the Anhui cohort data showed that underweight increased all-cause mortality risk with a stronger effect in Chinese men. This showed that while excess body weight conveys health risk, underweight in older age is also a health problem of concern. Further research would be required to understand the mechanism involved in the association of underweight in older Chinese adults with increased health risk.

The literature suggests that lean body mass, and not low-fat mass, was responsible for the high mortality detected in underweight older adults (Allison et al., 1997). Also, underweight elderly subjects are prone to sarcopenia, which is a condition characterised by reduced muscle mass that affects mobility and clinical outcome (Morley et al., 2011). Besides, sarcopenia is strongly associated with physical inactivity and ageing, which manifest as difficulty in maintaining muscle mass and strength (Morley, 1996; Morley et al., 2010; Morley, 2012). Therefore, there is a need for research to uncover ways to increase muscle mass to prevent frailty and improve brain health via physical activity.

There are some possible explanations for the harmful effect of overweight and obesity in terms of dementia risk and the increased risk of all-cause mortality in the underweight older Chinese adults, which showed a stronger effect in men compared to women after an extended follow up of ten years. Firstly, the Chinese cohort had an extended follow-up which allowed the dementia risk to be detected. This impact of length of cohort follow-up is plausible because the health consequences of overweight and obesity take time to manifest, and for dementia to develop, it could take as much as ten years or more depending on the baseline age of adiposity assessment in cohort studies (Johnson et al., 2006; Knopnan et al., 2007; Kivimaki et a., 2018). The meta-analyses stratified by duration of follow-up in chapter three suggests that a higher BMI decreases dementia risk by 5% in studies with a short follow-up (< 9 years). However, this inverse effect was not supported in studies with longer follow-up (≥9 years), as indicated by the non-significant increased risk. It could be because longer-term studies may be affected by several factors such as attrition, survivor bias and change in weight. It could also be that the change in weight is a more critical factor in the development of dementia risk, as also suggested from the meta-analyses that being overweight (not obese) reduces the risk of Alzheimer's disease while WC showed no significant association. In support of the harmful effect of excess weight, the evidence from Chinese data showed significantly increased dementia risk in the entire cohort with a more substantial effect in obese and overweight men.

Secondly, the higher dementia risk in Chinese obese and overweight men maybe because they are more likely to survive to an older age, whereas in China the underweight have an earlier age at mortality and they are more likely to be poorer (of low SES). Importantly, these underweight men died earlier, perhaps because of poverty-related illness with nutritional deprivation, infectious disease, lung disease, frailty, but not because of CVD. These are supported by the Anhui cohort data, which showed that the underweight older adults were less likely to have heart diseases, diabetes, uncontrolled and controlled hypertension, hyperlipidaemia, and stroke.

Thirdly, CVD shares risk factors with dementia, and the overweight and obese men who also carry these risk factors (such as hypertension, diabetes, hyperlipidaemia) survive for longer but then later develop dementia. These obese men are more likely to be urban, have low education, more likely to have hypertension, stroke, diabetes, hyperlipidaemia, more likely to be married, be sedentary and poorer. Indeed the findings from the cohort study showed that overweight/obesity in men increases the risk for dementia after a 10-year follow-up, but this is mediated partly by Activity of Daily Living (ADL) (they are also frail possibly as they were more likely to be sedentary), hypertension, stroke and depression than the men who do not develop dementia. These effects remained significant when only analysing non-smokers, so as hypothesised CVD risk mediates the association of Obesity/overweight in less educated poor sedentary urban married men.

The underweight men who survive are of higher education, more active, had less risk of CVD (hypertension, diabetes, hyperlipidaemia) and so are also less likely to be diagnosed with dementia. Women who are overweight have less risk of dementia, but this is no longer significant in multivariate analyses. In the developed countries, the US and Swedish women have higher education on average, but here obesity increases dementia risk (Gustafson et al., 2003; Hayden et al., 2006). In these countries, obesity is associated with poverty and low education (Sobal et al., 1989; Wang et al., 2007), which can increase dementia risk. However, being overweight in women reduced dementia risk (Atti et al., 2008; Tolppanen et al., 20014). In these cohorts, there were an insufficient sampling of men to show associations. For instance, the cohorts analysed for the studies by Atti et al (2008) and Tolppanen et al., (2014) had only 26.3% and 38.9% men in their samples, respectively.

The evidence from the focus group study showed that the participants were aware that overweight and obesity may be deleterious to health. The evidence from the views of the UK older adults suggested that overweight and obesity may contribute to chronic diseases, particularly cardiovascular diseases which leads to reduced survival. The study also suggested that the optimum body weight for minimum health risks and survival in older age may be within the recommended normal weight range and that moderating body weight to stay within this range may confer better survival. Considering the findings from the study in the UK, a similar focus group would be needed in China to inform policy and practice.

In all, since the so-called obesity paradox hypothesis of beneficial effects of excess body weight on health were refuted by the evidence from the research in the Chinese population, while the harmful consequences were detected, it led to the conclusion that overweight and obesity in older age and being underweight is deleterious to health.

Furthermore, the evidence of the significant risk factors for overweight and obesity in older age from the thesis showed that they included several factors that cut across the upstream and downstream social determinants of health. This encompasses rural compared to urban living, low education, and high income as upstream determinants while marital status of being unmarried/divorced, watching TV/reading newspapers, male sex and hypertension emerged as significant downstream determinants. These findings provided support for the literature which suggested that tackling overweight and obesity will require a range of policies and strategies that targets mainly the upstream social determinants of health. This is because there is growing evidence linking upstream social determinants with possible root causes of overweight and obesity in developed and developing countries. Besides, even though upstream determinants may be shaped by local environments, they tend to influence the downstream factors which would require individual approaches as part of a larger multilevel approach targeting all stakeholders from different aspects of the society including those in clinical practice.

It is clear from this doctoral thesis that overweight and obesity, and even underweight, in older adults are associated with health risks in terms of incident dementia and all-cause mortality risk. The major risk factors for overweight and obesity are modifiable by public health approaches to curb the epidemic. Evidence from this thesis supports weight reduction in overweight and obese older adults and encourages the management of body weight to attain and remain within normal weight limits. The use of anthropometric indices including both BMI and WC as officially recommended by the WHO for the UK and the Chinese government for China should be sustained.

REFERENCES

Aarsland, D., Ballard, C., McKeith, I., Perry, R.H. and Larsen, J.P (2001). Comparison of extrapyramidal signs in dementia with Lewy bodies and Parkinson's disease. *The Journal of neuropsychiatry and clinical neurosciences*, *13* (3), pp.374-379.

Abdullah, A., Peeters, A., de Courten, M., & Stoelwinder, J (2010). The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. *Diabetes research and clinical practice*, *89* (3), 309-319.

Abdullah, A., Stoelwinder, J., Shortreed, S., Wolfe, R., Stevenson, C., Walls, H., and Peeters, A. (2011). The duration of obesity and the risk of type 2 diabetes. *Public health nutrition*, *14* (1), 119-126.

Adam, T.C (2007). Epel ES. *Stress, eating and the reward system. Physiol Behav*, *91*, pp.449-458.

Adams, K.F., Schatzkin, A., Harris, T.B., Kipnis, V., Mouw, T., Ballard-Barbash, R., Hollenbeck, A. and Leitzmann, M.F (2006). Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *New England Journal of Medicine*, *355* (8), pp.763-778.

Ahtiluoto, S., Polvikoski, T., Peltonen, M., Solomon, A., Tuomilehto, J., Winblad, B., Sulkava, R. and Kivipelto, M (2010). Diabetes, Alzheimer disease, and vascular dementia: a population-based neuropathologic study. *Neurology*, *75* (13), pp.1195-1202.

Albanese, E., Launer, L.J., Egger, M., Prince, M.J., Giannakopoulos, P., Wolters, F.J. and Egan, K (2017). Body mass index in midlife and dementia: Systematic review and meta-regression analysis of 589,649 men and women followed in longitudinal studies. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *8*, pp.165-178.

Alford, S., Patel, D., Perakakis, N. and Mantzoros, C.S (2018). Obesity as a risk factor for Alzheimer's disease: weighing the evidence. *Obesity reviews*, *19*(2), pp.269-280.

Allison, D.B., Faith, M.S., Heo, M. and Kotler, D.P (1997). Hypothesis concerning the U-shaped relation between body mass index and mortality. *American journal of epidemiology*, *146* (4), pp.339-349.

Aloi, J.F., Vaswani, A., Russo, L., Sheehan, M. and Flaster (1995). The influence of menopause and hormonal replacement therapyon body cell mass and body fat mass. *American journal of obstetrics and gynecology*, *172* (3), pp.896-900.

Al-Safi, Z. A., and Polotsky, A. J. (2015). Obesity and menopause. *Best Practice & Research Clinical Obstetrics & Gynaecology*, *29* (4), 548-553.

Asarian, L. and Geary, N (2006). Modulation of appetite by gonadal steroid hormones. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *361*(1471), pp.1251-1263.

Anstey KJ, Cherubim N, Budge M, Young J (2011) Body mass index in midlife and late life as a risk factor for dementia: a meta-analysis of prospective studies. *Obes Rev* **12**, e 426-e437.

Anum, E.A. and Adera, T (2004). Hypercholesterolemia and coronary heart disease in the elderly: a meta-analysis. *Annals of epidemiology*, *14* (9), pp.705-721.

Arciero, P.J., Goran, M.I. and Poehlman, E.T (1993). Resting metabolic rate is lower in women than in men. *Journal of applied physiology*, *75* (6), pp.2514-2520.

Arvanitakis, Z., Wilson, R.S., Bienias, J.L., Evans, D.A. and Bennett, D.A (2004). Diabetes mellitus and risk of Alzheimer disease and decline in cognitive function. *Archives of neurology*, *61*(5), pp.661-666.

Atti A (2008) Late-life body mass index and dementia incidence: nine-year follow-up data from the Kungsholmen Project. J Am Geriatr Sock 56, 111-116.

Aunt, D., Sen, A., Prasad, M., Nora, T., Janky, I., Tonstad, S., Romundstad, P. and Vatten, L.J (2016). BMI and all-cause mortality: a systematic review and non-linear dose-response meta-analysis of 230 cohort studies with 3.74 million deaths among 30.3 million participants. *BMJ*, *353*.

Baigent, C. (2005). Cholesterol Treatment Trialists'(CTT) Collaborators: Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet*, *366*, pp.1267-1278.

Bailey, S. and Handu, D (2013). *Introduction to epidemiologic research methods in public health practice*. Jones & Bartlett Publishers. pp.43

Ball, K., Jeffery, R. W., Abbott, G., McNaughton, S. A., & Crawford, D. (2010). Is healthy behaviour contagious: associations of social norms with physical activity and healthy eating. *International Journal of Behavioural Nutrition and Physical Activity*, *7* (1), 86.

Banack, H.R. and Kaufman, J.S. (2014. The obesity paradox: understanding the effect of obesity on mortality among individuals with cardiovascular disease. *Preventive medicine*, *62*, pp.96-102.

Bandaru, V.V.R., Troncoso, J., Wheeler, D., Pletnikova, O., Wang, J., Conant, K. and Haughey, N.J., (2009). ApoE4 disrupts sterol and sphingolipid metabolism in Alzheimer's but not normal brain. *Neurobiology of aging*, *30* (4), pp.591-599.

Bastien, M., Poirier, P., Lemieux, I. and Després, J.P (2014). Overview of epidemiology and contribution of obesity to cardiovascular disease. *Progress in cardiovascular diseases*, *56*(4), pp.369-381.

Bays, H.E., Toth, P.P., Kris-Etherton, P.M., Abate, N., Aronne, L.J., Brown, W.V., Gonzalez-Campoy, J.M., Jones, S.R., Kumar, R., La Forge, R. and Samuel, V.T (2013). Obesity, adiposity, and dyslipidemia: a consensus statement from the National Lipid Association. *Journal of clinical lipidology*, *7* (4), pp.304-383.

Beaudart, C., Zaaria, M., Pasleau, F., Reginster, J.Y. and Bruyère, O (2017). Health outcomes of sarcopenia: a systematic review and meta-analysis. *PloS one*, *12* (1), p.e0169548.

Begum, H., Li, B., Shui, G., Cazenave-Gassiot, A., Soong, R., Ong, R.T.H., Little, P., Teo, Y.Y. and Wenk, M.R (2016). Discovering and validating between-subject variations in plasma lipids in healthy subjects. *Scientific reports*, *6*, p.19139.

Belanoff, J.K., Kalehzan, M., Sund, B., Fleming Ficek, S.K. and Schatzberg, A.F (2001). Cortisol activity and cognitive changes in psychotic major depression. *American Journal of Psychiatry*, *158*(10), pp.1612-1616.

Beleigoli, A. M., Boersma, E., Maria de Fátima, H. D., Lima-Costa, M. F., & Ribeiro, A. L. (2012). Overweight and class I obesity are associated with lower 10-year risk of mortality in Brazilian older adults: the Bambuí Cohort Study of Ageing. *PloS one*, *7* (12), e52111.

Bennett, G. G., Wolin, K. Y and Duncan, D. T. (2008). Social determinants of obesity. In F. B. Hu (Ed.), *Obesity epidemiology* (pp. 342–376). New York: Oxford University Press

Berraho, M., Nejjari, C., Raherison, C., El Achhab, Y., Tachfouti, N., Serhier, Z., Dartigues, J.F. and Barberger-Gateau, P (2010). Body mass index, disability, and 13-year mortality in older French adults. *Journal of ageing and health*, *22* (1), pp.68-83.

Bettany-Saltikov J (2012) How to do a Systematic Literature Review in Nursing: A Step-by-Step Guide, McGraw-Hill Education (UK).

Beydoun MA, Beydoun H, Wang Y (2008) Obesity and central obesity as risk factors for incident dementia and its subtypes: a systematic review and meta-analysis. Obesity Reviews 9, 204-218.

Bhaskaran, K., Douglas, I., Forbes, H., dos-Santos-Silva, I., Leon, D.A. and Smeeth, L (2014). Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5· 24 million UK adults. *The Lancet*, *384* (9945), pp.755-765.

Bhopal, R., 1999. Paradigms in epidemiology textbooks: in the footsteps of Thomas Kuhn. *American Journal of Public Health*, *89* (8), pp.1162-1165.

Bhopal, R.S (2016). *Concepts of epidemiology: integrating the ideas, theories, principles, and methods of epidemiology*. Oxford University Press.

Bhopal, Raj S (2008) *Concepts of Epidemiology: An Integrated Introduction to the Ideas, Theories, Principles and Methods of Epidemiology.* 2nd ed. Oxford: Oxford University Press.

Boa, C., Manila, M., Ye, Z., Wang, J., Jinn, M., He, W. and Chen, K (2015). Forecasting and analysing the disease burden of the aged population in China, based on the 2010 global burden of disease study. International journal of environmental research and public health, 12 (7), pp.7172-7184.

Borenstein Graves A, Mortimer JA, Bowen JD, McCormick WC, McCurry SM, Schellenberg GD, Larson EB (2001) Head circumference and incident Alzheimer's disease: modification by Apolipoprotein E. Neurology 57, 1453-1460.

Bornstein, S.R., Schuppenies, A., Wong, M.L. and Licinio, J (2006). Approaching the shared biology of obesity and depression: the stress axis as the locus of gene-environment interactions. *Molecular psychiatry*, *11*(10), p.892.

Bowman, K., Thambisetty, M., Kuchel, G.A., Ferrucci, L. and Melzer, D (2019). Obesity and Longer-Term Risks of Dementia in 65–74-Year-Olds. *Age and Ageing*, *48* (3), pp.367-373.

Boyatzis, R. E. (1998). *Transforming qualitative information: Thematic analysis and code development*. Sage.

Brasilia, N., Huffman, D.M., Muzumdar, R.H. and Bartke, A., 2012. The critical role of metabolic pathways in ageing. *Diabetes*, *61*(6), pp.1315-1322.

Braun, V. and Clarke, V (2006). Using thematic analysis in psychology. *Qualitative research in psychology*, *3* (2), pp.77-101.

Braun, V., Clarke, V., Hayfield, N. and Terry, G., 2019. Thematic analysis. *Handbook of Research Methods in Health Social Sciences*, pp.843-860.

Braveman, P., Egerter, S., & Williams, D. R. (2011). The social determinants of health: coming of age. *Annual review of public health*, *32*, 381-398.

Bremmer, M.A., Beekman, A.T.F., Deeg, D.J.H., Penninx, B.W.J.H., Dik, M.G., Hack, C.E. and Hoogendijk, W.J.G (2008). Inflammatory markers in late-life depression: results from a population-based study. *Journal of affective disorders*, *106* (3), pp.249-255.

Brewis, A. A. (2010). *Obesity: Cultural and biocultural perspectives*. Rutgers University Press.

Brown, R.E. and Kuk, J.L (2015). Consequences of obesity and weight loss: a devil's advocate position. *Obesity Reviews*, *16*(1), pp.77-87.

Bruce, N., Pope, D. and Stanistreet, D (2008). *Quantitative Methods for Health Research a Practical Interactive Guide to Epidemiology and Statistics.* Chichester, West Sussex: J. Wiley, Print. pp.3

Bryman, A., 2006. Integrating quantitative and qualitative research: how is it done? *Qualitative research*, *6*(1), pp.97-113.

Buchman AS, Wilson RS, Bienias JL, Shah RC, Evans DA, Bennett DA (2005) Change in body mass index and risk of incident Alzheimer disease. Neurology 65, 892-897.

Burton, R.F (2010). Waist circumference as an indicator of adiposity and the relevance of body height. *Medical Hypotheses*, *75* (1), pp.115-119.

Byers, A.L. and Yaffe, K (2011). Depression and risk of developing dementia. *Nature Reviews Neurology*, *7* (6), p.323.

Calle, E. E., Thun, M. J., Petrelli, J. M., Rodriguez, C., & Heath Jr, C. W. (1999). Body-mass index and mortality in a prospective cohort of US adults. *New England Journal of Medicine*, *341*(15), 1097-1105.

Callisaya, M., Moran, C. and Srikanth, V (2013). Type 2 Diabetes mellitus as a causal factor for dementia-is there sufficient evidence from interventional studies? *Australasian Epidemiologist*, *20*(1), p.26.

Canoy, D., Luben, R., Welch, A., Bingham, S., Wareham, N., Day, N. and Khaw, K.T (2004). Fat distribution, body mass index and blood pressure in 22 090 men and women in the Norfolk cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk) study. *Journal of hypertension*, *22* (11), pp.2067-2074.

Caruana, E.J., Roman, M., Hernández-Sánchez, J. and Solli, P (2015). Longitudinal studies. *Journal of thoracic disease*, *7* (11), p.E537.

Cereda, E., Sansone, V., Meola, G. and Malavazos, A.E (2007). Increased visceral adipose tissue rather than BMI as a risk factor for dementia. *Age and ageing*, *36*(5), pp.488-491.

Chan, J.C., Malik, V., Jia, W., Kadowaki, T., Yajnik, C.S., Yoon, K.H. and Hu, F.B (2009) Diabetes in Asia: epidemiology, risk factors, and pathophysiology. *Jama*, *301* (20), pp.2129-2140.

Chan, R. S., & Woo, J. (2010). Prevention of overweight and obesity: how effective is the current public health approach. *International journal of environmental research and public health*, *7* (3), 765-783.

Chatterjee, S., Peters, S.A., Woodward, M., Arango, S.M., Batty, G.D., Beckett, N., Beiser, A., Borenstein, A.R., Crane, P.K., Haan, M. and Hassing, L.B (2016). Type 2 diabetes as a risk factor for dementia in women compared with men: a pooled analysis of 2.3 million people comprising more than 100,000 cases of dementia. *Diabetes care*, *39*(2), pp.300-307.

Chen R, Tunstall-Pedoe H (2005). Socioeconomic deprivation and waist circumference in men and women: the Scottish MONICA surveys 1989–1995. Eur J Epidemiology; 20: 141–7

Chen, C.M. (2008). Overview of obesity in Mainland China. *Obesity reviews*, *9*, pp.14-21.

Chen, H., Yoshioka, H., Kim, G.S., Jung, J.E., Okami, N., Sakata, H., Maier, C.M., Narasimhan, P., Goeders, C.E. and Chan, P.H (2011). Oxidative stress in ischemic brain damage: mechanisms of cell death and potential molecular targets for neuroprotection. *Antioxidants & redox signalling*, *14* (8), pp.1505-1517.

Chen, R., Hu, Z., Qin, X., Xu, X. and Copeland, J.R (2004). A community-based study of depression in older people in Hefei, China—the GMS-AGECAT prevalence, case validation and socio-economic correlates. *International journal of geriatric psychiatry*, *19*(5), pp.407-413.

Chen, R., Tunstall-Pedoe, H., Morrison, C., Connaghan, J., and A 'Brook, R. (2004). Erratum: Trends and social factors in blood pressure control in Scottish MONICA surveys 1986–1995: the rule of halves revisited. *Journal of Human Hypertension*, *18* (10), 753-754.

Chen, R., Wei, L., Hu, Z., Qin, X., Copeland, J.R. and Hemingway, H (2005). Depression in older people in rural China. *Archives of internal medicine*, *165*(17), pp.2019-2025.

Cheng, F.W., Gao, X., Mitchell, D.C., Wood, C., Still, C.D., Rolston, D. and Jensen, G.L., (2016). Body mass index and all-cause mortality among older adults. *Obesity*, *24*(10), pp.2232-2239.

Cheung, B.M. and Li, C (2012. Diabetes and hypertension: is there a common metabolic pathway? *Current atherosclerosis reports*, *14* (2), pp.160-166.

Chew, H., Solomon, V.A. and Fonteh, A.N (2020). Involvement of Lipids in Alzheimer's disease Pathology and Potential Therapies. *Frontiers in Physiology*, *11*, p.598.

Chilisa, B. and Kawulich, B (2012). Selecting a research approach: Paradigm, methodology and methods. *C Wagner, B Kawulich, & M Garner, Doing social research: A global context*, pp.51-61.

Choi, K., Fabian, L., Mottey, N., Corbett, A. and Forster, J (2012). Young adults' favourable perceptions of snus, dissolvable tobacco products, and electronic cigarettes: findings from a focus group study. *American journal of public health*, *102*(11), pp.2088-2093.

Choy, L.T (2014). The strengths and weaknesses of research methodology: comparison and complimentary between qualitative and quantitative approaches. *IOSR Journal of Humanities and Social Science*, *19* (4), pp.99-104.

Christakis, N.A. and Fowler, J.H. (2007). The spread of obesity in a large social network over 32 years. New England journal of medicine, 357(4), pp.370-379.

Chrostowska, M., Szyndler, A., Hoffmann, M. and Narkiewicz, K. (2013). Impact of obesity on cardiovascular health. *Best practice & research Clinical endocrinology & metabolism*, *27*(2), pp.147-156.

Chrostowska, M., Szyndler, A., Paczwa, P. and Narkiewicz, K (2011). Impact of abdominal obesity on the frequency of hypertension and cardiovascular disease in Poland–Results from the IDEA study (international day for the evaluation of abdominal obesity). *Blood pressure*, *20*(3), pp.145-152.

Clark, D.O., Gao, S., Lane, K.A., Callahan, C.M., Baiyewu, O., Ogunniyi, A. and Hendrie, H.C (2014). Obesity and 10-year mortality in very old African Americans and Yoruba-Nigerians: exploring the obesity paradox. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *69*(9), pp.1162-1169.

Cohen, A. K., Rai, M., Rehkopf, D. H., & Abrams, B. (2013). Educational attainment and obesity: a systematic review. *Obesity Reviews*, *14*(12), 989-1005.

Cohen-Cole, E., & Fletcher, J. M. (2008). Is obesity contagious? Social networks vs. environmental factors in the obesity epidemic. *Journal of health economics*, *27*(5), 1382-1387.

Cole, Stephen R., Robert W. Platt, Enrique F. Schisterman, Haitao Chu, Daniel Westreich, David Richardson, and Charles Poole (2010): "Illustrating bias due to conditioning on a collider." *International journal of epidemiology* 39, no. 2, 417-420.

Connelly, L.M (2016). Trustworthiness in qualitative research. *Medsurg Nursing*, *25*(6), pp.435-437.

Consultation, W.E., 2008. Waist circumference and waist-hip ratio. *Report of a WHO Expert Consultation. Geneva: World Health Organization*, *2008*, pp.8-11.

Cope, D. G. (2014). Methods and meanings: credibility and trustworthiness of qualitative research. In *Oncology nursing forum* (Vol. 41, No. 1).

Copeland, J. R. M., Chen, R., Dewey, M., McCracken, C. F. M., Gilmore, C., Larkin, B., & Wilson, K. C. M (1999). Community-based case-control study of depression in older people: Cases and sub-cases from the MRC–ALPHA study. *The British Journal of Psychiatry*, *175* (4), 340-347.

Copeland, J. R. M., Dewey, M. E., & Griffiths-Jones, H. M. (1986). A computerized psychiatric diagnostic system and case nomenclature for elderly subjects: GMS and AGECAT. *Psychological medicine*, *16* (1), 89-99.

Copeland, J. R., Prince, M., Wilson, K. C. M., Dewey, M. E., Payne, J., and Gurland, B. (2002). The geriatric mental state examination in the 21st century. *International journal of geriatric psychiatry*, *17* (8), 729-732.

Copeland, J.R., Dewey, M.E. and Griffiths-Jones, H.M (1990). Dementia and depression in elderly persons: AGECAT compared with DSM III and pervasive illness. *International journal of geriatric psychiatry*, *5* (1), pp.47-51.

Copeland, J.R., Prince, M., Wilson, K.C.M., Dewey, M.E., Payne, J. and Gurland, B (2002). The geriatric mental state examination in the 21st century. *International journal of geriatric psychiatry*, *17* (8), pp.729-732.

Correa, M. M., Thume, E., De Oliveira, E. R. A., & Tomasi, E. (2016). Performance of the waist-to-height ratio in identifying obesity and predicting non-communicable diseases in the elderly population: A systematic literature review. *Archives of gerontology and geriatrics*, *65*, 174-182.

Craft, S. and Watson, G.S (2004). Insulin and neurodegenerative disease: shared and specific mechanisms. *The lancet neurology*, *3* (3), pp.169-178.

Creswell, J. W., & Poth, C. N. (2017). *Qualitative inquiry and research design: Choosing among five approaches*. Sage publications.

Creswell, J.W (2014). *A Concise Introduction to Mixed Methods Research*. SAGE Publications. Pp. 4

Creswell, J.W. and Clark, V.L.P (2017). *Designing and conducting mixed methods research*. Sage publications. Pp.5

Creswell, J.W., Klassen, A.C., Plano Clark, V.L. and Smith, K.C (2011). Best practices for mixed methods research in the health sciences. *Bethesda (Maryland): National Institutes of Health*, *2013*, pp.541-545.

Crossan, F (2003). Research philosophy: towards an understanding. *Nurse Researcher (through 2013)*, *11* (1), p.46.

Crotty, M (1998). *The foundations of social research: Meaning and perspective in the research process*. Sage.

Cui, R., Iso, H., Yamagishi, K., Saito, I., Kokubo, Y., Inoue, M., & Tsugane, S (2011). Diabetes mellitus and risk of stroke and its subtypes among Japanese: the Japan public health centre study. *Stroke*, *42* (9), 2611-2614.

Dahl AK, Löppönen M, Isoaho R, Berg S, Kivelä SL (2008) Overweight and obesity in old age are not associated with greater dementia risk. J Am Geriatrics Soc 56, 2261-2266.

Dahl, A.K., Fauth, E.B., Ernsth-Bravell, M., Hassing, L.B., Ram, N. and Gerstof, D (2013). Body mass index change in body mass index, and survival in old and very old persons. *Journal of the American Geriatrics Society*, *61* (4), pp.512-518.

Dahlgren, G. and Whitehead, M. (2007). *European strategies for tackling social inequities in health*. WHO, Regional Office for Europe.

Dallman, M.F (2006). Pecoraro NC, La Fleur SE, Warne JP, Ginsberg AB, Akana SF, Laugero KC, Houshyar H, Strack AM, Bhatnagar S, Bell ME. *Glucocorticoids, chronic stress, and obesity. Prog Brain Res*, *153*, pp.75-105.

Danat, I.M., Clifford, A., Partridge, M., Zhou, W., Bakre, A.T., Chen, A., McFeeters, D., Smith, T., Wan, Y., Copeland, J. and Anstey, K.J (2019. Impacts of overweight and obesity in older age on the risk of dementia: A systematic literature review and a meta-analysis. *Journal of Alzheimer's disease*, *70* (s1), pp. S87-S99.

David, C.N., de Mello, R.B., Bruscato, N.M. and Moriguchi, E.H. (2017). Overweight and abdominal obesity association with all-cause and cardiovascular mortality in the elderly aged 80 and over: A cohort study. *The journal of nutrition, health & ageing*, *21*(5), pp.597-603.

De Hollander, E., Van Zutphen, M., Bogers, R. P., Bemelmans, W. J., & De Groot, L. C. P. G. M. (2012). The impact of body mass index in old age on cause-specific mortality. *The journal of nutrition, health & ageing*, *16* (1), 100-106.

De Koning, L., Merchant, A.T., Pogue, J. and Anand, S.S (2007). Waist circumference and waist-to-hip ratio as predictors of cardiovascular events: meta-regression analysis of prospective studies. *European heart journal*, *28* (7), pp.850-856.

Decaria, J.E., Sharp, C. and Petrella, R.J (2012) Scoping review report: obesity in older adults. International journal of obesity (2005), 36(9), pp. 1141.

Denscombe, M (2008). Communities of practice: A research paradigm for the mixed methods approach. *Journal of mixed methods research*, *2* (3), pp.270-283.

Denzin, N.K. and Lincoln, Y.S (2008). *Strategies of qualitative inquiry* (Vol. 2). Sage.

Dhana, K., Berghout, M. A., Peeters, A., Ikram, M. A., Tiemeier, H., Hofman, A., and Franco, O. H. (2016). Obesity in older adults and life expectancy with and without cardiovascular disease. *International journal of obesity*, *40* (10), 1535.

Di Angelantonio, E., Bhupathiraju, S.N., Wormser, D., Gao, P., Kaptoge, S., de Gonzalez, A.B., Cairns, B.J., Huxley, R., Jackson, C.L., Joshy, G. and Lewington, S (2016). Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *The Lancet*, *388* (10046), pp.776-786.

Dinsa, G.D., Goryakin, Y., Fumagalli, E. and Suhrcke, M (2012). Obesity and socioeconomic status in developing countries: a systematic review. *Obesity Reviews*, *13* (11), pp.1067-1079.

Donini, L. M., Savina, C., Gennaro, E., De Felice, M. R., Rosano, A., Pandolfo, M. M., and Chumlea, W. C (2012). A systematic review of the literature concerning the relationship between obesity and mortality in the elderly. *The journal of nutrition, health & ageing*, *16* (1), 89-98.

Dorresteijn, J.A.N., Visseren, F.L.J. and Spiering, W (2012). Mechanisms linking obesity to hypertension. *Obesity Reviews*, *13* (1), pp.17-26.

Doyle, L., Brady, A.M. and Byrne, G (2009). An overview of mixed methods research. *Journal of research in nursing*, *14* (2), pp.175-185.

Drake, A.J. and Reynolds, R.M. (2010). Impact of maternal obesity on offspring obesity and cardiometabolic disease risk. Reproduction, 140(3), pp.387-398.

Duggleby, W (2005), "What about focus group interaction data?" *Qualitative health research,* vol. 15, no. 6, pp. 832-840.

Dugravot, A., Sabia, S., Stringhini, S., Kivimaki, M., Westerlund, H., Vahtera, J., Guéguen, A., Zins, M., Goldberg, M., Nabi, H. and Singh-Manoux, A (2010). Do socioeconomic factors shape weight and obesity trajectories over the transition from midlife to old age? Results from the French GAZEL cohort study–. *The American journal of clinical nutrition*, *92*(1), pp.16-23.

Dye, L., Boyle, N. B., Champ, C., & Lawton, C (2017). The relationship between obesity and cognitive health and decline. *Proceedings of the nutrition society*, *76* (4), 443-454.

Egger, G. and Swinburn, B (1997). An "ecological" approach to the obesity pandemic. *B*MJ, *315*(7106), pp.477-480.

Egger, G., Swinburn, B. and Rossner, S (2003). Dusting off the epidemiological triad: could it work with obesity? *Obesity Reviews*, *4* (2), pp.115-119.

Ehehalt, R., Keller, P., Haass, C., Thiele, C. and Simons, K (2003). Amyloidogenic processing of the Alzheimer β-amyloid precursor protein depends on lipid rafts. *The Journal of cell biology*, *160*(1), pp.113-123.

Elias-Sonnenschein, L. S., Viechtbauer, W., Ramakers, I. H., Verhey, F. R and Visser, P. J (2011). Predictive value of APOE-ε4 allele for progression from MCI to AD-type dementia: a meta-analysis. *Journal of Neurology, Neurosurgery & Psychiatry*, *82*(10), 1149-1156.

Emmerzaal, T.L., Kiliaan, A.J. and Gustafson, D.R. (2015). 2003-2013: a decade of body mass index, Alzheimer's disease, and dementia. *Journal of Alzheimer's disease*, *43* (3), pp.739-755.

Ettehad, D., Emdin, C.A., Kiran, A., Anderson, S.G., Callender, T., Emberson, J., Chalmers, J., Rodgers, A. and Rahimi, K (2016). Blood pressure-lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *The Lancet*, *387* (10022), pp.957-967.

Eurostat (2014) Population Projections. https://ec.europa.eu/eurostat/ (accessed June 2019)

Faas, M.M., Melgert, B.N. and de Vos, P (2010). A brief review on how pregnancy and sex hormones interfere with taste and food intake. *Chemosensory perception*, *3* (1), pp.51-56.

Faith, M.S., Butryn, M., Wadden, T.A., Fabricatore, A., Nguyen, A.M. and Heymsfield, S.B (2011). Evidence for prospective associations among depression and obesity in population-based studies. *Obesity Reviews*, *12* (5), pp.e438-e453.

Fakhouri, T.H., Ogden, C.L., Carroll, M.D., Kit, B.K. and Flegal, K.M (2012). Prevalence of obesity among older adults in the United States, 2007-2010 (No. 106). US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics.

Farruggia, M.C. and Small, D.M (2019). Effects of adiposity and metabolic dysfunction on cognition: a review. *Physiology & behavior*, *208*, p.112578.

Ferrucci, L. and Alley, D (2007). Obesity, disability, and mortality: a puzzling link. *Archives of internal medicine*, *167* (8), pp.750-751.

Fewtrell, M. S., Kennedy, K., Singhal, A., Martin, R. M., Ness, A., Hadders-Algra, M., and Lucas, A. (2008). How much loss to follow-up is acceptable in long-term randomised trials and prospective studies? *Archives of disease in childhood*, *93* (6), 458-461.

Fitzpatrick AL, Kuller LH, Lopez OL, Diehr P, O'Meara ES, Longstreth WT Jr, Luchsinger JA (2009) Midlife and late-life obesity and the risk of dementia: cardiovascular health study. Arch Neurol 66, 336-342.

Flegal, K.M., Graubard, B.I., Williamson, D.F. and Cooper, R.S (2011). Reverse causation and illness-related weight loss in observational studies of body weight and mortality. *American journal of epidemiology*, *173* (1), pp.1-9.

Flegal, K.M., Kit, B.K., Orpana, H. and Graubard, B.I (2013). Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *Jama*, *309*(1), pp.71-82.

Fleischmann, E., Teal, N., Dudley, J., May, W., Bower, J.D. and Salahudeen, A.K (1999). Influence of excess weight on mortality and hospital stay in 1346 haemodialysis patients. *Kidney International*, *55*(4), pp.1560-1567.

Flicker, L., McCaul, K.A., Hankey, G.J., Jamrozik, K., Brown, W.J., Byles, J.E. and Almeida, O.P (2010). Body mass index and survival in men and women aged 70 to 75. *Journal of the American geriatrics society*, *58* (2), pp.234-241.

Forny-Germano, L., De Felice, F.G. and Vieira, M.N.D.N (2019). The role of leptin and adiponectin in obesity-associated cognitive decline and Alzheimer's disease. *Frontiers in neuroscience*, *12*, p.1027.

Fowler, J.H. and Christakis, N.A. (2008). Dynamic spread of happiness in a large social network: longitudinal analysis over 20 years in the Framingham Heart Study. *B*MJ, *337*, p.a2338.

Fox, A., Feng, W., & Asal, V. (2019). What is driving global obesity trends? Globalization or "modernization"? *Globalization and health*, *15*(1), 32.

Franssen, F. M. E., O'Donnell, D. E., Goossens, G. H., Blaak, E. E., and Schols, A. M. W. J. (2008). Obesity and the lung: 5· Obesity and COPD. Thorax, 63(12), 1110-1117.

Freedman, D.M., Ron, E., Ballard-Barbash, R., Doody, M.M. and Linet, M.S (2006). Body mass index and all-cause mortality in a nationwide US cohort. *International journal of obesity*, *30*(5), p.822.

Friedman, A.L. and Shepeard, H (2007). Exploring the knowledge, attitudes, beliefs, and communication preferences of the general public regarding HPV: findings from CDC focus group research and implications for practice. *Health Education & Behaviour*, *34*(3), pp.471-485.

Frisardi, V., Solfrizzi, V., Seripa, D., Capurso, C., Santamato, A., Sancarlo, D., Vendemiale, G., Pilotto, A. and Panza, F (2010). Metabolic-cognitive syndrome: a crosstalk between metabolic syndrome and Alzheimer's disease. *Ageing research reviews*, *9*(4), pp.399-417.

Gafoor, R., Booth, H.P. and Gulliford, M.C (2018). Antidepressant utilisation and incidence of weight gain during 10 years' follow-up: population-based cohort study. *Bmj*, *361*.

Galster, G.C (2012). The mechanism (s) of neighbourhood effects: Theory, evidence, and policy implications. In *Neighbourhood effects research: New perspectives* (pp. 23-56). Springer, Dordrecht.

Gannon, O.J., Robison, L.S., Custozzo, A.J. and Zuloaga, K.L (2019). Sex differences in risk factors for vascular contributions to cognitive impairment & dementia. *Neurochemistry international*, *127*, pp.38-55.

García-Ptacek, S., Kåreholt, I., Farahmand, B., Cuadrado, M. L., Religa, D., & Eriksdotter, M. (2014). Body-mass index and mortality in incident dementia: a cohort study on 11,398 patients from Sweden, the Swedish Dementia Registry. *Journal of the American Medical Directors Association*, *15* (6), 447-e1.

Garrison, R.J., Kannel, W.B., Stokes III, J. and Castelli, W.P., 1987. Incidence and precursors of hypertension in young adults: the Framingham Offspring Study. *Preventive medicine*, *16*(2), pp.235-251.

GBD 2016 Neurology Collaborators. (2019). Global, regional, and national burden of neurological disorders, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016.

Gelber, R.P., Gaziano, J.M., Orav, E.J., Manson, J.E., Buring, J.E. and Kurth, T. (2008). Measures of obesity and cardiovascular risk among men and women. *Journal of the American College of Cardiology*, *52* (8), pp.605-615.

Gellert, C., Schöttker, B. and Brenner, H (2012). Smoking and all-cause mortality in older people: systematic review and meta-analysis. *Archives of internal medicine*, *172*(11), pp.837-844.

Gill, L.E., Bartels, S.J. and Batsis, J.A. (2015). Weight management in older adults. *Current obesity reports*, *4* (3), pp.379-388.

Giroud, M., Delpont, B., Daubail, B., Blanc, C., Durier, J., Giroud, M. and Béjot, Y (2017). Temporal trends in sex differences with regard to stroke incidence: the Dijon stroke registry (1987–2012). Stroke, 48(4), pp.846-849.

Gluckman, P.D. and Hanson, M.A. (2009. Developmental and epigenetic pathways to obesity: an evolutionary-developmental perspective. International journal of obesity, 32(S7), p.S62.

Gómez-Cabello, A., Pedrero-Chamizo, R., Olivares, P.R., Hernández-Perera, R., Rodríguez-Marroyo, J.A., Mata, E., Aznar, S., Villa, J.G., Espino-Torón, L., Gusi, N. and González-Gross, M (2012). Sitting time increases the overweight and obesity risk independently of walking time in elderly people from Spain. *Maturitas*, *73*(4), pp.337-343.

Gong, P., Liang, S., Carlton, E. J., Jiang, Q., Wu, J., Wang, L., and Remais, J. V. (2012). Urbanisation and health in China. *The Lancet*, *379*(9818), 843-852.

Gorospe, E.C. and Dave, J.K (2007). The risk of dementia with increased body mass index. *Age and Ageing*, *36* (1), pp.23-29.

Gortmaker, S.L., Swinburn, B.A., Levy, D., Carter, R., Mabry, P.L., Finegood, D.T., Huang, T., Marsh, T. and Moodie, M.L (2011). Changing the future of obesity: science, policy, and action. *The Lancet*, *378* (9793), pp.838-847.

Graham, H. (2009) Understanding health inequalities. Maidenhead: McGraw-Hill Open University Press.

Guallar-Castillón, P., Balboa-Castillo, T., López-García, E., León-Muñoz, L.M., Gutiérrez-Fisac, J.L., Banegas, J.R. and Rodríguez-Artalejo, F., 2009. BMI, waist circumference, and mortality according to health status in the older adult population of Spain. *Obesity*, *17* (12), pp.2232-2238.

Guerra, F., Stringhini, S., Vollenweider, P., Waeber, G., & Marques-Vidal, P. (2015). Socio-demographic and behavioural determinants of weight gain in the Swiss population. *BMC Public Health*, *15* (1), 73.

Guh, D.P., Zhang, W., Bansback, N., Amarsi, Z., Birmingham, C.L. and Anis, A.H (2009). The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC public health*, *9* (1), p.88.

Gurvich, C., Hoy, K., Thomas, N. and Kulkarni, J., 2018. Sex differences and the influence of sex hormones on cognition through adulthood and the ageing process. *Brain sciences*, *8* (9), p.163.

Gustafson D, Rothenberg E, Blennow K, Steen B, Skoog I (2003) An 18-year follow-up of overweight and risk of Alzheimer disease. Arch Intern Med 163, 1524-1528.

Gustafson, D.R. and Luchsinger, J.A (2013). High adiposity: risk factor for dementia and Alzheimer's disease? *Alzheimer's Research & Therapy*, *5* (6), p.57.

Gustafson, D.R., Bäckman, K., Joas, E., Waern, M., Östling, S., Guo, X. and Skoog, I (2012). 37 years of body mass index and dementia: observations from the prospective population study of women in Gothenburg, Sweden. *Journal of Alzheimer's disease*, *28* (1), pp.163-171.

Gustafson, D.R., Bäckman, K., Joas, E., Waern, M., Östling, S., Guo, X. and Skoog, I (2012). 37 years of body mass index and dementia: observations from the prospective population study of women in Gothenburg, Sweden. *Journal of Alzheimer's disease*, *28* (1), pp.163-171.

Hajek, A., Lehnert, T., Ernst, A., Lange, C., Wiese, B., Prokein, J., Weyerer, S., Werle, J., Pentzek, M., Fuchs, A. and Luck, T. (2015). Prevalence and determinants of overweight and obesity in old age in Germany. *BMC geriatrics*, *15* (1), p.83.

Haldar, S., Chia, S. C., and Henry, C. J. (2015). Body composition in Asians and Caucasians: comparative analyses and influences on cardiometabolic outcomes. In Advances in food and nutrition research (Vol. 75, pp. 97-154). Academic Press. 304.

Hall, J.E., Hildebrandt, D.A. and Kuo, J., 2001. Obesity hypertension: role of leptin and sympathetic nervous system. American journal of hypertension, 14(S3), pp.103S-115S.

Hartemink, N., Boshuizen, H.C., Nagelkerke, N.J., Jacobs, M.A. and van Houwelingen, H.C (2006). Combining risk estimates from observational studies with different exposure cutpoints: a meta-analysis on body mass index and diabetes type 2. *American journal of epidemiology*, *163*(11), pp.1042-1052.

Hatch, J. A. (2002). *Doing qualitative research in education settings*. Suny Press.

Hayden KM, Zandi PP, Lyketsos CG, Khachaturian AS, Bastian LA, Charoonruk G, Tschanz JT, Norton MC, Pieper CF, Munger RG, Breitner JC, Welsh-Bohmer KA, Cache County Investigators (2006) vascular risk factors for incident Alzheimer disease and vascular dementia: the Cache County Study. Alzheimer Dis Assoc Disord 20, 93-100.

Hennink, M.M (2007) *International focus group research: A handbook for the health and social sciences,* Cambridge University Press. Mass index." Nutrition & diabetes 1, no. 5 (2011): e6.

Herd, P., Goesling, B. and House, J.S., 2007. Socioeconomic position and health: the differential effects of education versus income on the onset versus progression of health problems. *Journal of health and social behaviour*, *48*(3), pp.223-238.

Hernán, M.A., Hernández-Díaz, S. and Robins, J.M. (2004). A structural approach to selection bias. *Epidemiology*, pp.615-625.

Herrera, B.M., Keildson, S. and Lindgren, C.M. (2011). Genetics and epigenetics of obesity. *Maturitas*, *69* (1), pp.41-49.

Hill, J.O., 2006. Understanding and addressing the epidemic of obesity: an energy balance perspective. *Endocrine Reviews*, *27*(7), pp.750-761.

Hogervorst, E (2017). Healthy lifestyles to prevent dementia and reduce dementia symptoms. *Working with Older People*.

Hogervorst, E., Clifford, A., Stock, J., Xin, X. and Bandelow, S (2012). Exercise to prevent cognitive decline and Alzheimer's disease: for whom, when, what, and (most importantly) how much. *J Alzheimer's Dis Parkinsonism*, *2*, p.e117.

Holloway, I. (2005). *Qualitative research in health care*. McGraw-Hill Education (UK).

Holsboer, F (2000). The corticosteroid receptor hypothesis of depression. *Neuropsychopharmacology*, *23* (5), pp.477-501.

Howe, C. J., Cole, S. R., Lau, B., Napravnik, S., & Eron Jr, J. J. (2016). Selection bias due to loss to follow up in cohort studies. *Epidemiology (Cambridge, Mass.)*, *27*(1), 91.

Hruby, A. and Hu, F.B (2015). The epidemiology of obesity: a big picture. *Pharmacoeconomics*, *33* (7), pp.673-689.

Hryhorczuk, C., Sharma, S. and Fulton, S.E (2013). Metabolic disturbances connecting obesity and depression. *Frontiers in neuroscience*, *7*, p.177.

Hu, F (2008). Obesity epidemiology. Oxford University Press. pp 23- 24

Huang, Y., Wang, Y., Wang, H., Liu, Z., Yu, X., Yan, J., & Wang, Z. (2019). Prevalence of mental disorders in China: a cross-sectional epidemiological study. *The Lancet Psychiatry*, *6*(3), 211-224.

Hughes TF, Borenstein AR, Schofield E, Wu Y, Larson EB (2009) Association between late-life body mass index and dementia: The Kame Project. Neurology 72, 1741-1746.

Huxley, R., Mendis, S., Zheleznyakov, E., Reddy, S. and Chan, J (2010). Body mass index, waist circumference and waist: hip ratio as predictors of cardiovascular risk—a review of the literature. *European journal of clinical nutrition*, *64* (1), pp.16-22.

Iliodromiti, S., Celis-Morales, C.A., Lyall, D.M., Anderson, J., Gray, S.R., Mackay, D.F., Nelson, S.M., Welsh, P., Pell, J.P., Gill, J.M. and Sattar, N (2018). The impact of confounding on the associations of different adiposity measures with the incidence of cardiovascular disease: a cohort study of 296 535 adults of white European descent. *European heart journal*, *39* (17), pp.1514-1520.

Jacobs, E.J., Newton, C.C., Wang, Y., Patel, A.V., McCullough, M.L., Campbell, P.T., Thun, M.J. and Gapstur, S.M (2010). Waist circumference and all-cause mortality in a large US cohort. *Archives of internal medicine*, *170* (15), pp.1293-1301.

James, P.A., Oparil, S., Carter, B.L., Cushman, W.C., Dennison-Himmelfarb, C., Handler, J., Lackland, D.T., LeFevre, M.L., MacKenzie, T.D., Ogedegbe, O. and Smith, S.C. (2014). 2014 evidence-based guideline for the management of high blood pressure in adults: a report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *Jama*, *311*(5), pp.507-520.

James, W.P.T (2008). The epidemiology of obesity: the size of the problem. *Journal of internal medicine*, *263*(4), pp.336-352.

Janssen, I. and Bacon, E (2008). Effect of current and midlife obesity status on mortality risk in the elderly. *Obesity*, *16* (11), pp.2504-2509.

Jantaratnotai, N., Mosikanon, K., Lee, Y. and McIntyre, R.S (2017. The interface of depression and obesity. *Obesity research & clinical practice*, *11*(1), pp.1-10.

Jellinger, K.A. and Attems, J (2011). Prevalence and pathology of dementia with Lewy bodies in the oldest old: a comparison with other dementing disorders. *Dementia and geriatric cognitive disorders*, *31* (4), pp.309-316.

Jellinger, K.A. and Korczyn, A.D (2018). Are dementia with Lewy bodies and Parkinson's disease dementia the same disease? *BMC medicine*, *16* (1), pp.1-16.

Jia, J., Wang, F., Wei, C., Zhou, A., Jia, X., Li, F., and Cui, Y. (2014). The prevalence of dementia in urban and rural areas of China. *Alzheimer's & Dementia*, *10*(1), 1-9.

Jia, L., Quan, M., Fu, Y., Zhao, T., Li, Y., Wei, C., and Shi, S. (2019). Dementia in China: epidemiology, clinical management, and research advances. *The Lancet Neurology*.

Jin, L., Shuran, L. and Weixi, Z (2001). Assessment of Computeried Diagnostic System of Geriatric Mental State Schedule Shortened Community Version (GMSA-AGECAT). *Chinese Mental Health Journal*, *15* (4), pp.220-222.

John, U., Hanke, M., Rumpf, H.J. and Thyrian, J.R (2005). Smoking status, cigarettes per day, and their relationship to overweight and obesity among former and current smokers in a national adult general population sample. *International journal of obesity*, *29* (10), pp.1289-1294.

Johnson DK, Wilkins CH, Morris JC (2006) Accelerated weight loss may precede diagnosis in Alzheimer disease. Arch Neurology 63, 1312-1317.

Johnson, R.B., Onwuegbuzie, A.J. and Turner, L.A (2007). Toward a definition of mixed methods research. *Journal of mixed methods research*, *1* (2), pp.112-133.

Jones, S. V and O'brien, J. T. (2014). The prevalence and incidence of dementia with Lewy bodies: a systematic review of population and clinical studies. *Psychological medicine*, *44* (4), 673-683.

Joshy, G., Korda, R. J., Bauman, A., Van Der Ploeg, H. P., Chey, T., & Banks, E. (2014). Investigation of methodological factors potentially underlying the paradoxical findings on body mass index and all-cause mortality. *PLoS One*, *9*(2), e88641.

Jura, M. and Kozak, L.P (2016). Obesity and related consequences to ageing. *Age*, *38* (1), p.23.

Jurcau, A. and Simion, A (2020). Oxidative Stress in the Pathogenesis of Alzheimer's disease and Cerebrovascular Disease with Therapeutic Implications. *CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders)*.

Juruena, M.F. and Cleare, A.J (2007) Overlap between atypical depression, seasonal affective disorder and chronic fatigue syndrome. *Rev Bras Psiquiatr*, *29* (Supl I), pp. S19-26.

Juutilainen, A., Kortelainen, S., Lehto, S., Rönnemaa, T., Pyörälä, K. and Laakso, M (2004). Gender difference in the impact of type 2 diabetes on coronary heart disease risk. *Diabetes care*, *27* (12), pp.2898-2904.

Karch, C. M., Cruchaga, C., & Goate, A. M. (2014). Alzheimer's disease genetics: from the bench to the clinic. *Neuron*, *83* (1), 11-26.

Keith, S. W., Fontaine, K. R., & Allison, D. B. (2013). Mortality rate and overweight: Overblown or underestimated? A commentary on a recent meta-analysis of the associations of BMI and mortality. *Molecular metabolism*, *2* (2), 65-68.

Khan KS, Kunz R, Kleijnen J, Antes G (2003) Five steps to conducting a systematic review. J R Soc Med 96, 118-121.

Kiliaan, A.J., Arnoldussen, I.A. and Gustafson, D.R (2014). Adipokines: a link between obesity and dementia? *The Lancet Neurology*, *13* (9), pp.913-923.

Kim, D. D., and Basu, A (2016). Estimating the medical care costs of obesity in the United States: a systematic review, meta-analysis, and empirical analysis. *Value in Health*, *19* (5), 602-613.

Kim, S. and Popkin, B.M. (2006). Commentary: Understanding the epidemiology of overweight and obesity—a real global public health concern. *International journal of epidemiology*, *35* (1), pp.60-67.

Kim, T.J. and von dem Knesebeck, O (2018). Income and obesity: what is the direction of the relationship? A systematic review and meta-analysis. *BMJ open*, *8*(1), p.e019862.

Kim, T.J., Roesler, N.M. and von dem Knesebeck, O (2017). Causation or selection–examining the relation between education and overweight/obesity in prospective observational studies: a meta-analysis. *Obesity Reviews*, *18* (6), pp.660-672.

King, N., Cassell, C. and Symon, G., 2004. Using templates in the thematic analysis of text. *Essential guide to qualitative methods in organizational research*, *2*, pp.256-70.

Kivimäki, M., Luukkonen, R., Batty, G.D., Ferrie, J.E., Pentti, J., Nyberg, S.T., Shipley, M.J., Alfredsson, L., Fransson, E.I., Goldberg, M. and Knutsson, A., 2018. Body mass index and risk of dementia: analysis of individual-level data from 1.3 million individuals. Alzheimer's & Dementia, 14(5), pp.601-609.

Kivipelto, M., Ngandu, T., Fratiglioni, L., Viitanen, M., Kåreholt, I., Winblad, B., Helkala, E.L., Tuomilehto, J., Soininen, H. and Nissinen, A (2005). Obesity and vascular risk factors at midlife and the risk of dementia and Alzheimer disease. *Archives of neurology*, *62* (10), pp.1556-1560.

Kivipelto, M., Ngandu, T., Fratiglioni, L., Viitanen, M., Kåreholt, I., Winblad, B., Helkala, E.L., Tuomilehto, J., Soininen, H. and Nissinen, A., 2005. Obesity and vascular risk factors at midlife and the risk of dementia and Alzheimer disease. *Archives of neurology*, *62* (10), pp.1556-1560.

Klein, S., Allison, D.B., Heymsfield, S.B., Kelley, D.E., Leibel, R.L., Nonas, C. and Kahn, R (2007). Waist circumference and cardiometabolic risk: a consensus statement from shaping America's health: Association for Weight Management and Obesity Prevention; NAASO, the Obesity Society; the American Society for Nutrition; and the American Diabetes Association. *Obesity*, *15* (5), pp.1061-1067.

Klop, Boudewijn, Jan Willem F. Elte, and Manuel Castro Cabezas. "Dyslipidemia in obesity: mechanisms and potential targets." *Nutrients* 5, no. 4 (2013): 1218-1240.

Kloppenborg, R.P., van den Berg, E., Kappelle, L.J. and Biessels, G.J (2008). Diabetes and other vascular risk factors for dementia: which factor matters most? A systematic review. *European journal of pharmacology*, *585* (1), pp.97-108.

Knopman DS, Edland SD, Cha RH, Petersen RC, Rocca WA (2007) Incident dementia in women is preceded by weight loss by at least a decade. Neurology 69, 739-746.

Koliaki, C., Liatis, S. and Kokkinos, A (2019). Obesity and cardiovascular disease: revisiting an old relationship. *Metabolism*, *92*, pp.98-107.

Krauss, R.M., Winston, M., Fletcher, B.J. and Grundy, S.M., 1998. Obesity: impact on cardiovascular disease. *Circulation*, *98* (14), pp.1472-1476.

Kristman, V., Manno, M., & Côté, P. (2004). Loss to follow-up in cohort studies: how much is too much? *European journal of epidemiology*, *19* (8), 751-760.

Krueger, R. A., & Casey, M. A. (2014). *Focus groups: A practical guide for applied research*. Sage publications.

Kruger, J., Ham, S.A. and Prohaska, T.R. (2009). Behavioural risk factors associated with overweight and obesity among older adults: the 2005 National Health Interview Survey. *Preventing chronic disease*, *6* (1), pp.A14-A14.

Kruger, R.A. (1994) *Focus Group: Practical Guide for Applied Research,* Sage.

Kyrou, I. and Tsigos, C (2009). Stress hormones: physiological stress and regulation of metabolism. *Current opinion in pharmacology*, *9* (6), pp.787-793.

Lajous, M., Bijon, A., Fagherazzi, G., Boutron-Ruault, M.C., Balkau, B., Clavel-Chapelon, F. and Hernán, M.A (2014). Body mass index, diabetes, and mortality in French women: explaining away a "paradox". *Epidemiology (Cambridge, Mass.)*, *25* (1), p.10.

Larsson, J., Unosson, M., Ek, A.C., Nilsson, L., Thorslund, S. and Bjurulf, P (1990). Effect of dietary supplement on nutritional status and clinical outcome in 501 geriatric patients—a randomised study. *Clinical nutrition*, *9* (4), pp.179-184.

Lavie, C.J., Alpert, M.A., Arena, R., Mehra, M.R., Milani, R.V. and Ventura, H.O (2013). Impact of obesity and the obesity paradox on prevalence and prognosis in heart failure. *JACC: Heart Failure*, *1* (2), pp.93-102.

Lawlor, D.A., Hart, C.L., Hole, D.J. and Smith, G.D (2006). Reverse causality and confounding and the associations of overweight and obesity with mortality. *Obesity*, *14* (12), pp.2294-2304.

Lee, C.M.Y., Huxley, R.R., Wildman, R.P. and Woodward, M (2008). Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: a meta-analysis. *Journal of clinical epidemiology*, *61* (7), pp.646-653.

Lee, J.Y., Kim, H.C., Kim, C., Park, K., Ahn, S.V., Kang, D.R., Khaw, K.T., Willett, W.C. and Suh, I (2016). Underweight and mortality. Public Health Nutrition, 19 (10), pp.1751-1756.

Leech, N. L., & Onwuegbuzie, A. J. (2007). An array of qualitative data analysis tools: a call for data analysis triangulation. *School psychology quarterly*, *22* (4), and 557.

Li, J., Wang, Y.J., Zhang, M., Xu, Z.Q., Gao, C.Y., Fang, C.Q., Yan, J.C. and Zhou, H.D (2011). Vascular risk factors promote conversion from mild cognitive impairment to Alzheimer disease. *Neurology*, *76* (17), pp.1485-1491.

Li, R., and Singh, M. (2014). Sex differences in cognitive impairment and Alzheimer's disease. *Frontiers in neuroendocrinology*, *35* (3), 385-403.

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS medicine 6, e1000100.

Lim, U., Ernst, T., Buchthal, S.D., Latch, M., Albright, C.L., Wilkens, L.R., Kolonel, L.N., Murphy, S.P., Chang, L., Novotny, R. and Le Marchand, L (2011). Asian women have greater abdominal and visceral adiposity than Caucasian women with similar body mass index. *Nutrition & diabetes*, *1*(5), pp.e6-e6.

Lin, Y., Fu, R., Grant, E., Chen, Y., Lee, J.E., Gupta, P.C., Ramadas, K., Inoue, M., Tsugane, S., Gao, Y.T. and Tamakoshi, A (2013). Association of body mass index and risk of death from pancreas cancer in Asians: findings from the Asia Cohort Consortium. *European journal of cancer prevention: the official journal of the European Cancer Prevention Organisation (ECP)*, *22* (3).

Liu, C. C., Kanekiyo, T., Xu, H., & Bu, G. (2013). Apolipoprotein E and Alzheimer disease: risk, mechanisms and therapy. *Nature Reviews Neurology*, *9* (2), 106.

Liu, P., Hao, Q., Hai, S., Wang, H., Cao, L. and Dong, B (2017). Sarcopenia as a predictor of all-cause mortality among community-dwelling older people: a systematic review and meta-analysis. *Maturitas*, *103*, pp.16-22.

Llibre Rodriguez JJ, Ferri CP, Acosta D, Guerra M, Huang Y, and Jacob KS, et al. Prevalence of dementia in Latin America, India, and China: a population-based cross-sectional survey. Lancet 2008; 372: 464–74.

Lovejoy, J.C (1998). The influence of sex hormones on obesity across the female life span. *Journal of Women's Health*, *7* (10), pp.1247-1256.

Lovejoy, J.C., Sainsbury, A. and Stock Conference 2008 Working Group (2009). Sex differences in obesity and the regulation of energy homeostasis. *Obesity Reviews*, *10* (2), pp.154-167.

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., Abraham, J., Adair, T., Aggarwal, R., Ahn, S.Y. and AlMazroa, M.A (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*, *380* (9859), pp.2095-2128.

Lu, Y., Hajifathalian, K., Ezzati, M., Woodward, M., Rimm, E.B. and Danaei, G (2014) Metabolic mediators of the effects of body-mass index, overweight, and obesity on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1· 8 million participants.

Lucca U, Tettamanti M, Garrì M, Riva E, Nobili A, Pasina L, Franchi C, Djade C, Recchia A (2012) Body mass index and dementia in the oldest-old: The Monzino 80-Plus Study. Alzheimers Dement 8, P326.

Lucca U, Tettamanti M, Logroscino G, Tiraboschi P, Landi C, Sacco L, Garrì M, Ammesso S, Bertinotti C, Biotti A (2015) Prevalence of dementia in the oldest old: the Monzino 80-plus population based study. Alzheimer's Dement 11, 258-270.e3.

Luchsinger JA, Patel B, Tang M, Schupf N, Mayeux R (2007) Measures of adiposity and dementia risk in elderly persons. Arch Neurol 64, 392-398.

Luppino, F. S., de Wit, L. M., Bouvy, P. F., Stijnen, T., Cuijpers, P., Penninx, B. W., & Zitman, F. G (2010). Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. *Archives of general psychiatry*, *67* (3), 220-229.

Mai, Y., Peng, X. and Chen, W (2013). How fast is the population ageing in China? Asian Population Studies, 9 (2), pp.216-239.

Mann, C.J (2003). Observational research methods. Research design II: cohort, cross-sectional, and case-control studies. *Emergency medicine journal*, *20*(1), pp.54-60.

Mann, J.N. and Thakore, J.H (1999). Melancholic depression and abdominal fat distribution: a mini review. *Stress*, *3*(1), pp.1-15.

Marmot, M. (2004) Status syndrome. *Significance*, **1**(4), pp. 150-154.

Marshall, C., & Rossman, G. B. (2014). *Designing qualitative research*. Sage publications.

Martins, L.B., Monteze, N.M., Calarge, C., Ferreira, A.V.M. and Teixeira, A.L (2019). Pathways linking obesity to neuropsychiatric disorders. *Nutrition*, *66*, pp.16-21.

Mata, J., Frank, R. and Hertwig, R (2015). Higher body mass index, less exercise, but healthier eating in married adults: Nine representative surveys across Europe. *Social Science & Medicine*, *138*, pp.119-127.

Mathus-Vliegen, E.M., Basdevant, A., Finer, N., Hainer, V., Hauner, H., Micic, D., Maislos, M., Roman, G., Schutz, Y., Tsigos, C. and Toplak, H., 2012. Prevalence, pathophysiology, health consequences and treatment options of obesity in the elderly: a guideline. Obesity Facts, 5(3), pp.460-483.

Matthews, F.E., Stephan, B.C., Robinson, L., Jagger, C., Barnes, L.E., Arthur, A. and Brayne, C (2016). A two-decade dementia incidence comparison from the Cognitive Function and Ageing Studies I and II. *Nature communications*, *7* (1), pp.1-8.

Maxwell, J. (1992). Understanding and validity in qualitative research. *Harvard educational review*, *62* (3), 279-301.

Mazza, A., Zamboni, S., Tikhonoff, V., Schiavon, L., Pessina, A.C. and Casiglia, E (2007). Body mass index and mortality in elderly men and women from general population. *Gerontology*, *53* (1), pp.36-45.

McCay, C. M., Crowell, M. F. & Maynard, L. A. (1935). The effect of retarded growth upon the length of life span and upon the ultimate body size. J. Nutr. 10, 63-79. 2.

McLaren, L., 2007. Socioeconomic status and obesity. *Epidemiologic Reviews*, *29* (1), pp.29-48.

Meng, X. F., Yu, J. T., Wang, H. F., Tan, M. S., Wang, C., Tan, C. C., & Tan, L. (2014). Midlife vascular risk factors and the risk of Alzheimer's disease: a systematic review and meta-analysis. *Journal of Alzheimer's disease*, *42* (4), 1295-1310.

Merrill, Ray M. *Statistical Methods in Epidemiologic Research*. Sudbury: Jones and Bartlett Publishers, Inc., 2015

Mi, Y. J., Zhang, B., Wang, H. J., Yan, J., Han, W., Zhao, J., & Tian, Q. B. (2015). Prevalence and secular trends in obesity among Chinese adults, 1991– 2011. *American journal of preventive medicine*, *49* (5), 661-669.

Miard, S. and Picard, F (2008). Obesity and ageing have divergent genomic fingerprints. *International journal of obesity*, *32* (12), pp.1873-1874.

Misra, A., Wasir, J.S. and Vikram, N.K. (2005). Waist circumference criteria for the diagnosis of abdominal obesity are not applicable uniformly to all populations and ethnic groups. *Nutrition*, *21* (9), pp.969-976.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G. and Prisma Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS med*, *6* (7), p.e1000097.

Monteiro, C.A., Moura, E.C., Conde, W.L. and Popkin, B.M., 2004. Socioeconomic status and obesity in adult populations of developing countries: a review. *Bulletin of the World Health Organization*, *82*, pp.940-946.

Morley, J.E (1996). Anorexia in older persons. *Drugs & aging*, *8*(2), pp.134-155.

Morley, J.E (2012). Sarcopenia in the elderly. *Family practice*, *29*(suppl_1), pp.i44-i48.

Morley, J.E., Abbatecola, A.M., Argiles, J.M., Baracos, V., Bauer, J., Bhasin, S., Cederholm, T., Coats, A.J.S., Cummings, S.R., Evans, W.J. and Fearon, K (2011). Sarcopenia with limited mobility: an international consensus. *Journal of the American Medical Directors Association*, *12*(6), pp.403-409.

Morley, J.E., Anker, S.D. and von Haehling, S (2014). Prevalence, incidence, and clinical impact of sarcopenia: facts, numbers, and epidemiology—update 2014.

Morley, J.E., Argiles, J.M., Evans, W.J., Bhasin, S., Cella, D., Deutz, N.E., Doehner, W., Fearon, K.C., Ferrucci, L., Hellerstein, M.K. and Kalantar-Zadeh, K (2010). Nutritional recommendations for the management of sarcopenia. *Journal of the American Medical Directors association*, *11*(6), pp.391-396.

Müezzinler, A., Mons, U., Gellert, C., Schöttker, B., Jansen, E., Kee, F., and Wolk, A. (2015). Smoking and all-cause mortality in older adults: results from the CHANCES consortium. American journal of preventive medicine, 49(5), e53-e63.

Mujica-Parodi, L.R., Renelique, R. and Taylor, M.K (2009). Higher body fat percentage is associated with increased cortisol reactivity and impaired cognitive resilience in response to acute emotional stress. *International journal of obesity*, *33*(1), pp.157-165.

Napier, A.D., Ancarno, C., Butler, B., Calabrese, J., Chater, A., Chatterjee, H., Guesnet, F., Horne, R., Jacyna, S., Jadhav, S. and Macdonald, A. (2014). Culture and health. *The Lancet*, *384* (9954), pp.1607-1639.

Neergaard JS, Dragsbaek K, Hansen HB, Henriksen K, Christiansen C, Karsdal MA (2016) Late-life risk factors for all-cause dementia and differential dementia diagnoses in women: a prospective cohort study. Medicine (Baltimore) 95, e3112.

Newell-Fugate, A.E (2017). The role of sex steroids in white adipose tissue adipocyte function. *Reproduction*, *153* (4), pp. R133-R149.

Neter, J.E., Stam, B.E., Kok, F.J., Grobbee, D.E. and Geleijnse, J.M., 2003. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension*, *42* (5), pp.878-884.

Neu, S. C., Pa, J., Kukull, W., Beekly, D., Kuzma, A., Gangadharan, P., and Orlandi, D. (2017). Apolipoprotein E genotype and sex risk factors for Alzheimer disease: a meta-analysis. *JAMA neurology*, *74* (10), 1178-1189.

Newman, A.B., Fitzpatrick, A.L., Lopez, O., Jackson, S., Lyketsos, C., Jagust, W., Ives, D., DeKosky, S.T. and Kuller, L.H. (2005). Dementia and Alzheimer's disease incidence in relationship to cardiovascular disease in the Cardiovascular Health Study cohort. *Journal of the American Geriatrics Society*, *53* (7), pp.1101-1107.

Nichols, E., Szoeke, C.E., Vollset, S.E., Abbasi, N., Abd-Allah, F., Abdela, J., Aichour, M.T.E., Akinyemi, R.O., Alahdab, F., Asgedom, S.W. and Awasthi, A (2019). Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet Neurology*, *18* (1), pp.88-106.

Ninomiya, T., 2014. Diabetes mellitus and dementia. *Current Diabetes Reports*, *14*(5), p.487.

Nourhashémi F, Deschamps V, Larrieu S, Letenneur L, Dartigues J-, Bamberger-Gateau P, PAQUID study. Personness Agées Quid (2003) Body mass index and incidence of dementia: The PAQUID study. Neurology 60, 117-119.

Nowell, L.S., Norris, J.M., White, D.E. and Moules, N.J (2017). Thematic Analysis: Striving to Meet the Trustworthiness Criteria. *International Journal of Qualitative Methods*, *16*(1), p.1609406917733847.

O'Cathain, A., Murphy, E. and Nicholl, J., 2007. Integration and publications as indicators of" yield" from mixed methods studies. *Journal of mixed methods research*, *1* (2), pp.147-163.

Omran, M.L. and Morley, J.E (2000). Assessment of protein energy malnutrition in older persons, Part II: Laboratory evaluation. *Nutrition*, *16* (2), pp.131-140.

Onwuegbuzie, A.J., Dickinson, W.B., Leech, N.L. & Zoran, A.G (2009), "A qualitative framework for collecting and analyzing data in focus group research", *International journal of qualitative methods,* vol. 8, no. 3, pp. 1-21

Owsley, C., Allman, R. M., Gossman, M., Kell, S., Sims, R. V., & Baker, P. S (2018). Mobility impairment and its consequences in the elderly. *The Gerontological Prism: Developing Interdisciplinary Bridges: Developing Interdisciplinary Bridges*, 165.

Palta, P., Samuel, L.J., Miller III, E.R. and Szanton, S.L (2014). Depression and oxidative stress: results from a meta-analysis of observational studies. *Psychosomatic medicine*, *76* (1), p.12.

Patel, A. V., Hildebrand, J. S., & Gapstur, S. M. (2014). Body mass index and all-cause mortality in a large prospective cohort of white and black US adults. *PloS one*, *9* (10).

Pedditizi, E., Peters, R. and Beckett, N (2016). The risk of overweight/obesity in mid-life and late-life for the development of dementia: a systematic review and meta-analysis of longitudinal studies. *Age and Ageing*, *45* (1), pp.14-21.

Piazza, P.V. and Le Moal, M (1997). Glukokortikoïede as'n biologiese substraat van beloning: fisiologiese en patofisiologiese implikasies. *Brein Ondersoek Resensies*, *25*, pp.359-372.

Plummer-D'Amato, P. (2008). Focus group methodology Part 1: Considerations for design. *International Journal of Therapy and Rehabilitation*, *15*(2), 69-73.

Poehlman, E.T. and Dvorak, R.V., 2000. Energy expenditure, energy intake, and weight loss in Alzheimer disease. *The American journal of clinical nutrition*, *71*(2), pp.650S-655S.

Pope, C. and Mays, N. (2006), *Qualitative research in health care,* Third; 3 edn, Blackwell publishing/BMJ Books, Malden, Massachusetts.

Popkin, B. M. (2010). The implications of the nutrition transition for obesity in the developing world. *Obesity epidemiology: from aetiology to public health*, 136-142.

Popkin, B. M. (2014). Synthesis and implications: China's nutrition transition in the context of changes across other low-and middle-income countries. *Obesity reviews*, *15*, 60-67

Popkin, B. M., Adair, L. S., and Ng, S. W. (2012). Global nutrition transition and the pandemic of obesity in developing countries. *Nutrition reviews*, *70* (1), 3-21.

Power BD, Alfonso H, Flicker L, Hankey GJ, Yeap BB, Almeida OP (2011) Body adiposity in later life and the incidence of dementia: the health in men study. PloS One 6, e17902.

Power, B.D., Alfonso, H., Flicker, L., Hankey, G.J., Yeap, B.B. and Almeida, O.P (2013). Changes in body mass in later life and incident dementia. *International psychogeriatrics*, *25* (3), p.467.

Preston, S.H. and Stokes, A. (2014). The obesity paradox: conditioning on disease enhances biases in estimating the mortality risks of obesity. *Epidemiology (Cambridge, Mass.)*, *25* (3), p.454.

Prince M, Wimo AG M, Ali G-C, Wu Y-T, Prina M. World Alzheimer Report (2015). The Global Impact of Dementia. An Analysis of Prevalence, Incidence, Cost and Trends. London: Alzheimer’s disease International, 2015.

Prince, M. J., De Rodriguez, J. L., Noriega, L., Lopez, A., Acosta, D., Albanese, E., ... & Guerra, M. (2008). The 10/66 Dementia Research Group's fully operationalised DSM-IV dementia computerized diagnostic algorithm, compared with the 10/66 dementia algorithm and a clinician diagnosis: a population validation study. *BMC public health*, *8* (1), 219.

Prince, M., Acosta, D., Chiu, H., Copeland, J., Dewey, M., Scazufca, M., and 10/66 Dementia Research Group. (2004). Effects of education and culture on the validity of the Geriatric Mental State and its AGECAT algorithm. *The British Journal of Psychiatry*, *185* (5), 429-436.

Prince, M., Acosta, D., Chiu, H., Scazufca, M., Varghese, M. and 10/66 Dementia Research Group, (2003). Dementia diagnosis in developing countries: a cross-cultural validation study. The Lancet, 361(9361), pp.909-917.

Prince, M., Acosta, D., Chiu, H., Scazufca, M., Varghese, M., & 10/66 Dementia Research Group. (2003). Dementia diagnosis in developing countries: a cross-cultural validation study. *The Lancet*, *361* (9361), 909-917.

Prince, M., Acosta, D., Ferri, C. P., Guerra, M., Huang, Y., Rodriguez, J. J. L., & Acosta, I. (2012). Dementia incidence and mortality in middle-income countries, and associations with indicators of cognitive reserve: a 10/66 Dementia Research Group population-based cohort study. *The Lancet*, *380*(9836), 50-58.

Prince, M., Acosta, D., Ferri, C.P., Guerra, M., Huang, Y., Rodriguez, J.J.L., Salas, A., Sosa, A.L., Williams, J.D., Dewey, M.E. and Acosta, I (2012). Dementia incidence and mortality in middle-income countries, and associations with indicators of cognitive reserve: a 10/66 Dementia Research Group population-based cohort study. *The Lancet*, *380*(9836), pp.50-58.

Prince, M., Ali, G.C., Guerchet, M., Prina, A.M., Albanese, E. and Wu, Y.T (2016). Recent global trends in the prevalence and incidence of dementia, and survival with dementia. *Alzheimer's research & therapy*, *8* (1), p.23.

Prince, M., Bryce, R., Albanese, E., Wimo, A., Ribeiro, W. and Ferri, C.P., 2013. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimer's & dementia*, *9*(1), pp.63-75.

Prince, M., Knapp, M., Guerchet, M., McCrone, P., Prina, M., Comas-Herrera, A., Wittenberg, R., Adelaja, B., Hu, B., King, D. and Rehill, A., 2014. Dementia UK: -overview.http://eprints.lse.ac.uk/59437/1/Dementia_UK Second_edition-Overview.pdf

Public Health England (2017): Health Matters: Obesity and the food environment: Scale of the problem https://www.gov.uk/government/publications/health-matters-obesity-and-the-food-environment/health-matters-obesity-and-the-food-environment--2) Accessed Jan 2020)

Pusztai, P., Sarman, B., Ruzicska, E., Toke, J., Racz, K., Somogyi, A. and Tulassay, Z (2008). Ghrelin: a new peptide regulating the neurohormonal system, energy homeostasis and glucose metabolism. *Diabetes/metabolism research and reviews*, *24* (5), pp.343-352.

Qin, X., & Pan, J. (2016). The medical cost attributable to obesity and overweight in China: Estimation based on longitudinal surveys. *Health economics*, *25*(10), 1291-1311.

Qizilbash, N., Gregson, J., Johnson, M.E., Pearce, N., Douglas, I., Wing, K., Evans, S.J. and Pocock, S.J (2015). BMI and risk of dementia in two million people over two decades: a retrospective cohort study. *The Lancet Diabetes & Endocrinology*, *3*(6), pp.431-436.

Radoi, V.A.L.E.N.T.I.N., Lixandru, D.A.N.I.E.L.A., Mohora, M.A.R.I.A. and Virgolici, B.O.G.D.A.N.A., (2012). Advanced glycation end products in diabetes mellitus: mechanism of action and focused treatment. *Proceedings of the Romanian Academy, Series B*, *1*, pp.9-19.

Rahmouni, K., Correia, M.L., Haynes, W.G. and Mark, A.L., 2005. Obesity-associated hypertension: new insights into mechanisms. *Hypertension*, *45*(1), pp.9-14.

Rapp, I. and Schneider, B (2013). The impacts of marriage, cohabitation and dating relationships on weekly self-reported physical activity in Germany: A 19-year longitudinal study. Social science & medicine, 98, pp.197-203.

Rapsomaniki, E., Timmis, A., George, J., Pujades-Rodriguez, M., Shah, A.D., Denaxas, S., White, I.R., Caulfield, M.J., Deanfield, J.E., Smeeth, L. and Williams, B (2014). Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1· 25 million people. *The Lancet*, *383* (9932), pp.1899-1911.

Reitz, C (2012). Dyslipidemia and dementia: current epidemiology, genetic evidence, and mechanisms behind the associations. *Journal of Alzheimer's disease*, *30*(s2), pp. S127-S145.

Reitz, C., Brayne, C., & Mayeux, R. (2011). Epidemiology of Alzheimer disease. *Nature Reviews Neurology*, *7* (3), 137

Riaz, H., Khan, M.S., Siddiqi, T.J., Usman, M.S., Shah, N., Goyal, A., Khan, S.S., Mookadam, F., Krasuski, R.A. and Ahmed, H (2018). Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. *JAMA network open*, *1*(7), pp.e183788-e183788.

Roos, E. T., Lallukka, T., Lahelma, E., and Rahkonen, O. (2016). Joint associations between smoking and obesity as determinants of premature mortality among midlife employees. The European Journal of Public Health, 27(1), 135-139.

Ross, M. H. (1961) Length of life and nutrition in the rat. J. Nutr. 75, 197-210. 3.

Rothman, K.J (2008). BMI-related errors in the measurement of obesity. *International journal of obesity*, *32* (S3), p.S56.

Rothman, K.J., 2012. *Epidemiology: an introduction*. Oxford university press.

Sabatine, M.S., Giugliano, R.P., Wiviott, S.D., Raal, F.J., Blom, D.J., Robinson, J., Ballantyne, C.M., Somaratne, R., Legg, J., Wasserman, S.M. and Scott, R (2015). Open-Label Study of Long-Term Evaluation against LDL Cholesterol (OSLER) Investigators. Efficacy and safety of evolocumab in reducing lipids and cardiovascular events. *N Engl J Med*, *372* (16), pp.1500-9.

Sebastião, E., Pak, J., Benner, D., Nakamura, P.M. and Papini, C.B (2019). Magnitude and Composition of Sedentary Behavior in Older Adults Living in a Retirement Community. *Journal of community health*, *44*(4), pp.805-814.

Sacks, G., Swinburn, B. and Lawrence, M (2009). Obesity Policy Action framework and analysis grids for a comprehensive policy approach to reducing obesity. *Obesity Reviews*, *10* (1), pp.76-86.

Saczynski, J. S., Beiser, A., Seshadri, S., Auerbach, S., Wolf, P. A., and Au, R. (2010). Depressive symptoms and risk of dementia: the Framingham Heart Study. *Neurology*, *75* (1), 35-41.

Saely, C.H., Geiger, K. and Drexel, H (2012). Brown versus white adipose tissue: a mini review. *Gerontology*, *58* (1), pp.15-23.

Sagawa, N., Yura, S., Itoh, H., Mise, H., Kakui, K., Korita, D., Takemura, M., Nuamah, M.A., Ogawa, Y., Masuzaki, H. and Nakao, K (2002). Role of leptin in pregnancy—a review. *Placenta*, *23*, pp. S80-S86.

Sahle, B.W., Breslin, M., Sanderson, K., Patton, G., Dwyer, T., Venn, A. and Gall, S (2019). Association between depression, anxiety and weight change in young adults. *BMC psychiatry*, *19* (1), p.398.

Samieri, C., Perier, M. C., Gaye, B., Proust-Lima, C., Helmer, C., Dartigues, J. F., & Empana, J. P. (2018). Association of cardiovascular health level in older age with cognitive decline and incident dementia. *Jama*, *320* (7), 657-664.

Samper-Ternent, R., & Al Snih, S. (2012). Obesity in older adults: epidemiology and implications for disability and disease. *Reviews in clinical gerontology*, *22* (1), 10-34.

Santos, C.Y., Snyder, P.J., Wu, W.C., Zhang, M., Echeverria, A. and Alber, J (2017). Pathophysiologic relationship between Alzheimer's disease, cerebrovascular disease, and cardiovascular risk: a review and synthesis. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *7*, pp.69-87.

Scarmeas N, Luchsinger JA, Schupf N, Brickman AM, Cosentino S, Tang MX, Stern Y (2009) Physical activity, diet, and risk of Alzheimer disease. JAMA 302, 627-637.

Schierberl Scherr, A. E., McClure Brenchley, K. J., and Gorin, A. A. (2013). Examining a ripple effect: do spouses’ behaviour changes predict each other’s weight loss? *Journal of obesity*, *2013*.

Schmidt, D.S. and Salahudeen, A.K (2007) Cardiovascular and survival paradoxes in dialysis patients: Obesity-survival paradox—still a controversy. In *Seminars in dialysis* (Vol. 20, No. 6, pp. 486-492). Oxford, UK: Blackwell Publishing Ltd.

Schosserer, M., Grillari, J., Wolfrum, C. and Scheideler, M (2018). Age-induced changes in white, brite, and brown adipose depots: a mini-review. *Gerontology*, *64*(3), pp.229-236.

Schulze, B., & Angermeyer, M. C. (2003). Subjective experiences of stigma. A focus group study of schizophrenic patients, their relatives and mental health professionals. *Social science & medicine*, *56* (2), 299-312.

Schwandt, T. A., Lincoln, Y. S., and Guba, E. G. (2007). Judging interpretations: But is it rigorous? Trustworthiness and authenticity in naturalistic evaluation. *New directions for evaluation*, *2007* (114), 11-25.

Seidell, J. C., and Halberstadt, J. (2015). The global burden of obesity and the challenges of prevention. *Annals of Nutrition and Metabolism*, *66* (Suppl. 2), 7-12.

Seidell, J.C., Verschuren, W.M., Van Leer, E.M. and Kromhout, D., 1996. Overweight, underweight, and mortality: a prospective study of 48287 men and women. *Archives of internal medicine*, *156* (9), pp.958-963.

Shah, H., Albanese, E., Duggan, C., Rudan, I., Langa, K.M., Carrillo, M.C., Chan, K.Y., Joanette, Y., Prince, M., Rossor, M. and Saxena, S. (2016.) Research priorities to reduce the global burden of dementia by 2025. *The Lancet Neurology*, *15* (12), pp.1285-1294.

Sharma, A., Lavie, C.J., Borer, J.S., Vallakati, A., Goel, S., Lopez-Jimenez, F., Arbab-Zadeh, A., Mukherjee, D. and Lazar, J.M (2015). A meta-analysis of the relation of body mass index to all-cause and cardiovascular mortality and hospitalization in patients with chronic heart failure. *The American journal of cardiology*, *115* (10), pp.1428-1434.

Sharma, A., Lavie, C.J., Borer, J.S., Vallakati, A., Goel, S., Lopez-Jimenez, F., Arbab-Zadeh, A., Mukherjee, D. and Lazar, J.M. (2015). A meta-analysis of the relation of body mass index to all-cause and cardiovascular mortality and hospitalization in patients with chronic heart failure. *The American journal of cardiology*, *115* (10), pp.1428-1434.

Sharma, A.M. and Padwal, R. (2010). Obesity is a sign–over-eating is a symptom: an aetiological framework for the assessment and management of obesity. *Obesity Reviews*, *11* (5), pp.362-370.

Sharp, S. I., Aarsland, D., Day, S., Sønnesyn, H., Alzheimer's Society Vascular Dementia Systematic Review Group, & Ballard, C. (2011). Hypertension is a potential risk factor for vascular dementia: a systematic review. *International journal of geriatric psychiatry*, *26* (7), 661-669.

Shenton, A. K. (2004). Strategies for ensuring trustworthiness in qualitative research projects. *Education for information*, *22*(2), 63-75.

Shoelson, S.E., Herrero, L. and Naaz, A., 2007. Obesity, inflammation, and insulin resistance. *Gastroenterology*, *132* (6), pp.2169-2180.

Short, K.R., Vittone, J.L., Bigelow, M.L., Proctor, D.N. and Nair, K.S (2004). Age and aerobic exercise training effects on whole body and muscle protein metabolism. *American Journal of Physiology-Endocrinology and Metabolism*, *286* (1), pp.E92-E101.

Singh-Manoux, A., Dugravot, A., Shipley, M., Brunner, E.J., Elbaz, A., Sabia, S. and Kivimaki, M (2018). Obesity trajectories and risk of dementia: 28 years of follow-up in the Whitehall II Study. *Alzheimer's & Dementia*, *14* (2), pp.178-186.

Smith, K. B., & Smith, M. S (2016). Obesity statistics. *Primary care: clinics in office practice*, *43* (1), 121-135.

Sobal, J., Hanson, K. L., & Frongillo, E. A. (2009). Gender, ethnicity, marital status, and body weight in the United States. *Obesity*, *17*(12), 2223-2231.

Soni, M., Orrell, M., Bandelow, S., Steptoe, A., Rafnsson, S., d'Orsi, E., Xavier, A. and Hogervorst, E (2019). Physical activity pre-and post-dementia: English Longitudinal Study of Ageing. *Ageing & mental health*, *23* (1), pp.15-21.

Srikanth, V., Maczurek, A., Phan, T., Steele, M., Westcott, B., Juskiw, D. and Münch, G (2011). Advanced glycation endproducts and their receptor RAGE in Alzheimer's disease. *Neurobiology of aging*, *32* (5), pp.763-777.

Srikanthan, P., Seeman, T.E. and Karlamangla, A.S (2009). Waist-hip-ratio as a predictor of all-cause mortality in high-functioning older adults. *Annals of epidemiology*, *19* (10), pp.724-731.

Starr, K.N.P. and Bales, C.W (2015). Excessive body weight in older adults. *Clinics in geriatric medicine*, *31* (3), pp.311-326.

Steffens, D. C., Krishnan, K. R. R., Crump, C., & Burke, G. L. (2002). Cerebrovascular disease and evolution of depressive symptoms in the cardiovascular health study. *Stroke*, *33* (6), 1636-1644.

Steffens, D.C., Bosworth, H.B., Provenzale, J.M. and MacFall, J.R (2002). Subcortical white matter lesions and functional impairment in geriatric depression. *Depression and Anxiety*, *15* (1), pp.23-28.

Stenger, K.M., Ritter-Gooder, P.K., Perry, C. and Albrecht, J.A (2014). A mixed methods study of food safety knowledge, practices and beliefs in Hispanic families with young children. *Appetite*, *83*, pp.194-201.

Stewart, R., Masaki, K., Xue, Q.L., Peila, R., Petrovitch, H., White, L.R. and Launer, L.J (2005). A 32-year prospective study of change in body weight and incident dementia: the Honolulu-Asia Aging Study. Archives of neurology, 62(1), pp.55-60.

Stokes, A., and Preston, S. H. (2015). Smoking and reverse causation create an obesity paradox in cardiovascular disease. Obesity, 23(12), 2485-2490.

Strandberg, T. E., Stenholm, S., Strandberg, A. Y., Salomaa, V. V., Pitkälä, K. H., & Tilvis, R. S. (2013). The "obesity paradox," frailty, disability, and mortality in older men: a prospective, longitudinal cohort study. *American journal of epidemiology*, *178*(9), 1452-1460.

Swinburn, B., Gill, T. and Kumanyika, S (2005). Obesity prevention: a proposed framework for translating evidence into action. *Obesity Reviews*, *6*(1), pp.23-33.

Swinburn, B.A., Sacks, G., Hall, K.D., McPherson, K., Finegood, D.T., Moodie, M.L. and Gortmaker, S.L (2011). The global obesity pandemic: shaped by global drivers and local environments. *The Lancet*, *378*(9793), pp.804-814.

Takata, Y., Ansai, T., Soh, I., Awano, S., Nakamichi, I., Akifusa, S., Goto, K., Yoshida, A., Fujii, H., Fujisawa, R. and Sonoki, K., 2013. Body mass index and disease-specific mortality in an 80-year-old population at the 12-year follow-up. *Archives of gerontology and geriatrics*, *57*(1), pp.46-53.

Tamakoshi, A., Yatsuya, H., Lin, Y., Tamakoshi, K., Kondo, T., Suzuki, S., Yagyu, K., Kikuchi, S. and JACC Study Group (2010). BMI and all-cause mortality among Japanese older adults: findings from the Japan collaborative cohort study. *Obesity*, *18*(2), pp.362-369.

Tashakkori, A. and Creswell, J.W., 2007. The New Era of Mixed Methods. *Journal of Mixed Methods Research*, *1* (1), pp.3-7.

Taylor, W.D., Aizenstein, H.J. and Alexopoulos, G.S (2013). The vascular depression hypothesis: mechanisms linking vascular disease with depression. *Molecular psychiatry*, *18*(9), pp.963-974.

Therrien, F., Drapeau, V., Lupien, S.J., Beaulieu, S., Doré, J., Tremblay, A. and Richard, D (2008). Awakening cortisol response in relation to psychosocial profiles and eating behaviors. *Physiology & behavior*, *93*(1-2), pp.282-288.

Thomas, D.R., Ashmen, W., Morley, J.E. and Evans, W.J (2000). Nutritional management in long-term care: development of a clinical guideline. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, *55*(12), pp.M725-M734.

Thompson, D. and Wolf, A.M., 2001. The medical-care cost burden of obesity. *Obesity reviews*, *2*(3), pp.189-197.

Tolppanen A, Ngandu T, KÃ¥reholt I, Laatikainen T, Rusanen M, Soininen H, Kivipelto M (2014) Midlife and late-life body mass index and late-life dementia: results from a prospective population-based cohort. J Alzheimers Dis 38, 201-209.

Torres, S.J. and Nowson, C.A (2007). Relationship between stress, eating behaviour, and obesity. *Nutrition*, *23* (11-12), pp.887-894.

Tran, B.X., Nair, A.V., Kuhle, S., Ohinmaa, A. and Veugelers, P.J. (2013). Cost analyses of obesity in Canada: scope, quality, and implications. *Cost-Effectiveness and Resource Allocation*, *11* (1), p.3.

Ul-Haq, Z., Mackay, D. F., Fenwick, E., & Pell, J. P. (2013). Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. *Obesity*, *21*(3), 322-327.

Van Dijk, S.J., Molloy, P.L., Varinli, H., Morrison, J.L. and Muhlhausler, B.S (2015) Epigenetics and human obesity. *International journal of obesity*, *39*(1), pp.85-97.

Vazquez, G., Duval, S., Jacobs Jr, D.R. and Silventoinen, K. (2007). Comparison of body mass index, waist circumference, and waist/hip ratio in predicting incident diabetes: a meta-analysis. *Epidemiologic Reviews*, *29*(1), pp.115-128.

Vekic, J., Zeljkovic, A., Stefanovic, A., Jelic-Ivanovic, Z. and Spasojevic-Kalimanovska, V., 2018. Obesity and dyslipidemia. *Metabolism*.

Villareal, D.T., Apovian, C.M., Kushner, R.F., Klein, S., American Society for Nutrition and NAASO, T.O.S. (2005) Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. The American Journal of Clinical Nutrition, 82(5), pp. 923.

Vincent, G.K. and Velkoff, V.A. (2010). The next four decades: The older population in the United States: 2010 to 2050 (No. 1138). US Department of Commerce, Economics and Statistics Administration, US Census Bureau.

Vincent, H.K., Vincent, K.R. and Lamb, K.M. (2010). Obesity and mobility disability in the older adult. *Obesity Reviews*, *11*(8), pp.568-579.

Visscher, T.L.S., Seidell, J.C., Menotti, A., Blackburn, H., Nissinen, A., Feskens, E.J.M., Kromhout, D. and Seven Countries Study Research Group (2000). Underweight and overweight in relation to mortality among men aged 40–59 and 50–69 years: the Seven Countries Study. *American journal of epidemiology*, *151*(7), pp.660-666.

Vogli, R.D., Kouvonen, A., Elovainio, M. and Marmot, M. (2014). Economic globalization, inequality and body mass index: a cross-national analysis of 127 countries. *Critical Public Health*, *24*(1), pp.7-21.

Walker, B.R (2001). Activation of the hypothalamic-pituitary-adrenal axis in obesity: cause or consequence? *Growth Hormone & IGF Research*, *11*, pp. S91-S95.

Wang, C., Chan, J.S., Ren, L. and Yan, J.H (2016). Obesity reduces cognitive and motor functions across the lifespan. *Neural plasticity*, *2016*.

Wang, Y., Mi, J., Shan, X. Y., Wang, Q. J., & Ge, K. Y. (2007). Is China facing an obesity epidemic and the consequences? The trends in obesity and chronic disease in China. *International journal of obesity*, *31*(1), 177.

Wang, Z., Liu, M., Pan, T. and Tong, S (2016). Lower mortality associated with overweight in the US National Health Interview Survey: is overweight protective? *Medicine*, *95* (2).

Wang, Z.J., Zhou, Y.J., Galper, B.Z., Gao, F., Yeh, R.W. and Mauri, L (2015). Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. *Heart*, pp. heartjnl-2014.

Waters, D.L., Ward, A.L. and Villareal, D.T (2013). Weight loss in obese adults 65 years and older: a review of the controversy. *Experimental gerontology*, *48* (10), pp.1054-1061.

Webber, S. C., Porter, M. M., and Menec, V. H. (2010). Mobility in older adults: a comprehensive framework. *The Gerontologist*, *50*(4), 443-450.

Weber-Hamann, B., Hentschel, F., Kniest, A., Deuschle, M., Colla, M., Lederbogen, F. and Heuser, I (2002). Hypercortisolemic depression is associated with increased intra-abdominal fat. *Psychosomatic medicine*, *64*(2), pp.274-277.

Weindruch, R. & Walford, R. L. (1982) Dietary restriction in mice beginning at 1 year of age: effects on lifespan and spontaneous cancer incidence Science (Washington, DC) 215, 1415-141

Weindruch, R., Walford, R.L., Fligiel, S. and Guthrie, D (1986). The retardation of aging in mice by dietary restriction: longevity, cancer, immunity and lifetime energy intake. *The Journal of nutrition*, *116* (4), pp.641-654.

Wells, G.A., Shea, B., O'connell, D., Peterson, J., Welch, V., Losos, M. and Tugwell, P (2011).The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses

White, H., Pieper, C. and Schmader, K (1998). The association of weight change in Alzheimer's disease with severity of disease and mortality: a longitudinal analysis. *Journal of the American Geriatrics Society*, *46*(10), pp.1223-1227.

Whitehead, M. and Dahlgren, G (2006). Concepts and principles for tackling social inequities in health: Levelling up Part 1. *World Health Organization: Studies on social and economic determinants of population health*, *2*.

Whitmer, R.A., Gunderson, E.P., Barrett-Connor, E., Quesenberry, C.P. and Yaffe, K. (2005). Obesity in middle age and future risk of dementia: a 27-year longitudinal population-based study. *B*MJ, *330*(7504), p.1360.

Whitmer, R.A., Gustafson, D.R., Barrett-Connor, E., Haan, M.N., Gunderson, E.P. and Yaffe, K. (2008). Central obesity and increased risk of dementia more than three decades later. *Neurology*, *71*(14), pp.1057-1064.

WHO, E.C. (2004). Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet (London, England)*, *363* (9403), p.157.

Wilkinson, R.G. and Marmot, M.G. (2006) Social determinants of health. Oxford: Oxford University Press.

Wilkinson, R.G. and Pickett, K.E. (2006) Income inequality and population health: a review and explanation of the evidence. Social science & medicine *(1982,* **62**(7), pp. 1768-1784.

Wilkinson, S. & Silverman, D. (2004) "10 Focus Group Research", *Qualitative research: Theory, method and practice,* pp. 177-199.

Willcox, B.J., Willcox, D.C., Todoriki, H., Fujiyoshi, A., Yano, K., He, Q., Curb, J.D. and Suzuki, M (2007). Caloric restriction, the traditional Okinawan diet, and healthy aging: the diet of the world's longest-lived people and its potential impact on morbidity and life span. *Annals of the New York Academy of Sciences*, *1114*(1), pp.434-455.

Williams, D.M., Raynor, H.A. and Ciccolo, J.T (2008). A review of TV viewing and its association with health outcomes in adults. *American Journal of Lifestyle Medicine*, *2*(3), pp.250-259.

Wilson KC, Chen R, Taylor S, McCracken CF, Copeland JR (1999). Socio-economic deprivation and the prevalence and prediction of depression in older community residents. The MRC-ALPHA Study. Br J Psychiatry 175: 549–53

Wimo, A., Guerchet, M., Ali, G. C., Wu, Y. T., Prina, A. M., Winblad, B., and Prince, M. (2017). The worldwide costs of dementia in 2015 and comparisons with 2010. *Alzheimer's & Dementia*, *13*(1), 1-7.

Winblad, B., Amouyel, P., Andrieu, S., Ballard, C., Brayne, C., Brodaty, H., & Fratiglioni, L (2016). Defeating Alzheimer's disease and other dementias: a priority for European science and society. *The Lancet Neurology*, *15*(5), 455-532.

Winsløw, U.C., Rode, L. and Nordestgaard, B.G (2015). High tobacco consumption lowers body weight: a Mendelian randomization study of the Copenhagen General Population Study. *International journal of epidemiology*, *44* (2), pp.540-550.

Winter, J.E., MacInnis, R.J., Wattanapenpaiboon, N. and Nowson, C.A (2014). BMI and all-cause mortality in older adults: a meta-analysis. *The American journal of clinical nutrition*, *99* (4), pp.875-890.

Withrow, D. and Alter, D.A (2011). The economic burden of obesity worldwide: a systematic review of the direct costs of obesity. *Obesity reviews*, *12*(2), pp.131-141.

Wolverhampton Profile Information and Statistics, (2014), *Mid-Year Population Estimates*. Available: http://www.wolverhamptoninprofile.org.uk/ (Accessed 31st January 2018).

Wong, L. P. (2008). Focus group discussion: a tool for health and medical research. *Singapore Med J*, *49*(3), 256-60.

Wong, M.W., Braidy, N., Poljak, A., Pickford, R., Thambisetty, M. and Sachdev, P.S (2017). Dysregulation of lipids in Alzheimer's disease and their role as potential biomarkers. *Alzheimer's & Dementia*, *13* (7), pp.810-827.

Woodward, M., Barzi, F., Martiniuk, A., Fang, X., Gu, D.F., Imai, Y., Lam, T.H., Pan, W.H., Rodgers, A., Suh, I. and Jee, S.H (2006). Cohort profile: the Asia Pacific cohort studies collaboration. *International Journal of Epidemiology*, *35*(6), pp.1412-1416.

World Health Organisation (2019): Dementia Key Facts: https://www.who.int/news-room/fact-sheets/detail/dementia (accessed Jan 2020).

World Health Organization (2000). Obesity: preventing and managing the global epidemic (No. 894). World Health Organization.

World Health Organization (2011). Waist circumference and waist-hip ratio: report of a WHO expert consultation, Geneva, 8-11 December 2008.

World Health Organization (2018). International Classification of Functioning, Disability and Health (ICF). https://www.who.int/classifications/icf/icfbeginnersguide.pdf?ua=1 (accessed July 2019)

Worsley, A. (1988). Cohabitation-gender effects on food consumption. *International Journal of Biosocial Research*.

Wu, Y. T., Ali, G. C., Guerchet, M., Prina, A. M., Chan, K. Y., Prince, M., & Brayne, C. (2018). Prevalence of dementia in mainland China, Hong Kong and Taiwan: an updated systematic review and meta-analysis. *International journal of epidemiology*, *47*(3), 709-719.

Xie, Y.J., Stewart, S.M., Lam, T.H., Viswanath, K. and Chan, S.S (2014). Television viewing time in Hong Kong adult population: associations with body mass index and obesity. *PLoS One*, *9*(1).

Xu, H., Cupples, L. A., Stokes, A., & Liu, C. T. (2018). Association of obesity with mortality over 24 Years of weight history: Findings from the Framingham Heart Study. JAMA network open, 1(7), e184587-e184587.

Yamazaki, K., Suzuki, E., Yorifuji, T., Tsuda, T., Ohta, T., Ishikawa-Takata, K. and Doi, H., 2017. Is there an obesity paradox in the Japanese elderly population? A community-based cohort study of 13 280 men and women. *Geriatrics & gerontology international*, *17* (9), pp.1257-1264.

Yang, G., Kong, L., Zhao, W., Wan, X., Zhai, Y., Chen, L. C., & Koplan, J. P. (2008). Emergence of chronic non-communicable diseases in China. *The Lancet*, *372* (9650), 1697-1705.

Yilmaz, K. (2013). Comparison of quantitative and qualitative research traditions: Epistemological, theoretical, and methodological differences. *European Journal of Education*, *48* (2), 311-325.

Yoshitake T, Kiyohara Y, Kato I, Ohmura T, Iwamoto H, Nakayama K, Ohmori S, Nomiyama K, Kawano H, Ueda K (1995) Incidence and risk factors of vascular dementia and Alzheimer's disease in a defined elderly Japanese population: the Hisayama Study. Neurology 45, 1161-1168.

Yu, B. P., Masoro, E. J., Murata, I., Bertrand, H. A. & Lynd, F. T. (1982) Life span study of SPF Fischer 344 male rats fed ad libitum or restricted diets: longevity, growth, lean body mass and disease J. Gerontol. 37, 130-141. 4.

Yu, E., Ley, S. H., Manson, J. E., Willett, W., Satija, A., Hu, F. B., & Stokes, A. (2017). Weight history and all-cause and cause-specific mortality in three prospective cohort studies. Annals of internal medicine, 166 (9), 613-620.

Yuan, J., Zhang, Z., Wen, H., Hong, X., Hong, Z., Qu, Q., Tang, M., Wu, J., Xu, Q., Li, H. and Cummings, J.L (2016). Incidence of dementia and subtypes: a cohort study in four regions in China. *Alzheimer's & Dementia*, *12* (3), pp.262-271.

Zade D, Beiser A, McGlinchey R, Au R, Seshadri S, Palumbo C, Wolf PA, DeCarli C, Milberg W (2013) Apolipoprotein epsilon 4 allele modifies waist-to-hip ratio effects on cognition and brain structure. Journal of Stroke and Cerebrovascular Diseases 22, 119-125.

Zamboni, M., Mazzali, G., Zoico, E., Harris, T.B., Meigs, J.B., Di Francesco, V., Fantin, F., Bissoli, L. and Bosello, O (2005) Health consequences of obesity in the elderly: a review of four unresolved questions. International journal of obesity, 29 (9), pp. 1011-1029.

Zhang, J.G., Wang, Z.H., Wang, H.J., Du, W.W., Su, C., Zhang, J., Jiang, H.R., Zhai, F.Y. and Zhang, B (2015). Dietary patterns and their associations with general obesity and abdominal obesity among young Chinese women. *European journal of clinical nutrition*, *69* (9), pp.1009-1014.

Zhang, X., Sun, Z., Zhang, X., Zheng, L., Liu, S., Xu, C., & Sun, Y. (2008). Prevalence and associated factors of overweight and obesity in a Chinese rural population. *Obesity*, *16* (1), 168-171.

Zore, T., Palafox, M. and Reue, K (2018). Sex differences in obesity, lipid metabolism, and inflammation—A role for the sex chromosomes? Molecular metabolism, 15, pp.35-44.

APPENDIX: 1 THE APPROVAL LETTER FROM THE RESEARCH ETHICS COMMITTEE OF THE FACULTY OF EDUCATION, HEALTH AND WELLBEING, UNIVERSITY OF WOLVERHAMPTON UK

UNIVERSITY OF WOLVERHAMPTON

Dr Alexandra Hopkins RN PhD MSc MBA RNT RCNT DANS
Dean of the Faculty of Education Health and Wellbeing

University of Wolverhampton
Walsall Campus
Gorway Road
Walsall
WS1 3BD
United Kingdom

Telephone Codes
UK: 01902 Abroad: +44 1902

Switchboard: 321000

Internet: www.wlv.ac.uk

26th March 2018

Isaac Danat (Ruoling Chen and Martin Partridge)
University of Wolverhampton
FEHW

Dear Isaac Danat (Ruoling Chen and Martin Partridge),

Re: The local authority may need to give ethical approval if the local day centre for older adults in Wolverhampton is a local authority service. (Health Professions, Psychology, Social Work & Social Care)

The Faculty Ethics Panel (Health Professions, Psychology, Social Work & Social Care) has considered and reviewed your submission.

On review your Research Proposal was passed and the Panel believes that the ethical issues inherent in your study have been adequately considered and addressed. The only minor changes are as follows: Please make sure that your respondents clearly do not have dementia as a diagnosis or are in the process of an assessment for this. Include independent persons contact details for complaints on the information sheet. Therefore the Panel is giving you full ethical approval for your study (Code 1 - Approved).

We would like to wish you every success with the project.

Yours sincerely

Hilary Paniagua
Dr. H. Paniagua PhD, MSc, BSc (Hons) Cert. Ed. RN RM
Chair – Faculty Ethics Sub-Panel

THE UNIVERSITY OF OPPORTUNITY

APPENDIX 2: APPROVAL LETTER FROM THE ORGANISATION FOR THE STUDY

[redacted] [redacted]

Sunday, 28 October 2018

Professor Ruoling Chen (Director of Studies)
Centre for Health and Social Care Improvement (CHSCI)
Faculty of Education, Health and Wellbeing (FEHW)
University of Wolverhampton

Dear Sir,
I write to confirm that I have given Isaac M. Danat, [redacted] permission to recruit the participants from our church for their research project on overweight/obesity, Fish consumption, Oral health and dementia.
Yours faithfully,

[redacted]

Parish Priest [redacted]

APPENDIX 3: LETTER TO ORGANISATION FOR PERMISSION TO RECRUIT PARTICIPANTS

Name:

Dear

As part of my PhD study in Public Health at the University of Wolverhampton, I am proposing to conduct a research project on "The impact of overweight and obesity on dementia risk and survival in older adults. To do this I require your support/help in allowing me recruit participants for the study from your organization. If you agree to be of help, it will involve you granting us permission and assistance in recruiting a few older adults of age 60 years and above for a focus group discussion, and if possible, conduct the study at your organisation. Though there are no direct benefits, but it will help find out about the effects of obesity and overweight on dementia risk and survival and the views of older adults on preventing it. This will improve knowledge and understanding of the relationship between excess body weight and dementia risk and guide strategies on reducing dementia in our society

I am therefore writing to seek your permission and help in recruiting participants for the study from your organization and I have enclosed a copy of the research protocol for your information. I look forward to hearing from you.

Yours sincerely

Researcher's signature

APPENDIX 4: PARTICIPANT INVITATION LETTER

Dear ……….

I am writing to invite you to participate in a research project, which I am conducting as part of a PhD degree study in Public Health at the University of Wolverhampton. I enclose 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 discussion, you would partake in two sessions on separate days of approximately 60 to 90 minutes per session. Anything you say would be confidential and any notes made as a result of the discussion would be destroyed afterwards. The interview would take place at the convenient location agreed with the participants at a time that is convenient to yourself. A report will be written of the findings and numbers will replace all names so that you cannot be identified.

If you feel that you would like to participate in this discussion please indicate on the attached sheet and send the letter by post using the provided self-address envelope with postage paid or hand it to the researcher when 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 your care will not be affected in any way.

Yours
sincerely,
Isaac
Danat
Contact email: [redacted]

APPENDIX 5: INFORMATION SHEETS FOR PARTICIPANTS

Study title: The impacts of obesity and overweight on dementia risk and survival: Exploring the views of older adults

Invitation:

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, / relatives. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

What is the purpose of the study?

Dementia is a big health problem worldwide. It is a condition marked by loss of memory and difficulty in thinking, problem-solving or language. It may also affect behavior or mood. There are about 47 million people with dementia in the world. The number is predicted to rise to 132 million by the year 2050. Dementia is also common in the UK and it affects about 670,000 people in England alone. Most of dementia cases occur in older age from 60 years
Obesity means excess body fats. Overweight refers to excess body weight for a given height. It is unclear from research if these two conditions are linked to dementia risk. There is, therefore, an ongoing debate on whether older adults with overweight or obesity have reduced risk of developing dementia than their normal weight counterparts.

The aim of the study is to gain understanding, from the viewpoint of older adults, on the effect of overweight and obesity on future dementia and also survival in older adults. It will also explore how to maintain body weight in older adults.

What is the area being studied?

The area for the study is Wolverhampton, UK.

Why is this study important? This is to increase knowledge and understanding of the effects of obesity and overweight on dementia risk. The findings will guide strategies on reducing dementia risk.

What question do you aim to answer? To help understand or clarify if older adults need to reduce, maintain or put on weight to reduce future dementia risk. The duration of the study is 60 to 90 minutes.

Why have I been chosen?

You were identified from the community you reside through your regular meetings of elderly people. You have been chosen because you met the inclusion criteria based on age, capacity to provide consent and to participate in the study. There will be total 5-8 participants in the study including you.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time without giving a reason.

What will happen if I decide to take part?

You will keep a copy of this information sheet and returned to us a signed consent form enclosed or attached. You will also keep a signed copy**.** You will then be involved in two focus group discussions, both on an arranged date convenient to all involved. The research will be approximately 60 to 90 minutes per focus group session. You will take part in an open discussion on the topic with other members of the group. It will involve a few questions put forward for a normal discussion just like you freely do in your everyday life.

If you decide that you want to withdraw your data or the contribution you made during the discussion, it should be done at least a week after the study or before we commence the data analysis. Be aware also that your name will not be used in gathering any information during the study. Instead codes will replace names; but if you decide to withdraw your data, there might be difficulty in identifying you by the codes.

What is expected of me? You are expected to attend and participate in the focus group discussion meeting. You are to freely express your views as you also listen to other participants views. You can contribute based on your personal view and help make good group interaction and mutual leaning.

Data collection method: The data will be collected during the discussion by audiotapes recording of the discussions.

What are the potential benefits and risks of taking part?

Though there are no direct benefits for you if you take part, by participating you will help us to find out about the effects of obesity and overweight on dementia risk and the views of the elderly on preventing it. This may improve knowledge and understanding of the relationship between excess body weight and dementia risk and help reduce dementia in our society.

There are no risks to 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 interview. 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 participate in will be stored on a password protected computer in a locked office. Only the researchers working on the project will have access to the information. You will not be identifiable in any publication or report as all identifying information will be removed and names will be changed.

If anything is raised during the interview which indicates that either you or someone else is at risk of harm, we must share these safeguarding concerns with an appropriate agency.

What will happen at the end of the research study?

At the end of the study, the findings will be published in a health journal or may be shared or presented at public health conferences locally and internationally. For instance, the British Medical journal, Lancet Public Health journal or the local University of Wolverhampton journal of Health and Social Care improvement.

What if I have a problem or concern?

If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions. You can contact Dr. Martin Partridge or Prof. Ruoling Chen using the following address:

Centre for Health and Social Care Improvement (CHSCI)
Faculty of Education, Health and Wellbeing (FEHW)
University of Wolverhampton
Millennium City Building
Wulfruna Street
Wolverhampton, WV1 1LY
UK
T: [redacted], F: [redacted]

Who has reviewed the study?

The University of Wolverhampton Research Ethics Committee have reviewed and approved this study.

Contact for further information

If you require more information about this study, you can use the following contact details:

Isaac Danat
Centre for Health and Social Care Improvement (CHSCI)
Faculty of Education, Health and Wellbeing (FEHW)
University of Wolverhampton
Millennium City Building
Wulfruna Street
Wolverhampton, WV1 1LY
UK
T: [redacted], F: [redacted]
[redacted]

Many thanks for agreeing to take part in this important study.

APPENDIX 6: PARTICIPANT CONSENT FORM

Title of Project:

Name of Researcher:

Please initial boxes

1. I confirm that I have read and understand the information sheet dated ………………. 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 at any time, 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 for my discussion to be audio recorded 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 consent	Date	Signature
………………………….	…………………….	………………………………
Researcher	Date	Signature

APPENDIX 7: PARTICIPANT BASIC INFORMATION FORM

Identification Code………………………..

Age.

Sex: ……………………………………………...

Ethnicity:
(a) White or white British
(b) Indian
(c) Pakistani
(d) Bangladeshi
(e) Chinese
(f) Other Asians
(g) Black Caribbean
(h) Black African
(i) Others

Education level:

(a) No formal education
(b) Primary Education
(c) Secondary Education
(d) Higher education

APPENDIX 8: DISCUSSION GUIDE FOR FOCUS GROUP STUDY

Introduction: By researcher

Background:

- ✓ Dementia is marked by loss of memory, difficulty in thinking or solving problems. It affects language and mood or behavior. People develop dementia as they grow older particularly from 60 years and above.

- ✓ Because it is big problem, we need to identify and understand what increases or reduce dementia in order to prevent it

- ✓ Obesity means excess body fats. Overweight refers to excess body weight for a given height.

- ✓ Recent studies showed that older people with overweight or even obesity may have a reduced risk of developing dementia in future.

- ✓ Some other studies also found thatexcess body weight may increase the risk of dementia.

- ✓ Your discussion today is part of the ongoing debate on whether older adults with overweight or obesity have reduced risk of developing dementia than their normal weight counterparts.

Main Question

Do overweight and obesity in older adults reduce future dementia?

Follow on questions

(a) Do older adults need to reduce weight to decrease dementia?

- ✓ If they need to reduce weight to decrease dementia, what body weight should be reduced (overweight or obesity)?

- ✓ Why do you think so?
- ✓ How could reducing body weight reduce dementia

(b) Should they maintain body weight

- ✓ If they should maintain body weight, what body weight should they keep (underweight, normal, overweight or obese weight)

- ✓ Why do you think so?
- ✓ How could maintaining the same weight reduce dementia

(c) Should they put on some bodyweight?

- ✓ What (increase in) body weight should they target to reduce the dementia? (normal, overweight or obesity)
- ✓ Why do we think so?
- ✓ How could putting on some body weight reduce dementia

Conclusion: By researcher

Discussion guide for Focus group study part B:

The influence of overweight and obesity on survival in older adults

Introduction: By researcher

Background:

- ✓ Dementia is marked by loss of memory, difficulty in thinking or solving problems. It affects language and mood or behavior. People develop dementia as they grow older particularly from 60 years and above.
- ✓ Because it is big problem, we need to identify and understand what increases or reduce dementia in order to prevent it
- ✓ Obesity means excess body fats. Overweight refers to excess body weight for a given height.
- ✓ Recent studies showed that older people with overweight or even obesity may have a reduced risk of developing dementia in future.
- ✓ Some other studies also found that excess body weight may increase the risk of dementia.
- ✓ As older adults grow older, they tend to experience other health problems that make they lose body weight, have dementia or even pass away early.
- ✓ Your discussion today is part of the ongoing debate on "what body weight is related to better survival in older adults".

Main Questions

Do overweight and obesity increase survival in older adults?

Follow on questions

(a) Do older adults need to reduce body weight to live longer?

- ✓ If they need to reduce body weight to live longer, what body weight should they target (overweight or obesity)?

Why do you think so?

- ✓ How could reducing body weight help older adults live longer

(d) Should they maintain body weight?

- ✓ If they should maintain body weight, what body weight should they keep (underweight, normal, overweight or obese weight)

- ✓ Why do you think so?
- ✓ What ways can older adults maintain body weight

(e) Should they put on some bodyweight?

- ✓ What (increase in) body weight should they target to help them live longer? (normal, overweight or obesity)
- ✓ Why do we think so?

Conclusion: By researcher

APPENDIX 9: SPECIMEN OF TRANSCRIPT FROM THE FOCUS GROUP STUDY

Moderator opening question: Do overweight and obesity in older reduce future dementia risk?

Speaker A

Well, I think if I should say something, obesity is not good at any age especially when you are an adult getting to a certain age. Each time we go to the GP one of the first worries is our weight, let's check their weight, and check your height. So it is not for nothing, I believe they do it because they want us to have a certain weight especially at a certain age. If I should say, obesity helps to increase the risk of dementia and a lot of things in our body. So, it is a disadvantage, not an advantage.

Speaker B

I don't know if it may or may not be so but what goes through my mind, obviously there is obese, very obese, extremely obese or whatever, so you know that's…. I have difficulty…. But what goes through my mind is in terms of the record of statistics. Because as I understand it If you are grossly obese then your life expectancy will be less anyway, so you might not get to the stage when you are going to be suffering from dementia. Whereas if you are of sort of reasonable weight and fit then you might be expected to live to when you are expected to (when are we expected to live to? 82 or something like that?). You might get to 82 quite satisfactory that, and maybe before you reach that age with some level of dementia. So, I do query the sort of way the statistics will actually work out but that is the way the statistics are isn't it.

Speaker B

I know of nothing that I know of that the more obese you are the less demented you are. All I am saying is that if you are very obese your life expectancy might be less which will distort the overall research figures. I am not knocking off the research. I am just saying it is a caution that needs to be there.

Speaker D:

My own background is physical education, teaching. My whole life has been one of being athletic, being in athletics, sports, that is being my whole life until last... really, I cut down in the last 30 years but the first 40 years as a full-time athlete really. So, I always held the desire to be as fit as I could be at any age I was at. So, I have put some weight on at this point in time which I am continuously reminded of by my wife and I am keen to try and make sure that that weight is reduced and does not get excessive because I am aware from all my studies and theories as an athletic life that overweight wasn't good for the functioning, the best functioning of my body to run, to jump. So, I always have that desire to have a healthy body. I always haven't succeeded in terms of alcohol

Speaker D: I do not have at this moment any definite view of the relationship with dementia, but I am aware that there is a great concern about the effects of lack of exercise or inappropriate exercise on the person's mental health and I do think that there is a probable link between not being appropriately fit and mental health. I do think to be mentally healthy is (a very, you know) something that is desirable. That is why I am so interested in what we are going to study, that is the relationship between diet, mental health, and wellbeing.

Speaker C: Em… I can only speak totally really the only people I know who have dementia or Alzheimer's or have had are all anything but overweight and I know several people are either a bit overweight or more than a bit overweight and there is no sign of mental problems like that. So (I mean) that is all I can say only of experience I have had of dementia. Being overweight seems to preserve you from possible dementia but that's only from the few people that I've come across.

Speaker E: I don't know but if you are overweight obviously it affects your physical ability doesn't it? you are not as active, so presumably, your muscles are not working as well as they could be if you're not overweight; so, does it affect the brain as well? It may well do I suppose. I think it is a very valid point that Speaker B has said that if you are a bit overweight you are not going to live as long, so perhaps it is not going to affect you so much. There are so many other factors that people say it affects dementia, aren't they? The latest one I heard is the time the other day that if you live in a polluted area you are more likely to get dementia. And you've got to keep your mind active as well, aren't you? It means being physically active as well.

Speaker C: On the other hand, there is the possibility if you're not active if you are a bit overweight, people who are overweight and more sedentary sitting down doing mental exercises, crossword... It could be…

Speaker A: Dementia is, I think it is forgetfulness, a kind of acute one. A few cases I'm aware of is for example in my family I have a few people who if they are like this in a discussion before a few minutes they sleep off. In some cases, you see them they are getting of age, certain age and the body mass is increasing. This helps them to sleep at every time, every time and when you are sleeping you are not remembering anything. So, it becomes an issue. If you take it, this is some cases I am aware of. You see that overweight actually has to do with forgetfulness, dementia, you get me? May be studies can verify this but If you go to certain hospitals, as he was saying (Speaker C) many people that have dementia, even people that are slim they can also suffer from dementia. So, linking it up with data and statistics might be a course of research as well. Yea, but for me, my experience I believe they have a correlation, they have a link.

Moderator: Do we think being overweight or obese will increase the chances of survival?

Speaker E: No

Speaker A: If we were in a famine situation, there is no food available and you had resources, yes you will probably live longer than somebody who was lean but that is just obviously in an extreme condition.

Speaker C: No, I think overweight is bad. I really think is bad. I don't think it causes or will cause dementia but I think overweight is bad. In all we do have overweight people, we had rationing, but we only eat too much, we all eat the wrong stuff. It is advertising factors, our kids want everything that is fattening, and there is that saying that anything that is fattening and something, and something is forbidden. I can't remember the saying, and that is not dementia. The rule is saying something everything is illicit, sweet, and something and something is forbidden. That is all the "good" things that make you fat, the cake.

Speaker B: I think if you are obese, it will shorten your life anyway, in a short space of time. Because it puts a strain on everything, the strain on your heart, on your limbs and your joints and everything. Because you shouldn't be that weight isn't? Body mass index isn't? Height against weight. You should be a stone or a stone and half of your height.

Speaker E: Overweight is bad in every sense, in every sense. If you go to the GP, he may check your weight then he will warn you. You stand a risk. Yes, it happened to me, told you last time I went to GP, he measured me, he said to me (speaker E) be careful, you have to reduce your weight; you have the risk of getting diabetes. When you get diabetes, you are not surviving, your chances of dying are there. You know, is not good for your BP, I have high blood pressure. Is it not good for blood pressure my survival is on question? So overweight is bad in every sense.

Speaker D: Being overweight must be bad. Having said that the medics can pop you up with this medicine and that medicine and that could keep you going. That is another distortion. In actual words, it must be a big danger sign to be way overweight.

Speaker C; I am on the long obese. I am. My weight should be about 9 and a half stones or is 13 to, almost 4 stone overweight.

Speaker D: how many kilos you weigh?

Speaker C: No. The doctors have told me so. I am not making it up. I cannot do any exercise. Only swim I can do or lie on my back or walk. I am apologising for not being able to walk faster. I have got a scooter. You see me on me scoter

Speaker A: No, I don't think it does. I don't think it does. You know if you look at weight as an end in itself I think our diet is important. How you achieve it and all the weight must be important. Now that we are getting older, the vitamins, the nutrients, the proteins, the good fats, and all the other things in order to keep the proper weight will all be important. Not just to look at some body's weight and that is that's the end in itself. You know how there is….will be important as well.

APPENDIX 10a: THE SAMPLE OF THE DICTIONARY OF DATABASE IN THE ANHUI COHORT STUDY FROM THE QUESTIONNAIRE IN CHINESE

调查表中的序号(NO. in questionnaire)	数据库中变量 (variables in database)	变量名称	Variable meaning	编码 code
A:一般资料				
	Age	年龄（岁）	Age	
	Age_group	年龄分组（岁）	**baseline age group**	
			60-64	0
			65-69	1
			70-74	2
			75-79	3
			≥80	4
a1、	**Sex**	**性别**	**Gender**	
		男性	Male	2
		女性	Female	1
	Smoke01	**吸烟（近两年）**	**Smoking over the last 2 years**	
		不	No	0
		yes	Yes	1
	Smoke	**吸烟**	**smoke**	
		从不吸烟	Never-	0
		曾经吸烟	Ex-	1
		现在吸烟	Current-	2
		未知	Not known	888
		缺失	Miss	999
	a6_m	**喝酒（近两年）**	**Drinking alcohol over the 2 years**	
		否	No	0
		天天经常偶尔	Daily/often/occationally	1

	hgt		Height (cm)	
	wgt		Weight (kg)	
	BMI		BMI (kg/m2)	
	gpBMI	BMI旧分组	BMI group	
		＜25	＜25	1
		25-30	25-30	2
		≥30	≥30	3
	BMICUT	BMI新分组	BMI new group	0
		<20	<20	1
		20-<23	20-<23	2
		23-<26	23-<26	3
		>= 26	>= 26	
	waist		Waist circumference (em)	
	waistcut	Waist分组	WC group	
		No Action	No Action	0
		Action Level 1	Action Level 1	1
		Action Level 2	Action Level 2	2
SES	urban_rural	**Living 城乡**	**Living in urban and rural**	
			城市	1
			农村	**2**
	education_level_m	**教育程度**	**Educational level**	
		≥高中（专）	>=High secondary school	4
		初中	Secondary school	3
		小学	primary school	2
		文盲	Illiterate	1
	occupation_m	职业	**Main occupation**	

	农民	Peasant	1
	工人	Manual labourer	2
	干部（教师和军人）	Official/Teacher	3
	商人/其他	Business/ Other	4
income	收入	**income satisfactory**	
	很满意	Very satisfactory	1
	满意	Satisfactory	2
	一般	Average	3
	差	Poor	4
income_m	收入	**income satisfactory**	
	很满意	Very satisfactory	1
	满意	Satisfactory	2
	一般	Average	3
	差	Poor	4
	income_m: 将'最近两年存在经济困难（d2=2）'并入'收入差(income=4)'		
D2	经济困难in the last years	**Financial difficulties over the last years**	
	没有	no	1
	有	yes	2
a10	对目前生活满意	**Satisfied with life/ current living**	
	很满意	Very satisfactory	1
	满意	Satisfactory	2
	一般	Average	3
	差	poor	4
a13	乐观与否	optimistic	
	是	yes	2
	否	no	1

APPENDIX 10b: THE MAIN SYNTAX OF DATA ANALYSIS FOR EACH CHAPTER

Chapter 4: Risk factors for overweight/obesity

```
CROSSTABS
  /TABLES=Sex BY BMI_wave3_obov
  /FORMAT=AVALUE TABLES
  /STATISTICS=CHISQ
  /CELLS=COUNT COLUMN
  /COUNT ROUND CELL.

*Age-sex adjusted
LOGISTIC REGRESSION VARIABLES BMI_wave3_obov
  /METHOD=ENTER Age_group sex qp871_A_03_m
  /CONTRAST (Age_group) =Indicator (2)
 /CONTRAST (sex) =Indicator (1)
 /CONTRAST (qp871_A_03_m) =Indicator (1)
  /PRINT=CI (95)
  /CRITERIA=PIN (0.05) POUT (0.10) ITERATE (20) CUT (0.5).

*Multivariate analysis for overweight/obesity
*Age, Sex, Smoking, Urban rural areas and educational level

LOGISTIC REGRESSION VARIABLES BMI_wave3_obov
  /METHOD=ENTER Age_group sex Smoke01 urban_rural education_level_m qp871_A_03_m
  /CONTRAST (Age_group) =Indicator (2)
 /CONTRAST (sex) =Indicator (1)
 /CONTRAST (Smoke01) =Indicator (1)
 /CONTRAST (urban_rural) =Indicator (1)
 /CONTRAST (education_level_m) =Indicator (4)
 /CONTRAST (qp871_A_03_m) =Indicator (1)
  /PRINT=CI (95)
  /CRITERIA=PIN (0.05) POUT (0.10) ITERATE (20) CUT (0.5).
```

Chapter 6: Impact of overweight and obesity on dementia risk: a cohort study and a meta-analysis

***Syntax for Cohort data analysis**

```
*Table 1 characteristics of participants within BM category

USE ALL.

COMPUTE filter_$= (Age_group<>0 and T_full_2978>=0 and dementia_W1<>2).

VARIABLE LABELS filter_$ 'Age_group<>0 and T_full_2978>=0 and
dementia_W1<>2 (FILTER)'.
```

```
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMATS filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.

CROSSTABS
  /TABLES=BMIct BY demetia_followup01
  /FORMAT=AVALUE TABLES
  /STATISTICS=CHISQ
  /CELLS=COUNT ROW
  /COUNT ROUND CELL.

CROSSTABS
  /TABLES=sex BY BMIct
  /FORMAT=AVALUE TABLES
  /STATISTICS=CHISQ
  /CELLS=COUNT ROW
  /COUNT ROUND CELL.

*Table 2 Odd ratios of dementia across four BMI groups
*Dementia all cohorts analysis
USE ALL.
COMPUTE filter_$= (Age_group<>0 and T_full_2978>=0 and dementia_W1<>2).
VARIABLE LABELS filter_$ 'Age_group<>0 and T_full_2978>=0 and
dementia_W1<>2 (FILTER)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMATS filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE
```

```
*Gender analysis (all cohort)

USE ALL.

COMPUTE filter_$= (Age_group<>0 and T_full_2978>=0 and dementia_W1<>2
and sex<>1).

VARIABLE LABELS filter_$ 'Age_group<>0 and T_full_2978>=0 and
dementia_W1<>2 and sex<>1 (FILTER)'.

VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.

FORMATS filter_$ (f1.0).

FILTER BY filter_$.

EXECUTE.
```

```
* Dementia (excluding wave 2) analysis

USE ALL.

COMPUTE filter_$= (Age_group<>0 and T_full_2978>=0 and dementia_W1<>2
and dementia_W2 <>2).

VARIABLE LABELS filter_$ 'Age_group<>0 and T_full_2978>=0 and
dementia_W1<>2 AND DEMENTIA_W <>2 (FILTER)'.

VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.

FORMATS filter_$ (f1.0).

FILTER BY filter_$.

EXECUTE.
```

```
*Gender analysis

DATASET ACTIVATE DataSet1.

SORT CASES BY sex.

SPLIT FILE SEPARATE BY sex.

SORT CASES BY smoke01.

SPLIT FILE LAYERED BY smoke01.
```

***MODEL 1**

```
LOGISTIC REGRESSION VARIABLES demetia_followup01
  /METHOD=ENTER BMI Age_group sex smoke01 a6_m urban_rural
education_level_m income marriage C5_m
/CONTRAST (Age_group) =Indicator (2)
  /CONTRAST (sex) =Indicator (1)
  /CONTRAST (a6_m) =Indicator (1)
  /CONTRAST (urban_rural) =Indicator (1)
  /CONTRAST (education_level_m) =Indicator
  /CONTRAST (income) =Indicator (2)
  /CONTRAST (marriage) =Indicator (1)
  /CONTRAST (C5_m) =Indicator (3)
  /PRINT=GOODFIT CI (95)
  /CRITERIA=PIN (0.05) POUT (0.10) ITERATE (20) CUT (0.5).
```

***MODEL 2**

```
DATASET ACTIVATE DataSet1.
  LOGISTIC REGRESSION VARIABLES demetia_followup01
  /METHOD=ENTER BMI Age_group sex smoke01 a6_m urban_rural
education_level_m income marriage C5_m
    group_hptn140 b5 ADL_group GMS_level
/CONTRAST (Age_group) =Indicator (2)
  /CONTRAST (sex) =Indicator (1)
  /CONTRAST (smoke01) =Indicator (1)
  /CONTRAST (a6_m) =Indicator (1)
  /CONTRAST (urban_rural) =Indicator (1)
  /CONTRAST (education_level_m) =Indicator
  /CONTRAST (income) =Indicator (2)
  /CONTRAST (marriage) =Indicator (1)
  /CONTRAST (C5_m) =Indicator (3)
  /CONTRAST (group_hptn140) =Indicator (1)
  /CONTRAST (b5) =Indicator (1)
```

```
  /CONTRAST (ADL_group) =Indicator (1)
  /CONTRAST (GMS_level) =Indicator (1)
  /PRINT=GOODFIT CI (95)
  /CRITERIA=PIN (0.05) POUT (0.10) ITERATE (20) CUT (0.5)
```

Chapter 7

```
CROSSTABS
  /TABLES= Sex BY BMIct
  /FORMAT=AVALUE TABLES
  /STATISTICS=CHISQ
  /CELLS=COUNT ROW TOTAL
  /COUNT ROUND CELL.
```

```
DATASET ACTIVATE DataSet1.
USE ALL.
COMPUTE filter_$= (Age_group<>0 and T_full_w4>3).
VARIABLE LABELS filter_$ 'Age_group<>0 and T_full_w4>3 (FILTER)'.
VALUE LABELS filter_$ 0 'Not Selected' 1 'Selected'.
FORMATS filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE.
```

***Model 1** (age, sex, smoking status, alcohol drinking and urban areas)

```
COXREG T_full_w4
  /STATUS=Death_2011 (1)
  /CONTRAST (BMIct) =Indicator (2)
  /CONTRAST (waist_mc) =Indicator (1)
  /CONTRAST (Age_group) =Indicator (2)
  /CONTRAST (sex) =Indicator (1)
  /CONTRAST (smoke01) =Indicator (1)
  /CONTRAST (a6_m) =Indicator (1)
```

```
/CONTRAST (urban_rural) =Indicator (1)
  /METHOD=ENTER BMIct Age_group sex smoke01 a6_m urban_rural
  /PRINT=CI (95)
  /CRITERIA=PIN (.05) POUT (.10) ITERATE (20).
```

***Model 2**

*Model 2   age, sex, smoking status, alcohol drinking, urban areas, income level educational level Activity of daily living and dementia_dep

```
COXREG T_full_w4
  /STATUS=Death_2011 (1)
  /CONTRAST (BMIct) =Indicator (2)
  /CONTRAST (waist_wc) =Indicator (1)
  /CONTRAST (Age_group) =Indicator (2)
  /CONTRAST (smoke01) =Indicator (1)
  /CONTRAST (a6_m) =Indicator (1)
/CONTRAST (urban_rural) =Indicator (1)
  /CONTRAST (income) =Indicator (2)
  /CONTRAST (education_level_m) =Indicator (2)
/CONTRAST (ADL_group) =Indicator (1)
/CONTRAST (b2) =indictor (1)
/CONTRAST (b5) =indictor (1)
/CONTRAST (b6) =indictor (1)
 /CONTRAST (dementia_dep18) =Indicator (1)
  /METHOD=ENTER BMIct Age_group smoke01 a6_m urban_rural income education_level_m ADL_group b2 b5 b6 dementia_dep18
  /PRINT=CI (95)
  /CRITERIA=PIN (.05) POUT (.10) ITERATE (20).
```

***Syntax for meta-analysis data analysis**

```
metan LnRR SeLnRR, label(namevar=BMI_type) random effect (Relative Risk) eform

metan LnRR SeLnRR, label(namevar=study_id) fixed effect (Relative Risk) eform

metan LnRR SeLnRR if Ref3==4 | Ref4==4, label(namevar=study_id)random effect(Relative Risk) eform

metan LnRR SeLnRR if  wc_lastg==1 | wc_lastg ==2, label(namevar=study_id)sortby (Year) by(wc_dv) fixed effect(Relative Risk) eform

metan LnRR SeLnRR if  BMI_type==2, label(namevar=study_id) sortby (Year) by(year_stu) random effect(Relative Risk) eform


metabias LnRR SeLnRR, graph (begg)

metabias LnRR SeLnRR if Study_md==1, egger

metabias LnRR SeLnRR if Study_no==1, egger

metafunnel LnRR SeLnRR if Study_no==1, x label(0.1 0.2 0.4 0.6 0.8 1 2 3 4 5 10 20) xtitle(Relative Risk) eform

metabias LnRR SeLnRR, graph egger
```

APPENDIX 11: TABLE OF CHARACTERISTICS FOR STUDIES IN THE SYSTEMATIC REVIEW OF IMPACTS OF OVERWEIGHT AND OBESITY IN OLDER ADULTS ON DEMENTIA RISK

First Author (publication year): study place	Participants' recruitment and characteristics	Sample size; follow up	Baseline measure of overweight and obesity	Endpoint outcomes: Dementia cases and diagnosis criteria	Data analysis, Adjustment for confounders	Findings
Yoshitake (1995): Japan.	Age≥65 years, with mean age of 74 and 73 years for women and men respectively. Recruited Japanese residing in the community within Hisayama town in Kyushu with 60% being females.	Sample size 828. Females 494 and men 334. Followed from 1985-1992. The total Follow up was 7 years; with 2 yearly monitoring. Two people were lost in follow up	BMI based on measurements and used as continuous variable.	103 dementia cases (65 females, 38 males). There were 42 AD, 50 VaD, 2 mixed cases and 9 Others. Diagnosis based on DSM-III-R for dementia. AD and VaD diagnosed mainly by NINCDS-ADARDA and NINCDS-AIREN respectively.	AD and VaD risks estimated using cox proportionate hazard analysis. Adjusted covariate was age.	The HR for AD and VaD were 0.75 (0.54-1.03) and 1.31 (0.98-1.74) respectively in relation to continuous BMI.

Borenstein Graves (2001): USA	Japanese Americans aged ≥ 65 years with mean age 72.6 (SD 6.1) were recruited in King County, WA (of which 96% were 100% Japanese descent) Ni-Hon-Sea Project	Sample size 1,869. Follow up from 1992-1996 with mean of 3.8 years.	BMI calculated based on measured weight and heights and Continuous BMI used in the study.	AD cases were 59. Diagnosis based on DSM-IV and NINCDS-ADRDA criteria	Cox proportionate hazard regression models were used with age as time axis and adjustments for sex, education, height, verbal IQ scores, Head Circumference. For analysis stratified by sex, adjusted for head circumference and APOE Ɛ4 alleles	The fully adjusted HR was 1.06 (0.90-1.25) for continuous BMI and AD. The HR in women was 1.06 (0.87-1.31) and in men it was 1.05 (0.82-1.34)
Gustafson (2003): Sweden.	Age≥70 years. Recruited 392 individuals (166 men, and 226 women). Response rate 85%. Ten demented at baseline were excluded from study.	Sample size 382; Follow up≥ 18 years. Total risk-years 4,194.8 (2,705.6 in women and 1,489.2	Measured body weight and heights. BMI used as continuous variable.	93 dementia cases (women 59 and men 34). Diagnosis based on DSM-III. AD and VaD diagnosed mainly by NINCDS-ADARDA and NINCDS-AIREN respectively.	Dementia, AD, and VaD risks in women were estimated using cox proportionate hazard regression analysis. Controlled covariates included diastolic blood pressure, Cardiovascular diseases, Socioeconomic status, cigarette smoking and	After all adjustments, the Hazard ratio (95%CI) for dementia was 1.13 (1.04-1.24), 1.13 (1.04-1.24) and 1.15 (1.05-1.26) for BMI at ages of 70, 75 and 79 respectively. The AD risk was 1.36 (1.16-1.59), 1.35 (1.19-1.53) and 1.23 (1.10-1.37) for BMI at ages of 70, 75 years and 79 years respectively. For VaD, it was 1.01 (0.88-1.15), 1.07 (1.02-1.12) and

					treatments for hypertension.	1.00 (0.89-1.13) respectively for BMI at ages of 70 years, 75 years and 79 years. The calculated time at risk for dementia was 962.2 risk years.
Nourhashemi (2003): France	Recruited 3,777 elderly subjects aged ≥65 years that were part of the longitudinal PAQUID study. 3,636 (response rate 96.3%) were involved in the study.	Sample size used was 3,557. Follow up was 8 years with different time point at 1, 3, 5 and 8 years. Loss in follow-up was 89 (2.4%).	Self-reported weight and heights. Mini-Nutritional assessment cut offs for BMI were used; underweight BMI<21, normal BMI 21-22, overweight BMI 23-26 and Obese BMI ≥27	Incident dementia cases after 8 years was 4.4% (66), at 5 years 2.6% (52), at 3 years 3.7% (85) and 1 year (1% (18). Diagnosis involved MMSE and by DSM-III-R criteria.	Cox proportional hazard models used with adjustments for sex, age and education. Initial analysis used all incident dementia cases (Model 1) and followed by exclusion of diagnosed cases at 1- and 3-years' follow-up (model 2). Logistic regression estimated evolution of dementia risk over time with adjustments for sex, age, age-sex interaction, educational level,	The risk ratio (95%CI) for dementia in those with BMI<21 compared to those with BMI 23-26 was 1.483 (1.078-2.040) and 1.185 (0.716-1.960) for model 1 and 2. The risk ratio for BMI 21-22 was 1.072 (0.759-1.514 and 0,709 (0.401-1.254) for model 1 and 2. For BMI ≥27 they were 0.833 (0.589-1.178) and 0.716 (0.429-1.195) respectively. The Odds ratio at 3 years, 5 years and 8 years' assessments was 1.56 (0.85—2.86), 1.24 (0.61-2.54) and 1.05 (0.51-2.26) respectively for BMI<21.

					alcohol and tobacco consumption	
Buchman (2005): USA	Data from the Religious Orders Study of older Catholic clergy (≥65 years; mean age 80.2) that were recruited from 40 groups across the USA.	Sample size 820. Study from 1994-2003. The mean follows up was 5.6 years.	Measured heights and weight were used. Continuous BMI was used (mean baseline BMI 27.4Kg/m²)	151 AD cases. Diagnoses involved neurological assessment and 20 tests of cognitive function and NNCDS/ADRDA.	Cox proportionate hazard regression model was used and adjusted for age, sex and education and chronic diseases	The adjusted HR was 0.94 (0.91-0.98) for baseline continuous BMI and AD; and for annual change in BMI it was 0.73 (0.63-0.85).
Hayden (2006): USA	5,092 aged ≥ 65 years were recruited (response rate 85.5%). 355 excluded for having dementia after baseline. assessment.	Sample size 3, 264. Follow up 3.2 years. Loss in follow up was 1,429 (30.2%). Reasons for loss in follow-up; 626 died and 803 refusals or no trace.	Self- or proxy reported height and weight were employed. BMI assessed as obese (BMI≥ 30) or not obese (BMI<30)	Dementia 141 (AD=104, VaD=37). 44 other types (Lewy body, parkinsonism, and others). Dementia diagnosis involved MMSE, IQ-code, and using DSM-III-R criteria and NINCDS-ADRDA criteria used for AD. VaD was classified by the NINDS-AIRLN criteria.	Discrete-time survival models used with control for possible confounders. Hazard ratios for AD and VaD stratified by sex were calculated with adjustments for current age, sex, education and number of APOE e4 alleles.	The fully adjusted dementia, AD and VaD risks for BMI≥30 as compared to BMI<30 was 1.76(1.03-2.88), 1.93(1.05-3.36) and 1.16(0.37-3.12). The risks of AD for males and females was 1.48(0.41-4.18) and 2.23(1.09-4.30) respectively. For VaD it was 0.71(0.04-4.31) and

						1.30(0.32-4.29) for males and females respectively.
Lunchsinger et al. (2007) US	Age ≥65 years (mean 77). 2,126 randomly selected Medicare participants were recruited for study.	Sample sizes for analysis of BMI 893, WC 907, and weight change 709. At first follow-up 1,484 had anthropometric data. 255 excluded for baseline dementia with 1,372 remaining. The lost to follow-up rate was 30.2% over a mean period of 5.1 years.	Weight, height and WC were measured. BMI quartiles used; 1st BMI <23.4, 2nd BMI 23.4-26.2, 3rd BMI 26.3-29.6, 4th BMI >29.6. WC quartiles used; 1st ≤83cm, 2nd 84-90cm, 3rd, 91-97cm, 4th >97cm. Yearly weight change categorised into 3 groups: weight loss (>1 kg), stable weight (1kg of loss to 1kg of gain), and	181 dementia, 112 AD, and 53 dementia-associated with stroke (DAS). Dementia diagnosis by agreement from committee of neurologists, psychiatrists, and neuropsychologists using the DSM-IV criteria for dementia, NINCDS-ADRDA for AD. VaD was established if it started within 3 months of stroke diagnosis.	The Cox proportional hazard regression model was used to estimate HR with adjustments for age, sex, education years, ethnic group, and APOE 4 status. Secondary analysis was used to adjust for diabetes mellitus, hypertension, low density lipoprotein level, heart disease, stroke, and current smoking	In a fully adjusted model, the risk of dementia, AD and DAS were 0.9(0.9-1.0), 0.9(0.9-1.0), and 1.1(0.9-1.3) respectively for continuous BMI. For the second BMI quartile compared to the first, it was 0.7 (0.5-1.0), 0.9(0.5-1.4) and 0.4(0.2-1.0) respectively. For the Third quartile it was 0.6(0.4-0.9), 0.5(0.2-0.9) and 0.9(0.4-1.8). For the fourth quartile it was 0.8(0.5-1.2), 0.9(0.5-1.6) and 0.8(0.4-1.7) respectively. In those <76 years the risk for dementia was 0.4 (0.2-0.9), 0.3(0.1-0.8) and 1.0(0.4-2.1) for the second, third and fourth quartiles (reflecting U-shape). In ≥76 years, relationship is inverse, with risk of 0.6 (0.4-1.1) for the fourth quartile. The fully adjusted risk of dementia for the 3rd (91-97cm) and

			weight gain (>1 kg)			4th WC quartile (>97cm) was 0.94 (0.6-1.4) and 1.1 (0.7-1.8). In those <76 years it was 2.3(0.9-5.8) and 5.1, 1.0-26.4) for dementia and AD but in those >76 years it was 1.0(0.6-1.7) and 0.8(0.4-1.8)
Atti et al 2008 (Sweden)	Age 75 years. 1,810 were recruited (Response rate 80.2%). 1435 left after taking out; 110 (dropped out or died prior to clinical stage), 225 (demented), 40 (very old ≥95 years, MMSE score<20 or educational level unknown).	Sample size 1,255 (87.5%) with BMI data. The lost to follow-up rate was 12.5% over the 9 years period.	Weight and height were measured. BMI based on standard cut-offs of ≥30 for obese, 25-29.9 for overweight and 20-24.9 for normal. The underweight threshold was set at 20, because few participants had very low BMI. BMI change was assessed as decrease	189 dementia cases. Dementia status was established using the DSM-III-R criteria using a double step approach and also from Medical records and death certificates.	A Cox-regression hazard models was used to estimate the hazard ratio (HR) for dementia at different periods and adjusted for age, sex, education, baseline MMSE, depressive symptoms, chronic disease, and impairment in activities of daily living	After full adjustments, the risk was 0.98 (0.94-1.00) for continuous BMI. It was 0.97 (0.71-1.34) and 0.75(0.59-0.96) for BMI<20 and ≥25 when compared to 20-24.9 after 9 years follow up. For dementia at 3-9 years only, the risk was 0.96 (0.92-1.01), 0.91(0.59-1.40) and 0.72(0.52-1.02) for continuous BMI and for BMI<20 and ≥25. For dementia at 6-9 years, the risk was 0.97(0.91-1.04), 0.74(0.36-1.53) and 0.66(0.40-1.07) respectively. The risk for overweight male and females was 0.62(0.36-1.08) and 0.73(0.55-0.95)

			(>10% or 5-10%), stable (±5%) or increase (5-10% or >10%).			respectively. The risk of AD was reduced for overweight (RR 0.66, 0.50-0.88). For the overweight APOE e4 carriers and non-carriers it was 0.83(0.54-1.30) and 0.66(0.47-0.91). The risk for BMI decrease of >10% was 1.58(1.02-2.46) and 2.18(1.27-3.74) after 6 and 3 years respectively. No significant associations for other BMI changes.
Dahl et al 2008 (Finland)	Age 65-92 years. Recruited 1,196 (response rate 93.2%). After 8 years, 419 died (35%), 33 moved on (2.8%) leaving 744. A further 126 refused participation	Sample size 605 left for analysis from 618 (83%) due to refusal, missed clinical examination and baseline dementia diagnoses. The loss to follow-up rate was about 17% over the 8 years period	Measured weight and height. BMI categorized as ≥30 for obese, 25-29.9 for overweight and 18.5-24.9 for normal weight, <18.5 for underweight	86 cases of dementia. Dementia status was established using the DSM-IV criteria and all the information collected from laboratory test, medical records, and caregiver/nursing staff data and based on agreement between two physicians and a geriatrician.	A 3-step Cox-regression hazard models was performed to estimate the hazard ratio (HR) for dementia and adjusted for age, sex, education, diabetes mellitus, CVD (stroke coronary heart disease, hypertension, and atrial fibrillation),	In a fully adjusted model, the HR and 95%CI for continuous BMI was 0.92, 95% CI 0.87-0.97). After exclusion of dementia within 4 years after baseline, the risk was 0.93 (0.86-0.99). The risk for women and men (with low BMI scores) was 0.90(0.84-0.96 and 0.94(0.84-1.07) respectively. The dementia risk for Continuous BMI were 0.90 (0.84-0.96) and 0.95(0.84-1.07)

	with 618 (87%) left.				smoking, and alcohol use.	respectively for women and men. The risk for older age (71-92 at baseline) was 0.92(0.86-0.98), and younger age group (65-70 at baseline) was 0.91(0.82-1.03).
Hughes et al. (2009) USA	1,985 Japanese Americans (males and females) aged ≥65 years (mean 71.8 years) were recruited. Of this, 149 had dementia and were excluded with 1,836 dementia free left.	Sample size 1,478. Follow up was biennially (2, 4, 6, 8 years) with total of 8 years. The lost to follow-up rate was 19.5%. Reasons: No anthropometric data 221 lacked other follow-up data 137.	Height, weight, WC, and hip circumference measured. After follow-up, only weight measured. BMI base on International Obesity Taskforce cut-offs for Asians; Obese≥25.0, Overweight 23.0-24.9, normal 18.5-22.9 and underweight <18.5 while WC (inches)	129 dementia, 71 AD, and 22 VaD cases. Dementia and its subtypes diagnosis confirmed by committee of experts according to the DSM-IV criteria for dementia, the NINCDS-ADRDA for AD, and several criteria for VaD among which is NINCDS-ADDTC.	Cox regression hazard models was used to calculate HR for continuous baseline BMI, WC, and WHR and continuous BMI change adjusting for age, sex education, smoking, alcohol intake, regular exercise, hypertension, hypercholesterolemia, angina pectoris, diabetes, heart attack, TIA, stroke, ApoE genotype status	After full adjustments, the risk of dementia, AD and VaD were 0.80 (0.38-1.68), 0.68(0.31-1.51) and 0.40(0.06-2.51) respectively for baseline BMI In the fully adjusted model, for BMI change, the risk of dementia, AD and VaD are 0.31(0.09-1.02), 0.21(0.06-0.80) and 0.43(0.02-10.60). No association was found between the risk of dementia, AD, and VaD with baseline WC and WHR (result not reported by authours).

			and WHR used as secondary measures of adiposity.			
Fitzpatrick et al 2009 (USA)	Age 65 -97 years (mean age 74.7years). 3,602 were recruited for the Cardiovascular Health Cognition Study after completing cranial MRI and MMSE in1992/94.	Sample size 2,798. Follow up 5.4 years. Exclusions before final sample: Prevalent dementia 277, and Mild Cognitive Impairment 577.	Measured weight (kg), standing height (m) and waist/hip circumference (cm) at Late life. Weight for midlife was self-reported but height measured. The BMI was categorized into 4 groups using >30 for obese, >25-30 for overweight, 25-30 for normal weight, and <20 for underweight. WHR	480 dementia cases, 245 AD, 62 VaD. 151 both AD and VaD (mixed dementia). Dementia diagnosis by team of psychiatrists and neurologists using Cranial MRI. For dementia subtypes classification, the NINCDS-ADRDA and NINCDS-ADDTC were used for AD and VaD respectively.	A Cox- proportional hazard regression models was used to estimate the hazard ratio (HR) for dementia with adjustment for age, sex, race, education, CVD risk factors (smoking, diabetes mellitus, coronary heart disease, hypertension history, total cholesterol, ankle-arm blood pressure, C-reactive protein, Interleukin-6, kilocalories consumed /week, APOE genotype).	The fully adjusted risk for Late life Continuous BMI and dementia was 0.95(0.92-0.98). For BMI<20, BMI>25-30 and BMI>30 the risks were 1.62(1.02-2.64), 0.90(0.70-1.16) and 0.63(0.44-0.91) when compared to BMI 20-25. The risks of AD were 1.42(0.74-2.70), 0.74(0.52-1.05) and 0.58(0.36-0.96); and for VaD they were 2.15(1.11-4.19), 1.20(0.83-1.76) and 0.72(0.41-1.27) respectively for BMI<20, BMI 25-30 and BMI>30 as compared to BMI 20-25.The fully adjusted risk for midlife continuous BMI and dementia was .01(0.98-1.04). For BMI<20, BMI>25-30 and BMI>30 the risks were

			calculated as ratio of waist to hip circumference			1.20(0.66-2.17), 1.01(0.83-1.35) and 1.36(0.94-1.95).The risks of AD were 1.47(0.70-3.09), 1.04(0.74-1.47) and 1.25(0.74-2.11); and for VaD they were 0.87(0.31-2.40), 1.00(0.70-1.44) and 1.33(0.78-2.29) respectively for BMI<20, BMI 25-30 and BMI>30 as compared to BMI 20-25.
Scarmeas (2009): USA	Participants aged ≥65 years were Medicare beneficiaries from 2 cohorts recruited via Washington Heights-Inwood Columbia Aging project (WHICAP).	Sample sizes 1,880. They were followed from 1992-2006. The Follow-up duration was 5.4 years (SD 3.3).	BMI from measured heights and weight were used as continuous variable.	282 AD cases Diagnosis by DSM-III-R and NINCDS-ADRDA criteria.	Cox regression models controlled for age, sex, ethnicity, education, APOE status, Calorie intake, smoking, depression, leisure activities, comorbidity index, baseline clinical dementia rating score, time between first dietary score and physical activity assessment	After all adjustments the HR was 0.96 (0.93-0.99) for continuous BMI and AD

Power et al. (2011) Australia	12,203 of age 64-84 years (mean 72.1) were recruited by the aid of the copy of electoral roll for the Health in Men Study (Response rate 63%).	Sample size 12,047. Mean follow up 9.7 years. Exclusions prior to sample size included underweight 87, baseline dementia 32 and Substance abuse or HIV 37.	Measured weight, height and WC. BMI according to WHO; Normal 18.5≤BMI<25 , overweight 25≤BMI<30), obese and (BMI≥30). Mild central obesity 94 cm ≤ WC<102 cm Marked central obesity WC ≥102 cm. Also, a WHR with ≥0.9 signify obesity.	1,271 incident dementia. Diagnosis based on data from Western Australia Data Linkage System (WADLS) using ICD-9 and ICD-10 codes from the international classification of disease.	Cox regression models calculated crude and adjusted HR of dementia for each adiposity marker, controlling for age, marital status, educational level, alcohol intake, physical activity, diabetes prevalent, dyslipidaemia, CHD, and fat intake from milk. Repeated analysis (sensitivity) excluded first 2 years dementia cases or deaths.	The fully adjusted dementia risk HR (95%CI) for BMI 25-<30 and ≥30 was 0.82(0.70-0.95) and 0.82(0.67-1.01) respectively as compared to BMI<25. The risk for WC 94-<102cm and ≥102 was 1.02(0.87-1.20) and 0.88(0.74-1.04) as compared to WC<94. The risk for WHR≥9.0 compared to <9.0 was 0.82(0.69-0.98). Sensitivity analysis showed fully adjusted risk of 0.82(0.70-0.95), and 0.84 (0.69-1.03) for BMI 25-<30 and ≥30. No change for WC (result not reported by authours) while for WHR≥9 it was 0.81(0.68-0.98).
Lucca (2012): Italy	Recruited 2,813 aged ≥80 years in the Monzino-80-plus study. Data	Sample size 1,035. Total followed-up period was 5.5 years. Loss in follow up 6.8%.	Self- or caregiver reported weight and heights used. BMI assessed as continuous	373 dementia cases. Dementia diagnosis by DSM-IV criteria	Logistic and cox-regression models used with adjustments for age, sex, education, current smoking, alcohol	The fully adjusted incident dementia risk for continuous BMI was 0.966(0.934-0.997), p=0.0328. For BMI<18.5Kg/m² and BMI≥25Kg/m². They were

	available for 2,504 individuals (Lucca et al., 2015*). For the study, 1,110 were involved.		or categorical. Underweight BMI<18.5kg/m², normal BMI 18.5-24.9 kg/m² and Overweight obesity ≥25kg/m².		consumption, physical activity, depression, diabetes, hypertension, heart failure, atrial fibrillation, myocardial infarction, ictus and COPD.	0.62 (0.41-0.97) and 0.73(0.55-0.97) respectively when compared to BMI18.5-24.9Kg/m².
Tolppanen (2014): Finland	Recruited 1,511 aged 65-79 years (Response rate75.6%). 1,304 (38.9% males, 61.1% females) had complete data for midlife (mean age 50.2 SD 6.0) and late life study (mean age 71.2 SD 4.0).	Sample sizes 1,262 and 1,256 for dementia and AD for late life study. Sample sizes 1,304 and 1,289 for dementia and AD midlife study. Follow-up duration was 10 years for late life and 26 years for midlife.	Measured BMI were used as continuous and/or categorical BMI. Cut offs included <25 kg/m² for Normal BMI, 25-30kg/m² for overweight and 30kg/m² for obesity. Change in BMI (BMI baseline-BMI 1998) was used.	42 dementia out of which 33 was AD for late life study. There were 141 MCI cases. Dementia diagnosis by 3 steps approach based on MMSE, and DSM-IV criteria. The probable and possible AD was based on the NINCDS-ADRDA criteria. The modified Mayo Clinic AD research Centre criteria was used for mild cognitive impairment (MCI) diagnosis.	Cox regression models used. Fully adjusted model includes age, gender, ApoE status and region of residence, smoking and socioeconomic factors, likely mediators, serum cholesterol levels, systolic blood pressures, cardio- and cerebrovascular diseases and diabetes	The fully adjusted dementia risk for late life continuous BMI was 0.94(0.86-1.03). The risk was 0.51(0.25-1.04) and 0.55(0.23-1.34) for BMI<25-30 Kg/m² and ≥30Kg/m² respectively when compared to BMI<25Kg/m². The AD risk was 0.89(0.81-0.98) for continuous BMI; and it was 0.57(0.27-1.19) and 0.40(0.15-1.08) for BMI 25-29Kg/m² and BMI ≥30Kg/m² respectively. The dementia risk for Midlife continuous BMI was 1.07(1.00-1.14); and it was 1.04(0.58-1.87) and 1.81(0.91-3.57) for

						BMI<25-30 Kg/m^2 and ≥30Kg/m^2 ^{2}. For AD, it was 0.89(0.47-1.68) and 1.57(0.75-3.29) for BMI<25-30 Kg/m^2 and ≥30Kg/m^2 respectively. The dementia and AD risks for decrease in BMI were 1.14(1.03-1.25) and 1.20(1.09-1.33) respectively.

Neergaard (2016): Denmark	5,855 post-menopausal Danish women of mean age 70.1 were recruited.	Sample size 5,512; after excluding pre-existing dementia (15) and those with missing data (328). The follow-up was 15 years (Mean 11.9 ±3.9).	Measured heights and weight were used. underweight BMI<18.5, Normal weight BMI≥18.5-<25, Overweight BMI ≥25-<30 and obese BMI≥30	592 dementia cases. These included AD (250), VaD (43) and Other/unspecified dementia (299). ICD-10 was used to classify dementia diagnosis. Also from data of the National Danish Patient Registry and the National Danish Causes of Death Registry.	Cox proportionate hazard regression model was used and adjusted for age, education, smoking, alcohol consumption, physical activity, history of depression, cerebral embolism/haemorrhage, systolic blood pressure, fasting glucose levels and cholesterol levels.	The fully adjusted dementia risk was 0.88(0.45-1.72), 0.75(0.62-0.89) and 0.79(0.62-1.01) for BMI<18.5, BMI ≥25-<30 and BMI≥30 respectively when compared to BMI≥18.5-<25. The AD risk was 0.92(0.34-2.51), 0.72(0.54-0.96) and 0.74(0.51-1.09) for BMI<18.5, BMI ≥25-<30 and BMI≥30 respectively. For VaD, the risk was 0.68(0.33-1.40) and 1.28(0.57-2.86) for BMI ≥25-<30 and BMI≥30 respectively (No data for BMI<18.5). The risk for Other/unspecified dementia it was 0.93(0.38-2.28), 0.75(0.58-0.98) and 0.75(0.52-1.06) for BMI<18.5, BMI ≥25-<30 and BMI≥30 respectively.

APPENDIX 12: MULTIVARIATE-ADJUSTED ANALYSIS OF BMI AND DEMENTIA RISK (NORMAL BMI AS REFERENCE CATEGORY)

Body mass index **(kg/m²)**	**Dementia risk**				**Dementia risk (excluding wave 2**			
	Model 2				Model 2			
	OR‡	95%CI		*P*	OR‡	95%CI		*P*
(All)								
Underweight (<18.5)	0.44	0.21	0.95	0.036	0.40	0.12	1.31	0.130
Normal (18.5-<24)	Ref				Ref			
Overweight (24-<27.9)	1.00	0.74	1.35	0.996	1.26	0.85	1.87	0.247
Obese (>=28)	0.94	0.60	1.49	0.800	1.44	0.81	2.55	0.217
(Men only)								
Underweight (<18.5)	0.79	0.22	2.79	0.713				
Normal (18.5-<24)	Ref				Ref			
Overweight (24-<27.9)	2.12	1.30	3.47	0.003	2.83	1.51	5.30	0.001
Obese (>=28)	2.59	1.25	5.36	0.010	3.88	1.62	9.27	0.002
(Women only)								
Underweight (<18.5)	0.35	0.13	0.91	0.031	0.527	0.15	1.81	0.309
Normal (18.5-<24)	Ref				Ref			
Overweight (24-<27.9)	0.61	0.41	0.91	0.015	0.70	0.41	1.21	0.206
Obese (>=28)	0.48	0.26	0.90	0.022	0.69	0.30	1.56	0.370

APPENDIX 13: MULTIVARIATE ANALYSIS OF WC QUARTILES AND DEMENTIA RISK

Waist Circumference (WC)	**Dementia risk**				**Dementia risk (excluding wave 2)**			
	Model 2				Model 2			
Quartile	OR‡	95%CI		*P*	OR‡	95%CI		*P*
(All)								
Q1 **(<76.0)**	1.18	0.83	1.68	0.363	1.42	0.88	2.29	0.146
Q2 **(75.0-<85.0)**	Ref				Ref			
Q3 **(83.0-<93.0)**	1.33	0.92	1.93	0.133	1.45	0.86	2.45	0.161
Q4 **(>=93.0)**	0.88	0.57	1.36	0.569	1.45	0.82	2.58	0.203
Total								
(Men)								
Q1 **(<78.0)**	1.33	0.74	2.41	0.344	1.63	0.73	3.61	0.231
Q2 **(78.0-<85.0)**								
Q3 **(85.0-<95.0)**	1.45	0.77	2.73	0.247	1.89	0.80	4.46	0.145
Q4 **(>=95.0)**	1.37	0.66	2.85	0.406	2.71	1.06	6.95	0.038
Total								
(Women)								
Q1 **(<75.0)**	1.13	0.72	1.79	0.592	1.25	0.67	2.31	0.488
Q2 **(75.0-<82.0)**	Ref				Ref			
Q3 **(82.0-<91.0)**	1.30	0.81	2.09	0.284	1.27	0.64	2.51	0.498
Q4 **(>=91.0)**	0.71	0.41	1.23	0.224	0.96	0.44	2.11	0.922
Total								

APPENDIX 14: MULTIVARIATE ANALYSIS OF WC/√ HEIGHT QUARTILES AND DEMENTIA RISK

	Dementia risk								**Dementia risk (Excluding wave 2)**							
Waist Circumference /√ height	Model 1				Model 2				Model 1				Model 2			
Quartile	OR[†]	95%CI		*P*	OR[‡]	95%CI		*P*	OR[†]	95%CI		*P*	OR[‡]	95%CI		*P*
All																
Q1 **(<6.1)**	1.29	0.90	1.84	0.161	1.35	0.94	1.93	0.105	1.49	0.92	2.42	0.108	1.56	0.96	2.54	0.076
Q2 **(6.1-<6.7)**	Ref				Ref				Ref				Ref			
Q3 **(6.7-<7.3)**	1.39	0.95	2.02	0.089	1.44	0.99	2.11	0.059	1.57	0.93	2.65	0.090	1.64	0.97	2.78	0.066
Q4 **(>=7.3)**	1.16	0.77	1.73	0.478	1.19	0.79	1.79	0.395	1.74	1.01	2.98	0.045	1.79	1.04	3.10	0.037
Total																
Men																
Q1 **(<6.1)**	1.24	0.70	2.19	0.455	1.37	0.77	2.45	0.289	1.78	0.81	3.94	0.155	1.93	0.85	4.39	0.116
Q2 **(6.1-<6.7)**	Ref		Ref						Ref							
Q3 **(6.6-<7.3)**	1.44	0.76	2.72	0.259	1.49	0.78	2.84	0.229	2.64	1.12	6.20	0.026	3.07	1.27	7.39	0.013
Q4 **(>=7.3)**	1.54	0.76	3.09	0.228	1.57	0.77	3.22	0.218	3.31	1.35	8.15	0.009	3.64	1.42	9.35	0.007
Total																
Women																
Q1 **(<6.1)**	1.35	0.85	2.16	0.204	1.37	0.77	2.45	0.289	1.35	0.72	2.53	0.349	1.32	0.70	2.51	0.397
Q2 **(6.1-<6.7)**	Ref				Ref				Ref				Ref			
Q3 **(6.6-<7.3)**	1.32	0.81	2.13	0.262	1.49	0.78	2.84	0.229	1.09	0.55	2.16	0.816	1.11	0.55	2.24	0.763
Q4 **(>=7.3)**	1.03	0.62	1.69	0.920	1.57	0.77	3.22	0.218	1.18	0.59	2.36	0.642	1.28	0.63	2.57	0.498
Total																

APPENDIX 15: MULTIVARIATE ANALYSIS OF CONTINUOUS ADIPOSITY DATA AND DEMENTIA RISK

Continuous Variables	**Dementia risk**								**Dementia risk (Excluding wave 2)**							
	Model 1				Model 2				Model 1				Model 2			
	OR†	95%CI		*P*	OR‡	95%CI		*P*	OR†	95%CI		*P*	OR‡	95%CI		*P*
ALL																
BMI	1.01	0.97	1.05	0.548	1.01	0.97	1.05	0.709	1.06	1.01	1.12	0.023	1.06	1.00	1.11	0.035
WC	1.00	0.98	1.01	0.567	1.00	0.98	1.01	0.560	1.01	0.99	1.03	0.368	1.01	0.99	1.03	0.401
WC/√ height	0.98	0.83	1.16	0.839	0.98	0.83	1.16	0.832	1.13	0.91	1.41	0.282	1.12	0.90	1.41	0.315
Men																
BMI	1.10	1.03	1.18	0.003	1.09	1.02	1.17	0.010	1.17	1.08	1.27	0.000	1.17	1.08	1.27	0.000
WC	1.01	0.99	1.03	0.436	1.01	0.99	1.03	0.515	1.03	0.999	1.06	0.061	1.03	1.00	1.06	0.066
WC/√ height	1.16	0.87	1.55	0.317	1.14	0.85	1.53	0.386	1.44	1.01	2.05	0.043	1.44	1.00	2.06	0.047
Women																
BMI	0.96	0.92	1.01	0.115	0.96	0.91	1.01	0.101	0.99	0.93	1.06	0.794	0.99	0.93	1.06	0.819
WC	0.99	0.97	1.01	0.165	0.99	0.97	1.01	0.238	0.99	0.972	1.02	0.631	1.00	0.973	1.02	0.772
WC/√ height	0.89	0.73	1.09	0.250	0.91	0.73	1.12	0.352	0.95	0.71	1.26	0.720	0.98	0.72	1.32	0.878

APPENDIX 16: RISK OF INCIDENT DEMENTIA IN RELATION TO CATEGORIZED BMI GROUP META-ANALYSIS ANALYSIS

BMI variable (study reference)	Nos of studied populations	Nos of Participants	Nos of dementia cases	RR (95% CI)
<u>Categorized BMI</u> **analysis (I)**				
Overweight (a,b,e,f) [a]	6	11,864	1,568	0.87(0.66-1.14)
Obesity (a,b,e,f) [a]	5	11,644	1,585	0.86 (0.60-1.22)
Underweight (a,b,e, f) [a]	5	12,899	1,882	0.92 (0.64-1.33)
<u>Categorized BMI</u> **analysis (II)**				
Overweight (c, g)	4	15,608	1,453	0.98 (0.54-1.77)
Obesity (c,d,g) *	5	18,872	1,594	1.17 (0.65-2.10)

a (Luca et al., 2012), **b** (Atti et al.,2008), **c** (Power et al.,2011), **d**(Hayden et al., 2006), **e** (Fitzpatrick et al., 2009) and **f** (Neergaard et al., 2016) and **g** (Tolpppanen et al.,2014)

Note: all findings in the Table were from Random Effects Model in meta-analysis.

[a] Analysis included data from new unpublished Chinese study

(I) using normal-weight as a reference group, (II) using under-weight and normal-weight as a reference group (* one study (Hayden et al) compared obesity versus other weight)

APPENDIX 17: MUTIVARIATE ANALSYSIS OF BMI AND ALL-CAUSE MORTALITY IN SMOKERS

BMI, Kg/m²	Nos. of deaths /participants	Person-years	Rate of incidence (per 1000 p-y)	Model 1 † (smokers)				Model 2 ‡ (smokers)			
				HR	95CI		p-value	HR	95CI		p-value
All participants											
Underweight (<18.5)	35/106	528.4	66.2	1.78	0.78	4.07	0.174	1.56	0.66	3.68	0.306
Normal (18.5-<24)	196/1038	6078.5	32.2	Ref							
Overweight (24-<27.9)	87/650	4012	21.7	0.56	0.30	1.05	0.070	0.49	0.26	0.92	0.027
Obese (>=28)	26/184	1174.3	22.1	0.90	0.35	2.30	0.826	0.81	0.31	2.14	0.670
(Men)											
Underweight (<18.5)	23/53	265.18	86.7	2.52	1.08	5.86	0.032	2.35	0.98	5.60	0.054
Normal (18.5-<24)	112/517	3048.8	36.7	Ref							
Overweight (24-<27.9)	51/310	1915.6	26.6	0.67	0.35	1.28	0.222	0.55	0.28	1.09	0.085
Obese (>=28)	16/83	506.74	31.6	0.79	0.24	2.58	0.691	0.80	0.24	2.68	0.718
(Women)											
Underweight (<18.5)	12/53.	263.23	45.59								
Normal (18.5-<24)	84/521	3029.7	27.73	no enough data				no enough data			
Overweight (24-<27.9)	36/340	2096.4	17.17								
Obese (>=28)	10/101	667.59	14.98								

Model 1: age, sex, smoking status, alcohol drinking and urban areas; **Model 2**: age, sex, smoking status, alcohol drinking, urban areas, income level educational level Activity of daily living **(EXCLUDING PRE-EXISTING DISEASES, FIRST 3 YEARS DATA)**

APPENDIX 18: MULTIVARIATE ANALYSIS OF WC WITH ALL-CAUSE MORTALITY IN NON-SMOKERS

(EXCLUDING PRE-EXISTING DISEASES AND FIRST 3 YEARS DATA)

Waist circumference	Model 1 ǂ				Model 2 *			
	HR	95CI		p-value	HR	95CI		p-value
All participants								
No action	Ref				Ref			
Action level 1	0.86	0.54	1.366	0.521	0.88	0.55	1.4	0.578
Action level 2	0.99	0.63	1.55	0.964	0.99	0.62	1.579	0.967
(Men)								
No action	Ref				Ref			
Action level 1	0.87	0.4	1.911	0.726	0.95	0.43	2.126	0.901
Action level 2	1.14	0.54	2.427	0.733	1.13	0.51	2.47	0.766
(Women)								
No action	Ref				Ref			
Action level 1	0.83	0.47	1.477	0.527	0.78	0.44	1.398	0.406
Action level 2	0.90	0.52	1.55	0.696	0.89	0.50	1.57	0.689

Pre-existing diseases: heart disease, stroke, diabetes and depression/dementia

APPENDIX 19: MULTIVARIATE ANALYSIS OF WC WITH ALL-CAUSE MORTALITY IN SMOKERS

(Excluding pre-existing diseases and first 3 years data**)**

Waist circumference	Model 1 ǂ				Model 2 *			
	HR	95CI		p-value	HR	95CI		p-value
All participants								
No action	Ref				Ref			
Action level 1	0.93	0.4	2.136	0.857	0.95	0.4	2.248	0.909
Action level 2	0.38	0.12	1.16	0.090	0.44	0.14	1.374	0.159

Pre-existing diseases: heart disease, stroke, diabetes and depression/dementia

Note: reduced sample size did not permit analysis by gender for smokers.

APPENDIX 20: MULTIVARIATE-ADJUSTED ANALYSIS OF WC (CHINESE CUT-OFFS) AND ALL-CAUSE MORTALITY IN THOSE WITH DEMENTIA (NO ACTION AS **REFERENCE)**

Waist circumference	**Nos. of deaths**		**Rate of incidence (per 1000 p-y)**	**Model 1 †**				**Model 2 ǂ**			
Group (cm^2)	**/participants**	**Person-years**		**HR**	**95CI**		**p-value**	**HR**	**95CI**		**p-value**
(All)											
No action	54/134	573.69	94.1	Ref				Ref			
Action level 1	16./41	181.27	88.3	1.27	0.70	2.31	0.428	1.28	0.69	2.35	0.431
Action level 2	5/35.	193.42	25.9	0.34	0.13	0.89	0.027	0.40	0.15	1.11	0.078
(Men only)											
No action	31/66.	264.23	117.3	Ref				Ref			
Action level 1	5/6.	25.35	197.2	1.97	0.69	5.59	0.203	1.33	0.39	4.56	0.654
Action level 2	0/3	23.37	0.0	No	data			No	data		
(Women only)											
No action	23/68	309.46	74.3	Ref				Ref			
Action level 1	11/55.	155.92	70.5	1.22	0.55	2.68	0.624	1.40	0.59	3.30	0.443
Action level 2	5/32.	170.03	29.4	0.40	0.15	1.05	0.064	0.56	0.17	1.81	0.334