

Characterizing the changing morbidity and cause-specific mortality burden of the obesity epidemic in England

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Abstract

Nearly two-thirds of adults are overweight or obese in England. Whilst cardiovascular disease (CVD) mortality rates have contributed to declines in all-cause mortality, there is limited research on these shifts and the impact of mortality and morbidity as a result. My thesis aims to estimate the trends and diversification of obesity-related mortality and morbidity in patients and to estimate the contributors to morbidity in obese individuals by applying a clinical definition for obesity. Data was extracted from the Clinical Practice Research Datalink, consisting of primary healthcare records, for over 1.4 million adults in England with at least one body mass index (BMI) measurement between 1998 and 2019, linked to national death registration data and hospital data. I used discrete Poisson regression to analyse obesity-related mortality and incidence trends and binomial logistical regression to analyse the prevalence of comorbidities by BMI category. I utilised joinpoint regression to estimate if the trends are significant across the study period. In the final aspect of my PhD, I calculated crude prevalence to identify the most prominent conditions in obese individuals, using a novel definition. Between 2004 and 2019, I observed declines in all-cause and CVD mortality rates, and as a result, cancers became the primary contributor of death in males in all BMI categories and females in the overweight category by 2019. Across obesity-related co-morbidities, in the obese category, type 2 diabetes remains one of the most prevalent conditions, but conditions are diversifying, and osteoarthritis and depression are becoming major contributors to incidence and prevalence. Amongst those with obesity, high blood pressure, joint pain, and respiratory conditions are the most prominent conditions. Shifts in the major contributors to mortality and morbidity indicate a greater focus on prevention and management for a broader set of diseases for continued improvement in health in obese individuals and the general population.

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Abbreviations

ADL	Activities of daily living
BMI	Body mass index
CI	Confidence interval
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CPRD	Clinical Practice Research Datalink
CVD	Cardiovascular disease
DALY	Disability adjusted life years
eGFR	Estimated glomerular filtration rate
FTO	Fat mass and obesity-associated
GBD	Global Burden of Disease
HDL	High-density lipoprotein
HES	Hospital Episode Statistics
HSE	Health Survey for England
ICD	International Classification of Diseases
ID	Identifiers
IHD	Ischaemic heart disease
IMD	Index of Multiple Deprivation
ISAC	Independent Scientific Advisory Committee
NCD	Non-communicable disease
NICE	National Institute for Health and Care Excellence
ONS	Office of National Statistics
OR	Odds ratio
PCOS	Polycystic ovary syndrome
QOF	Quality and Outcomes Framework
WC	Waist circumference
WHO	World Health Organization

Statement of originality

I declare the work in this thesis is my own original research—including study design, data application, all analyses, and the write-up— and any work that is not my own has been cited.

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1. Rationale, aims, and thesis overview

1.1 Rationale

The obesity epidemic is a major public health problem affecting virtually every part of the world, with global obesity prevalence tripling between 1975 (4.7%) and 2016 (13.1%) (1, 2). As of 2019, there was an estimated 5 million deaths and 160 million disability adjusted life years (DALYs) as a result of obesity, with the projected deaths and DALYs to increase by 43% and 40%, respectively, between 2020 and 2030 (2). If the trends in obesity prevalence continue to rise as previously observed, by 2035 nearly 51% of the global population will be overweight or obese (3). The long-term impact of these trends in obesity is now one of the most discussed topics in public health today.

Having an overweight or obese body mass index (BMI) increases the risk of a broad set of well-established diseases and conditions, such as multiple cardiovascular diseases (CVDs), certain cancers, respiratory conditions, and musculoskeletal disorders. We know that all-cause mortality rates are declining, and as a result people are expected to be living longer but with major illness. Yet, the degree of changes for both mortality and morbidity by BMI, and more specifically obesity, across a variety of obesity-related conditions is unknown. It is plausible that with improved mortality, along with an increase in burden of disease, there is a change in the primary contributors to both obesity-related mortality and morbidity. Understanding these trends and any potential shifts in the contributors to obesity-related mortality and morbidity is essential to provide insight for health care planning and how the health system can support improved outcomes, treatment, and prevention.

In this context, obesity is defined as a risk factor, as opposed to a disease. As obesity is a multifaceted condition, there is a significant amount of discourse on if/when obesity should be

considered a disease. Redefining obesity as a disease using a clear set of criteria for adiposity levels and prevalent diseases, it becomes imperative to understand the population burden of clinical obesity. By investigating the burden of disease associated with mortality, morbidity, and a clinical obesity diagnosis, this research supports prevention strategies, public health interventions, and improvements to clinical care and treatment for individuals with obesity.

1.2 Aims and objectives

The aim of this PhD is to characterise the trends of obesity-related mortality and morbidity and prevalence of clinical obesity in English adults from 1999 to 2019. There are three specific objectives:

1. To examine the changes in mortality rates and how the proportional composition of deaths by cause has changed in overweight and obese adults from 2004 to 2019 in England.
2. To determine whether the spectrum and character of dominant morbidities associated with obesity is changing through prevalence and incidence of obesity-related morbidities in adults from 2004 to 2019 in England.
3. To implement a new definition of clinical obesity, according to the *Lancet Diabetes & Endocrinology* Obesity Commission, and estimate period prevalence (from 2015 to 2019) and mortality risk (from 2010 to 2019) of clinical obesity in English adults.

1.3 Structure of the thesis

Chapter 2 of this thesis explores the factors which have been influencing the obesity epidemic. I discuss the history of obesity, the factors which impact obesity prevalence from a global and a UK perspective, as well as trends and complications associated to obesity. Chapter 3 details

the dataset I used for this research, the Clinical Practice Research Datalink (CPRD), which includes the data retrieval and cleaning process, and a brief description of the population included in the cleaned dataset. Chapter 4 addresses the results of my first aim—mortality rate trends and burden of mortality by diseases. This chapter goes over the changing mortality trends and their significance, and how these then impact the proportional contribution to mortality across all causes of death. Chapter 5 looks at the trends in both prevalence and incidence of obesity-related morbidities, assessing whether these trends are significant and whether they are similar or divergent. In Chapter 6, I utilise the Obesity Commission’s definition of clinical obesity and apply this to my population to understand the prevalence of clinical obesity and the mortality risk by adiposity levels and a broad set of causes of death. Chapter 7 is the final chapter of this PhD, in which I discuss my findings, how these may overlap, and the clinical and public health implications of these unexplored outcomes of the obesity epidemic.

2. Introduction

2.1 History of obesity

Obesity is a complex condition, defined by an excess accumulation of adiposity, with the potential to impair health (4, 5). Obesity has been a popular topic of discussion since the late 20th century, with levels reaching epidemic proportions, but can also be dated back to sixth century BCE (6). The Indian physician Sushruta considered obesity to be attributed to a sedentary lifestyle and linked to diabetes, disease, and death (6, 7). More frequently mentioned for obesity ideologies is Hippocrates, who stated, “Corpulence is not only a disease itself, but the harbinger of others” (8). Both individuals cited an imbalance of humours (or fluids) as a cause, and exercise as treatment to restore the balance of fluids in the body (7-9). Obesity indicated affluence and wealth throughout famines and food shortages but was also stigmatised as a result of the continuous investigation of the health consequences associated (10, 11). As medical knowledge progressed, an index for relative body weight to estimate obesity and body fat mass became imperative for comparative disease research.

2.1.1 Measuring obesity and body mass index

After a medical insurance company identified the relationship between high body weight and an increase in mortality risk, in 1941 they developed best weight-for-height tables which consisted of weight relative to height in 1 inch increments by different frame sizes (small, medium, and large) and correlated this with their mortality data (12-14). This resulted in an identification of an ‘ideal’ or ‘healthy weight’ which was based on those who were enrolled in their insurance plan (12, 13). These weight categorisations were widely used, but there was still no agreed upon definition for researchers to use. Other definitions to identify overweight and obesity included weight divided by height ratio and the weight divided by height cubed (14).

As obesity prevalence continued to increase, there was still no standard definition to identify overweight and obesity, and research showed that the ratio of weight to height squared is a better measure (compared to weight to height ratio) of overweight as it is less sensitive to height variations in populations, has a high correlation to body fat estimates (primarily skinfold thickness and body density), and does not use population averages of weight by mortality risk (14). Thus in 1972, a 19th century definition for relative body weight was coined BMI and became the standard index to identify overweight and obesity in research, though discussions on whether it is the best measurement for adiposity and health consequences are continuous (14-18).

BMI is calculated by using weight in kilograms divided by height in meters squared (kg/m^2) and is considered a proxy measurement for body fat percentage (18, 19). BMI was characterised by the World Health Organization (WHO) with the following classifications: underweight: $\text{BMI} < 18.5 \text{ kg/m}^2$; normal weight: $\text{BMI} \geq 18.5$ and $< 24.9 \text{ kg/m}^2$; overweight: $\text{BMI} \geq 25$ and $< 29.9 \text{ kg/m}^2$; and obese: $\geq 30 \text{ kg/m}^2$. The obese category can be further separated into obese class I: $\text{BMI} \geq 30 \text{ kg/m}^2$ and $< 34.9 \text{ kg/m}^2$; obese class II: $\geq 35 \text{ kg/m}^2$ and $< 39.9 \text{ kg/m}^2$; and obese class III $\geq 40 \text{ kg/m}^2$ (16). These categories were designated as they are associated to how excess body fat increases the risk of morbidity and mortality and is closely related to adiposity (16).

BMI is often criticised for not directly assessing body fat or differentiating between lean or fat mass. Measuring techniques such as bioelectrical impedance and dual-energy X-ray absorptiometry are considered the gold standards as they directly measure body mass, but they are impractical for routine use (20). Research also indicates using measures for central obesity

such as waist circumference (WC), are as highly correlated to BMI and show similar risk of disease (21). However, when measuring WC to assess central adiposity and risk of disease, there are validity and variability concerns. WC measurements can be taken from four different areas on the waist, and recommendations differ based on the agency, such as WHO or National Institute of Health (22). Without a standard definition, the location of a WC measurement would affect the risk of disease (22, 23). Further, techniques are not well familiarised in the clinical setting, resulting in considerable measurement error with measurements ranging from 1.3 to 6.5 centimetres when taken by trained nurses, and from 0.7 to 12 centimetres when taken by physicians (24). Until a standard definition of the location of a WC measurement is implemented, followed by training to ensure the location for the measurement is well understood and multiple measurements are taken to improve validity, BMI has a higher reliability for assessing adiposity (24-26). Thus, BMI has become the standard, being an appropriate and reliable measurement to estimate the risk of morbidity and mortality associated to obesity (20).

2.2 The obesity epidemic

Whilst updating the International Classification of Diseases (ICD), the WHO recognised obesity as a disease in 1948 (27). Since the 1970s, worldwide obesity prevalence has nearly tripled and continues to increase in all regions and sexes (28). Globally in 2016, 39% of adults were overweight and 13% were obese (5). If trends continue to increase as expected, the World Obesity Federation predicted, globally, over 50% of individuals will be either overweight or obese, and 25% will be obese by 2035 (29).

From a regional perspective, the Americas had the highest prevalence of overweight and obesity, accounting for 63% of adults in 2016 (30). The European Region closely followed the

Americas with a prevalence of overweight and obesity of 59% in 2016 (31). From 1975 to 2016, the prevalence of obesity in Europe increased by 138% and in the past decade increased by 20% (31). As of 2018, the prevalence of overweight and obesity in England is higher than the European prevalence at 63% (32).

In England, obesity rates increased from 15% in 1993 and despite a deceleration in the increase of rates from 2001, obesity rates reached 28% in 2019 (4, 32). The prevalence of obesity in the UK is two-thirds the prevalence in the US, which accounts for the highest levels of obesity globally at 42% (2017-2020), but alarming findings indicate that the trends in the UK are closely following that of the US, only a few years behind (33-35). Models project that the maximum obesity prevalence will be reached by 2031 at 44% in the US compared to 37% by 2034 in the UK (34).

2.3 Drivers of obesity

Obesity is the result of energy intake exceeding energy expenditure. However, this is a simplistic way of viewing obesity when in fact it is a multifaceted disease and there is not one direct cause of obesity. From biological reasons to changes in modern society, obesity has risen due to a multitude of reasons interacting with each other.

2.3.1 Biology

As a result of food scarce environments, we as humans had adapted to seek out high-calorie, energy-dense foods and to biologically resist dieting (36). This also led to a genetic predisposition of storing excess body fat, which was an evolutionary response, so we did not die of starvation or weight-loss inducing illnesses (36, 37). This response has translated to

obesity as fire, tools, and social behaviour became prominent and we no longer needed these biological mechanisms to the same extent, yet these genes were not completely removed (37).

About 40-65% of obesity risk is due to genetics and there are at least 900 genetic variants that can contribute to obesity (36, 37). In the majority of cases, there is not one large genetic mutation, but rather an accumulation of a lot of minor genetic mutations (37). The *ob* gene, discovered in 1994, expressed predominantly in adipose tissue, produces a hormone called leptin (38, 39). When body fat is low, leptin stimulates hunger, but when body fat is increased, it acts as an appetite suppressor (36, 38-41). Leptin was originally thought to be lacking in individuals with obesity, but it is actually elevated resulting in reduced satiety, increased consumption, and increased BMI levels (36, 39, 40). Later in 2007, the fat mass and obesity-associated (FTO) gene variant was discovered through genome wide association studies and is unequivocally associated to obesity (42, 43). Having two FTO variants is associated to a 1.67 times higher risk of developing obesity and a weight increase of 3kg (43-45).

2.3.2 The ‘obesogenic environment’

From 1910 to 1960, there was a decrease in physical activity and food consumption in high-income countries (considered the move-less stay lean phase), which resulted in a balance of energy intake and expenditure, however, from 1960 onwards, this phase shifted to maintaining a decrease in physical activity but an increase energy intake (the eat more, gain weight phase) (46). This is considered the ‘energy-balance flipping point’, which is illustrated using food supply data in the US, where energy intake exceeded energy expenditure and weight gain was occurring at individual and population level. The flipping point is attributed to a multitude of reasons, from our lifestyle and behaviour as a result of living in an increasing obesogenic

environment, referring to the environment which promotes obesity through lifestyle and behaviours (43).

Energy expenditure declines are attributed to technological advances where there is an increase in cars, computers, and machinery, with occupations becoming more sedentary as a result. With people driving more and walking less, there is a decline in physical activity considering more time is spent sitting in traffic on the way to work, but also because of a decrease in manual labour jobs (36, 46, 47). Technological advances also increases leisure time with more time spent watching television, on electronic devices, and playing computer games (36, 47).

Sedentary lifestyle and climate change are also factors attributed to obesity. Increasing ambient temperatures increases our energy expenditure and as our bodies are trying to keep cool, our food intake declines. However, with physical activity declining and our time indoors increasing, the use of air conditioning is rising. Thus, our body working to stay cool is interrupted as the air conditioning decreases energy expenditure and impacts food intake reductions (43, 48).

The largest contributor to the obesogenic environment is changes in the food system. Food has been able to be produced more quickly with cheaper manufacturing, resulting in less expensive food more widely available, but often lower in quality (36, 42, 43, 47). More accessibility to these products has contributed to a reduction in home cooking and an increase in fast food consumption, which is often high calorie and energy dense, and large in portion size (43, 46). Having easier access to fast foods with high energy intake is a sufficient explanation to the rise in obesity rates in the UK from the 1980s to today (46).

2.4 Risk factors of obesity

2.4.1 Gender

Gender is one factor which significantly influences obesity risk. With increases occurring in both sexes between 1970 and 2016, obesity prevalence increased in women from 69 million to 390 million, compared to men which increased from 31 million to 281 million (28). Globally, the prevalence of obesity is higher in women at 15% than men at 11% (5). Overweight has a less prominent difference, with a prevalence of 40% in women and 39% in men (31).

Based on 2016 WHO estimates, this is not the case in Europe, where overweight and obesity rates were higher in men at 63% than women at 54% (31). Similarly, the rates of overweight or obesity in England was 69% in men and 59% in women (32). However, obesity rates in Europe was 24% in women and 22% in men; in England, the prevalence of obesity was 26% of women compared 25% of men (31, 32).

The discrepancy between overweight global rates and European rates can be explained by a country's income level. A literature review found when combining all countries, prevalence of overweight was larger in women than men (49). When only including high-income countries, there was a greater prevalence of overweight in men than women. Obesity prevalence remained larger in women than men when separated by income level. There is not one distinct reason for obesity rates higher in women than men, but rather a combination of lifestyle (diet, physical activity), biological (menopause), social, and cultural factors (49-51).

2.4.2 Age

Rates of obesity increase with age, with peaks in late middle age and declining thereafter (52). In England, obesity levels were over 30% between ages 45 and 74 and dropped in the 75+ age

group (32). In men, the 45 to 54 age group had the highest prevalence of obesity at 36% whilst women had the highest levels of obesity in the 55 to 64 age group at 37% (4).

There is clear evidence that body composition changes with age (53-57). Fat free mass peaks at around 20 years of age and declines from 30 years of age (53, 55, 56). Conversely, fat mass increases from 30 years of age and peaks between 60 and 70 years of age (56). In addition to energy expenditure declining throughout adulthood, with increasing age and fat distribution, this leads to an increase in overweight and obesity rates (56, 58).

At 70 years of age, both fat mass and lean mass decline, known as sarcopenia, which is one explanation for a lower level of obesity in this age group (56, 57). However, there is the concern of sarcopenic obesity, which is when muscle mass and function declines, but adiposity increases, especially in individuals in older age groups (59). The clinical impact of sarcopenic obesity is great, linked to a high risk of comorbidities (depression, knee osteoarthritis), metabolic disorders (dyslipidaemia), geriatric syndromes (frailty), and death (59, 60). The prevalence of sarcopenic obesity is estimated to be 11% globally in older adults, but as a result of the increasing obesity prevalence and the aging population, this is expected to increase (61, 62). This is a significant health challenge for older individuals, but also for clinicians as there is no standard definition for a diagnosis, with gaps in care for preventing and managing the condition (59). Considering age and obesity are risk factors for increased mortality rates, the lower obesity rates in older age could also be due to those with a lower BMI having a higher survival into older age (53).

2.4.3 Socioeconomic status

Globally, obesity rates are the lowest in low-income countries and highest in high-income countries, however the difference in rates are declining (63). As countries develop economically, obesity prevalence is expected to follow the pattern of higher income countries, where within a population, the obesity prevalence amongst the wealthier groups changes little and the burden of obesity shifts and a larger proportion become overweight or obese in the lower socioeconomic population (64).

In high-income countries, the burden of obesity is highest among the poorest people (63). In England, deprivation is the main indicator used for area-level socioeconomic status. The proportion of men who were obese is the smallest in the least deprived quintile at 21% and highest in the most deprived quintile at 30% (65). In women, the disparity between quintiles is more pronounced where women have the lowest obesity prevalence in the least deprived quintile at 19% and the highest obesity prevalence in the most deprived quintile at 36% (65). The health inequalities are apparent considering hospital admissions directly attributed to obesity are over three times higher in the most deprived areas compared to the least (66).

2.4.4 Ethnicity

In England, 72% of the Black population were overweight or obese, the highest proportion of overweight or obesity of all ethnic groups in the country. In contrast, 37.5% of the Chinese population were overweight or obese, accounting for the lowest proportion. Asians, 'other white', and mixed ethnicities had a prevalence of overweight or obesity ranging from 57-59%; whereas white British and 'other' ethnic groups had a similar prevalence of 65% and 66%, respectively, being overweight or obese (67).

BMI cut-offs were intended to be used in association to disease risk, however, how different ethnicities carry body fat and the impact of these differences on disease risk was not originally considered (68, 69). Research has consistently shown that there is a higher prevalence of type 2 diabetes at lower BMI levels in certain populations (70). Specifically in Asian populations, there is a higher risk of type 2 diabetes at lower BMIs compared to Europeans, and despite having the same body fat percentage, BMI is shown to be 3-4 units lower compared to Caucasians (68), (71).

The National Institute for Health and Care Excellence (NICE) recently updated their guidelines for BMI cut-offs to estimate cardiometabolic risk more accurately (72, 73). As South Asian, Chinese, 'other' Asian, Middle Eastern, Black African, and African Caribbean population are at greater risk of diabetes risk with lower BMI levels, compared to their white counterparts, NICE recommends overweight classified as a BMI $\geq 23 \text{ kg/m}^2$ and $< 27.4 \text{ kg/m}^2$ and obese classified as a BMI $\geq 27.5 \text{ kg/m}^2$ (72). However, these cut-offs have primarily been investigated in association to type 2 diabetes risk, thus they may not be appropriate to assess the risk of outcomes such as CVD or all-cause mortality (69).

2.5 Obesity sequelae

2.5.1 Cardiovascular disease

An obese BMI increases the risk of multiple CVDs. The incidence of hypertension among obese individuals is five times greater compared to normal weight individuals (74). Having persistent hypertension increases the risk of stroke, myocardial infarction, heart failure, arterial aneurysm, and kidney disease (75-78). The risk of heart disease and stroke—which are the second and fourth leading causes of death in the UK—increases by 28% and 64%, respectively,

compared to a normal weight BMI (79-81). In a UK population-based study, once a BMI of 25 kg/m² was reached, the risk of mortality from CVD increased 29% for every 5 kg/m² increase in BMI (75). For CVD-specific diseases, the mortality risk increased by 164% for hypertensive heart disease, 82% for heart failure, and 57% for ischaemic heart disease in the obese category compared to normal weight (75).

2.5.2 Type 2 diabetes

The relationship between obesity and diabetes is so intertwined, the term ‘diabesity’ was coined to describe the overlap of both conditions (82, 83). In the UK, about 90% of type 2 diabetes is attributed to overweight or obesity (74). In a meta-analysis assessing multiple high-income countries, including the UK, there was a seven times greater risk among obese individuals and five times greater risk among overweight individuals, compared to normal weight (84, 85). In England, the risk of diabetes is five times higher among obese individuals compared to normal weight (84). Those with diabetes live on average six years less than those who do not as there is a greater risk of CVD, blindness, amputation, depression, kidney disease, and respiratory conditions, further influencing the risk of mortality, morbidity, and quality of life (74, 83, 84).

2.5.3 Cancers

As the second leading cause of death in the UK, with smoking the leading cause, obesity is attributed to 4-8% of cancer cases and increases the risk of cancer mortality by 17% (86-89). There are at least 13 types of cancers which are knowingly associated to obesity, some of which have convincing evidence that they are caused by obesity (90, 91). Of the 13 cancers, three are among the most difficult to treat—oesophageal, pancreatic and gallbladder—and two are some of the most prevalent cancers—breast and colorectal (89, 92). In the UK, breast cancer is the most common cancer accounting for 15% of cancer cases and colorectal is the fourth most

common, behind prostate and lung cancer, accounting for 11% of cases (92). A meta-analysis observed the risk of mortality among individuals with obesity increased by 23% for breast cancer, 24% for colorectal cancer, and 28% for pancreatic cancer compared to individuals without obesity (87).

Obesity is also highly associated to gynaecological cancers, endometrial cancer being one of the most common, and countries with the highest obesity rates also have some of the highest rates of endometrial cancer (92, 93). Research has shown 41% of all endometrial cancers have the potential to be attributed to excess weight (if assuming causality), with the largest associations occurring with each 5 kg/m² increase in BMI (94, 95). However, observational studies suggest that intentional weight loss significantly reduces the risk of endometrial cancer, and whilst other gynaecological cancers were investigated, no significant changes occurred (96, 97). Ovarian cancer is also strongly associated with obesity and for each 5 kg/m² increase in BMI, the risk of different histotypes of ovarian cancer increases between 13% and 19% (98). The link between other gynaecological cancers and obesity is more limited, but evidence suggests screening is lower in females with obesity due to stigma, lack of appropriate equipment or training, and attitude of the health care workers (93).

2.5.4 Musculoskeletal

The prevalence of musculoskeletal disorders was 25% among obese individuals compared to the average prevalence of 17% in England (99). Whilst musculoskeletal disorders do not directly lead to increased mortality, the effect on morbidity is substantial. Back pain has a positive association with obesity (100). In 2017 in England, the prevalence of back pain was 39% among those with obesity, compared to 29% of those without obesity (101). Osteoarthritis is the most researched musculoskeletal condition associated to obesity, specifically in the knee

and, less often studied, in the hip (102). With each 5 kg/m² increase in BMI, there is a 35% increase in risk of knee osteoarthritis and 11% increase in hip osteoarthritis (103, 104).

2.5.5 Mental health

Anxiety disorders and depression are the most prevalent mental health conditions, both of which can lead to poor health outcomes and increased morbidities (105). Meta-analyses show positive associations between obesity and anxiety (pooled odds ratio (OR): 1.40) and depression (OR: 1.57; OR: 1.40) (30, 100, 106, 107). The risk of obesity and depression has been studied often, with analyses also showing that the risk of obesity was increased among those who were depressed (OR: 1.40) (107).

2.6 Cardiometabolic factors, obesity, and mortality risk

Several studies report those with an increased BMI are more protected from mortality, specifically from CVD, compared to normal weight individuals (108). This concept is known as the obesity paradox. This protective effect has been shown only in overweight and obese class I individuals, and less so for class II or class III obesity (109). The obesity paradox is often criticised as it implies obesity does not increase mortality risk, despite having the knowledge that it increases the risk of all-cause and cause-specific mortality (94). Further, studies which indicate an obesity paradox are largely influenced by methodological factors and patient characteristics such as using only retrospective data; not having the ability to adjust for covariates or potential confounders (i.e., age and prior health status); and not accounting for an exclusion period or lead-in time to mitigate the impact of weight loss due to illness, referred to as reverse causality (110, 111).

Factors which impact the obesity paradox, which are not always considered in research, include cardiorespiratory fitness and exercise capacity, resulting in a phenotype called “fat but fit” (108). Both of these measures have evidence showing a greater cardiorespiratory fitness level and exercise capacity can reduce the risk of CVD events regardless of BMI status, and mitigate the effect of the obesity paradox (112, 113). Other obesity phenotypes include metabolically healthy or unhealthy obesity (108). These phenotypes depend on an individual’s BMI but also their cardiometabolic risk factors, which is relevant for clinical knowledge on obesity-related mortality and morbidity across different phenotypes (114). However, there is no standard definition for these obesity phenotypes, and different criteria have been proposed which include an obese BMI, but also clinical biomarkers such as triglycerides, HDL, blood pressure, and fasting blood glucose (114). Thus across-study comparisons are not currently possible to gain a better understanding of the risk of mortality and a BMI phenotype.

2.7 Economic impact of the obesity epidemic

Obesity currently costs the NHS £6.5 billion per year, and the NHS costs attributed to overweight and obesity are projected to be £9.7 billion by 2050 (115, 116). In the UK, the increase in obesity prevalence is projected to add nearly 1.3 million incident cases of type 2 diabetes, CVD, and cancers (combined) by 2030 (117). These estimates would increase healthcare costs by about £2 billion, indicating as BMI increases so does healthcare resource utilisation (84, 117, 118). For instance, patients with class III obesity and type 2 diabetes had greater healthcare costs than their counterparts without type 2 diabetes, primarily driven by prescription use (118). In individuals with CVD and class III obesity, the mean number of prescriptions was five times greater and healthcare costs were 10 times greater, compared to those with a normal weight BMI and low CVD risk (119).

Whilst the UK has lower obesity prevalence than the US, the UK has a larger aging population, resulting in a higher health expenditure. For example, in the US, the annual increase in healthcare costs from obesity-associated diseases is about 15%, of which 4% is due to the aging population. However, in the UK, healthcare costs are estimated to have an annual increase of about 25%, of which 10% is due to the aging population (117).

2.8 Obesity mortality and morbidity trends

2.8.1 Mortality

Globally, there were an estimated five million obesity-related deaths in 2019, an increase from the four million deaths from high BMI in 2015 (2, 120). In previous years, trends showed a reduction in all-cause and cause-specific mortality rates. Deaths from all-causes declined by 14% from 2007 to 2017 worldwide (121). In most western European countries, mortality rates declined between 2005 and 2015 with the fastest rates of improvement occurring in the early 2000s, declining 2-3% per year (122-124). Concurrently with mortality rates declining in western Europe, life expectancy increased between six to eight years since the 1970s and in England alone, the life expectancy from 1910 to 2010 increased almost three years per decade (125, 126). However, since 2011, these improvements have slowed, with the slowdown in England and Wales greater than in other high-income countries (127, 128).

In 2017, non-communicable disease (NCD) death rates decreased by 8% from 2007 and 2017 globally, with NCDs accounting for 73% of global deaths by 2017 (121). The success of improvements in overall and NCD-specific mortality rates is a result of the declines in CVD mortality rates, which has been considered a major public health achievement (125, 129-132). Globally, CVD mortality rates declined 10% in addition to declines in mortality rates from

cancers (4%), respiratory diseases (14%), and digestive disease (11%), with no changes in neurological mortality (121).

Between 2000 and 2010 in high income countries, the average annual decline in CVD mortality was 3%, with the UK experiencing some of the highest declines at 5% per year (121, 131). In the UK, between 1983 and 2013, CVD mortality rates declined 67%, compared to an 18% reduction in cancer mortality rates (129, 130). As a result of the large declines in CVD mortality, in addition to the cancer mortality rates declining at a slower rate, research suggests that the number of deaths and mortality rates from cancer is now larger than CVD in the UK and other high-income countries (122, 129, 130).

Despite such success in declining all-cause and CVD mortality, improvements in both life expectancy and mortality rates have stagnated in many western European countries, but the greatest plateau of the declines occurred in the UK (126, 133). From 2011, mortality rates have been plateauing in most English populations, mostly from the stagnation of CVD mortality improvements (123, 133-135). The causes of the slowdown of improvements is complex, but many studies cite that the increasing prevalence of overweight and obesity is the main contributor (123, 131, 136, 137). Other factors impacting the stagnation include the increasing aging population, the impact of obesity on type 2 diabetes and CVD risk, and growing inequalities from factors such as socioeconomic status (123, 126, 134). Research in the US shows that mortality rates are now increasing and considering the trends in mortality rates and life expectancy have been consistent across high-income countries, the health and longevity of populations is expected to decline elsewhere (131, 138).

2.8.2 Morbidity

In 2016, obesity was one of the leading risk factors for morbidity in England (139). A study from the Global Burden of Disease (GBD) 2015 Obesity Collaborators found the prevalence of high BMI increased faster than the disease burden associated to obesity, largely due to declines in CVD mortality (120). Compared to 20-30 years ago, there have been improvements in CVD risk factors among obese individuals, but CVD is still a major morbidity affecting obese individuals, considering CVD was still the leading cause of DALYs due to obesity in 2015 (120, 140).

The slight improvement observed for CVD risk factors provides further evidence of morbidities changing. For example, chronic kidney disease was the second leading cause of DALYS and increased from 11.5% to 18% between 1990 and 2015. Further, musculoskeletal disorders, diabetes and cancers accounted for <10% total of BMI-related DALYs, but increases in prevalence were observed between 1990 and 2015 for the three diseases and conditions (120).

This suggests that despite a decline in CVD mortality, the burden of morbidities has been increasing for other conditions and the risk of disabilities and complications which take a longer period of time to develop, such as musculoskeletal disorders and renal failure, are likely to be increasing among obese individuals (141, 142). Multiple studies note that the increase in exposure to obesity due to better risk factor management is likely going to increase the prevalence of these conditions over time (141, 143, 144).

2.9 Obesity as a disease

Defining obesity as a disease is a highly controversial topic. On one side, there is the concern of over-medicalising the condition which would result in a greater stigma of those with obesity,

a lower adherence to behavioural changes, and an increase in potentially unnecessary treatments (145, 146). However, defining it as a disease would confirm that obesity, like any other chronic condition, leads to illness independently of any other morbidities (146, 147). A *Lancet Diabetes and Endocrinology* Obesity Commission has established a clinical definition of obesity and a set of criteria to diagnose obesity as a disease. This is to differentiate obesity as a risk factor and obesity as a disease. Obesity as a risk factor predicts for future disease or mortality, but obesity as a disease would assess the clinical manifestations of obesity which have materialised independently of other comorbidities. This implementation results in a clinical definition of obesity, known as clinical obesity, which denotes when excess adiposity impacts normal functioning of tissues and organs, in addition to limiting the ability to perform activities of daily living (ADL) (146).

2.10 Summary

The rates of obesity continue to increase worldwide. The reason for the increase in obesity prevalence is not attributed to one single factor, but rather a combination of modifiable and non-modifiable risk factors which together are driving the epidemic. However, the drivers that may seem to be modifiable such as diet and physical activity are closely connected with socioeconomic status, having a major effect on health inequalities. Those with obesity are at significantly higher risk of a number of diseases and conditions, and whilst these associations are well known, there is space to look further into how the mortality risks and prevalence of these diseases and conditions are shifting as the obesity epidemic continues.

3. Methods and data used

3.1 Background

CPRD will be utilised for all aims in this PhD. It was chosen due to its large, longitudinal database, data quality standards, and linkage data to death registration and hospitalisations. The patients in the database are also largely representative of the UK population, providing the necessary generalisability across the English population for age, sex, ethnicity, and BMI when compared to Health Survey for England (HSE) and the UK census (94, 148, 149).

3.2 Clinical Practice Research Datalink

CPRD is one of the largest databases that collects medical records from primary care (150). Established in 1987, it was previously known as the General Practice Research Database and changed to CPRD in 2012 (150, 151). The database collects longitudinal anonymised patient data from 986 practices in the UK, accounting for over 21 million patients (total number of GP practices and patients ever included in the database) (152). As of March 2023, there were nearly three million current patients from 373 practices currently contributing to the database, accounting for both 4.5% of the UK population and UK general practices (152).

3.2.1 Quality checks

Practices are included in the CPRD database once agreeing at practice level to provide data monthly (150). The data, collected and recorded by practices, goes through data quality checks to ensure the data collected is continuously high quality and is ‘up to standard’. Two measures are applied for data quality assurance. A gap analysis occurs to check if there are any gaps in the reporting of patient data and death records to ensure the expected number of deaths and patients who leave the practice (i.e., transferred-out patients) are appropriately recorded (153). If there are any meaningful gaps, the checks must identify when there are no longer any gaps

in the records, and a practice meets quality standard at the earliest date with no gap, becoming the up to standard date.

Patient data also has to reach quality standard by CPRD to be deemed ‘acceptable’. There are multiple criteria to be reached but it aims to identify any concern of the validity of the patient’s record by excluding patients who have non-continuous follow up or inconsistent data records (153). A few criteria resulting in exclusion are empty or invalid registration date, transfer out date with no reason, and health care records prior to birth. Patients also have the option to opt out of sharing data with CPRD database (150).

3.2.2 Data availability

The CPRD dataset is formatted into care-specific datasets, separated by the type of information the health care professional records, including clinical, additional, referral, immunisation, test, and therapy data (150). There are also patient, practice, staff, and consultation data files which provide administrative information. These specified datafiles and their details are in Table 1.

Table 1. CPRD Datafiles Details

Data type	Details	Used in this study?
Patient	Demographics Registration date Transfer out date (if available) Acceptable status	Yes
Practice	Administrative data Location of practice Up to standard date (if available)	Yes
Staff	Practice staff details	No
Consultation	Type of consultation	No
Clinical	Medical history events such as: Symptoms Diagnoses Deaths	Yes
Additional Clinical Details	Data linked to events in the clinical file (i.e., BMI measurement value) Uses additional details identifier to link to clinical file	Yes
Referral	Referral details to external care centres	Yes
Immunisation	Immunisation records	No
Test	Test data coded using a read code to identify the type of test used and entity type for the test result	Yes
Therapy	All prescriptions	No

Read codes, of which there are 96,000, are entered by the healthcare professional and specifies symptoms, diagnoses, and any tests that were performed (150, 154). The name of the test and the corresponding results are identified using a numerical code called entity types. For instance, if a patient were diagnosed with high blood pressure, a high blood pressure read code and medical code (which is a unique CPRD code for medical terms selected by the GP) would be entered into the medical records. These records would then indicate that that patient had high blood pressure. To get the actual blood pressure readings, there is an entity type which provides the numerical measurements of the blood pressure. Entity types also cover responses from a healthcare professional's questions (i.e., smoking status) or a measurement result (i.e., height), with the response or value result (i.e., ex-smoker; height in centimetres). CPRD entity values are used to identify the study population (155).

3.2.3 Access

CPRD has ethics approval, supporting research using anonymised patient data and linked patient data, from the Health Research Authority (REC reference: 21/EM/0265) (156). CPRD completes NHS Data Security and Protection Toolkit assessment annually to ensure standard of holding data securely is met (157). Once GP data is received by CPRD, anonymisation according to the Information Commissioner's Office code of practice is reached and patient privacy is protected. All CPRD studies required scientific approval from the MHRA Independent Scientific Advisory Committee (ISAC) when I applied, but as of June 2021, access is now through CPRD's Research Data Governance (158). The CPRD registered study protocol ID for this research is 21_000310. The ISAC application with approval is provided in the Appendix.

3.3 Linkage availability

CPRD provides linkage data to a subset of English practices, accounting for 58% of all CPRD practices (150). Linked data includes Office of National Statistics (ONS), Hospital Episode Statistics (HES), Index of Multiple Deprivation (IMD), and multiple disease registers such as cancer and myocardial infarction. In this PhD, linkage data utilised ONS for death registration, HES for hospital admissions and outcomes for outpatient and inpatient (admitted patient care) hospitalisations, and IMD for deprivation data. The process of linkage is based on a sequential algorithm based on NHS number, sex, date of birth, and/or postcode. Around 95% are matched with exact correspondence with NHS number, sex, date of birth.

CPRD covers all of the UK, however, linkage data from ONS (i.e., mortality) is only available in England, which is why the analysis is only in English adults. ONS provides both the primary cause of death and date of death. HES data contains the primary diagnosis during a

hospitalisation as well as each diagnosis that may occur whilst hospitalised which was not the primary cause. HES was also utilised to extract ethnicity data. Both CPRD and HES collect patient ethnicity data, but 79% of inpatients in HES have ethnicity data, compared to 36% of patients in CPRD (148, 149). When CPRD is linked to HES ethnicity data, 64% of all acceptable patients have an ethnicity coded, and once combined over 90% of patients in HES and CPRD had the same ethnicity recorded (149). When extracting ethnicity data I used the first ethnicity recorded in HES, but if there was no ethnicity recorded in the HES extraction, then the first ethnicity in CPRD was used. The ethnicity groupings are: Asian, Black, White, Mixed, other, and missing.

Patient-level IMD data from 2010 was used to represent the midyear of this research, providing patient postcode linked deprivation measures. IMD measures the level of deprivation in a small area of England. It aims to cover economic, housing, and social problems by ranking the following indicators: income; employment; health and disability; education skills and training; barriers to housing and services; living environment; and crime (159). These indicators can be used separately, but for this research the combined indicators with weights are utilised, creating a single index. For comparability, quintiles are used, which are based on each small area in England where a person lives and their deprivation level with 1 as the least deprived areas and 5 the most deprived areas (159).

3.4 Defining the study population

Once access to the CPRD dataset was approved, I defined my study population by extracting patients from the ‘clinical’ database with entity value 13, indicating those who had at least one BMI measurement available. The BMI measurement was located in the ‘additional’ database

and was linked using anonymised patient identifiers and identifier for the measurement. This resulted in a dataset with 6,093,353 patients.

3.4.1 Initial data cleaning of CPRD dataset

Patients were excluded for a few administrative reasons. If a patient's first registration date was not the same as the current registration date they were excluded, as this may indicate gaps in the registration and temporary patients. The purpose of this was to only include permanent patients at the practice to acquire the most longitudinal data available and most accurate BMI measurement data throughout follow up. Patients who had a BMI measurement within 12 months of their registration date at the practice were also excluded. Newly registered patients at the general practice often get their BMI measured for administrative purposes, but for this research we only wanted BMI measures that were taken for medical purposes at the clinician's discretion.

Patients were excluded if their BMI measurement was prior to 1998 and after 2019. Data from 1998 was selected as the start year as it was when ONS death registration data became available. Whilst data was acquired until November 2021, due to the COVID-19 pandemic, the end of follow up was December 2019 to ensure mortality rates and cause of death were not skewed.

The plausibility range for BMI was 10-70 kg/m², excluding any extreme outliers for both abnormally low and high BMIs. Further, only adults aged 18 years and older were included, but this was an open cohort study so once a patient turned 18 years old and fit the other criteria, they were then included in the study.

As preparing for pregnancy and being pre- and post-natal influences lifestyle and behaviours, in addition to weight gain throughout pregnancy, cleaning for pregnancy in the dataset was imperative. Using a website called CALIBER, now replaced by Health Data Research UK, I searched read codes which indicated pregnancy and extracted them (160). I then matched the patients in my dataset that had a pregnancy read code, and using the date a pregnancy read code was entered and the date of a BMI measurement, I excluded BMI measurements which were taken 6 months prior to pregnancy and 15 months after pregnancy.

To account for duplicated data, rows with identical patient identifiers (IDs), BMI measurement dates, and BMI measurements were removed. There were cases where there were duplicated patient IDs and measurement dates, but the BMI measurement was different. Multiple measurements on the same day could indicate measurement error on behalf of the patient, person measuring, or measuring supplies (scale or tape measure). However, there is no way to know the true reason for these cases, so instead of taking the first measurement provided or averaging the measurements, a random measurement was selected. To select a random measurement, a seed was set, and two new variables were created, both consisting of different random normally distributed values. The first variable was sorted in ascending order by patient ID followed by the second variable, then the first row for each patient with a distinct measurement date was selected.

There were also certain cases where the gender was coded as neither male nor female, so they were excluded.

3.4.2 Preparing for linked data

Prior to requesting linked data (ONS, HES, and IMD), the start and end of follow up for each patient was established using the CPRD dataset to ensure the BMI measurements were within the defined study period (1 January 1998 – 31 December 2019) and other dates of interest. The start of follow up was the latest date of the following: practice up to standard date, registration date, linkage availability date, or the study start date (this is aim-specific and defined in subsequent chapters). The end of follow up was the earliest date of the following: transferring out of practice date, date of death, last collection date of the practice, end of linked data availability, or the end of the study period (31 December 2019). The linkage availability dates differ depending on the data, specified in Table 2.

Table 2. Linkage start and end dates for data availability

Data source	Start	End
ONS death	1 January 1998	16 November 2020
HES outpatient	1 April 2003	31 October 2020
HES admitted patient care	1 April 1997	31 October 2020

Linked data had to be requested for the subset of patients that had it available to them. To comply with CPRD rules, known as data minimisation, 1,500,000 random patients were selected to get linkage data. To choose these participants, two new variables were created consisting of random normal distribution values. Once the patient IDs were sorted in ascending order, the first 1,500,000 participants were selected. The linkage data for these participants were requested and received.

Despite the CPRD dataset containing date of death for patients, the ONS death data is the most reliable source for this information, thus the end of follow up for participants was updated once receiving linkage data. The same criteria were applied, but instead using the ONS date of death that was provided rather than CPRD-provided date of death.

Once these inclusion and exclusion criteria were applied and participants were identified based on the start and end of follow up, there were 1,495,193 participants with linkage data included in the study population. A full flow-chart specifying the cleaning practices of the dataset is shown in Figure 1.

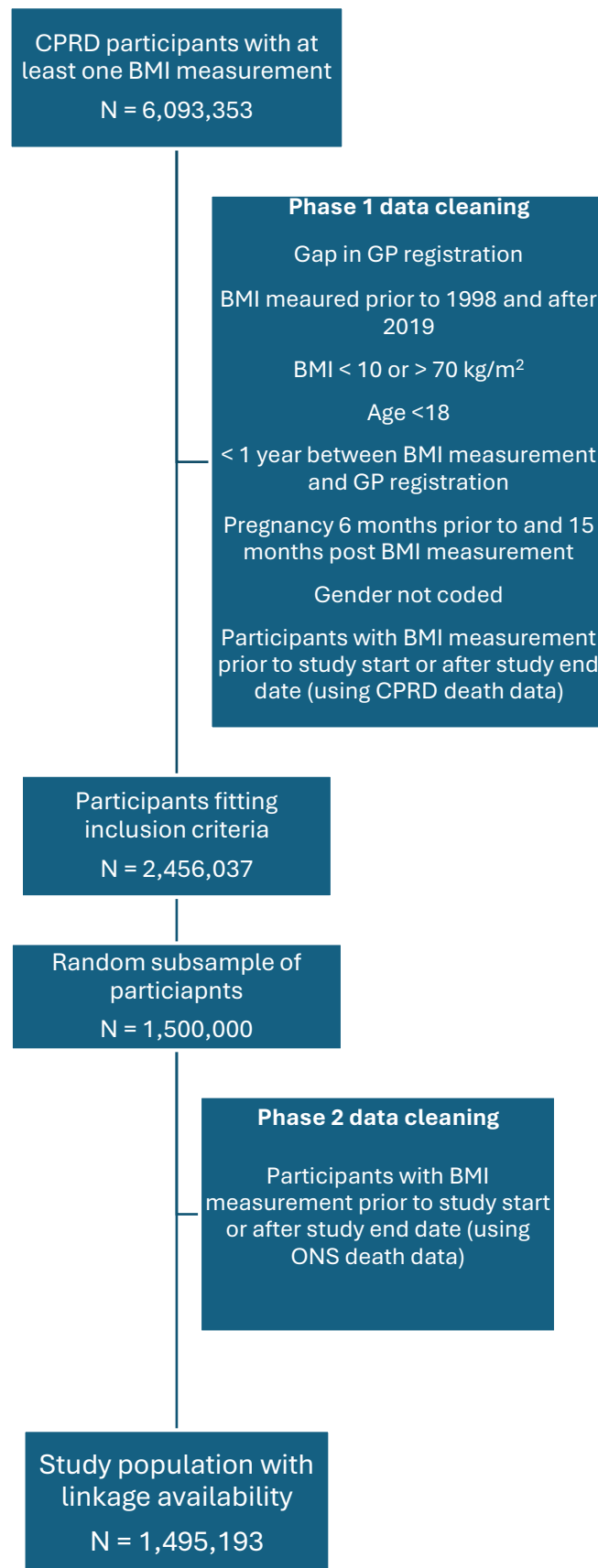


Figure 1. Exclusion Flowchart

The data cleaning process in this section created a multi-purpose dataset for each aim of this PhD, as these inclusion and exclusion criteria applied were comprehensive. Further data cleaning is conducted as there are different criteria applied for each analysis, including different definitions for BMI categories. These will be specified in subsequent chapters, but for each aim the primary exposure of interest is overweight and obese aim-specific outcomes, thus those in the underweight category were included in all models but are not shown in the results.

Finally, the aim of this PhD is to understand the overall trends in the spectrum of mortality and morbidity associated with obesity across the general population in England, not to determine the mechanisms which may affect these trends. For this reason, smoking status was not accounted for in the analyses. Future studies including the mechanisms which may impact mortality and morbidity trends such as smoking status, drinking status, hypertension or type 2 diabetes control, would be important analyses to understand these trends based on the population's lifestyle and morbidity management.

3.5 Study population characteristics

As this is a longitudinal cohort, participants will have multiple BMI measurements throughout the study period. Of the 1,495,193 participants, there are over 7.8 million BMI measurements. The largest proportion of participants (28%) had one BMI measurement, followed by two measurements (17%) and three measurements (11%). After 15 BMI measurements, there was less than 1% of participants for each number of measurements. The maximum number of measurements was 337 for one participant. I aggregated the proportion of individuals who had 27 or more BMI measurements taken, of which only accounted for 1.8% of the study population (Figure 2).

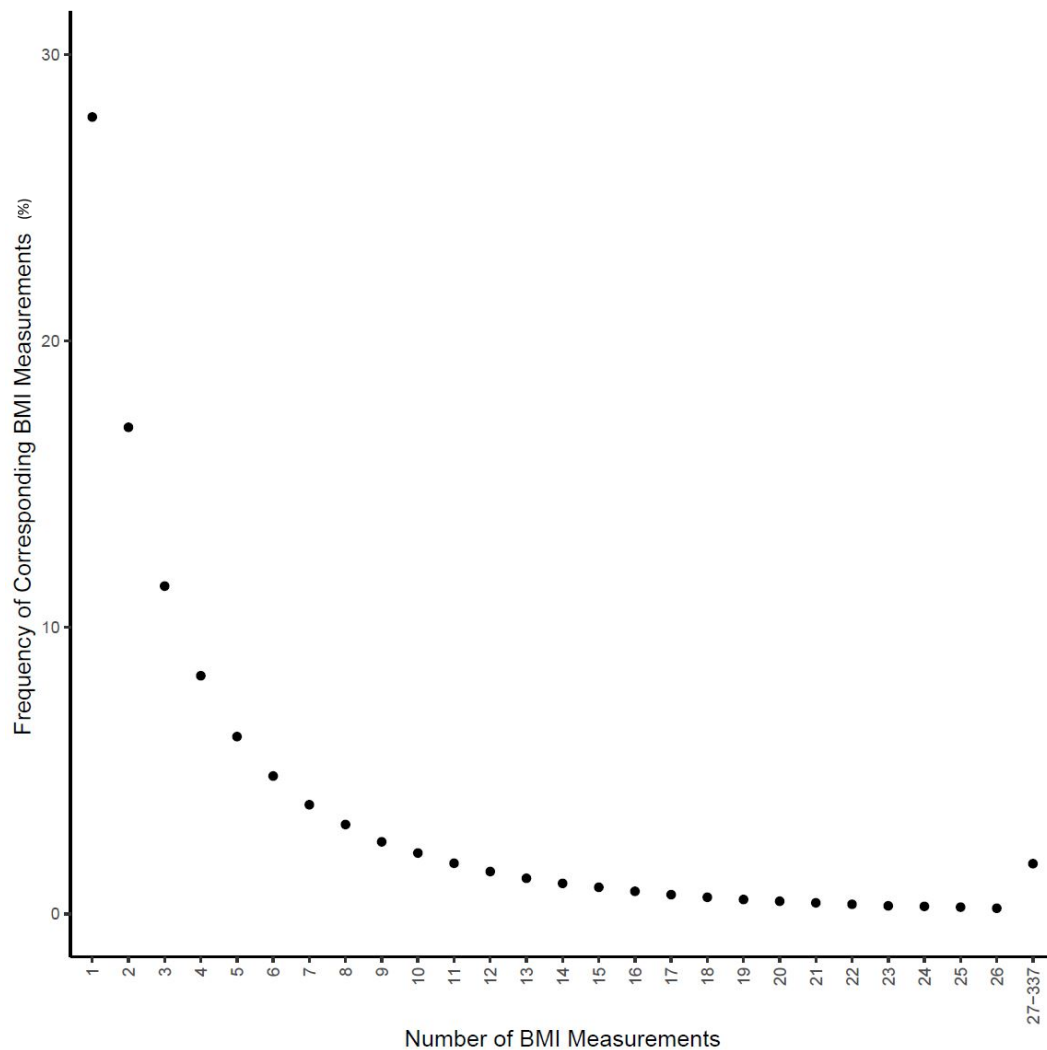


Figure 2. Scatter plot with the proportion of BMI measurements available per participant (measurements 27-337 was aggregated due to the small number of occurrences).

With the knowledge that 28% of participants had only one BMI measurement, I examined the proportion of individuals who did not have a BMI measurement for a given study year. Table 3 shows that there was a high proportion of individuals across all BMI categories that individuals either do not visit the GP every year, or do not get them measured when attending the GP.

The normal weight category generally had the highest proportion of individuals with a missing BMI measurements in a given year in this analysis, and the obese category had the lowest

proportion of individuals with a missing BMI measurement, indicating there are more measurements taken each year for this group. After analysing five million electronic health records 2000-2017, a UK primary care study found about one-third of patients had a BMI measurement each year, and on average patients have a BMI every two years (161). Further, having a low or high BMI increases the likelihood of having a BMI measurement taken, which is consistent to what I observed (Table 3).

Table 3. Proportion of individuals without a BMI measurement in a given year of the study period

Year	Underweight	Normal weight	Overweight	Obese
1998	0	0	0	0
1999	33.8	36.0	32.3	27.2
2000	40.5	43.7	40.2	34.2
2001	37.9	43.2	40.1	33.2
2002	44.5	49.3	45.8	38.4
2003	47.7	51.3	47.6	41.1
2004	49.2	53.0	49.1	41.3
2005	52.1	57.0	52.4	43.7
2006	49.2	53.2	48.8	39.9
2007	53.0	56.9	52.6	43.3
2008	54.0	59.0	54.5	44.7
2009	55.3	60.7	56.4	45.8
2010	57.9	62.8	58.3	47.3
2011	57.7	63.5	58.8	48.4
2012	56.4	61.9	57.4	48.1
2013	57.3	62.8	59.2	50.4
2014	60.4	66.3	63.4	54.5
2015	61.1	68.1	65.4	56.3
2016	62.8	70.7	68.3	60.0
2017	63.2	69.2	66.9	59.3
2018	59.5	67.3	64.6	57.1
2019	61.8	68.4	65.7	58.0

1998 is 0% as 1 January 1998 initial study start year and BMI measurements were not utilised prior to that date

To truly understand the study population and how variables may change throughout the study period (such as age and BMI), participants are accounted for each time they have a BMI measurement (Table 4). Throughout the study period, the median BMI remained fairly stable. Yet, the proportion of obese participants increased from 1998 and peaked in 2010, where 39%

of participants were obese, followed by a slight decrease. Further, deprivation was mostly consistent, with an increase in the proportion of least deprived participants in 2017. As median age increased, the proportion of females decreased and both the proportion of smoking and drinking declined in the study period.

Table 4. Descriptive statistics by year using each BMI measurement available in the dataset

	N	BMI (kg/m ²)	Obese (%)	Age (years)	Female (%)	Most Deprived (%)	Least Deprived (%)	Current Smoker (%)	Current Drinker (%)
1998	84,227	27 (24, 31)	28.1	55 (41, 67)	65.9	16.1	20.5	20.5	74.2
1999	109,061	27 (24, 31)	31.2	56 (42, 68)	64.3	15.9	21.0	20.5	74.2
2000	153,165	27 (24, 31)	32.5	56 (42, 68)	63.4	15.6	21.7	20.8	74.2
2001	232,698	27 (24, 32)	34.3	56 (41, 69)	62.6	15.2	21.9	21.1	75.1
2002	298,027	28 (24, 32)	35.5	57 (42, 69)	62.0	15.1	21.8	21.0	75.3
2003	358,055	28 (24, 32)	34.5	57 (42, 70)	60.8	15.6	21.1	20.0	74.3
2004	420,781	28 (24, 32)	34.7	58 (43, 70)	59.7	15.9	20.7	19.2	73.4
2005	452,294	28 (24, 32)	35.9	58 (43, 70)	59.6	16.9	19.9	19.0	72.1
2006	553,635	28 (24, 32)	36.1	58 (43, 70)	59.6	17.0	19.9	18.8	71.8
2007	569,221	28 (24, 32)	37.1	58 (43, 70)	59.5	17.2	19.6	18.2	71.5
2008	584,074	28 (24, 33)	38	58 (43, 70)	59.5	17.7	19.6	17.9	71.3
2009	586,728	28 (24, 33)	38.7	58 (43, 70)	59.6	17.5	20.0	17.8	71.2
2010	562,669	28 (24, 33)	38.7	58 (43, 71)	58.7	18.1	19.7	17.8	70.7
2011	547,397	28 (24, 33)	38.5	59 (44, 71)	58.6	17.8	19.8	17.5	70.3
2012	539,633	28 (24, 32)	37.2	59 (45, 71)	57.9	17.7	20.1	17.1	70.2
2013	504,226	28 (24, 32)	36.8	60 (45, 71)	57.9	17.3	20.0	16.5	70.0
2014	403,470	28 (24, 32)	36.7	59 (45, 71)	58.4	16.6	21.2	15.8	70.1
2015	308,969	28 (24, 32)	37.1	60 (45, 72)	58.6	17.2	21.6	15.5	70.1
2016	202,492	28 (24, 32)	37.2	59 (45, 71)	58.4	16.9	24	15.1	69.6
2017	152,784	28 (24, 32)	36.6	58 (45, 71)	58.4	16.9	26.6	14.8	69.8
2018	129,831	28 (24, 32)	35.8	59 (45, 71)	58.2	17.0	25.7	14.7	70.1
2019	106,471	28 (24, 32)	36.4	59 (46, 72)	57.8	18.0	23.4	14.7	70.2

N: number of participants included in each year of the study period. This includes participants as many times as they had a BMI measurement taken; BMI: Median BMI (IQR); % Obese: the proportion of participants who had an obese BMI measurement; Age: median age (IQR); % Female: the proportion of females in the study population; Most deprived: proportion of participants in quartile 5, the most deprived quartile; Least deprived: proportion of participants in quartile 1, the least deprived quartile; Current smoker: proportion of participants who are current smokers; Current drinker: proportion of participants who are current drinkers

When accounting for the whole population by BMI, the largest proportion of participants in the overweight (36%) and obese (44%) categories were in the middle-aged group (45-64 years), whereas the majority of underweight and normal weight participants were younger (Table 5).

The majority of the study population were women in all BMI categories, accounting for 77% of underweight participants. The gender gap closed slightly in the overweight category which was 48% men and 52% women. Participants across all BMI categories were majority of white ethnicity. The least deprived IMD quintile accounted for the smallest proportion of obese individuals (17%), with the greatest proportion in the fourth IMD quintile (22%).

Table 5. Descriptive statistics of participants at using each BMI measurement available in the dataset

	Underweight	Normal Weight	Overweight	Obese
	(<18.5 kg/m²)	(18.5-24.9 kg/m²)	(25-29.9 kg/m²)	(>30 kg/m²)
	N = 189,135	N = 2,227,689	N = 2,564,098	N = 2,878,986
Age (Years)				
<44	67,522 (36%)	762,973 (34%)	557,771 (22%)	695,880 (24%)
45-64	35,913 (19%)	603,547 (27%)	921,616 (36%)	1,276,309 (44%)
65-74	26,539 (14%)	365,949 (16%)	585,733 (23%)	595,143 (21%)
75+	59,161 (31%)	495,220 (22%)	498,978 (19%)	311,654 (11%)
Median (IQR)	60 (32, 78)	56 (38, 73)	61 (47, 72)	57 (45, 67)
Gender				
Male	42,772 (23%)	743,274 (33%)	1,232,242 (48%)	1,167,840 (41%)
Female	146,363 (77%)	1,484,415 (67%)	1,331,856 (52%)	1,711,146 (59%)
Ethnicity				
Asian	6,011 (3.2%)	72,065 (3.2%)	85,215 (3.3%)	70,092 (2.4%)
Black	1,828 (1.0%)	28,707 (1.3%)	43,691 (1.7%)	58,714 (2.0%)
Mixed	1,014 (0.5%)	12,105 (0.5%)	11,609 (0.5%)	12,833 (0.4%)
Other	2,625 (1.4%)	33,690 (1.5%)	31,861 (1.2%)	28,238 (1.0%)
White	165,030 (87%)	1,928,396 (87%)	2,236,817 (87%)	2,573,153 (89%)
Missing	12,627 (6.7%)	152,726 (6.9%)	154,905 (6.0%)	135,956 (4.7%)
Index of Multiple Deprivation				
Quintile 1 (Least deprived)	36,328 (19%)	523,771 (24%)	564,713 (22%)	498,722 (17%)
Quintile 2	37,955 (20%)	505,372 (23%)	591,745 (23%)	597,466 (21%)
Quintile 3	36,653 (19%)	437,877 (20%)	518,120 (20%)	584,836 (20%)
Quintile 4	39,471 (21%)	414,884 (19%)	491,002 (19%)	624,767 (22%)
Quintile 5 (Most Deprived)	38,182 (20%)	338,058 (15%)	391,821 (15%)	567,480 (20%)
Missing	546 (0.3%)	7,727 (0.3%)	6,697 (0.3%)	5,715 (0.2%)
Smoking Status				
Current	62,481 (33%)	488,512 (22%)	416,871 (16%)	441,397 (15%)
Never	87,937 (46%)	1,193,392 (54%)	1,315,823 (51%)	1,454,692 (51%)
Ex	34,817 (18%)	520,527 (23%)	804,484 (31%)	947,460 (33%)
Missing	3,900 (2.1%)	25,258 (1.1%)	26,920 (1.0%)	35,437 (1.2%)
Drinking Status				
Current	108,633 (57%)	1,590,333 (71%)	1,910,120 (74%)	2,013,642 (70%)
Never	46,494 (25%)	389,311 (17%)	426,946 (17%)	569,068 (20%)
Ex	7,752 (4.1%)	59,727 (2.7%)	70,393 (2.7%)	99,145 (3.4%)
Missing	26,256 (14%)	188,318 (8.5%)	156,639 (6.1%)	197,131 (6.8%)

Unless otherwise stated, estimates are reported as median (IQR) or number (%).

3.5.1 Follow-up of participants, causes of mortality and morbidity

Participants contributed over 10 million person years throughout this study period, with an individual contributing a median of six person years. The end of follow-up was defined as the date of death, the end of the study, the date of the last data collection from the GP, or a participant transferring out of CPRD. The primary reason for end of follow-up was due to the last collection date of the GP, accounting for 56% of reasons for leaving the dataset (Table 6). The median age at death was 80 years and 82 years old for males and females, respectively. Approximately 7% of participants died in the study period (Table 6). I assessed the top 10 causes of death and diagnosis at hospitalisation in males and females (Table 7). The largest proportion of deaths occurred from ischemic heart disease (IHD), accounting for 11% and 7% of all deaths in males and females, respectively. Lung cancer was the second greatest cause of death accounting for 7% of deaths in males and 6% of deaths in females. Similar causes of death were observed for both males and females at different proportions, such as chronic obstructive pulmonary disease (COPD), pneumonia, acute myocardial infarction, stroke, and unspecified cancer. About 4% of males died from prostate cancer and about 5% of females died from breast cancer. Oesophageal cancer and colon cancer were in the top 10 causes of death for males, but not females, whereas unspecified dementia and pancreatic cancers were for females but not males.

Table 6. Follow-up summary statistics

Person years	
Total	10,603,055
Median (IQR)	6.4 (2.8, 10.7)
Age at death	
Median (IQR)	81 (73, 87)
Reason for end of follow-up (%)	
Death	7.5%
End of study period	10.4%
Transfer out of CPRD	26.2%
Last collection date of GP	55.9%

Unless otherwise stated, estimates are reported as median (IQR) or number (%).

Table 7. Top 10 causes of death across males and females

Males		Females	
Cause of death	Percent (%)	Cause of death	Percent (%)
Ischemic heart disease	11.0	Ischemic heart disease	7.2
Lung cancer	7.4	Lung cancer	6.4
Acute myocardial infarction	7.4	Pneumonia	5.8
Other COPD	5.8	Other COPD	5.4
Pneumonia	4.9	Acute myocardial infarction	4.9
Prostate cancer	4.4	Breast cancer	4.5
Stroke	3.0	Stroke	4.3
Oesophageal cancer	2.3	Unspecified dementia	3.7
Unspecified cancer	2.2	Unspecified cancer	2.3
Colon cancer	2.2	Pancreatic cancer	2.0

The majority of hospitalisations (nearly 80%) were due to unknown causes in both males and females (Table 8). Other diagnoses occurred at much smaller scales, with chronic kidney disease accounting for about 2% of diagnoses in males, and breast cancer diagnoses occurring for 0.70% in females.

Table 8. Top 10 primary diagnosis from hospitalisation across males and females

Males		Females	
Diagnosis	Percent (%)	Diagnosis	Percent (%)
Unknown and unspecified causes of morbidity	79.0	Unknown and unspecified causes of morbidity	80.0
Chronic kidney disease	1.5	Breast cancer	0.70
Prostate cancer	0.50	Chronic kidney disease	0.60
Ischemic heart disease	0.40	Abdominal and pelvic pain	0.40
Pain in throat and chest	0.40	Pain in throat and chest	0.30
Schizophrenia	0.30	Other cataract	0.30
Other cataract	0.30	Back pain (dorsalgia)	0.30
Pneumonia	0.30	Perineal laceration during delivery	0.30
Colon cancer	0.20	Pneumonia	0.20
Lung cancer	0.20	Senile cataract	0.20

3.5.2 HSE comparisons

CPRD has been compared to HSE to ensure it is representative of the English population in prior studies (94, 148, 149). To ensure my cleaned dataset is representative, I conducted simple comparisons of crude prevalence data to HSE data on the proportion of overweight and obesity by sex and by IMD (Figure 3). When comparing the two datasets, the prevalence of overweight and obesity were only one percentage point different for both males and females. When stratifying by IMD, there is a slight under-representation of males in the overweight category in the more deprived IMD quintiles and an over-representation of overweight and obese males in the least deprived IMD quintiles. Further, these differences were not observed in females, which is consistent with literature which states that females and individuals in more deprived IMD quintiles are more likely to visit the GP, with more deprived individuals having anthropometric measurements more often (161, 162).

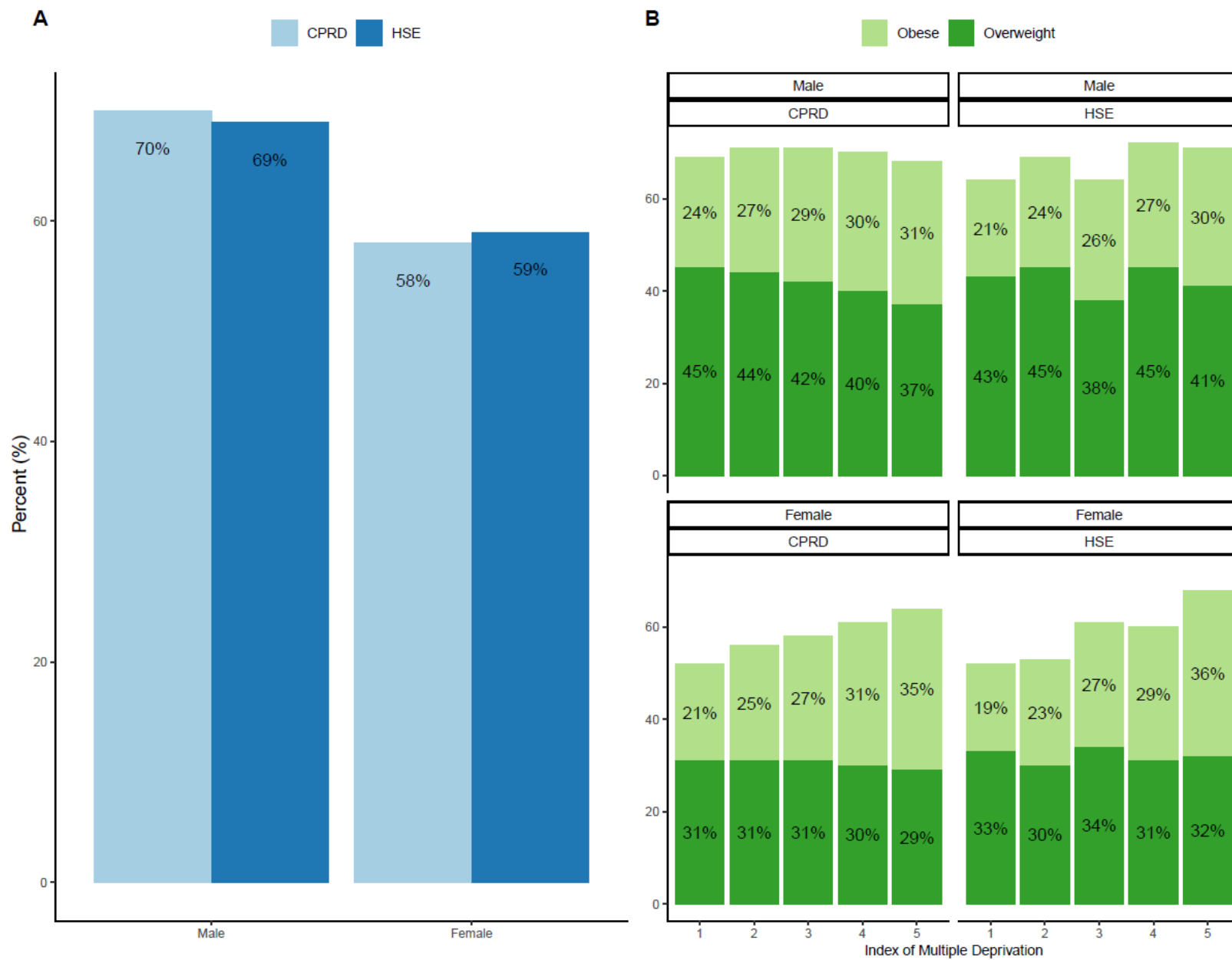


Figure 3. Comparing the cleaned CPRD dataset to HSE: A) The crude prevalence of overweight or B) The crude prevalence of overweight and obesity by IMD

4. Mortality trends

4.1 Background

It is widely understood that mortality rates have declined greatly due to improvements in CVD mortality rates. However, recent years indicate that these reductions are not going to continue and are either going to plateau or increase. These shifts in mortality rates have the potential to interact with the obesity epidemic, considering obesity is a large contributor to the stagnation in mortality rate improvements, yet few studies have investigated these mortality changes by BMI, by obesity-related causes of death, and by the total burden of mortality impacted by obesity. This chapter aims to examine the changes in mortality rates and how the proportional composition of deaths by cause has changed in overweight and obese adults from 2004 to 2019 in England.

4.2 Methods

4.2.1 Sample selection and analytic dataset

This research aim used the CPRD dataset linked with ONS to analyse trends in mortality rates and the proportional contributions of the mortality burden by BMI. The initially cleaned dataset described in Chapter 3 was cleaned further for this aim. First, due to the low numbers of deaths in the first year of the study, resulting in unrealistically low mortality rates, the study began in 1999 rather than 1998. Second, to limit reverse causality—where weight loss can be caused by severe illness—we excluded BMI measurements from participants who had less than a five year follow up period in the study. Meaning the final analytic sample only included participants who were still being followed up five years after their BMI measurement. Considering it was likely participants had more than one BMI measurement throughout the study period, only the BMI measurement that did not have five years follow up was excluded, not necessarily the participant. To account for this survival period, BMIs between 1999 and 2014 were utilised,

thus, the beginning of the analysis to assess mortality rates is from 1 January 2004 through 31 December 2019. After applying these criteria, the final study cohort consisted of 880,683 participants.

4.2.2 Predictors and mortality

BMI was categorised based on WHO classifications as follows: underweight: BMI < 18.5 kg/m²; normal weight: BMI ≥ 18.5 and < 24.9 kg/m²; overweight: BMI ≥ 25 and < 29.9 kg/m²; and obese: ≥ 30 kg/m² (163).

Mortality records for participants were extracted from ONS death registration data. Mortality outcomes were separated into three tiers to ensure obesity-associated causes of death were accounted for in broad and granular categories: all-cause mortality (Tier 1); broad categories of mortality (Tier 2); specific causes of mortality (Tier 3). Tier 2 outcomes were separated into CVDs, cancers, other NCDs (referred to as non-cancer, non-CVD NCDs) and other causes of death. Tier 3 outcomes include more specific NCDs consisting of CVD and cancers, but also digestive diseases excluding liver, endocrine, liver, neurological, renal, respiratory, infections, and other causes of death. These outcomes were identified by the ICD-10 code for the primary cause of death listed in the death registration data (Table 9).

Table 9. Mortality outcomes of interest by tier and corresponding ICD-10 codes

Mortality	ICD chapters/codes
Tier 1 outcomes	
All-causes	
Tier 2 outcomes	
Non-cancer, non-CVD NCDs	D-H, J-R
CVD	I
Cancer	C
Other	
Tier 3 outcomes	
Respiratory	J, G47.3
Endocrine	E
Neurological	G, F01-03
Liver	K70-77
Renal	N
Digestive excluding liver	K
Infections	A, B, J00-22
Other	

Other variables accounted for in the dataset include IMD for patient postcode linked deprivation measures from 2010, ethnicity extracted from HES—both of which were explained in detail in Chapter 3—and alcohol consumption and smoking status (current, never, ex, missing).

4.2.3 Statistical analysis

A discrete Poisson regression model was used to estimate tier specific mortality rates by BMI. Prior to running all models, I checked each model for over-dispersion, which was not present, thus confirming Poisson regression was the appropriate methodology for this research objective. A participant was included in the analysis each calendar year from the time of their first BMI measurement to the end of their follow up. As BMI is a time-dependent variable, the BMI was updated for each year of follow up. The first BMI measurement available was used for the first year of study inclusion, and if a BMI was available for each subsequent year, the

first BMI measurement of that year was used. If a BMI measurement was not taken in a subsequent year, the last BMI measurement available from a prior year was used instead. Age, death status, and exposure length of each participant was updated each year as well.

A participant's exposure length ranged from 0 to 1 and was the number of days the participant was in each calendar year divided by the total number of days in the same year. If a participant died on 14 July 2013, for example, their exposure length would be 195/365. This exposure length for each year a participant is being followed up in the study is then input as the offset in the Poisson regression model to account for the different follow up time of each individual participant.

To account for death being a mutually exclusive event and to ensure risks were not influencing the Poisson regression results, I utilised competing risk analyses wherein separate models for each cause of death were run. Further, separate models were run for males and females and each model was fitted for interaction terms between BMI, age, and calendar year. Mortality rates were age-standardised using male/female-combined ONS mid-year population estimates in 2011 (chosen as it is the median of the study period), to ensure the mortality rates were comparable between years and gender (164). These mortality rates were then used to calculate the proportional contribution of Tier 2 and Tier 3 outcomes to the total mortality burden by BMI.

After running the Poisson regression model, and predicting the mortality rates for each year, a joinpoint model was used to identify change in mortality rates trends. Joinpoint is a statistical software through the National Cancer Institute in the US which takes trend data—i.e., mortality rate by year— and standard errors, fits these variables a model and determines if any change is

statistically significant (165). The output is the annual average percent change, which is the annual change in mortality rates per year by BMI category and outcomes (Tiers 2 and 3 only).

4.2.4 Stratified and sensitivity analyses

Stratified Poisson models were run for age, ethnicity, and deprivation levels. Age was assessed for pre-mature mortality only, thus those 35-74 years of age were of interest (very few deaths occurred for those <35); ethnicity was classified as Asian, Black, Mixed, Other, and White. Deprivation was separated into quintiles with 1 indicating the least deprived and 5 the most deprived. Whilst stratifying for these variables, those who had missing IMD or ethnicity information were excluded from the analysis. Thus, there was not enough power for the statistical analysis—due to the number of deaths and exposure length per category—and once accounting for Tier 2 and Tier 3 outcomes, the models could not converge. This was not a problem for the age-stratified model, however, the stratified analyses for ethnicity and IMD were only conducted for Tier 1 outcomes.

A sensitivity analysis was run using the ethnicity-specific BMI thresholds, as specified by NICE recommendations. Across Asian and Black ethnicities, BMI categories are as follows: underweight: BMI <18.4 kg/m²; normal weight: BMI ≥ 18.5 kg/m² and < 22.9 kg/m²; overweight: BMI ≥ 23 kg/m² and < 27.4 kg/m²; obese: BMI ≥ 27.5 kg/m² (72).

A sensitivity analysis using a two-year exclusion period, rather than the five-year that was ultimately selected for the main analysis, was also conducted. Finally, the observations from this CPRD dataset was compared to Health Survey for England to assess representativeness.

4.3 Results

4.3.1 Primary analyses

4.3.1.1 All-cause mortality

Between 2004 and 2019, all-cause mortality rates per 1000 person years declined across all BMI categories for males (Table 10, Figure 3A). The largest magnitude of decline occurred in obese individuals by 3.2% (95% CI: -4.2%, -2.2%) on average per year (23.3 to 14.6 deaths per 1000 person years). Mortality rates declined by 2% on average per year in the normal weight category (95% CI: -4.2%, -0.2%) from 17.4 to 12.4 deaths per 1000 person years and overweight category (95% CI: -2.8%, -1.3%) from 16.3 to 12.9 per 1000 person years.

In contrast, in females the only significant change in mortality rates occurred in the obese category (Table 10, Figure 3B). All-cause mortality rates declined from 12.5 to 9.4 deaths per 1000 person years accounting for a 2% (95% CI: -3.0%, -1.2%) decline per year.

4.3.1.2 Tier 2 mortality outcomes

Across Tier 2 outcomes in males, CVD had the largest declines in the obese category 7% (95% CI: -8.2%, -5.2%) by on average per year (Table 10, Figure 4A). Average declines of 5% per year also occurred for overweight (95% CI: -6.1%, -4.1%) and normal weight (95% CI: -5.4%, -3.8%) categories. No significant changes occurred for cancer mortality in any BMI category. Finally, for non-cancer, non CVD NCDs, overweight males had significant changes in mortality rates, increasing by about 2% (95% CI: 0.2%, 3.5%) on average per year, but no changes occurred in the normal weight or obese categories.

Declines were observed in females for CVD by about 4% per year in the obese (95% CI: -6.2%, -2.7%) and overweight (95% CI: -4.9%, -2.5%) and by 2% (95% CI: -4.3%, -0.6%) per year in the normal weight category (Figure 4B). Conversely, mortality rates increased on

average per year in non-cancer, non-CVD NCDs by 7% (95% CI: 4.3%, 8.2%) in the overweight category and by 4% (95% CI: 1.6%, 5.9%) in the normal weight category, with no changes in the obese category. No changes were observed for cancers in females in any of the BMI categories.

4.3.1.3 Tier 3 mortality outcomes

In males, mortality rates declined in normal weight individuals for liver and endocrine conditions (Figure 5A). Liver disease mortality rates declined by 90% (95% CI: -95.7%, -83.5%) on average per year from 0.28 to <0.0001 deaths per 1000 years. For endocrine conditions, mortality rates declined by 12% (95% CI: -18.1%, -5.2%) per year from 0.48 to 0.17 deaths per 1000 person years. There were no changes in mortality rates observed for liver or endocrine conditions in either the overweight or obese categories. There were no other declines in other Tier 3 outcomes, however, mortality rates increased in all BMI categories for neurological mortality. The largest increase was in the obese category, increasing 305% (95% CI: 122.7%, 550.2%) on average per year from <0.0001 to 0.88 deaths per 1000 person years; in normal weight, mortality rates increased by 9% (95% CI: 3.4%, 13.7%) from 0.38 to 1.1 deaths per 1000 person years on average per year in normal weight and by 7% (95% CI: 3.0%, 11.8%) per year from 0.58 to 1.3 deaths per 1000 person years in the overweight category. No other increases were observed in males for non-cancer, non-CVD NCDs.

In females, the only declines in mortality rates occurred for endocrine mortality in the obese category which decreased 11% (95% CI: -15.7%, -6.3%) on average per year from 0.95 to 0.47 deaths per 1000 person years (Figure 5B). Liver disease mortality rates increased by 976% (95% IC: 509.3%, 2408.4%) in the obese category only from <0.0001 to 0.04 deaths per 1000 person years. Neurological conditions had increases in all BMI categories, with the largest

change in the normal weight category with an increase of 17% (95% CI: 14.9%, 19.9%) on average per year from 0.11 to 1.3 deaths per 1000 person years. The overweight category increased by 15% (95% CI: 10.4%, 20.5%) on average per year from 0.13 to 1.2 deaths per 1000 person years.

Table 10. Age-adjusted all-cause mortality (tier 1), tier 2, and tier 3 mortality rates in 2004 and 2019 per 1000 person years and average percent change in death rate across BMIs, by sex

	Normal Weight			Overweight			Obese		
	2004 rate	2019 rate	Average change per year (%)	2004 rate	2019 rate	Average change per year (%)	2004 rate	2019 rate	Average change per year (%)
MALES									
Tier 1									
All-cause	17.4 (15.0, 19.9)	12.4 (10.6, 14.3)	-2.5 (-4.4, -0.1)	16.3 (14.3, 18.4)	12.9 (11.3, 14.4)	-2.0 (-2.8, -1.3)	23.3 (19.4, 27.2)	14.6 (12.4, 16.8)	-3.2 (-4.2, -2.2)
Tier 2									
Non-cancer, non-CVD NCD	3.6 (2.5, 4.7)	4.6 (3.4, 5.7)	0.5 (-1.5, 2.6)	3.3 (2.27, 4.3)	4.4 (3.5, 5.4)	1.8 (0.2, 3.5)	4.2 (2.4, 5.9)	4.2 (2.9, 5.5)	0.5 (-1.2, 2.3)
Cardiovascular Disease	7.9 (6.2, 9.5)	3.3 (2.3, 4.2)	-4.6 (-5.4, -3.8)	7.4 (5.9, 8.8)	3.2 (2.4, 3.9)	-5.1 (-6.1, -4.1)	12.4 (9.5, 15.4)	4.4 (3.1, 5.7)	-6.8 (-8.4, -5.4)
Cancer	5.1 (3.9, 6.4)	3.3 (2.4, 4.3)	-1.2 (-3.2, 0.7)	4.6 (3.6, 5.7)	4.4 (3.6, 5.3)	-1 (-4.5, 1.8)	4.8 (3.2, 6.4)	4.6 (3.5, 5.7)	-1.8 (-3.6, 0.1)
Other	0.86 (0.33, 1.4)	1.3 (0.66, 1.9)	-0.3 (-5.1, 4.5)	1.1 (0.58, 1.62)	0.87 (0.44, 1.3)	-1.3 (-3.4, 0.9)	1.87 (0.65, 3.1)	1.5 (0.76, 2.1)	-1.7 (-4.6, 1.3)
Tier 3									
Cancers	5.1 (4.4, 5.8)	3.3 (2.8, 3.8)	-1.1 (-3.2, 0.8)	4.6 (4.0, 5.2)	4.4 (3.9, 5.0)	-1 (-4.4, 1.5)	4.8 (4.0, 5.6)	4.6 (3.9, 5.3)	-1.7 (-3.5, 0.1)
Cardiovascular Disease	7.9 (6.8, 9)	3.3 (2.8, 3.8)	-4.6 (-5.4, -3.8)	7.4 (6.4, 8.3)	3.2 (2.8, 3.5)	-5.1 (-6.1, -4.1)	12.4 (10.3, 14.5)	4.4 (3.8, 5.1)	-6.7 (-8.2, -5.2)
Digestive Excluding Liver	0.44 (0.38, 0.5)	0.68 (0.58, 0.78)	-1 (-5.3, 3.3)	0.8 (0.7, 0.9)	0.5 (0.44, 0.56)	-2.4 (-6.3, 1.7)	0.78 (0.65, 0.91)	0.92 (0.78, 1.06)	-0.9 (-8.1, 7.1)
Endocrine	0.49 (0.42, 0.56)	0.18 (0.15, 0.2)	-11.8 (-18.1, -5.2)	0.43 (0.38, 0.49)	0.13 (0.11, 0.14)	-7.7 (-17.2, 2.7)	0.67 (0.56, 0.79)	0.38 (0.32, 0.44)	-4.4 (-10, 1.5)
Infections	1.2 (1, 1.4)	1 (0.9, 1.2)	-1.7 (-4.8, 1.3)	0.77 (0.68, 0.87)	0.93 (0.82, 1.05)	0.4 (-1.9, 2.8)	2.1 (1.7, 2.4)	1.2 (1, 1.4)	1.4 (-2.7, 5.7)
Liver	0.28 (0.24, 0.32)	<0.0001	-89.6 (-95.7, -83.5)	0.13 (0.12, 0.15)	0.089 (0.079, 0.089)	-4 (-9.4, 1.5)	0.064 (0.053, 0.074)	0.25 (0.22, 0.29)	8.1 (-13.1, 25.2)
Neurological	0.38 (0.33, 0.43)	1.1 (0.94, 1.3)	9.1 (3.4, 13.7)	0.58 (0.51, 0.66)	1.4 (1.2, 1.5)	7.2 (3.0, 11.8)	<0.0001	0.88 (0.75, 1)	304.7 (122.7, 550.2)
Other	0.29 (0.25, 0.34)	0.88 (0.75, 1)	5.6 (-2, 11.3)	0.32 (0.28, 0.37)	0.37 (0.33, 0.42)	2.2 (-1.9, 6.3)	1.1 (0.91, 1.3)	0.46 (0.39, 0.5)	-3.8 (-11.8, 5.4)
Renal	0.11 (0.1, 0.13)	0.26 (0.22, 0.3)	0.6 (-13.9, 11.5)	0.22 (0.19, 0.24)	0.51 (0.45, 0.57)	-3.3 (-10.4, 4.2)	0.53 (0.44, 0.61)	0.49 (0.41, 0.56)	-1.3 (-8.6, 6.9)
Respiratory	1.2 (1.1, 1.4)	1.7 (1.4, 2)	-0.3 (-2.6, 1.9)	1.1 (0.97, 1.3)	1.4 (1.2, 1.6)	1.2 (-1.2, 3.6)	0.84 (0.7, 0.84)	1 (0.86, 1.2)	-0.5 (-3.3, 2.5)
FEMALES									
Tier 1									
All-cause	8.5 (7.3, 9.7)	10 (8.7, 11.3)	-0.2 (-2.9, 3.1)	7.8 (6.6, 9.0)	7.8 (6.6, 8.9)	0 (-1.3, 1.2)	12.5 (10.3, 14.7)	9.4 (8.0, 10.8)	-2.1 (-3.0, -1.2)
Tier 2									
Non-cancer, non-CVD NCD	1.9 (1.3, 2.5)	3.7 (2.9, 4.5)	3.6 (1.6, 5.9)	1.4 (0.91, 2)	3.0 (2.2, 3.7)	6.2 (4.3, 8.2)	3.5 (2.4, 4.7)	3 (2.2, 3.7)	0.1 (-1.7, 1.9)
Cardiovascular Disease	3.6 (2.8, 4.4)	2.9 (2.2, 3.7)	-2.4 (-4.3, -0.6)	3 (2.2, 3.8)	2.0 (1.4, 2.6)	-3.6 (-4.9, -2.5)	5.5 (4, 7)	3 (2.2, 3.8)	-4.4 (-6.2, -2.7)
Cancers	2.5 (1.8, 3.1)	2.6 (2, 3.3)	0 (-1.6, 1.2)	2.9 (2.2, 3.6)	2.1 (1.5, 2.7)	0.1 (-3, 2.9)	2.7 (1.7, 3.7)	2.6 (1.9, 3.3)	-1.1 (-4.7, 2.7)
Other	0.45 (0.17, 0.73)	0.67 (0.33, 1.01)	-0.8 (-3.4, 1.9)	0.46 (0.16, 0.75)	0.69 (0.35, 1.03)	-2.1 (-5.6, 1.2)	0.73 (0.19, 1.3)	0.81 (0.38, 1.2)	-1.6 (-5.9, 2.7)
Tier 3									
Cancers	2.5 (2.1, 2.9)	2.6 (2.3, 3)	-0.9 (-2.1, 0.3)	2.9 (2.4, 3.3)	2.1 (1.8, 2.4)	0.1 (-3, 3.1)	2.7 (2.2, 3.2)	2.6 (2.2, 3)	-1.1 (-4.6, 2.5)
CVD	3.6 (3.1, 4.2)	2.9 (2.6, 3.3)	-2.6 (-4.5, -0.6)	3 (2.5, 3.5)	2 (1.7, 2.3)	-3.7 (-5, -2.5)	5.5 (4.6, 6.5)	3 (2.5, 3.4)	-4.4 (-6.2, -2.6)
Digestive Excluding Liver	0.28 (0.24, 0.32)	0.27 (0.23, 0.3)	-1.6 (-4.5, 1.5)	0.2 (0.17, 0.23)	0.47 (0.4, 0.54)	-1.6 (-6.9, 4.1)	0.5 (0.41, 0.59)	0.55 (0.47, 0.64)	-1 (-4.3, 2.5)
Endocrine	0.31 (0.27, 0.36)	0.12 (0.089, 0.12)	-33.4 (-73.2, 63.4)	0.2 (0.17, 0.23)	0.15 (0.13, 0.18)	-2.5 (-7.8, 3.1)	0.95 (0.78, 1.11)	0.47 (0.4, 0.54)	-11.1 (-15.7, -6.3)
Infections	0.56 (0.48, 0.64)	0.85 (0.74, 0.96)	0.8 (-1.9, 3.5)	0.14 (0.12, 0.16)	0.44 (0.38, 0.51)	9.5 (3.0, 16.6)	0.76 (0.63, 0.9)	0.67 (0.57, 0.77)	-0.2 (-3.2, 2.9)
Liver	0.09 (0.079, 0.11)	0.037 (0.028, 0.037)	-30.5 (-71.9, 68.7)	0.16 (0.13, 0.18)	0.067 (0.049, 0.067)	-3.1 (-10.7, 5.3)	<0.0001	0.042 (0.031, 0.042)	976 (509.3, 2408.4)
Neurological	0.11 (0.097, 0.13)	1.3 (1.2, 1.51)	17.4 (14.9, 19.9)	0.13 (0.11, 0.15)	1.2 (1.1, 1.4)	15.4 (10.4, 20.5)	0.49 (0.4, 0.57)	0.82 (0.7, 0.95)	5 (-0.5, 12.9)
Other	0.31 (0.26, 0.35)	0.96 (0.84, 1.09)	3.8 (0.8, 7)	0.37 (0.31, 0.43)	0.48 (0.41, 0.55)	-0.4 (-5, 4.4)	0.87 (0.72, 1)	0.36 (0.31, 0.41)	-0.5 (-5.4, 4.6)
Renal	0.17 (0.15, 0.2)	0.15 (0.13, 0.17)	-0.2 (-7, 6.9)	0.14 (0.12, 0.16)	0.13 (0.11, 0.15)	0.4 (-14.2, 16.3)	0.27 (0.22, 0.32)	0.18 (0.16, 0.21)	-3.2 (-13.5, 8.3)
Respiratory	0.53 (0.45, 0.6)	0.70 (0.61, 0.79)	-0.4 (-6, 5.3)	0.56 (0.47, 0.64)	0.67 (0.57, 0.76)	1.2 (-2.1, 4.6)	0.42 (0.35, 0.49)	0.66 (0.56, 0.76)	5.3 (-1.1, 9.6)

CVD: cardiovascular disease; NCD: Non-communicable disease

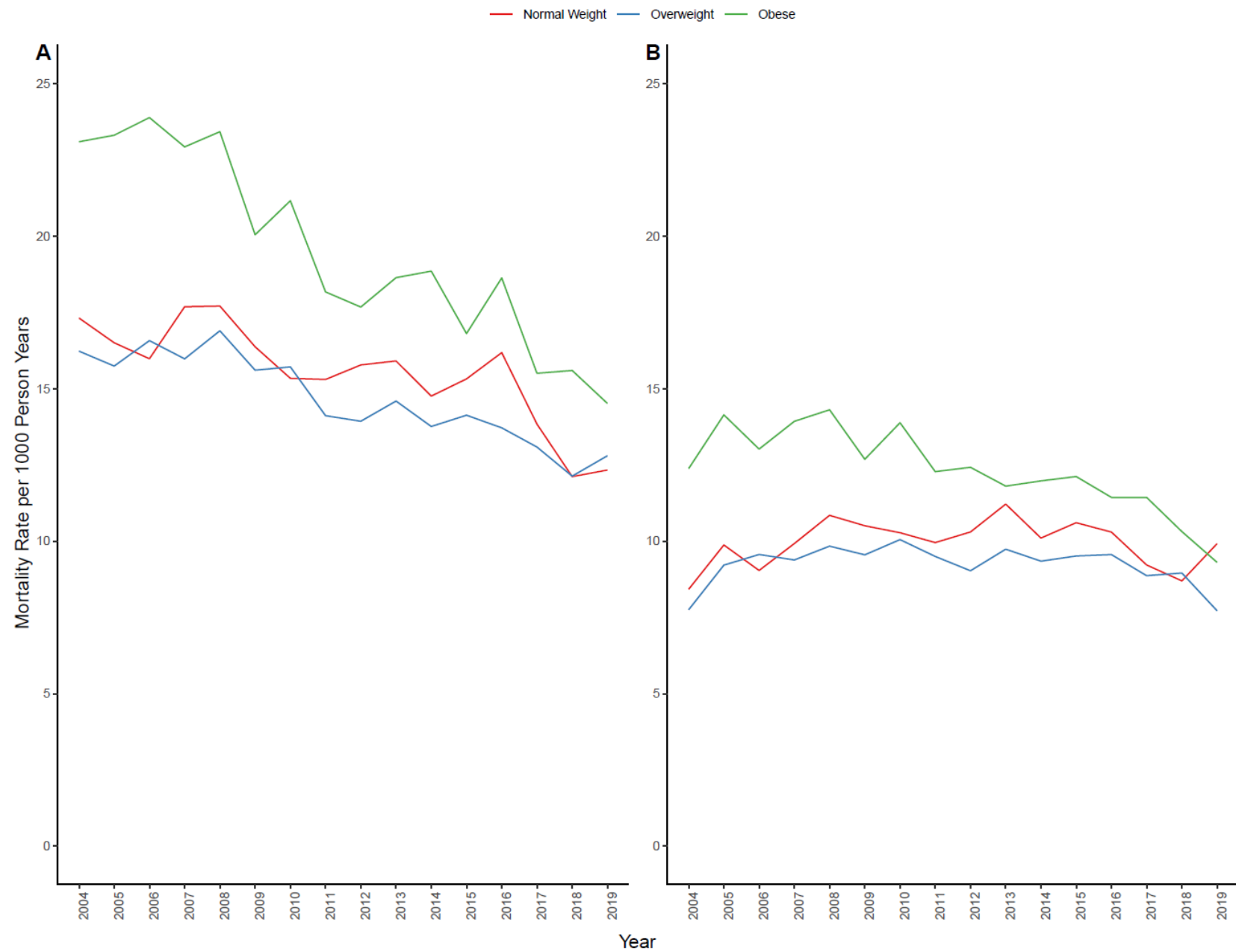


Figure 4. Age-adjusted all-cause mortality rates in (A) males and (B) females



Figure 5. Age-adjusted mortality rates in Tier 2 outcomes in (A) males and (B) females

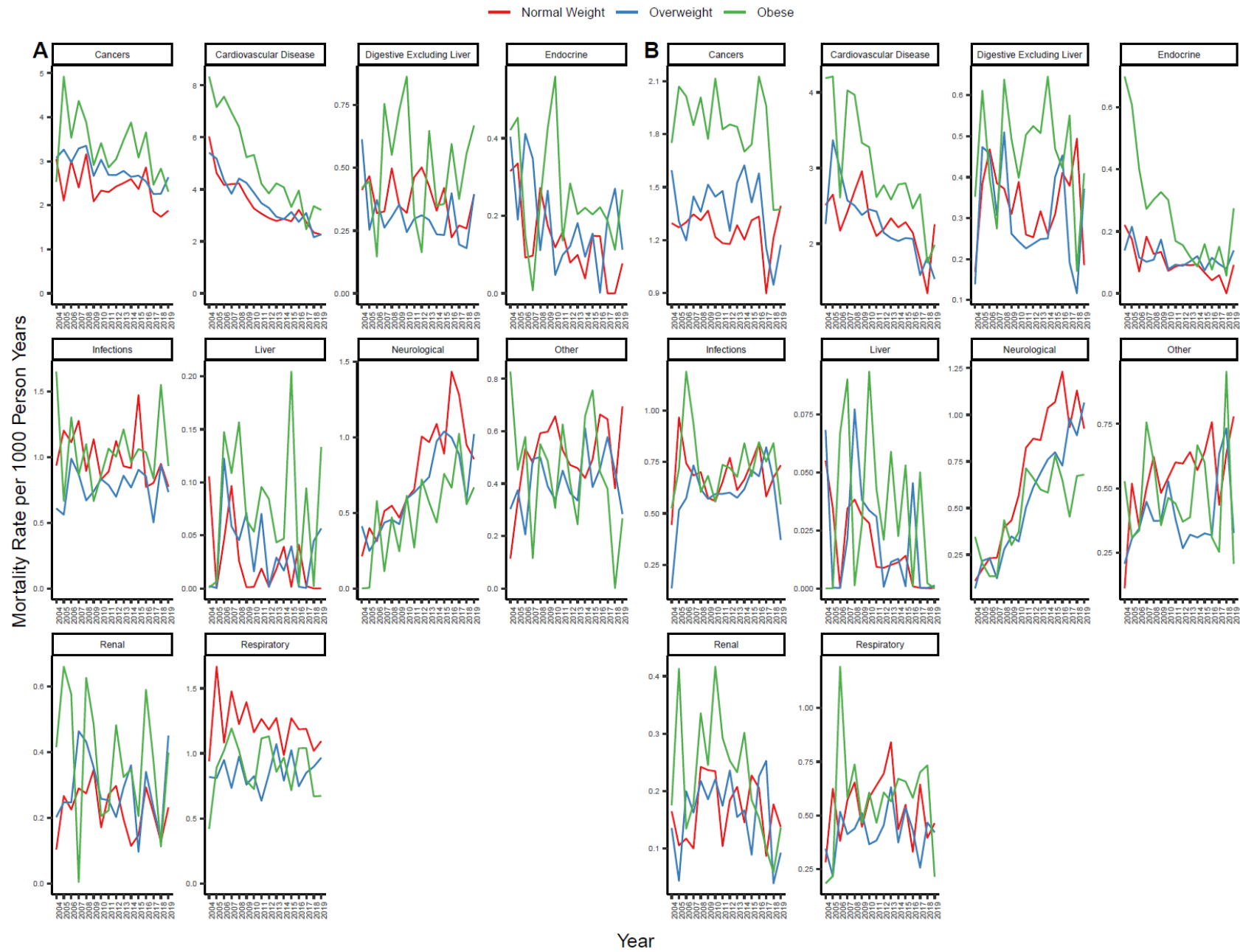


Figure 6. Age-adjusted mortality rates in Tier 3 outcomes in (A) males and (B) females

4.3.1.4 Proportional mortality

In males, between 2004 and 2019 the proportion of deaths from CVD declined by a similar magnitude from 45% to about 25% in both normal weight and overweight categories and from 54% to 30% in the obese category. Across cancers, the proportion of deaths declined from 29% to 27% in the normal weight category whilst increases occurred from 28% to 35% in the overweight category and from 21% to 31% in the obese category (Figure 6A). The proportion of deaths in males from non-cancer, non-CVD NCDs increased in all BMI categories, from 21% to 37% in normal weight; from 20% to 34% in overweight, and from 18% to 29% in obese.

Once breaking down these non-cancer, non-CVD NCD outcomes further, the proportion of deaths from neurological, renal, and respiratory conditions increased in all BMI categories in males (Figure 7). Proportionally, neurological conditions increased from about 0% to 6% in the obese category, from 2% to 9% in the normal weight category, and from 4% to 11% in the overweight category. The proportion of deaths from respiratory diseases increased from 7% to 14% in the normal weight category, 4% to 6% in obese category, and 7% to 11% in the overweight category. Renal diseases had the greatest increases in mortality contribution in the normal weight category from 0.6% to 2%, and in the overweight category from 1% to 4%, and a smaller increase in the obese category from 2% to 3%. Another increase in the proportion of deaths occurred in digestive diseases excluding liver disease which increased from 3% to 6% in both normal weight and obese categories. Liver disease proportional mortality only increased in the obese category from 0.30% to 2%. The proportion of deaths from cancer is now higher than that of CVD in males across all BMI categories (Table 11; Figure 7A).

In females, the CVD mortality burden declined from 39% to 26% in the overweight category, 43% to 30% in the normal weight category, and 44% to 32% in the obese category. The

proportion of deaths from cancers declined from 37% to 27% in overweight and a small decline occurred in normal weight from 29% to 27%. Conversely, the proportion of deaths from cancers in the obese category increased from 22% to 28% (Figure 6B).

In females, the proportion of deaths from non-cancer, non-CVD NCDs increased in all BMI categories, from 19% to 38% in overweight, 23% to 37% in normal weight, and 28% to 32% in the obese category (Table 12). The proportion of deaths from neurological conditions and respiratory conditions increased in all BMI categories. For neurological mortality contribution, increases occurred from 1% to 13% in normal weight, 2% to 16% in overweight, and 4% to 9% in obese categories. Respiratory disease mortality increased the most proportionally in the obese category from 3% to 7% with smaller increases in the overweight category from 7% to 9% and in the normal weight category from 6% to 7%. Digestive diseases excluding liver disease increased in the overweight category from 3% to 6% and obese category from 4% to 6%. Finally, liver disease only increased in the obese category from 0% to 0.4%. In females, the proportion of deaths from cancers is higher than CVD in the overweight category (Figure 7B).

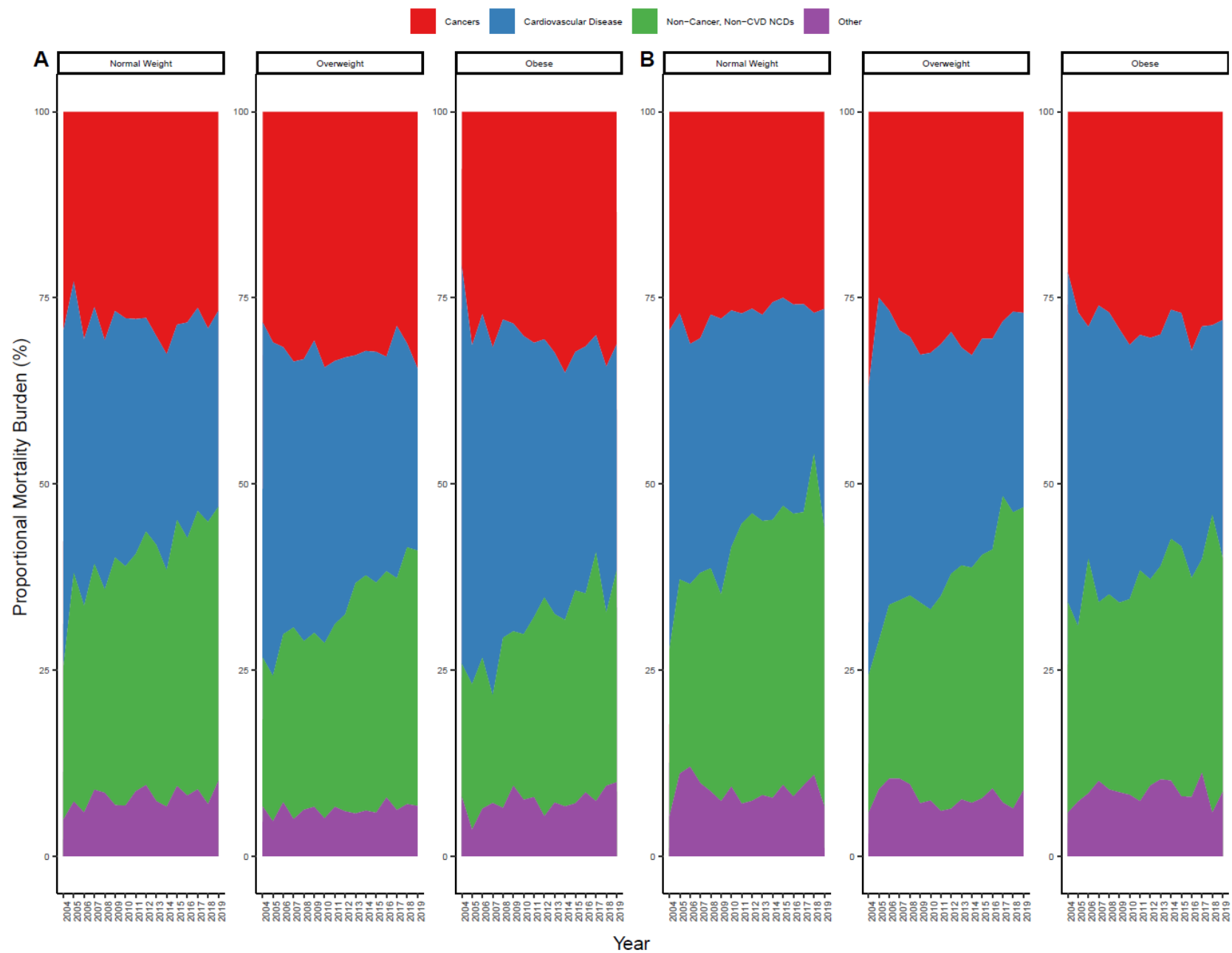


Figure 7. Proportional composition of Tier 2 outcomes between 2004 and 2019 in (A) males and (B) females

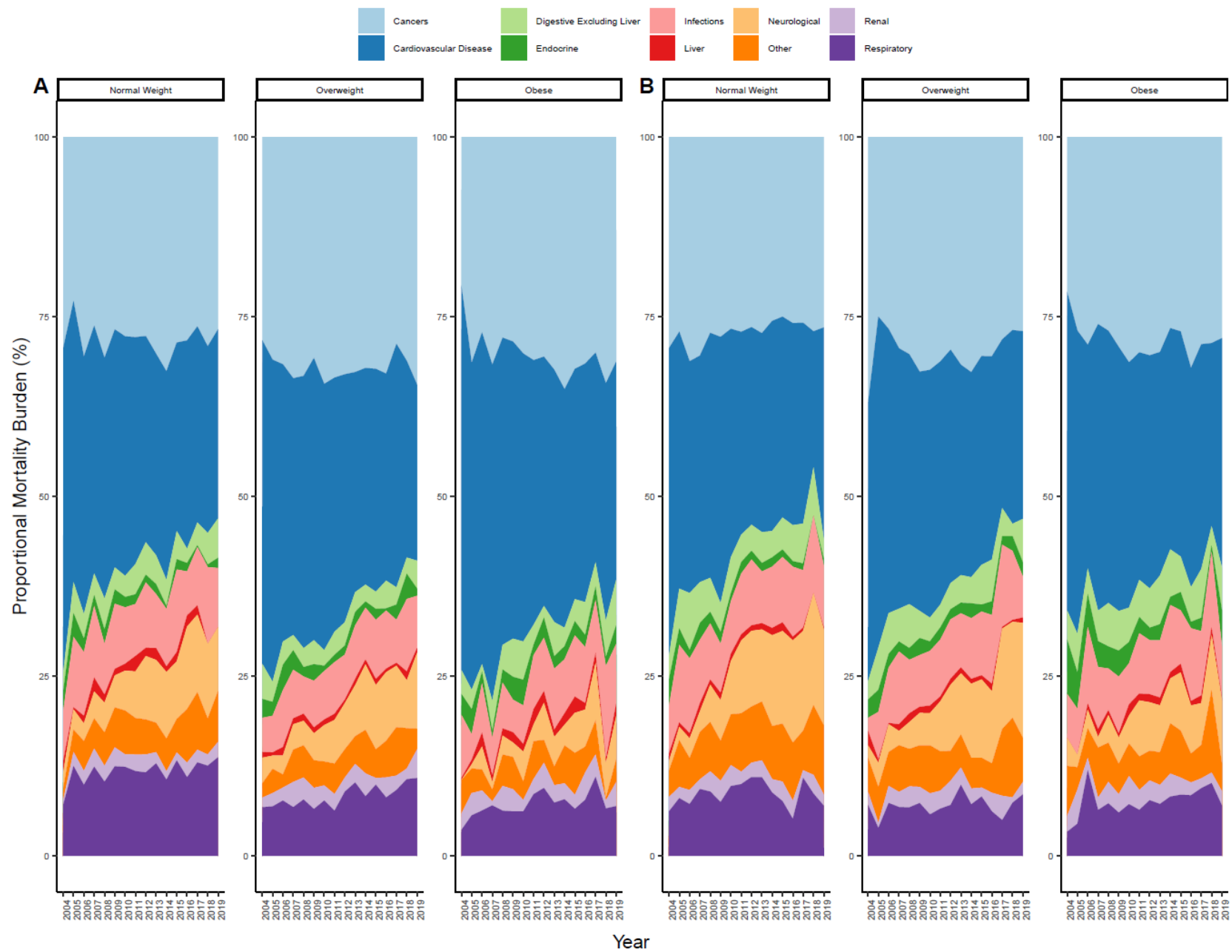


Figure 8. Proportional composition of Tier 3 outcomes between 2004 and 2019 in (A) males and (B) females

Table 11. Tier 3 outcomes and the proportional contribution (%) of mortality rankings in 2004 and 2019 by BMI in males

Normal Weight			
2004		2019	
Cardiovascular Disease	45.2 (42.8, 47.5)	Cancers	26.8 (25.4, 28.1)
Cancers	29.4 (27.8, 30.9)	Cardiovascular Disease	26.3 (24.9, 27.7)
Respiratory	7.1 (6.8, 7.5)	Respiratory	13.7 (13.0, 14.4)
Infections	6.9 (6.6, 7.3)	Neurological	8.9 (8.4, 9.4)
Endocrine	2.8 (2.7, 2.9)	Infections	8.2 (7.8, 8.7)
Digestive Excluding Liver	2.5 (2.4, 2.7)	Other	7.1 (6.7, 7.4)
Neurological	2.2 (2.1, 2.3)	Digestive Excluding Liver	5.5 (5.2, 5.8)
Other	1.7 (1.6, 1.8)	Renal	2.1 (2.0, 2.2)
Liver	1.6 (1.5, 1.7)	Endocrine	1.4 (1.3, 1.5)
Renal	0.60 (0.60, 0.70)	Liver	0 (0, 0)

Overweight			
2004		2019	
Cardiovascular Disease	45.0 (42.7, 47.3)	Cancers	34.5 (32.7, 36.3)
Cancers	28.3 (26.8, 29.7)	Cardiovascular Disease	24.5 (23.2, 25.7)
Respiratory	6.8 (6.4, 7.1)	Respiratory	10.8 (10.3, 11.4)
Digestive Excluding Liver	4.9 (4.6, 5.1)	Neurological	10.5 (10, 11.1)
Infections	4.7 (4.5, 5.0)	Infections	7.2 (6.9, 7.6)
Neurological	3.6 (3.4, 3.8)	Renal	4.0 (3.8, 4.2)
Endocrine	2.6 (2.5, 2.8)	Digestive Excluding Liver	3.9 (3.7, 4.1)
Other	2.0 (1.9, 2.1)	Other	2.9 (2.7, 3.0)
Renal	1.3 (1.3, 1.4)	Endocrine	1.0 (0.9, 1.0)
Liver	0.80 (0.80, 0.90)	Liver	0.70 (0.70, 0.70)

Obese			
2004		2019	
Cardiovascular Disease	53.5 (50.7, 56.2)	Cancers	31.3 (29.6, 32.9)
Cancers	20.7 (19.6, 21.7)	Cardiovascular Disease	30.3 (28.8, 31.9)
Infections	8.8 (8.4, 9.3)	Infections	8.3 (7.9, 8.7)
Other	4.7 (4.4, 4.9)	Respiratory	6.9 (6.6, 7.3)
Respiratory	3.6 (3.4, 3.8)	Digestive Excluding Liver	6.3 (6.0, 6.6)
Digestive Excluding Liver	3.3 (3.2, 3.5)	Neurological	6.0 (5.7, 6.3)
Endocrine	2.9 (2.7, 3.0)	Renal	3.3 (3.2, 3.5)
Renal	2.3 (2.1, 2.4)	Other	3.2 (3.0, 3.3)
Liver	0.30 (0.30, 0.30)	Endocrine	2.6 (2.5, 2.7)
Neurological	0 (0, 0)	Liver	1.7 (1.6, 1.8)

Table 12. Tier 3 outcomes and the proportional contribution (%) of mortality rankings in 2004 and 2019 by BMI in females

Normal Weight			
2004		2019	
Cardiovascular Disease	42.8 (39.9, 45.7)	Cardiovascular Disease	29.5 (27.5, 31.5)
Cancers	29.4 (27.4, 31.4)	Cancers	26.5 (24.7, 28.3)
Infections	6.6 (6.2, 7.1)	Neurological	13.3 (12.4, 14.3)
Respiratory	6.2 (5.8, 6.6)	Other	9.6 (9.0, 10.3)
Endocrine	3.7 (3.4, 3.9)	Infections	8.5 (7.9, 9.1)
Other	3.6 (3.4, 3.9)	Respiratory	7.0 (6.5, 7.5)
Digestive Excluding Liver	3.3 (3, 3.5)	Digestive Excluding Liver	2.7 (2.5, 2.9)
Renal	2.0 (1.9, 2.1)	Renal	1.5 (1.4, 1.6)
Neurological	1.3 (1.2, 1.4)	Endocrine	1.0 (1.0, 1.1)
Liver	1.1 (1.0, 1.2)	Liver	0.30 (0.30, 0.30)

Overweight			
2004		2019	
Cardiovascular Disease	38.7 (36.0, 41.3)	Cancers	27.0 (25.2, 28.9)
Cancers	37.0 (34.5, 39.6)	Cardiovascular Disease	26.1 (24.3, 27.9)
Respiratory	7.1 (6.6, 7.6)	Neurological	16.0 (14.9, 17.1)
Other	4.8 (4.4, 5.1)	Respiratory	8.6 (8.0, 9.1)
Digestive Excluding Liver	2.5 (2.4, 2.7)	Other	6.1 (5.7, 6.6)
Endocrine	2.5 (2.4, 2.7)	Digestive Excluding Liver	6.0 (5.6, 6.5)
Liver	2.0 (1.9, 2.2)	Infections	5.7 (5.3, 6.1)
Infections	1.8 (1.7, 1.9)	Endocrine	2.0 (1.9, 2.1)
Renal	1.8 (1.7, 1.9)	Renal	1.7 (1.6, 1.8)
Neurological	1.7 (1.6, 1.8)	Liver	0.70 (0.70, 0.80)

Obese			
2004		2019	
Cardiovascular Disease	44.3 (41.3, 47.3)	Cardiovascular Disease	31.9 (29.7, 34.1)
Cancers	21.5 (20.1, 23)	Cancers	28.0 (26.1, 29.9)
Endocrine	7.6 (7.1, 8.1)	Neurological	8.8 (8.2, 9.4)
Other	7.0 (6.5, 7.5)	Infections	7.2 (6.7, 7.7)
Infections	6.1 (5.7, 6.5)	Respiratory	7.0 (6.6, 7.5)
Digestive Excluding Liver	4.0 (3.7, 4.3)	Digestive Excluding Liver	5.9 (5.5, 6.3)
Neurological	3.9 (3.6, 4.2)	Endocrine	5.0 (4.7, 5.3)
Respiratory	3.4 (3.1, 3.6)	Other	3.8 (3.6, 4.1)
Renal	2.2 (2.0, 2.3)	Renal	2.0 (1.8, 2.1)
Liver	0 (0, 0)	Liver	0.40 (0.40, 0.40)

4.3.2 Age-stratified analyses

4.3.2.1 *Premature mortality for all-cause outcomes*

To understand changes in health status, and considering BMI declines after a certain age, I analysed the trends in premature mortality (individuals <75 years old) by BMI (Table 13). In males, all-cause mortality rates declined by 4% (95% CI: -5.3%, -2.8%) per year in the obese category, with no changes in the overweight or normal weight categories. In females, a 2% (95% CI: -4%, -0.4%) decline per year occurred in the normal weight category, with no changes in the overweight or obese categories (Table 13).

4.3.2.2 *Premature mortality across tier 2 outcomes*

Across Tier 2 outcomes in males <75 years old, CVD mortality rates declined by 7% (95% CI: -9%, -5.5%) per year in the obese category and by 4% (95% CI: -7.0%, -1.6%) per year in overweight category (Table 13). Cancer mortality rates declined by 3% (95% CI: -4.7%, -0.7%) per year in obese males. No changes were observed for non-cancer, non-CVD NCD mortality rates.

In females <75 years old, CVD mortality rates declined by 6% (95% CI: -8.2%, -4.4%) per year in the obese category and by 4% (95% CI: -6.1%, -1.8%) per year in the overweight category, with no change in the normal weight category (Table 13). Cancers had a borderline decrease of about 2% (95% CI: -3.8%, 0%) per year in the normal weight category, with no other changes in BMIs. For non-cancer, non-CVD NCDs, there were no changes in any of the BMI categories.

4.3.2.3 *Premature mortality across tier 3 outcomes*

Similarly to the main analysis, when assessing Tier 3 outcomes, the changes in mortality rates were often due to extremely small mortality rates over the study period.

In males, endocrine mortality declined in the normal weight category by 9% (95% CI: -15.7%, -3.1%) per year and in the obese category by 8% (95% CI: -13.0%, -3.8%) per year. Mortality rates in males declined from digestive diseases excluding liver disease by 6% (95% CI: -11.3%, -0.4%) per year in the obese category.

In females, mortality rates only changed for respiratory mortality in the overweight category, declining by 7% (95% CI: -13.0%, -1.8%) per year. Otherwise, no other changes occurred.

Table 13. Age-adjusted all-cause mortality (tier 1), tier 2, and tier 3 mortality rates in 2004 and 2019 per 1000 person years and average percent change in death rate across BMIs in those <75 years old, by sex

	Normal Weight			Overweight			Obese		
	2004 rate	2019 rate	Average % change per year (%)	2004 rate	2019 rate	Average % change per year (%)	2004 rate	2019 rate	Average % change per year (%)
MALES									
Tier 1									
All-cause	3.1 (2.2, 3.9)	2.2 (1.6, 2.9)	-1.5 (-4.2, 1.1)	2.3 (1.7, 2.8)	1.6 (1.2, 2)	-0.6 (-3.8, 1.5)	5.2 (4, 6.4)	2.6 (2, 3.2)	-4.1 (-5.3, -2.8)
Tier 2									
Non-cancer, non-CVD NCDs	0.52 (0.16, 0.87)	0.54 (0.22, 0.86)	-0.5 (-4.2, 3.2)	0.25 (0.08, 0.43)	0.34 (0.16, 0.51)	1.8 (-1.3, 5.1)	0.72 (0.29, 1.2)	0.45 (0.21, 0.69)	-2.3 (-5, 0.5)
Cardiovascular Disease	0.91 (0.46, 1.4)	0.54 (0.22, 0.86)	-5.3 (-12.2, 1.1)	0.99 (0.64, 1.3)	0.28 (0.11, 0.44)	-5.4 (-7, -3.9)	2.6 (1.8, 3.4)	0.53 (0.26, 0.79)	-7.0 (-8.9, -5.1)
Cancer	1.5 (0.89, 2.1)	0.86 (0.45, 1.3)	-0.6 (-4.4, 3.2)	0.91 (0.57, 1.26)	0.91 (0.62, 1.2)	0.8 (-2.3, 3.7)	1.6 (0.92, 2.2)	1.33 (0.9, 1.8)	-2.7 (-4.7, -0.7)
Other	0.15 (-0.06, 0.35)	0.28 (0.03, 0.53)	5.7 (-1.4, 14.4)	0.11 (-0.02, 0.25)	0.07 (-0.01, 0.16)	0 (-4.5, 4.7)	0.32 (0.01, 0.64)	0.28 (0.09, 0.48)	-2 (-8, 4.2)
Tier 3									
Cancers	1.5 (0.89, 2.1)	0.86 (0.45, 1.27)	-0.6 (-4.4, 3.2)	0.91 (0.57, 1.3)	0.91 (0.62, 1.19)	0.8 (-2.3, 3.7)	1.6 (0.92, 2.2)	1.3 (0.9, 1.8)	-2.7 (-4.7, -0.7)
Cardiovascular Disease	0.91 (0.46, 1.4)	0.54 (0.22, 0.86)	-5.3 (-12.2, 1.1)	0.99 (0.64, 1.3)	0.28 (0.11, 0.44)	-5.4 (-7, -3.9)	2.6 (1.78, 3.4)	0.53 (0.26, 0.79)	-7.0 (-8.9, -5.1)
Digestive Excluding Liver	<0.0001	0.15 (-0.02, 0.32)	0.8 (-6.5, 8.3)	0.03 (-0.03, 0.09)	0.05 (-0.02, 0.12)	-2.1 (-8.3, 4.2)	0.19 (-0.07, 0.46)	0.1 (-0.01, 0.22)	-5.6 (-11.3, -0.4)
Endocrine	0.18 (-0.02, 0.39)	0.09 (-0.08, 0.26)	-9.3 (-15.7, -3.1)	<0.0001	<0.0001	-3.4 (-11.3, 3.6)	0.06 (-0.06, 0.18)	0.04 (-0.03, 0.11)	-8.2 (-13, -3.8)
Infections	0.08 (-0.07, 0.22)	0.09 (-0.03, 0.2)	-4.3 (-11.5, 2.5)	0.07 (-0.03, 0.16)	0.07 (-0.01, 0.14)	-0.9 (-7.5, 5.9)	0.19 (-0.03, 0.41)	0.11 (-0.01, 0.23)	-4.7 (-10.6, -0.8)
Liver	0.15 (-0.06, 0.35)	<0.0001	1.1 (-5.4, 9.6)	0.09 (-0.03, 0.2)	0.02 (-0.02, 0.07)	-1.2 (-6.1, 4.2)	0.07 (-0.07, 0.2)	0.11 (-0.01, 0.23)	-2.2 (-9.4, 5.6)
Neurological	0.13 (-0.05, 0.31)	0.09 (-0.03, 0.2)	-1.6 (-9.3, 11.9)	0.03 (-0.03, 0.09)	0.05 (-0.02, 0.12)	7.8 (-1, 19)	<0.0001	0.1 (-0.01, 0.22)	-0.5 (-11, 9.9)
Other	<0.0001	0.09 (-0.08, 0.26)	5.2 (-3.9, 15.8)	<0.0001	0.2 (0.02, 0.37)	3.1 (-4.8, 11.8)	0.2 (-0.03, 0.42)	0.11 (-0.01, 0.23)	-5.3 (-13.5, 3.3)
Renal	<0.0001	<0.0001	-6.4 (-16.7, 2.7)	<0.0001	<0.0001	2.5 (-7.3, 14.7)	<0.0001	0.03 (-0.03, 0.1)	-3.4 (-18.7, 12.6)
Respiratory	0.13 (-0.05, 0.31)	0.32 (0.08, 0.56)	0.6 (-4.5, 5.9)	0.16 (0.02, 0.29)	0.22 (0.08, 0.36)	1.7 (-2.8, 6.6)	0.33 (0.04, 0.62)	0.14 (0, 0.27)	-2.3 (-5.7, 1.2)
FEMALES									
Tier 1									
All-cause	2.3 (1.7, 2.8)	1.3 (0.9, 1.7)	-2.2 (-4, -0.4)	2 (1.5, 2.5)	1.2 (0.8, 1.6)	-1.1 (-2.7, 0.6)	2.2 (1.5, 2.8)	1.8 (1.3, 2.3)	-1.4 (-5.1, 0.9)
Tier 2									
Non-cancer, non-CVD NCDs	0.39 (0.15, 0.63)	0.15 (0.02, 0.28)	-3.8 (-13.4, 7.9)	0.39 (0.16, 0.62)	0.16 (0.03, 0.3)	1.1 (-3.6, 6.1)	0.78 (0.4, 1.2)	0.38 (0.16, 0.59)	-2.5 (-5.2, 0.3)
Cardiovascular Disease	0.67 (0.35, 1.0)	0.17 (0.03, 0.31)	-4 (-9.5, 1.3)	0.56 (0.28, 0.83)	0.28 (0.11, 0.46)	-4.2 (-7, -1.6)	0.7 (0.36, 1.0)	0.4 (0.18, 0.62)	-6.2 (-8.2, -4.4)
Cancers	1.0 (0.62, 1.4)	0.84 (0.53, 1.15)	-1.9 (-3.8, 0)	0.95 (0.6, 1.3)	0.58 (0.33, 0.84)	-0.3 (-5.2, 4.1)	0.59 (0.27, 0.90)	0.93 (0.59, 1.3)	1.6 (-6.3, 7.5)
Other	0.19 (0.02, 0.36)	0.12 (0, 0.24)	-1.1 (-6.4, 4.6)	0.14 (0, 0.28)	0.16 (0.03, 0.3)	0.6 (-3.5, 5)	0.09 (-0.03, 0.21)	0.1 (-0.01, 0.2)	-2.2 (-8.2, 3.6)
Tier 3									
Cancers	1.0 (0.62, 1.4)	0.84 (0.53, 1.15)	-1.9 (-3.8, 0)	0.95 (0.6, 1.3)	0.58 (0.33, 0.84)	-0.3 (-5.2, 4.1)	0.59 (0.27, 0.9)	0.93 (0.59, 1.26)	1.6 (-6.3, 7.5)
Cardiovascular Disease	0.67 (0.35, 1)	0.17 (0.03, 0.31)	-4 (-9.5, 1.3)	0.56 (0.28, 0.83)	0.28 (0.11, 0.46)	-4.2 (-7, -1.6)	0.7 (0.36, 1)	0.4 (0.18, 0.62)	-6.2 (-8.2, -4.4)
Digestive Excluding Liver	0.08 (-0.03, 0.19)	0.03 (-0.03, 0.09)	-5.8 (-13.6, 2.2)	0.03 (-0.03, 0.1)	0.05 (-0.02, 0.13)	3.5 (-1.6, 9.3)	0.04 (-0.04, 0.13)	<0.0001	-5.8 (-17.8, 5.5)
Endocrine	0.08 (-0.03, 0.19)	<0.0001	-5.5 (-14.4, 5.4)	0.03 (-0.03, 0.1)	<0.0001	3 (-6, 14.6)	0.14 (-0.02, 0.29)	0.06 (-0.02, 0.15)	-5.8 (-13.1, 0.9)
Infections	0.04 (-0.04, 0.12)	<0.0001	0.3 (-9, 10.7)	<0.0001	<0.0001	2.7 (-6.8, 13.7)	0.22 (0.03, 0.42)	0.03 (-0.03, 0.09)	-1.8 (-9.7, 7.1)
Liver	0.03 (-0.03, 0.09)	0.03 (-0.03, 0.09)	-5.2 (-15.9, 11.2)	0.07 (-0.03, 0.17)	0.05 (-0.02, 0.13)	-0.5 (-7.6, 7)	<0.0001	0.03 (-0.03, 0.09)	1 (-8.2, 10.2)
Neurological	<0.0001	0.09 (-0.01, 0.2)	4.4 (-12.1, 22.6)	0.03 (-0.03, 0.1)	0.03 (-0.03, 0.08)	7.6 (-1.8, 19.9)	0.16 (-0.06, 0.39)	0.03 (-0.03, 0.09)	-4.2 (-18.1, 11.5)
Other	0.19 (0.02, 0.35)	0.09 (-0.01, 0.2)	0.4 (-4.8, 6.3)	0.13 (0, 0.26)	0.06 (-0.02, 0.14)	0.2 (-10.7, 7.7)	0.22 (0.03, 0.42)	0.09 (-0.01, 0.2)	-2.6 (-8.8, 3.8)
Renal	<0.0001	<0.0001	-5.7 (-17.9, 6.6)	<0.0001	0.03 (-0.03, 0.1)	7 (-5.4, 20.6)	0.04 (-0.04, 0.12)	<0.0001	-2.1 (-10, 7.2)
Respiratory	0.16 (0, 0.32)	0.03 (-0.03, 0.09)	-1.9 (-6.9, 3.1)	0.22 (0.04, 0.4)	0.11 (0, 0.21)	-7.2 (-13, -1.8)	0.04 (-0.04, 0.13)	0.22 (0.06, 0.39)	0.5 (-4.2, 5.4)

4.3.3 All-cause mortality trends by IMD

When stratifying by IMD, there were 877,187 people with IMD data available (Table 14). For all-cause mortality rates in 2004, the largest difference between the most deprived quintile and least deprived quintile was in overweight males with mortality rates 46% higher in 2004 and 68% higher in 2019. In females, in 2004 the overweight category had a mortality rate 68% larger in the most deprived quintile compared to the least, this difference declined to 47% by 2019, where the obese category had a 59% higher mortality rate in the most deprived compared to the least deprived.

In both 2004 and 2019, obese males in the most deprived quintile had the highest all-cause mortality rates (Table 14). In the obese category, all-cause mortality rates declined by about 4% per year in the least deprived quintile (95% CI: -7.9%, -0.3%), quintile 2 (95% CI: -6.2%, -1.1%), and quintile 4 (95% CI: -5.8%, -0.9%). In the overweight category in males, 2-3% declines per year were observed for all quintiles, except for the second quintile.

In females, whilst the mortality rates were highest in the obese category in most deprived quartile in 2004, females in the second quintile in the obese category and most deprived quintile in the normal weight category were the highest by 2019. In the obese category, mortality rates in the least deprived quintile declined by 4% (95% CI: -6.1%, -0.9%) per year, by 2% per year in the most deprived quintile (95% CI: -4.3%, -0.5%) and quintile 2 (95% CI: -3.9%, -0.1%). In the overweight category, all-cause mortality rates in the least deprived quintile increased by nearly 3% (95% CI: 0.1%, 6.2%) per year, but no other changes occurred.

Table 14. Age-adjusted all-cause mortality (tier 1) mortality rates in 2004 and 2019 per 1000 person years and average percent change in death rate across BMIs, by sex and IMD

	Normal Weight			Overweight			Obese		
	2004 rate	2019 rate	Average change per year (%)	2004 rate	2019 rate	Average change per year (%)	2004 rate	2019 rate	Average change per year (%)
MALES									
Quintile 1 (Least Deprived)	18.4 (13.2, 23.6)	8.8 (5.9, 11.7)	-3 (-4.9, -1.1)	16.3 (11.6, 21)	9.5 (7.1, 11.9)	-3.4 (-5.2, -1.5)	22.2 (11.7, 32.8)	13.9 (9.6, 18.1)	-4.2 (-7.9, -0.3)
Quintile 2	17.1 (12.2, 21.9)	16.1 (11.7, 20.5)	-0.9 (-3, 1.2)	10.4 (7.1, 13.7)	14.7 (11.3, 18)	-0.2 (-2.4, 2.0)	18.1 (11.6, 24.6)	14.7 (9.9, 19.5)	-3.7 (-6.2, -1.1)
Quintile 3	17.7 (12.2, 23.3)	10.7 (6.6, 14.9)	-4.1 (-6.4, -2.4)	16.5 (12, 21)	13 (9.3, 16.8)	-1.7 (-3.2, -0.3)	20.5 (12.9, 28)	14.7 (9.5, 19.8)	-1.8 (-3.9, 0.3)
Quintile 4	12.5 (7.8, 17.1)	15.2 (9.9, 20.6)	-0.3 (-2.6, 2)	16.7 (12, 21.5)	12.8 (9, 16.6)	-2.1 (-3.6, -0.6)	27.5 (18, 37)	12.3 (7.8, 16.8)	-3.4 (-5.8, -0.9)
Quintile 5 (Most Deprived)	23.9 (16.3, 31.5)	15.3 (9.4, 21.1)	-1.7 (-4.6, 1.1)	26.2 (18.9, 33.4)	19.3 (13.5, 25.2)	-1.7 (-2.9, -0.6)	34.4 (21.7, 47.2)	20.9 (13.4, 28.4)	-2 (-5, 1.2)
FEMALES									
Quintile 1 (Least Deprived)	7.7 (5.1, 10.3)	8.0 (5.8, 10.1)	0.5 (-3.2, 3.7)	5.2 (3.1, 7.3)	6.9 (4.7, 9.1)	2.5 (0.1, 6.2)	11.4 (5.4, 17.4)	6.4 (4, 8.7)	-3.6 (-6.1, -0.9)
Quintile 2	8.7 (5.9, 11.5)	9.5 (6.8, 12.1)	-0.2 (-1.2, 0.9)	7.3 (4.7, 9.9)	8 (5.6, 10.5)	0.1 (-1.3, 1.6)	13.3 (7.7, 18.8)	13.8 (10, 17.6)	-2.0 (-3.9, -0.1)
Quintile 3	7.5 (5, 10)	12.7 (9.1, 16.2)	0.8 (-1.7, 3.1)	7.7 (5.1, 10.4)	6.3 (4, 8.6)	0.1 (-1.1, 1.4)	10.3 (6.4, 14.2)	10 (6.6, 13.5)	0.1 (-1.7, 1.9)
Quintile 4	9.8 (6.8, 12.7)	11.2 (7.7, 14.7)	2 (-2.5, 5.8)	7.6 (5, 10.1)	8.7 (5.7, 11.6)	0.6 (-0.9, 2.2)	10.8 (6.7, 14.9)	6.3 (3.9, 8.7)	-2.1 (-4.3, 0.3)
Quintile 5 (Most Deprived)	10 (6.7, 13.3)	13.3 (8.6, 18)	2.8 (-0.4, 6)	10.7 (7.2, 14.2)	11.3 (7.5, 15.1)	-0.2 (-1.7, 1.4)	18.6 (12.4, 24.9)	11.7 (7.9, 15.6)	-2.3 (-4.3, -0.5)

4.3.4 All-cause mortality trends by ethnicity

To stratify by ethnicity, those who did not have any ethnicity coded for were excluded. This resulted in a dataset of 810,324 individuals. As a result, about 93% of the participants were white and due to such small sample sizes for the non-white ethnicities, instances occurred where some of the ethnicities had no observations certain years and/or had different study start or end dates (Table 15).

In 2004, males in the ‘other’ ethnicity group who were obese had the highest mortality rate, but by 2019, obese males in the ‘mixed’ ethnicity group had the highest, which throughout the study period increased by 19% (95% CI: 0.3%, 39.3%) per year. This was the only significant increase in mortality rates. However, males in both the ‘white’ ethnicity group and the obese category had mortality rates decline by 2% (95% CI: -3.4%, -0.6%) per year.

Females in the ‘mixed’ ethnicity group had the largest mortality rate in 2004, which declined by 13% (95% CI: -24.2%, -0.9%) per year. By 2019, the largest mortality rate was in females in the ‘other’ ethnicity group and had an obese BMI, but no significant changes occurred in females in the obese category by ethnicity group. Females in the ‘black’ ethnicity group and obese BMI declined by 11% (95% CI: -19.2%, -1.8%) per year. Increases in mortality rates occurred for the ‘white’ ethnicity group by 3% (95% CI: 1.5%, 4.4%) per year in the normal weight and by 2% (95% CI: 0.2%, 2.8%) per year in the overweight categories.

Table 15. Age-adjusted all-cause mortality (tier 1) mortality rates in 2004 and 2019 per 1000 person years and average percent change in death rate across BMIs, by sex and ethnicity

	Normal Weight			Overweight			Obese		
	2004 rate	2019 rate	Average change per year (%)	2004 rate	2019 rate	Average change per year (%)	2004 rate	2019 rate	Average change per year (%)
MALES									
Asian	19.0 (-2.5, 40.6)	1.9 (-1.8, 5.6)	-7.0 (-15.3, 2.5)	8.1 (-7.8, 23.9)	12.2 (1.5, 22.9)	-6.5 (-16.3, 5.8)	15.2 (-5.9, 36.3)	60.5 (1.2, 119.8)	2.3 (-13.3, 21.6)
Black	4.9 (-4.7, 14.6) †	19.6 (-18.8, 58.1)	4.8 (-13.3, 22.6)	63.8 (-8.4, 136)	62.9 (-8.3, 134.1)	-8.6 (-18.2, 1.5)	11.9 (-4.6, 28.3) ‡	18.3 (-7.1, 43.7)	-7.2 (-23.1, 8.5)
Mixed	19.6 (-18.8, 58.1) §	5.6 (-5.4, 16.7) #	1.5 (-21.0, 25.4)	8.9 (-8.5, 26.3) ‡	29.4 (-28.3, 87.1)**	8.2 (-13.4, 39.4)	20.2 (-7.8, 48.3) ¶	73.7 (-28.4, 175.8)**	19.1 (0.3, 39.3)
Other	5.6 (-2.2, 13.4) †	8.4 (-8.1, 24.9)	-10.5 (-25.4, 3.3)	15.2 (-14.6, 45)	2 (-2.0, 6.1)	-3.9 (-11.3, 5.2)	58.9 (-56.5, 174.3)*	25.4 (-9.8, 60.6)	-2.7 (-12.5, 8.5)
White	13.3 (11.1, 15.6)	13.2 (11.1, 15.2)	-0.2 (-1.6, 1.1)	12.0 (10.1, 13.8)	13.2 (11.5, 14.8)	0.7 (-1.8, 2.5)	18.0 (14.3, 21.8)	14.5 (12.2, 16.8)	-2 (-3.4, -0.6)
FEMALES									
Asian	4.4 (-4.2, 13.1)	8.2 (-1.1, 17.4)	10.9 (-10.1, 45.4)	7.9 (-3, 18.8)	11.6 (0.2, 23)	-1 (-13.4, 15.1)	3.7 (-3.6, 11)	1.6 (-1.6, 4.8)	-1.6 (-14.8, 14.7)
Black	8.6 (-8.2, 25.3)	14.7 (-14.1, 43.6) #	1 (-14.8, 20.3)	58.9 (-22.7, 140.5)	1.4 (-1.4, 4.2)	-11.3 (-19.2, -1.8)	16.1 (-6.2, 38.4)	11.2 (-1.5, 23.9)	-1.7 (-16.4, 17)
Mixed	68.5 (-26.4, 163.4)	8.5 (-8.2, 25.3)	-13 (-24.2, -0.9)	58.9 (-56.5, 174.3) ‡	19.6 (-7.6, 46.8)**	-7.5 (-49.6, 106.5)	11 (-4.2, 26.1) ¶	9.8 (-9.4, 29)	0.8 (-24.6, 30.6)
Other	11.8 (-11.3, 34.9)	13.5 (-1.8, 28.8)	-7 (-20.1, 6.6)	5.2 (-5, 15.5)*	1.6 (-1.6, 4.8)	4 (-12.2, 24)	6.3 (-6.1, 18.8)	21.7 (2.7, 40.7)	0.2 (-17.4, 24)
White	6.5 (5.4, 7.7)	10.3 (8.9, 11.7)	3.0 (1.5, 4.4)	6.2 (5, 7.3)	8.2 (6.9, 9.4)	1.5 (0.2, 2.8)	8.9 (7, 10.9)	9.8 (8.3, 11.2)	0.3 (-1.7, 2.7)

Study start and end years differed depending on the ethnicity as follows: *2005; †2006; ‡2007; §2008; ¶2009; #2017; **2018

4.3.5 Sensitivity analyses

4.3.5.1 *Two-year exclusion period*

When determining the exclusion period between a BMI measurement and loss to follow-up from death, transferring out of CPRD, or the end of the study period, a two-year exclusion period was considered. In the male all-cause mortality analysis, the obese category had a mortality rate of 13 deaths per 1000 person years, compared to normal weight at 12 deaths per 1000 person years. As the study period progressed, by 2019 normal weight mortality rates were 9 per 1000 person years and obese mortality rates were 8 per 1000 person years (Figures 8A, 9A, 10A).

In females, similar patterns were observed where obese females began the study with a mortality rate of 7 deaths per 1000 person years compared to normal weight at 6 deaths per 1000 person years. By 2019, the rates shifted where normal weight had a mortality rate of 7 deaths per 1000 person years and the obese mortality rate was 6 deaths per 1000 person years (Figures 8B, 9B, 10B).

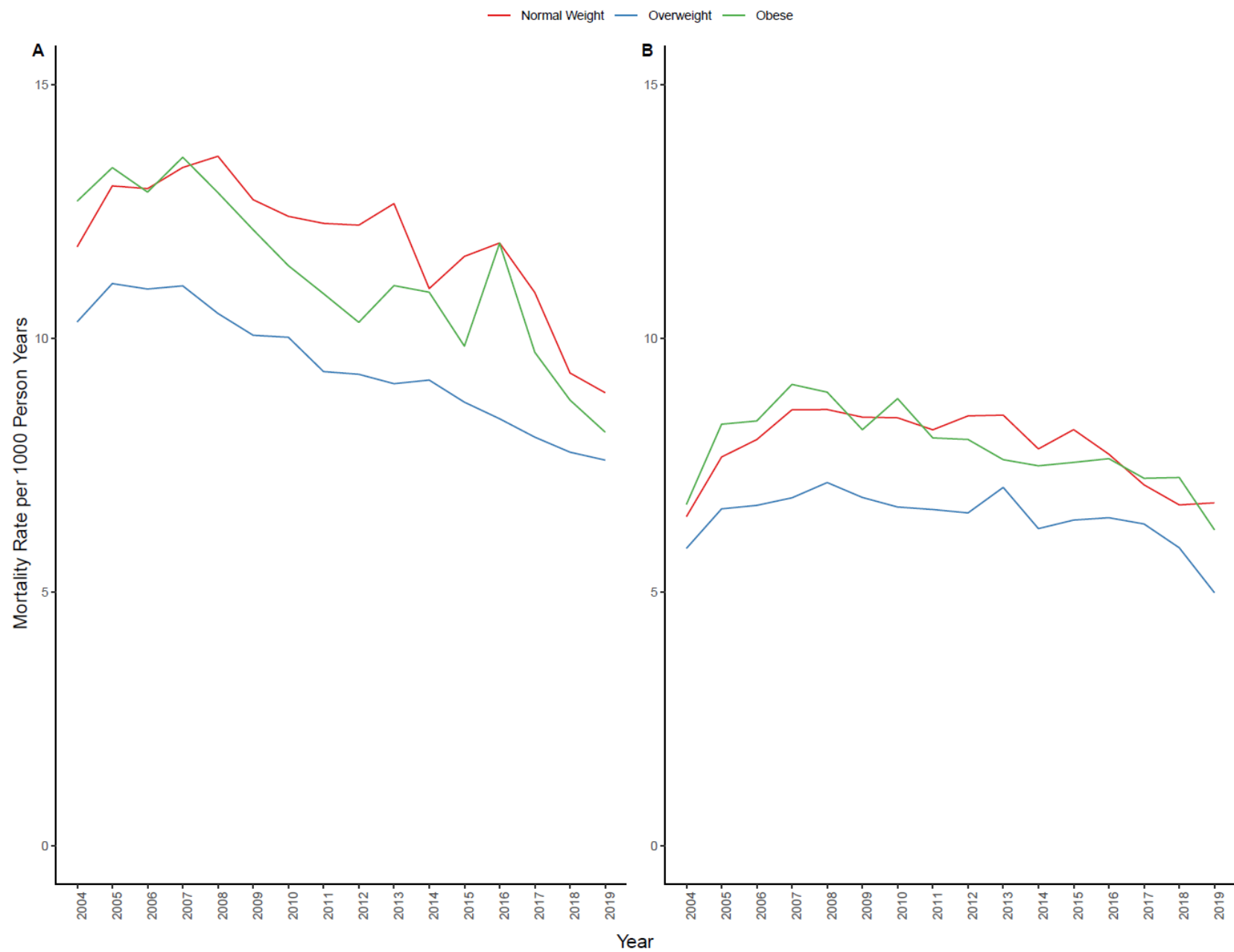


Figure 9. Sensitivity analysis with a two-year exclusion period: age-adjusted mortality rates in Tier 1 outcomes in (A) males and (B) females



Figure 10. Sensitivity analysis with a two-year exclusion period: age-adjusted mortality rates in Tier 2 outcomes in (A) males and (B) females

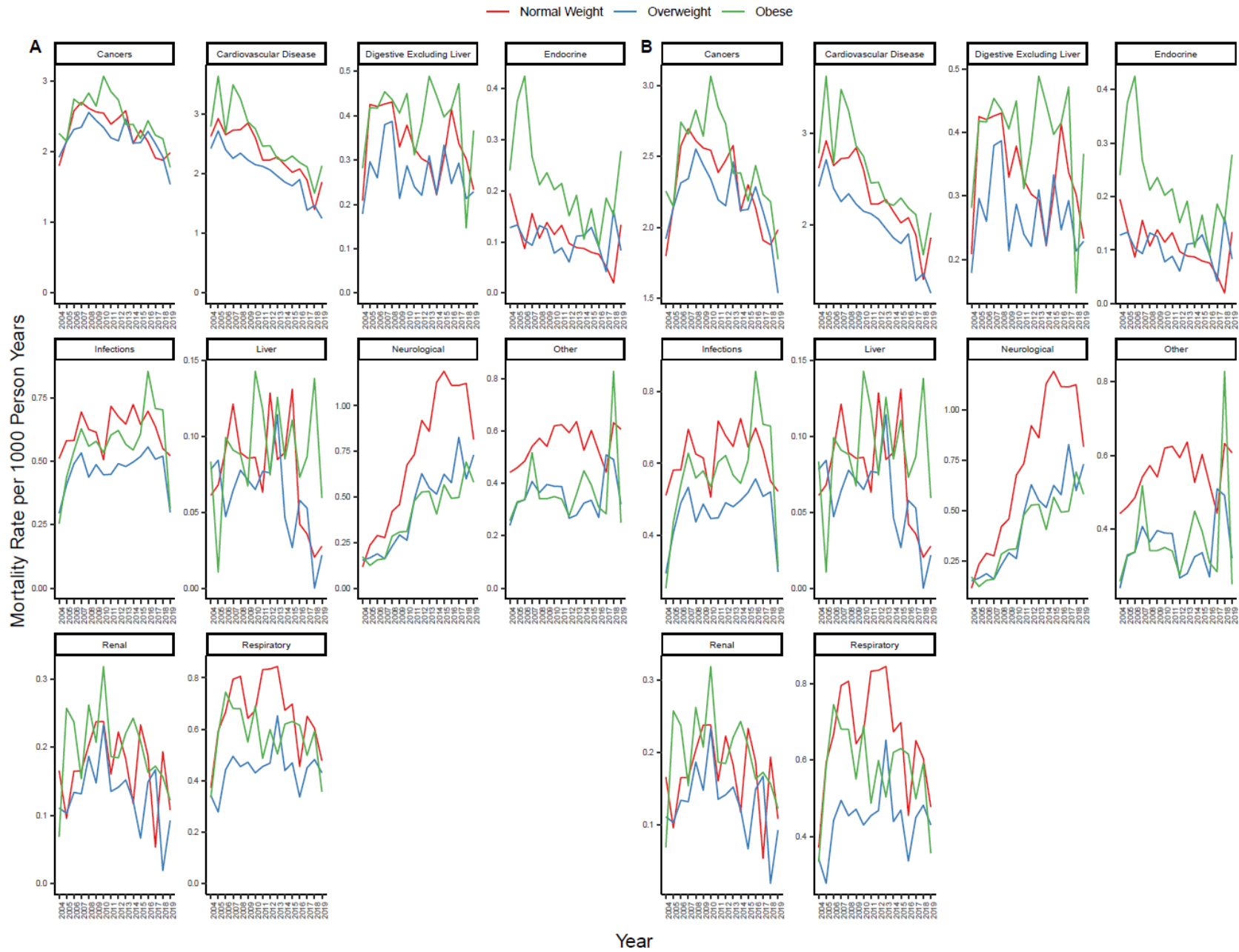


Figure 11. Sensitivity analysis with a two-year exclusion period: age-adjusted mortality rates in Tier 3 outcomes in (A) males and (B) females

4.3.5.2 Ethnicity-specific BMI

As previously stated, over 70,000 participants with no ethnicity data available were excluded to ensure the proper BMI cutoff was applied for each ethnicity.

Once applying these adjusted cutoffs all-cause mortality rates declined for the obese category only, by 3% (95% CI: -4.1%, -1.3%) per year, but no changes in normal weight or overweight categories (Table 16). When assessing Tier 2 outcomes in males, CVD mortality declined between 6% (95% CI: -7.7%, -4.1%) in the obese category and 3% (95% CI: -6.4%, -0.7%) per year in the overweight category. Non-cancer, non-CVD NCDs increased in overweight males by nearly 5% (95% CI: 1.4%, 6.6%) per year. A borderline decline occurred for cancer mortality in the obese category, declining about 2% (95% CI: -3.5%, 0.0%) per year. For Tier 3 outcomes, an 89% (95% CI: -95.7%, -83.4%) decline occurred for liver disease mortality and a 12% (95% CI: -18.6%, -4.3%) decline occurred for endocrine mortality, both in the normal weight category. In the overweight category, a 248% (95% CI: 75.9%, 501.9%) increase per year occurred for renal mortality rates. Neurological mortality rates increased across all BMI categories, by 288% (95% CI: 112.2%, 542.3%) per year in the obese category and 9% per year in the normal weight (95% CI: 3.8%, 14.8%) and (95% CI: 4.4%, 12.1%) in the overweight categories.

In females, all-cause mortality rates increased by 2% (95% CI: 0.9%, 3.3%) per year in the normal weight category (Table 16). Across Tier 2 mortality outcomes, CVD mortality rates declined by 4% (95% CI: -5.4%, -1.7%) per year in the obese category only. Mortality rates from non-cancer, non-CVD NCDs increased by 7% (95% CI: 5.8%, 9.4%) per year in the overweight and by 5% (95% CI: 2.7%, 6.8%) per year in the normal weight categories. Finally for Tier 2, no changes occurred for cancer mortality. For Tier 3 outcomes, endocrine mortality declined by 10% (95% CI: -15.2%, -4.9%) per year in the obese category, but increased by

16% (95% CI: 11.9%, 21.6%) per year in the overweight category. Neurological mortality rates increased for all BMI categories by 22% (95% CI: 16.9%, 27.2%) in normal weight, 17% (95% CI: 11.2%, 22.2%) in overweight, and 11% (95% CI: 4.5%, 19.0%) in obese females. Liver disease mortality rates increased by 1028% (95% CI: 539.7%, 2482.7%) per year in the obese category.

Table 16. Age-adjusted all-cause mortality (tier 1), tier 2, and tier 3 mortality rates in 2004 and 2019 per 1000 person years and average percent change in death rate using ethnicity-specific BMIs, by sex

	Normal Weight			Overweight			Obese		
	2004 rate	2019 rate	Average % change per year (%)	2004 rate	2019 rate	Average % change per year (%)	2004 rate	2019 rate	Average % change per year (%)
MALES									
Tier 1									
All-cause	14.3 (12, 16.5)	12.7 (10.8, 14.7)	-1 (-2.2, 0.2)	13 (11.1, 14.9)	13 (11.4, 14.6)	-0.1 (-2.9, 1.8)	18.7 (15.2, 22.3)	14.9 (12.6, 17.1)	-2.7 (-4.1, -1.3)
Tier 2									
Non-cancer, non-CVD NCDs	2.9 (2.4, 3.4)	4.8 (4.1, 5.6)	3.1 (-2.8, 7.6)	2.3 (1.9, 2.6)	4.5 (4, 5)	4.5 (1.4, 6.6)	3.6 (2.9, 4.3)	4.1 (3.5, 4.7)	1 (-0.9, 2.9)
Cardiovascular Disease	6.1 (5.1, 7)	3.1 (2.6, 3.6)	-4.9 (-6.2, -4.1)	5.6 (4.7, 6.4)	3.1 (2.7, 3.5)	-3.3 (-6.4, -0.7)	8.7 (7, 10.3)	4.7 (4, 5.4)	-6.0 (-7.7, -4.1)
Cancer	4.7 (4, 5.4)	3.4 (2.9, 4)	-0.7 (-2.7, 1.3)	4.2 (3.6, 4.8)	4.5 (4, 5.1)	-0.3 (-4.4, 2.7)	4.7 (3.8, 5.6)	4.6 (3.9, 5.3)	-1.8 (-3.5, 0)
Other	0.57 (0.48, 0.66)	1.3 (1.1, 1.5)	4.8 (-4.7, 12)	0.97 (0.83, 1.1)	0.89 (0.78, 1)	0.2 (-1.8, 2.3)	1.7 (1.4, 2.1)	1.4 (1.2, 1.7)	-1 (-3.9, 2.2)
Tier 3									
Cancers	4.7 (4, 5.4)	3.4 (2.9, 4)	-0.7 (-2.7, 1.3)	4.2 (3.6, 4.8)	4.5 (4, 5.1)	-0.3 (-4.4, 2.7)	4.7 (3.8, 5.6)	4.6 (3.9, 5.3)	-1.8 (-3.5, 0)
Cardiovascular Disease	6.1 (5.1, 7)	3.1 (2.6, 3.6)	-4.9 (-6.2, -4.1)	5.6 (4.7, 6.4)	3.1 (2.7, 3.5)	-3.3 (-6.4, -0.7)	8.7 (7, 10.3)	4.7 (4, 5.4)	-6.0 (-7.7, -4.1)
Digestive Excluding Liver	0.24 (0.2, 0.27)	0.72 (0.61, 0.83)	-0.1 (-5.9, 5.9)	0.69 (0.59, 0.79)	0.51 (0.45, 0.57)	-0.9 (-5.9, 4.2)	0.65 (0.52, 0.77)	0.91 (0.78, 1.1)	2 (-8.3, 13.9)
Endocrine	0.52 (0.44, 0.6)	0.2 (0.17, 0.23)	-11.8 (-18.6, -4.3)	0.46 (0.39, 0.52)	0.13 (0.11, 0.15)	-6.3 (-16.3, 4.9)	0.62 (0.5, 0.74)	0.38 (0.32, 0.43)	-4.6 (-9.9, 1.2)
Infections	0.65 (0.55, 0.75)	1.1 (0.91, 1.2)	-0.4 (-3.7, 3)	0.55 (0.47, 0.63)	0.95 (0.84, 1.1)	1.3 (-1.3, 3.9)	1.6 (1.3, 1.9)	1.2 (1, 1.4)	2.5 (-2.2, 7.4)
Liver	0.19 (0.16, 0.21)	<0.0001	-89.6 (-95.7, -83.4)	0.1 (0.088, 0.12)	0.092 (0.081, 0.1)	-2.5 (-9, 4.3)	0.064 (0.052, 0.076)	0.25 (0.22, 0.29)	8.1 (-12.2, 25.5)
Neurological	0.4 (0.34, 0.47)	1.2 (0.98, 1.3)	9.7 (3.8, 14.8)	0.32 (0.27, 0.37)	1.4 (1.2, 1.6)	8.6 (4.4, 12.1)	<0.0001	0.87 (0.74, 1)	288.4 (112.2, 542.3)
Other	0.26 (0.22, 0.3)	0.93 (0.79, 1.1)	6 (-2.4, 13.6)	0.34 (0.29, 0.39)	0.38 (0.33, 0.42)	3.5 (-1.8, 9.3)	1 (0.82, 1.2)	0.46 (0.39, 0.53)	-2.9 (-11.2, 6.6)
Renal	0.12 (0.1, 0.14)	0.28 (0.23, 0.32)	1.3 (-9.1, 9.5)	<0.0001	0.52 (0.46, 0.58)	247.5 (75.9, 501.9)	0.56 (0.45, 0.66)	0.48 (0.41, 0.56)	-1.4 (-8.6, 6.7)
Respiratory	1.1 (0.92, 1.3)	1.8 (1.5, 2.1)	2.2 (-3.4, 6.4)	0.79 (0.67, 0.9)	1.4 (1.3, 1.6)	1.7 (-0.8, 4.3)	0.83 (0.68, 0.99)	1 (0.85, 1.2)	-0.5 (-3.9, 3)
FEMALES									
Tier 1									
All-cause	7 (5.8, 8.1)	10.2 (8.9, 11.6)	2.1 (0.4, 3.9)	7.2 (6, 8.4)	7.9 (6.7, 9.1)	0.7 (-0.4, 1.8)	10.7 (8.6, 12.8)	9.4 (8, 10.8)	-0.5 (-3.3, 2.2)
Tier 2									
Non-cancer, non-CVD NCDs	1.3 (1.1, 1.5)	3.9 (3.4, 4.4)	4.8 (2.7, 6.8)	1.3 (1.1, 1.5)	3 (2.6, 3.5)	7.3 (5.8, 9.4)	3.2 (2.6, 3.9)	3 (2.5, 3.4)	0.8 (-2.1, 3.8)
Cardiovascular Disease	3.1 (2.6, 3.6)	3 (2.6, 3.4)	-1.8 (-4, 0.6)	2.8 (2.3, 3.2)	2 (1.7, 2.4)	-2.6 (-5.6, 0.4)	4 (3.2, 4.8)	3.1 (2.6, 3.5)	-3.6 (-5.4, -1.7)
Cancers	2.3 (2, 2.7)	2.7 (2.4, 3.1)	-0.7 (-2, 0.7)	2.8 (2.3, 3.2)	2.1 (1.8, 2.4)	-0.5 (-2.4, 1.6)	2.8 (2.2, 3.3)	2.7 (2.3, 3.1)	-0.6 (-2.4, 1.9)
Other	0.25 (0.21, 0.29)	0.7 (0.6, 0.79)	0.9 (-2.4, 4.3)	0.41 (0.34, 0.48)	0.71 (0.6, 0.81)	-0.8 (-3.8, 2.3)	0.67 (0.54, 0.8)	0.73 (0.62, 0.84)	-1.4 (-5, 2.5)
Tier 3									
Cancers	2.3 (2, 2.7)	2.7 (2.4, 3.1)	-0.7 (-2, 0.7)	2.8 (2.3, 3.2)	2.1 (1.8, 2.4)	-0.5 (-2.4, 1.6)	2.8 (2.2, 3.3)	2.7 (2.3, 3.1)	-0.6 (-2.4, 1.9)
Cardiovascular Disease	3.1 (2.6, 3.6)	3 (2.6, 3.4)	-1.8 (-4, 0.6)	2.8 (2.3, 3.2)	2 (1.7, 2.4)	-2.6 (-5.6, 0.4)	4 (3.2, 4.8)	3.1 (2.6, 3.5)	-3.6 (-5.4, -1.7)
Digestive Excluding Liver	0.065 (0.055, 0.076)	0.28 (0.24, 0.31)	8.1 (-9, 21)	0.21 (0.18, 0.25)	0.48 (0.41, 0.55)	-0.9 (-6, 4.5)	0.48 (0.39, 0.58)	0.48 (0.41, 0.55)	-2.6 (-8, 4.5)
Endocrine	0.2 (0.18, 0.25)	0.11 (0.092, 0.12)	-33.9 (-74.2, 69.2)	0.21 (0.18, 0.25)	0.16 (0.13, 0.18)	-1.6 (-6.8, 4)	1 (0.81, 1.2)	0.47 (0.4, 0.54)	-10.2 (-15.2, -4.9)
Infections	0.4 (0.33, 0.46)	0.88 (0.76, 0.99)	2.0 (-0.9, 5.0)	0.076 (0.063, 0.089)	0.45 (0.38, 0.52)	15.9 (11.9, 21.6)	0.56 (0.45, 0.68)	0.67 (0.57, 0.77)	0.7 (-2.5, 4.1)
Liver	0.1 (0.084, 0.12)	<0.0001	-31.7 (-73, 72.4)	0.17 (0.14, 0.19)	0.06 (0.051, 0.069)	55.7 (-51.8, 407.1)	<0.0001	0.036 (0.031, 0.042)	1028.2 (539.7, 2482.7)
Neurological	0.063 (0.053, 0.074)	1.4 (1.2, 1.6)	21.7 (16.9, 27.2)	0.065 (0.054, 0.076)	1.3 (1.1, 1.5)	16.5 (11.2, 22.2)	0.32 (0.26, 0.39)	0.82 (0.7, 0.94)	11.3 (4.5, 19.0)
Other	0.2 (0.19, 0.26)	1 (0.87, 1.1)	8 (2.7, 13.4)	0.24 (0.2, 0.28)	0.49 (0.42, 0.56)	1.5 (-4.3, 7.4)	0.92 (0.74, 1.1)	0.36 (0.31, 0.41)	0 (-6.8, 7.1)
Renal	0.126 (0.11, 0.15)	0.16 (0.14, 0.18)	0.2 (-8, 9.2)	0.15 (0.13, 0.18)	0.14 (0.12, 0.16)	6.7 (-15.1, 29.5)	0.24 (0.19, 0.29)	0.18 (0.16, 0.21)	-4.4 (-9.9, 1.5)
Respiratory	0.3 (0.29, 0.4)	0.72 (0.63, 0.82)	0.7 (-5.3, 7)	0.59 (0.49, 0.69)	0.68 (0.58, 0.78)	1.6 (-1.5, 4.8)	0.39 (0.31, 0.47)	0.66 (0.56, 0.76)	6.4 (-1, 11.7)

4.4 Discussion

4.4.1 Overview

In this English population-based study investigating the changing mortality spectrum associated with overweight and obesity, all-cause mortality is declining with the greatest declines in obese males and females than in those who were overweight or normal weight. The all-cause mortality rates were driven primarily by the large declines in CVD mortality. In Tier 2 outcomes, non-cancer, non-CVD NCDs are the only outcomes with increasing mortality rates, with the exception of the obese category. Finally, once analysing the mortality burden in Tier 3 outcomes, cancers became the primary contributor of death in males in all BMI categories, and females in the overweight category.

4.4.2 Key findings

For males in the obese category, all-cause mortality rate declined by 37% and CVD mortality rate by 64%. For females in the obese category, all-cause mortality rates declined by 25% and CVD mortality rates declined by 45%. It is clear the changes in all-cause mortality rates are significantly driven by the reductions in CVD mortality, especially considering no changes occurred in mortality rates for non-cancer, non-CVD NCDs, or cancers in the obese category.

The decline in CVD mortality and its impact is important considering the CVD declines which occurred in the normal weight and overweight categories in females were not large enough for all-cause mortality to subsequently decline. This is likely due to the increases in non-cancer, non-CVD NCD mortality rates in the normal weight and overweight categories, which was not the case in the obese category. Further, the strength of the reductions in CVD mortality in males is clear considering mortality rates from non-cancer, non-CVD NCDs increased in both the

normal weight and overweight categories, yet a significant decline was maintained in all-cause mortality.

The primary reason for significant increases in non-cancer, non-CVD NCDs when examining Tier 3 outcomes was the increasing rates in mortality from neurological conditions. Increases in neurological mortality rates occurred in all BMI categories for both males and females, but normal weight and overweight had smaller increases compared to the obese category. However, it is important to note that the extreme changes in some of the Tier 3 outcomes was due to having a very small mortality rate changing to another relatively small value, including in neurological mortality rates in obese males and females.

Cancer mortality rates did not change throughout the study period, excluding normal weight males. As a result of these slow improvements in cancer mortality rates, in addition to the stable decline in CVD mortality occurring simultaneously, the burden of mortality across all causes of death is diversifying. Mortality from cancers is now the leading cause of death, replacing CVD in all BMIs in males and overweight females. In normal weight and obese females, despite increases in the proportion of deaths from cancers in obese females only, CVD is still the leading cause of death in these categories. Thus, whilst mortality rates from CVD declined significantly, the change in mortality rates from cancers were small in females, and non-cancer, non-CVD NCDs mortality rates continue to rise. As a result, the proportion of deaths from causes such as neurological and respiratory conditions are on the rise.

4.4.3 Comparing to the literature

These findings are consistent with previous research indicating that there have been steady declines in both all-cause mortality and CVD mortality (122, 166, 167). Some research

suggests that increasing obesity prevalence is either slowing or offsetting the reduction in CVD rates, but we found no stagnation in mortality rates in this large sample of the English population (129, 131, 167, 168). Improvements in treatment, risk factor management, and lifestyle changes appear to have offset the impact of obesity as a risk factor for CVD (166).

Mortality rates for CVD and cancer narrowed over the study period for all BMI categories. There has been a 19% decline in cancer mortality rates in the UK between 1971 and 2019; yet, in our study normal weight males were the only group to have had a significant decrease in cancer mortality rates (169, 170). Further, data in the UK shows that cancer is the leading cause of death for males and females, accounting for 25% of deaths as of 2021. Whilst this is the case in males in my research, we did not observe this for females in all BMI categories (170).

Among specific types of non-cancer, non-CVD NCDs mortality, neurological conditions mainly contributed to the increasing mortality rates and mortality burden. This is consistent with prior literature showing the number of deaths from neurological conditions increased 39% in England (171). In this analysis, the proportion of deaths from neurological conditions, primarily consisting of dementia and Alzheimer's disease, and is one of the main reasons for the diversification of mortality from CVD. This is consistent with previous trend studies, with the proportion of deaths from dementia and Alzheimer's deaths in the UK increasing from 5% in 2001 to 13% in 2018 (166).

Respiratory mortality also increased proportionally across all causes, for both males and females in all BMI categories ranging from 7% in normal weight females and obese males and females to 14% in normal weight males. At a global scale, respiratory mortality accounts for about 7% of deaths, but in the UK that increases to 9% (170, 172). In contrast to my results,

which showed no change in respiratory mortality rates for males or females, except for a 5% increase in obese females, literature shows respiratory mortality rates declining in males, and no change in females (173).

4.4.4 Strengths and limitations

A major strength of this study is the use of the CPRD dataset, a large, generalisable dataset which allows for longitudinal analysis. Data is routinely collected from the GP practices and linked to ONS to provide comprehensive real-world data. However, that also comes with limitations. Our dataset was restricted to persons with a BMI measurement, so we could not look at whether there are considerable differences between patients who get their BMI measured compared to those who do not. Yet, when comparing CPRD dataset and HSE overweight and obesity prevalence, my CPRD dataset is confirmed to be representative of the population in England in regards to BMI overweight and obesity with IMD (32, 174).

A factor which may have influence increases in mortality rates is the changes in policy practices implemented during this study. The Quality and Outcomes Framework (QOF) was introduced in 2004 in UK primary care where GP practices were financially incentivised for the attainment of specific quality indicators (175). However, when comparing the descriptive statistics by year in Chapter 3, no stark differences were observed for the variables we considered in the study. Secondly, how the primary cause of death is defined could contribute to the increase in mortality rates from certain causes of death, and their proportional contribution. For instance, from 2014 an increased policy focus on dementia diagnosis and care resulted in higher recording of dementia as the primary cause of death more often than previous years (176). These trends are also being observed in the US and Australia, with dementia being coded as the primary cause of death, resulting in increases in dementia mortality rates, but also declines

in CVD mortality (177). Whether these are true increases, or because of changes in coding practices for primary and secondary causes of death in England, Australia, and United States, is not known (176, 177). We are unable to account for changes in policy and coding practices in the analysis but recognizing this as a potential reason for the increase in neurological mortality rates, for instance, is important in the interpretation of the results.

The impact of CVD declines in overweight males (5% per year), is important considering non-cancer, non-CVD NCDs mortality rates increased (2% per year), mainly due to the increase in neurological mortality rates (7% per year). However, despite this increase, males in the overweight category still had a decline in all-cause mortality on average per year, which shows the strength of the decline in CVD mortality, but also indicates the need to look at the estimated mortality rates and sample size.

It is important to consider the small mortality rates observed between 2004 and 2019 for some of the NCDs (i.e. neurological mortality). There was an increase in average percent change per year (primarily in those aged 75+ as indicated in the premature mortality results), and contribution to proportional mortality. In males in the obese category, for example, the mortality rate in 2004 was negligible, and whilst there was an increase on average per year, the rates were still small by 2019. In males and females in the normal weight and overweight categories, the increases for neurological mortality were significant, and the ranges for the 95% CIs indicate the estimates for both of these categories were well-powered, despite the normal weight category having a slightly more precise 95% CI than overweight. The obese category had a very large range of 95% CIs, indicating more uncertainty in the result. Despite this, these results are likely a true estimate, as competing risks were accounted for in the models, literature indicates neurological mortality is increasing in the UK, and CVD improvements gives rise to

other causes of death becoming more prominent, as shown in the proportional mortality results. However, it would be beneficial to include a larger sample size for future analyses and focusing on the specific NCDs which are on the rise, especially when stratifying further by variables such as BMI, IMD, and ethnicity in order to observe more precise estimates.

Reverse causality is a concern in any study of BMI and mortality. To ensure illness was not causing participants to lose weight prior to death, a five-year survival period was selected over two-year to ensure reverse causality was accounted for. However, there is the possibility that participants had lost weight more than five years prior to their death due to illness. Further, the five-year exclusion period significantly reduced the sample size and is a likely contributor to low death rates. Whilst CPRD has rich data to allow for a stratified analysis of males and females, in addition to ten mortality outcomes, further stratification was not plausible for IMD and ethnicity besides all-cause mortality. A larger sample size to allow more precise death rates, whilst still accounting for reverse causality, would be ideal.

I was able to utilise ethnicity-specific BMI categories, but these adjusted thresholds have only been examined to identify cardiometabolic risk, not overall mortality (69). When these updated thresholds were applied, the majority of previously significant declines were no longer significant, especially in all-cause mortality. Whether this was due to having a smaller sample, the thresholds are not appropriate indicators for mortality risk, or because they truly were no changes throughout the study period is not clear.

4.5 Summary

In summary, between 2004 and 2019 there were large declines in all-cause and CVD mortality in males and females in England, with the greatest reductions among obese individuals driven

by the reduction in deaths from CVD. Non-cancer, non-CVD mortality rates increased for normal weight and overweight categories, but not the obese category in males or females. Once NCDs were analysed granularly, cancers became the leading contributor of deaths amongst males in all BMI categories and females in the overweight category, whilst the proportion of deaths from neurological, respiratory, and digestive excluding liver disease also increased. The causes of death across BMI categories are becoming more diverse, indicating the need for further screening, prevention, and treatment implementation for a broader set of diseases.

5. Morbidity trends

5.1 Background

Whilst previous studies have suggested that the long-term increases in life expectancy have slowed in the past decade in England, there were still improvements through 2019 as shown in Chapter 4 (126). The continued improvements have been largely due to CVD mortality declines, but as individuals are living longer and the obesity rates are increasing, there is concern that the prevalence of individuals living with comorbidities such as COPD, dementia, stroke, and type 2 diabetes will increase (178). Yet, the changes in prevalence and incidence of these diseases and other obesity-related morbidities by BMI is unclear. Similarly, how the burden of disease is changing impacts both an individual's quality of life and the societal cost of caring for and treating those with these diseases. This chapter aims to quantify the prevalence and incidence trends in obesity-related morbidity in adults in England to identify the variation and shifts in comorbid conditions by BMI.

5.2 Methods

5.2.1 Study population

The CPRD dataset linked with HES data was utilised for this aim. The study period was amended to begin 1 January 2004 through 31 December 2019 to account for the implementation of the QOF. The purpose of QOF was to financially incentivise primary care physicians for improving care to patients through factors such as chronic disease management and public health measures, and attaining specific quality indicators (175). Limiting the analysis of this aim to start in 2004 reduces bias related to changes in, especially since read codes are utilised in this aim. There were 1,401,325 participants who fit the inclusion criteria as outlined in Chapter 3, in addition to having a BMI from 2004 through 2019.

5.2.2 BMI exposure and outcomes

In this chapter, there was no exclusion for individuals based on their survival time, allowing for a more granular analysis of obesity. BMI was categorised based on WHO classifications as follows: underweight: BMI < 18.5 kg/m²; normal weight: BMI ≥ 18.5 and < 24.9 kg/m²; overweight: BMI ≥ 25 and < 29.9 kg/m²; obese class I BMI ≥ 30 and < 35 kg/m²; and obese class II+: BMI ≥ 35 kg/m² (163).

Comorbidity diagnoses for participants were extracted from HES and CPRD read codes. HES data consisted of admitted patient care data and outpatient data. The primary diagnosis for a hospitalisation was extracted through ICD-10 codes based on the conditions of interest. Read codes were extracted from Clinical, Test, and Referral databases within CPRD depending on the diagnosis of interest.

Instead of focusing on all of the conditions, I am exploring specific comorbid conditions which were chosen based on the leading contributors to mortality from Chapter 4 or are well-known comorbidities closely associated to obesity. The outcomes of interest include Alzheimer's and dementia; cerebrovascular disease; heart failure; IHD; COPD; depression; liver disease; obesity-related cancers; osteoarthritis and joint disorders; renal failure; type 2 diabetes; and ulcers. The ICD-10 codes are shown in Table 17 whereas the read codes are in the Appendix.

Table 17. Morbidity outcomes of interest by ICD-10 codes

Morbidity	ICD-10 codes
Alzheimer disease and dementia	F00-03, G30
Atrial fibrillation	I48
Cerebrovascular disease	I60-69
Ischaemic heart disease	I20-25
Heart failure	I50
COPD	J41-J44
Depression	F32, F33
Liver disease	K70-77
Obesity-related cancers	C15, C16, C18-20, C22, C23, C25, C50, C54.1, C56, C64, C70, C73, C90
Osteoarthritis and joint pain	M15-M19, M22-M25, M47
Renal failure	N17-N19
Sleep apnoea	G47.3
Type 2 diabetes	E11
Ulcers	K25-28

COPD: chronic obstructive pulmonary disorder

5.2.3 Statistical analysis

This chapter is focused on variation and trends in prevalence and incidence rates of comorbid conditions according to levels of BMI. To utilise the longitudinal nature of CPRD, the same methodology from Chapter 4 was applied where a participant was included from the time of their first BMI measurement and each subsequent calendar year until the end of follow-up. Further, accounting for the time-dependency of BMI, BMI was updated each calendar year. The baseline measurement of the respective calendar year was used each year they were included in the analysis. If no measurement was available in a certain year, the most recent BMI measurement from the previous year was used instead. Both prevalence and incidence models were age-standardised based on the male/female-combined ONS mid-year population estimates in 2011 (chosen as it is the median of the study period), to ensure the mortality rates were comparable between years and gender (164). Finally, joinpoint models were utilised to understand whether the trends were significantly changing.

5.2.3.1 Prevalence

A prevalent condition was defined as a condition or disease which was diagnosed up to five years prior to or within the calendar year a BMI measurement occurred. (Thus, a condition that was diagnosed more than five years before the BMI measurement but was not noted again would not be considered a prevalent condition.) Once a person was diagnosed with a prevalent condition, it was considered prevalent until the end of follow-up which was the date of death, date of transferring out of CPRD, or end of the study period. A binomial logistic regression model was utilised to estimate the predicted prevalence for each comorbidity accounting for calendar year, BMI, and age as three-way interaction terms, with separate models for males and females.

5.2.3.2 Incidence

Incidence was defined as the first ever instance of a diagnosis. The diagnosis did not need to be on the same date as a BMI measurement, but in the calendar year of a measurement between 2004 and 2019. Only new cases were considered incident, despite certain conditions being recurrent. A discrete Poisson regression model was used to estimate incidence rates by BMI comorbidity accounting for calendar year, BMI, and age as three-way interaction terms, with separate models for males and females.

The same time-to-event methods were used for incidence as they were for mortality rates in Chapter 4. Follow-up ended the date of the first occurrence of a specific disease. For example, if a participant was diagnosed with type 2 diabetes on 5 May 2007, that was the end of follow-up for type 2 diabetes only and the exposure length would be 125/365. For every other comorbidity of interest, follow-up continued until the date of diagnosis, death, leaving CPRD, or end of the study. The exposure length, between 0 and 1, was the offset in the Poisson model to account for differing follow-up periods of participants.

5.2.3.3 Secondary analyses

Two secondary analyses were conducted in this chapter. To account for the potential of reverse causality when estimating incidence rates, as an individual's BMI may change prior to being diagnosed with a comorbidity, I applied a five-year survival period for individuals, meaning individuals who were not still being followed up five years after a BMI measurement were not included in the analysis. Prevalence and incidence rate trends were also age-stratified to identify any differences by age groups. Age groups were as follows: <44, 45-64, and 65+.

5.3 Results

5.3.1 Prevalence

5.3.1.1 Prevalence difference of comorbidities by BMI level

As the BMI scale increases, the prevalence of comorbid conditions rises significantly, resulting in obesity class II+ having the highest prevalence rates compared to other BMI categories for both males and females. Type 2 diabetes stands out for its association with BMI—compared to normal weight, prevalence is 2.5-fold as high for obese class I and 5-fold as high for obese class II+ (Figure 12, Figure 13). For sleep apnoea there was a 2.5-fold higher prevalence for obese class II+ compared to normal weight in males but increased to 4-fold by 2019; the prevalence amongst females was negligible in 2004, and by 2019 was 6-fold higher. A second group of conditions—osteoarthritis, renal disease, depression, atrial fibrillation, and heart failure—have about a 2-fold prevalence difference from normal weight to obese class II+. COPD and liver disease are both conditions which did not differ in prevalence at the beginning of the study when comparing the obese classes to normal weight, however, by 2019, a prevalence difference of about 1.5-fold emerged between obese class II+ and COPD and liver disease (Figure 12, Figure 13). A 1.5-fold prevalence difference also occurred for IHD but was consistent across the study period. Finally, there was no difference in prevalence of obesity-

related cancers by BMI level. Whilst prevalence rates are often higher in females than males, with exception to type 2 diabetes, heart failure, and IHD, the magnitude of differences in rates between obese class II+ and normal weight are similar.

When assessing the most prevalent comorbidity across the study period, the prevalence of type 2 diabetes was highest in the obese class II+ throughout the study period in males (Figure 12, Table 18). In males in 2004, IHD was the most prevalent condition in normal weight and overweight categories, but by 2019, osteoarthritis and depression were some of the most prominent conditions. In females, depression, closely followed by osteoarthritis and other joint disorders, had the highest prevalence rates in all BMI categories (Figure 13, Table 18).

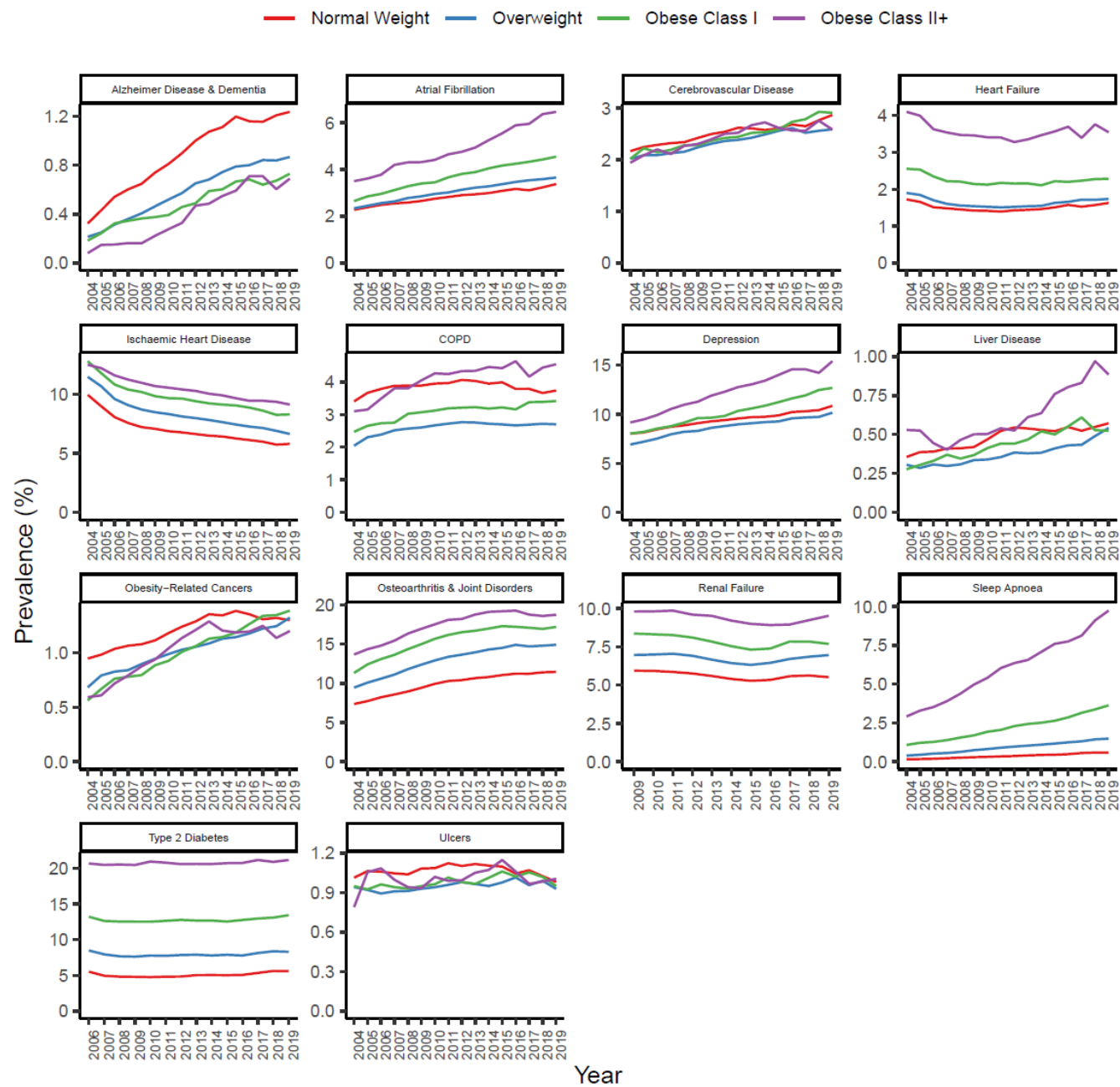


Figure 12. Age-adjusted prevalence (%) between 2004 and 2019 in males

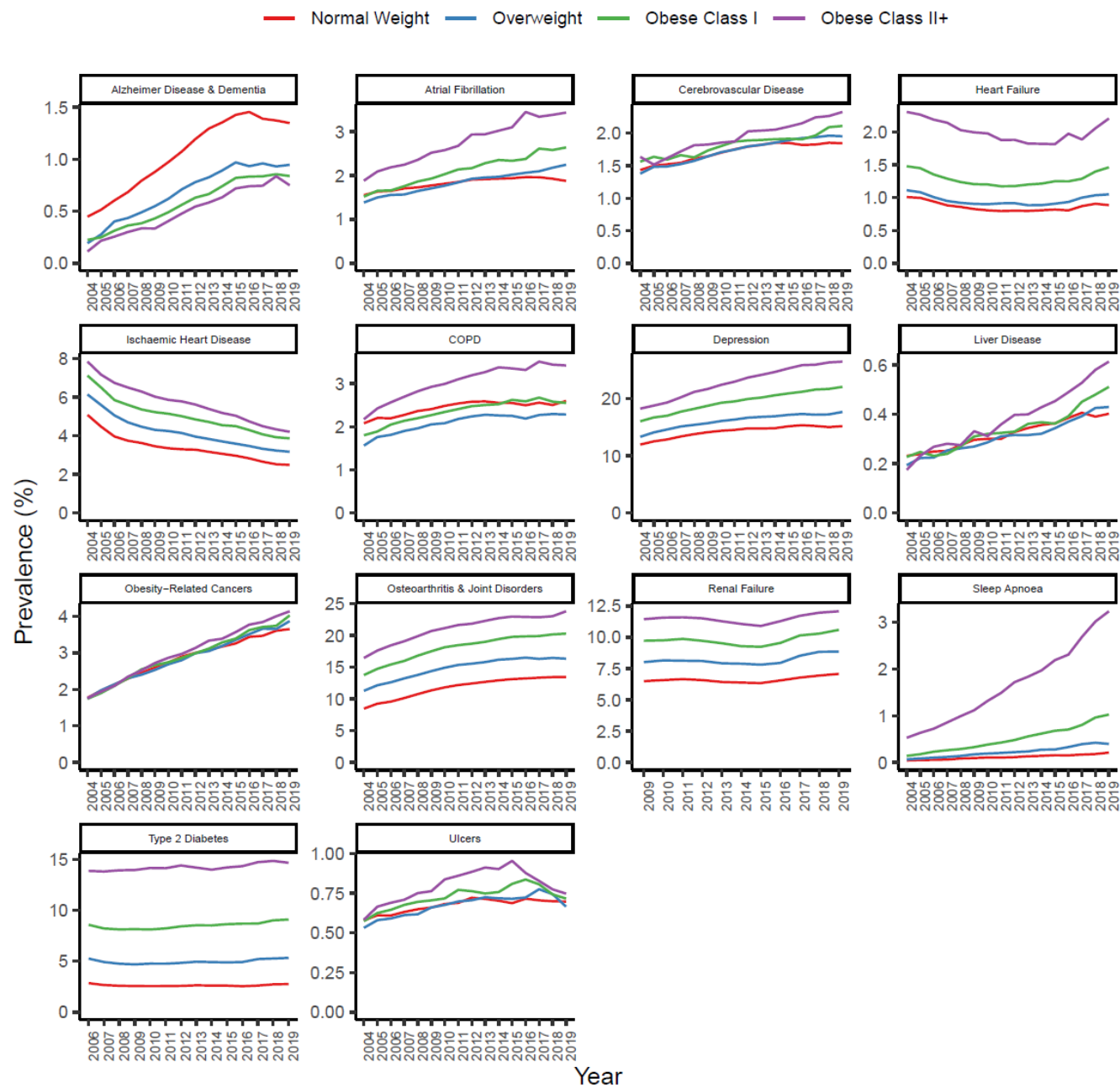


Figure 13. Age-adjusted prevalence (%) between 2004 and 2019 in females

5.3.1.2 Overall magnitude of change for prevalence

Overall, the largest increases in prevalence occurred in Alzheimer's disease and dementia, followed by sleep apnoea, obesity-related cancers, atrial fibrillation, liver disease, depression, and COPD for both males and females. Whilst increases did occur across each BMI category for these conditions, the rate of increase in prevalence of these comorbidities—excluding liver disease and sleep apnoea in males—was greater in the obese class II+ compared to normal weight (Table 18).

5.3.1.3 Magnitude of change for prevalence in males

In males, the prevalence of Alzheimer's disease and dementia increased by 14% per year in the obese class II+ (95% CI: 12.1%, 17.3%) category compared to a 9% increase per year in normal weight (95% CI: 8.6%, 9.9%). Atrial fibrillation prevalence increased by 4.5% (95% CI: 4.0%, 5.1%) in the obese class II+ category, compared to 2.4% (95% CI: 2.0%, 2.8%) per year in the normal weight category. The prevalence of COPD increased 2.5% (95% CI: 2.1%, 3.0%) per year in the obese class II+ compared to 0.4% (95% CI: 0.0%, 0.8%) per year in the normal weight category. This also occurred for depression in males, which increased 3.4% (95% CI: 3.1, 3.8) per year in obese class II+ and 2% in normal weight (95% CI: 1.8%, 2.1%). In obesity-related cancers, the incidence rate amongst the obese class II+ increased by 4.7% per year (95% CI: 4.1%, 5.3%) compared the normal weight category which increased by 2.1% (95% CI: 1.2%, 1.4%). IHD prevalence declined across all BMI categories, but the rate of decline was lower in the obese class II+ category, declining by 2.1% per year (95% CI: -2.2%, -1.9%) compared to a 3.6% (95% CI: -3.7%, -3.4%) decline per year in the normal weight category.

The prevalence trends and magnitudes of change across males were similar for cerebrovascular disease and liver disease. For instance, cerebrovascular disease increased by 1.8% in the normal weight category (95% CI: 1.5%, 2.0%) and 1.9% in the obese class II+ (95% CI: 1.2%, 2.4%).

This also occurred for liver disease which increased by 3.7% (95% CI: 2.4%, 6.4%) per year in obese class II+ and by 2.6% (95% CI: 2.0%, 3.2%) in normal weight. The prevalence of heart failure declined throughout the study period, and declines were <1% per year in both obese class II+ (95% CI: -1.3%, -0.1%) and normal weight (95% CI: -0.7%, -0.2%).

The increase in prevalence of sleep apnoea was greater in normal weight, increasing by 9.9% (95% CI: 9.2%, 11.1%) per year compared to an increase of 8.5% (95% CI: 7.9%, 8.9%) per year in the obese class II+ category. The increase in prevalence in males was also greater for osteoarthritis and joint disorders which increased by 3% (95% CI: 2.9%, 3.2%) in normal weight and by 2% (95% CI: 1.7%, 2.3%) in obese class II+.

5.3.1.4 Magnitude of change for prevalence in females

The prevalence of most comorbidities increased at a greater rate across the obese class II+ compared to the normal weight category in females (Table 18). Alzheimer's and dementia prevalence increased by 12.6% (95% CI: 10.5%, 14.8%) per year in obese class II+ compared to 7.7% (95% CI: 6.7%, 7.8%) per year in normal weight. Liver disease prevalence increased by 8.2% (95% CI: 6.2%, 9.7%) per year in the obese class II+ and 3.7% (95% CI: 3.3%, 4.4%) per year in normal weight. Obesity-related cancers also increased by 5.9% (95% CI: 5.7%, 6.2%) in obese class II+ and by 4.9% (95% CI: 4.7%, 5.3%) in normal weight. The prevalence of atrial fibrillation increased by 3.7% (3.2%, 4.2%) per year in the obese class II+ category, compared to 1.2% (95% CI: 1.0%, 1.3%) per year in the normal weight category.

The rates of increase in prevalence for sleep apnoea were similar between the normal weight and obese class II+, increasing between 11-13% on average per year. Similarly, the rates of increases which occurred for cerebrovascular disease, COPD, and depression were similar in

both obese class II+, increasing between 2.5-3% per year, and in normal weight, increasing by 1.3-1.6% per year. Osteoarthritis and joint pain increased at a greater rate in normal weight than obese class II+, by 3% (95% CI: 2.9%, 3.1%) in normal weight and by 2.2% (95% CI: 2.2%, 2.4%) in obese class II+.

IHD declined throughout the study period, but declines were similar in obese class II+ by 4.1% (-4.4%, -3.9%) and in normal weight by 4.5% (95% CI: -4.9%, -3.7%) per year. Heart failure also declined at a smaller rate, by <1% per year in obese class II+ (95% CI: -0.8%, -0.1%) and normal weight (95% CI: -1.2%, -0.4%).

Table 18. Age-adjusted prevalence (%) of obesity-related morbidities in 2004 and 2019 and average percent change of prevalence rate, by sex

	Normal Weight			Overweight			Obese Class I			Obese Class II+		
	2004 rate	2019 rate	Average % change per year (%)	2004 rate	2019 rate	Average % change per year (%)	2004 rate	2019 rate	Average % change per year (%)	2004 rate	2019 rate	Average % change per year (%)
MALES												
Alzheimer Disease & Dementia	0.32 (0.28, 0.36)	1.2 (1.1, 1.3)	9.2 (8.6, 9.9)	0.21 (0.18, 0.24)	0.87 (0.79, 0.95)	9.5 (8.7, 10.7)	0.18 (0.14, 0.23)	0.73 (0.62, 0.84)	9.2 (7.6, 10.9)	0.086 (0.028, 0.14)	0.69 (0.51, 0.87)	14.4 (12.1, 17.3)
Atrial Fibrillation	2.3 (2.2, 2.4)	3.4 (3.2, 3.6)	2.4 (2, 2.8)	2.3 (2.2, 2.4)	3.7 (3.5, 3.8)	3.1 (2.9, 3.2)	2.6 (2.5, 2.8)	4.5 (4.3, 4.8)	3.6 (3.3, 3.8)	3.5 (3.2, 3.8)	6.5 (6.0, 6.9)	4.5 (4.0, 5.1)
Cerebrovascular Disease	2.2 (2, 2.3)	2.9 (2.7, 3)	1.8 (1.5, 2.0)	2 (1.9, 2.1)	2.6 (2.5, 2.7)	1.6 (1.3, 1.8)	2 (1.9, 2.2)	2.9 (2.7, 3.1)	2.2 (1.9, 2.5)	1.9 (1.7, 2.2)	2.6 (2.3, 2.9)	1.9 (1.2, 2.4)
COPD	3.4 (3.3, 3.6)	3.7 (3.5, 3.9)	0.4 (0.0, 0.8)	2.0 (2.0, 2.1)	2.7 (2.6, 2.8)	1.6 (1.3, 1.8)	2.5 (2.3, 2.6)	3.4 (3.2, 3.6)	2 (1.7, 2.4)	3.1 (2.8, 3.4)	4.5 (4.1, 5.0)	2.5 (2.1, 3.0)
Depression	8 (7.7, 8.3)	10.9 (10.4, 11.3)	1.9 (1.8, 2.1)	6.9 (6.7, 7.2)	10.2 (9.8, 10.5)	2.5 (2.3, 2.8)	8 (7.7, 8.4)	12.7 (12.2, 13.2)	3.1 (3, 3.2)	9.2 (8.6, 9.8)	15.4 (14.6, 16.2)	3.4 (3.1, 3.8)
Heart Failure	1.7 (1.6, 1.8)	1.6 (1.5, 1.8)	-0.5 (-0.7, -0.2)	1.9 (1.8, 2)	1.7 (1.6, 1.8)	-0.5 (-0.8, -0.2)	2.6 (2.4, 2.7)	2.3 (2.1, 2.5)	-0.9 (-1.1, -0.6)	4.1 (3.7, 4.5)	3.5 (3.2, 3.9)	-0.7 (-1.3, -0.1)
Ischaemic Heart Disease	10.0 (9.7, 10.2)	5.8 (5.6, 6.1)	-3.6 (-3.7, -3.4)	11.5 (11.3, 11.7)	6.7 (6.4, 6.9)	-3.5 (-3.6, -3.3)	12.8 (12.5, 13.2)	8.3 (8, 8.7)	-2.8 (-3, -2.6)	12.5 (11.9, 13.1)	9.1 (8.6, 9.7)	-2.1 (-2.2, -1.9)
Liver Disease	0.36 (0.29, 0.42)	0.57 (0.49, 0.66)	2.6 (2.0, 3.2)	0.31 (0.26, 0.35)	0.54 (0.47, 0.61)	4.5 (3.6, 5.1)	0.28 (0.22, 0.33)	0.52 (0.44, 0.61)	3.8 (2.2, 6.3)	0.53 (0.38, 0.67)	0.89 (0.71, 1.06)	3.7 (2.4, 6.4)
Obesity-Related Cancers	0.95 (0.87, 1)	1.3 (1.2, 1.4)	2.1 (1.8, 2.3)	0.68 (0.63, 0.74)	1.3 (1.2, 1.4)	3.9 (3.6, 4.3)	0.56 (0.49, 0.64)	1.4 (1.2, 1.5)	6.1 (5.4, 6.8)	0.59 (0.45, 0.73)	1.2 (1, 1.4)	4.7 (4.1, 5.3)
Osteoarthritis & Joint Disorders	7.4 (7.1, 7.6)	11.5 (11.1, 11.8)	3.0 (2.9, 3.2)	9.5 (9.2, 9.7)	14.9 (14.6, 15.3)	3.0 (2.8, 3.1)	11.3 (11, 11.7)	17.2 (16.7, 17.7)	2.5 (2.3, 2.7)	13.7 (13, 14.3)	18.8 (17.9, 19.6)	2.0 (1.7, 2.3)
Renal Failure*	5.9 (5.8, 6.1)	5.5 (5.3, 5.8)	-0.7 (-1.6, -0.2)	7 (6.9, 7.1)	7 (6.7, 7.2)	-0.2 (-1.1, 0.3)	8.4 (8.2, 8.6)	7.7 (7.3, 8)	-0.8 (-1.9, -0.2)	9.8 (9.4, 10.2)	9.5 (8.9, 10.1)	-0.4 (-1.2, -0.1)
Sleep Apnoea	0.16 (0.12, 0.2)	0.58 (0.5, 0.67)	9.9 (9.2, 11.1)	0.39 (0.34, 0.45)	1.5 (1.4, 1.6)	9.2 (8.9, 9.5)	1.1 (0.96, 1.2)	3.6 (3.4, 3.9)	8.6 (8.2, 8.9)	2.9 (2.6, 3.2)	9.7 (9.1, 10.3)	8.5 (7.9, 8.9)
Type 2 Diabetes^	5.5 (5.4, 5.7)	5.6 (5.4, 5.9)	0.4 (-0.4, 0.9)	8.5 (8.3, 8.6)	8.3 (8.1, 8.5)	0 (-0.6, 0.4)	13.2 (12.9, 13.5)	13.4 (13, 13.9)	0.2 (0, 0.4)	20.7 (20.1, 21.2)	21.2 (20.3, 22)	0.1 (0, 0.3)
Ulcers	1 (0.92, 1.1)	0.98 (0.87, 1.09)	-0.1 (-0.6, 0.2)	0.94 (0.87, 1)	0.93 (0.84, 1.01)	0.6 (0.2, 1)	0.95 (0.84, 1.06)	0.95 (0.83, 1.07)	0.8 (0.2, 1.3)	0.79 (0.63, 0.95)	1 (0.81, 1.2)	0.7 (-0.5, 1.9)
FEMALES												
Alzheimer Disease & Dementia	0.45 (0.41, 0.49)	1.3 (1.3, 1.4)	7.3 (6.7, 7.8)	0.19 (0.16, 0.22)	0.95 (0.86, 1.03)	11.3 (10.2, 12.5)	0.23 (0.18, 0.27)	0.84 (0.73, 0.95)	9.4 (8.6, 10.4)	0.11 (0.064, 0.16)	0.75 (0.6, 0.9)	12.6 (10.5, 14.8)
Atrial Fibrillation	1.6 (1.5, 1.6)	1.9 (1.8, 2)	1.2 (1.0, 1.3)	1.4 (1.3, 1.5)	2.2 (2.1, 2.4)	3.0 (2.7, 3.2)	1.5 (1.4, 1.6)	2.6 (2.4, 2.8)	3.7 (3.2, 4.2)	1.9 (1.7, 2.1)	3.4 (3.1, 3.7)	3.7 (3.2, 4.2)
Cerebrovascular Disease	1.4 (1.4, 1.5)	1.8 (1.7, 2)	1.6 (1.5, 1.8)	1.4 (1.3, 1.5)	2 (1.8, 2.1)	2.4 (2.1, 2.6)	1.6 (1.4, 1.7)	2.1 (1.9, 2.3)	2.0 (1.5, 2.4)	1.6 (1.5, 1.8)	2.3 (2.1, 2.6)	2.7 (2.3, 3.1)
COPD	2.1 (2, 2.2)	2.6 (2.5, 2.7)	1.3 (1, 1.6)	1.6 (1.5, 1.6)	2.3 (2.2, 2.4)	2.3 (1.9, 2.7)	1.8 (1.7, 1.9)	2.6 (2.4, 2.7)	2.5 (2, 2.8)	2.2 (2, 2.4)	3.4 (3.1, 3.7)	3.0 (2.7, 3.2)
Depression	12 (11.7, 12.2)	15.2 (14.8, 15.5)	1.5 (1.3, 1.6)	13.3 (13, 13.7)	17.7 (17.2, 18.1)	1.8 (1.6, 2)	16 (15.5, 16.5)	22.1 (21.4, 22.7)	2.1 (2.1, 2.2)	18.2 (17.7, 18.8)	26.5 (25.7, 27.3)	2.5 (2.4, 2.7)
Heart Failure	1 (0.95, 1.1)	0.89 (0.81, 0.96)	-0.7 (-1.2, -0.4)	1.1 (1, 1.2)	1.1 (1, 1.1)	-0.4 (-0.8, 0)	1.5 (1.4, 1.6)	1.5 (1.3, 1.6)	-0.1 (-0.6, 0.2)	2.3 (2.1, 2.5)	2.2 (2, 2.4)	-0.4 (-0.8, -0.1)
Ischaemic Heart Disease	5.1 (4.9, 5.2)	2.5 (2.4, 2.6)	-4.5 (-4.9, -3.7)	6.1 (6, 6.3)	3.2 (3, 3.3)	-4.3 (-4.4, -4.2)	7.1 (6.9, 7.4)	3.9 (3.6, 4.1)	-4 (-4.1, -3.7)	7.8 (7.5, 8.2)	4.2 (3.9, 4.5)	-4.1 (-4.4, -3.9)
Liver Disease	0.23 (0.19, 0.27)	0.4 (0.35, 0.46)	3.7 (3.3, 4.4)	0.19 (0.16, 0.23)	0.43 (0.37, 0.49)	5.3 (4.8, 5.9)	0.23 (0.18, 0.28)	0.51 (0.42, 0.6)	5.3 (4.5, 6.2)	0.17 (0.12, 0.23)	0.61 (0.49, 0.73)	8.2 (6.2, 9.7)
Obesity-Related Cancers	1.8 (1.7, 1.9)	3.6 (3.5, 3.8)	4.9 (4.7, 5.3)	1.8 (1.7, 1.9)	3.9 (3.7, 4)	5.4 (4.9, 6)	1.7 (1.6, 1.9)	4.0 (3.8, 4.3)	5.8 (5.6, 6)	1.8 (1.6, 1.9)	4.1 (3.8, 4.4)	5.9 (5.7, 6.2)

Osteoarthritis & Joint Disorders	8.5 (8.3, 8.7)	13.5 (13.2, 13.8)	3.0 (2.9, 3.1)	11.3 (11.1, 11.5)	16.4 (16, 16.7)	2.4 (2.2, 2.5)	13.8 (13.4, 14.1)	20.3 (19.8, 20.8)	2.5 (2.3, 2.6)	16.5 (16, 17)	23.8 (23.1, 24.5)	2.2 (2, 2.4)
Renal Failure*	6.5 (6.4, 6.6)	7.1 (6.9, 7.3)	0.7 (0.3, 1.1)	8 (7.9, 8.1)	8.9 (8.6, 9.1)	1 (0.1, 1.5)	9.7 (9.5, 9.9)	10.6 (10.2, 11)	0.8 (0.2, 1.2)	11.4 (11.2, 11.7)	12.1 (11.5, 12.6)	0.5 (-0.1, 0.8)
Sleep Apnoea	0.045 (0.028, 0.061)	0.21 (0.17, 0.25)	10.9 (9.6, 13.0)	0.07 (0.048, 0.091)	0.4 (0.34, 0.46)	12.7 (11.6, 14.2)	0.14 (0.1, 0.18)	1.0 (0.9, 1.2)	14.1 (13.2, 15.2)	0.53 (0.44, 0.62)	3.2 (3, 3.5)	12.7 (11.9, 13.5)
Type 2 Diabetes^	2.8 (2.8, 2.9)	2.8 (2.6, 2.9)	-0.5 (-0.7, -0.1)	5.3 (5.1, 5.4)	5.3 (5.1, 5.5)	0.2 (-0.4, 0.6)	8.6 (8.4, 8.8)	9.1 (8.7, 9.5)	0.4 (0.2, 0.7)	13.9 (13.5, 14.2)	14.7 (14.1, 15.2)	0.4 (0.2, 0.6)
Ulcers	0.6 (0.52, 0.6)	0.7 (0.63, 0.77)	1.1 (0.8, 1.4)	0.53 (0.48, 0.59)	0.67 (0.59, 0.74)	1.5 (0.5, 2.5)	0.57 (0.5, 0.65)	0.72 (0.61, 0.82)	1 (0.2, 1.6)	0.58 (0.49, 0.68)	0.75 (0.62, 0.87)	1.2 (0.6, 1.7)

*Renal failure start of follow up was 2009; ^Type 2 diabetes start of follow up was 2006

5.3.2 Incidence

5.3.2.1 *Incidence difference of comorbidities by BMI level*

The greatest incidence difference among males occurred in type 2 diabetes and sleep apnoea, wherein the incidence rate among the obese class II+ is approximately 8 to 10-fold higher compared to normal weight incidence rates (Figure 14). In males, heart failure has about a 2.5-fold incidence rate in obese class II+ compared to normal weight and the differences are clear in atrial fibrillation and osteoarthritis and joint disorders, with a 2-fold incidence rate in obese class II+ compared to normal weight (Figure 14). When comparing incidence rates across the BMI categories in females, obese class II+ had higher rates than normal weight by about 10-fold higher in type 2 diabetes; about a 4-fold higher rates in sleep apnoea; a nearly 3-fold higher rates in atrial fibrillation; about 2-fold in osteoarthritis and joint disorders and renal failure; and about 1.5-fold for heart failure and depression (Figure 15).

At the beginning of the study, in males, type 2 diabetes had the highest incidence rate the obese categories, but depression was highest in normal weight category and osteoarthritis and joint disorders was the highest in the overweight category. This shifted to osteoarthritis and other joint disorders by 2019, though type 2 diabetes incidence was still highest for males in the obese class II+ category (Table 19, Figure 14). In females in 2004, osteoarthritis and other joint disorders had the highest incidence rates overweight and obese categories, whereas in normal weight the highest incident rates were for depression. By 2019, the incidence rates for osteoarthritis and joint disorders were highest in all BMI categories in females (Table 19, Figure 15).

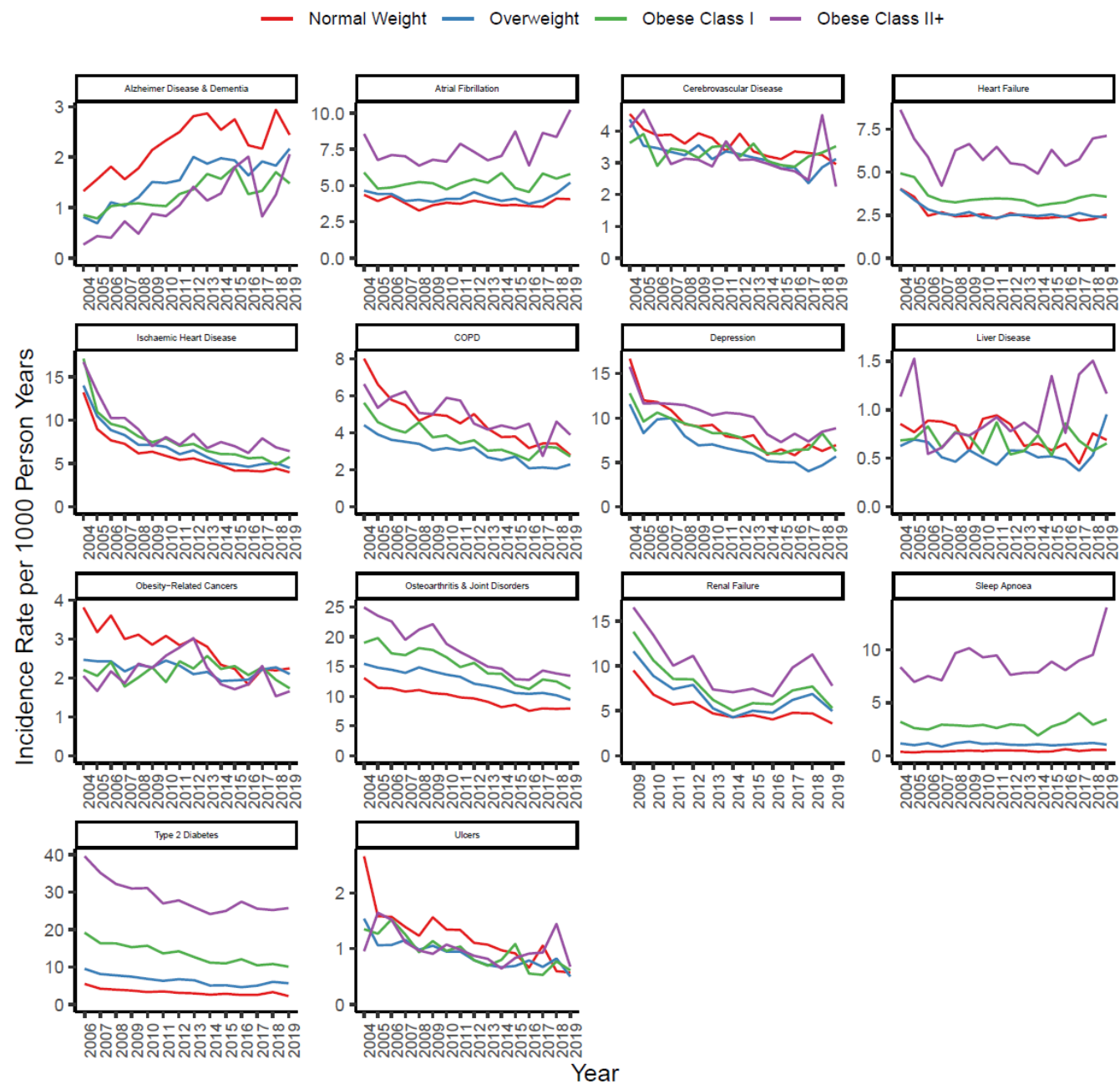


Figure 14. Age-adjusted incidence rates per 1000 person years between 2004 and 2019 in males

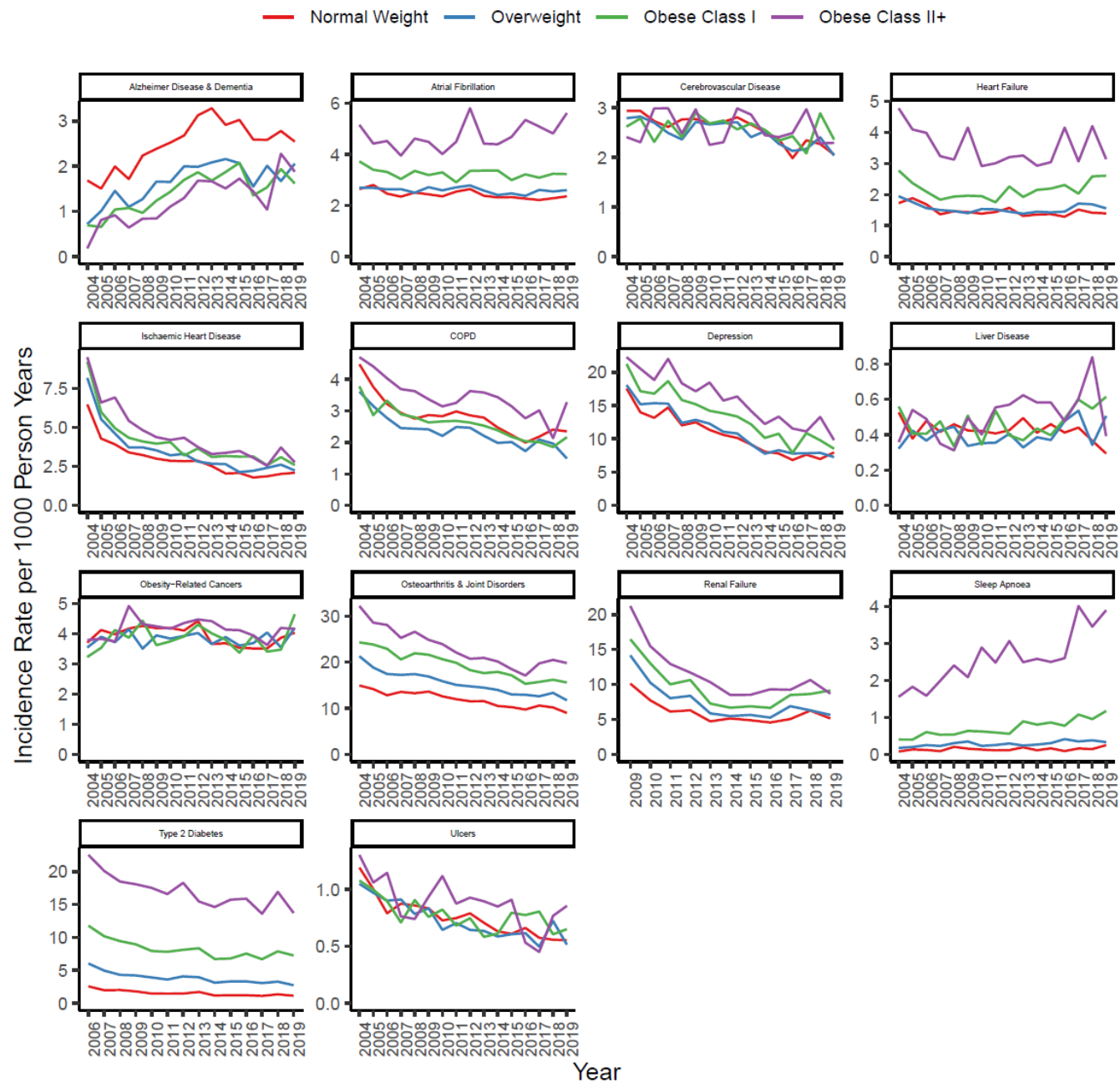


Figure 15. Age-adjusted incidence rates per 1000 person years between 2004 and 2019 in females

5.3.2.2 Magnitude of change for incidence rates in males

In males, incidence rates increased in Alzheimer's and dementia, increasing at a greater rate in obese class II+ by 11.4% (95% CI: 6.5%, 17.8%) per year compared to by 4% (95% CI: 1.7%, 6.0%) per year in normal weight (Table 19). A borderline increase also occurred for sleep apnoea by 4.3% (95% CI: 0.9%, 8.1%) per year in obese class II+ compared to 2.2% (95% CI: 0.0%, 4.3%) per year in the normal weight category. For all other conditions, incidence rates declined in males throughout the study period. The rate of decline in type 2 diabetes was borderline larger in normal weight, declining by 6.1% (95% CI: -7.9%, -3.8%) per year compared to obese class II+ which declined by 2.6% (95% CI: -3.8%, -1.6%) per year.

However, the rates of change were about the same or were not significant across BMI categories for the other comorbidities in males (Table 19). COPD incidence rates declined by 6% (95% CI: -7.0%, -4.2%) per year in normal weight compared to 3.5% (95% CI: -5.6%, -1.6%) per year in obese class II+. IHD declined by 7.9% (95% CI: -8.9%, -6.3%) per year in normal weight and by 5.2% (95% CI: -7.0%, -3.2%) in the obese class II+ category. Incidence rates for osteoarthritis and joint disorders declined by 4.9% (95% CI: -6.2%, -3.8%) per year in obese class II+ and by 3.4% (95% CI: -4.0%, -2.9%) per year in normal weight.

5.3.2.3 Magnitude of change for incidence rates in females

Similarly to males, incidence rates in females increased in Alzheimer's and dementia (Table 19). However, unlike males, there was no difference in the rate of change between normal weight or obese class II+. In the obese II+ category, the incidence rate for Alzheimer's and dementia increased by 8.7% (95% CI: 2.2%, 20.8%) per year compared to a 3.1% (95% CI: 1.6%, 4.3%) increase per year in the normal weight category. Increases also occurred for sleep apnoea, by 3-6% per year in the overweight, obese class I, and obese class II+ categories, but no significant change occurred for the normal weight category.

IHD declined by 8.1% (95% CI: -9.9%, -5.7%) in the normal weight category and by 7.6% (95% CI: -9.1%, -5.7%) per year in the obese class II+ category. Type 2 diabetes declined by 6% (95% CI: -8.4%, -4.0%) per year in normal weight and by 3.1% (95% CI: -4.6%, -1.8%) per year in the obese class II+ category. Atrial fibrillation only declined in the normal weight category, by 1% (95% CI: -1.6%, -0.20%) per year, with no other significant declines.

A summary of these joinpoint trends, indicating whether the prevalence and incidence rates increased, decreased, or had no change on average per year is shown in Table 20.

Table 19. Age-adjusted incidence rates of obesity-related morbidities in 2004 and 2019 per 1000 person years and average percent change of incidence rate, by sex

	Normal Weight			Overweight			Obese Class I			Obese Class II+		
	2004 rate	2019 rate	Average % change per year (%)	2004 rate	2019 rate	Average % change per year (%)	2004 rate	2019 rate	Average % change per year (%)	2004 rate	2019 rate	Average % change per year (%)
MALES												
Alzheimer Disease & Dementia	1.3 (1.1, 1.6)	2.4 (2, 2.9)	4.0 (1.7, 6.0)	0.81 (0.63, 1)	2.17 (1.76, 2.57)	6.2 (4.1, 8.2)	0.85 (0.53, 1.2)	1.48 (0.96, 2)	3.7 (-0.4, 9.4)	0.27 (0.01, 0.53)	2.1 (0.89, 3.2)	11.4 (6.5, 17.8)
Atrial Fibrillation	4.4 (3.8, 4.9)	4.1 (3.4, 4.7)	-0.8 (-2.1, 0.5)	4.6 (4.2, 5.1)	5.2 (4.6, 5.9)	1.2 (-0.9, 2.2)	5.9 (5.1, 6.7)	5.8 (4.8, 6.8)	0.5 (-0.8, 1.6)	8.6 (6.8, 10.4)	10.2 (7.9, 12.5)	1.3 (-0.8, 3.4)
Cerebrovascular Disease	4.5 (4, 5.1)	3.0 (2.4, 3.5)	-2.1 (-3.2, -1.1)	4.4 (3.9, 4.8)	3.1 (2.6, 3.6)	-2.1 (-3.4, -1.1)	3.6 (3, 4.3)	3.5 (2.7, 4.3)	-0.8 (-2.5, 0.8)	4.1 (2.9, 5.3)	2.3 (1.3, 3.2)	-2.1 (-4.4, 0.1)
COPD	8.0 (7.2, 8.8)	2.8 (2.2, 3.4)	-6.0 (-7.0, -4.2)	4.4 (4, 4.9)	2.3 (1.9, 2.7)	-4.4 (-5.4, -3.5)	5.6 (4.8, 6.4)	2.7 (2, 3.4)	-4.3 (-6, -2.8)	6.6 (5.2, 8.1)	3.9 (2.6, 5.2)	-3.5 (-5.6, -1.6)
Depression	16.7 (15, 18.4)	7 (5.7, 8.2)	-4.5 (-7.3, -2.7)	11.5 (10.4, 12.7)	5.7 (4.7, 6.6)	-6.3 (-8, -4.8)	12.8 (11, 14.6)	6.3 (5, 7.6)	-3.3 (-5, -2)	15.8 (12.9, 18.6)	8.8 (6.3, 11.3)	-3.8 (-5.5, -2.4)
Heart Failure	4.0 (3.5, 4.6)	2.5 (2, 3)	-4.0 (-4.9, -2.6)	4 (3.6, 4.5)	2.4 (1.9, 2.8)	-3.1 (-3.8, -2.4)	4.9 (4.2, 5.7)	3.6 (2.8, 4.4)	-2.7 (-3.6, -1.4)	8.6 (6.9, 10.4)	7.1 (5.2, 9)	-2.3 (-4.5, 1.2)
Ischaemic Heart Disease	13.2 (12, 14.4)	4.0 (3.3, 4.7)	-7.9 (-8.9, -6.3)	14 (13, 15)	4.5 (3.9, 5.1)	-7.7 (-8.7, -6)	17.1 (15.4, 18.7)	5.8 (4.7, 6.8)	-7.5 (-8.6, -5.7)	16.7 (14.1, 19.3)	6.4 (4.6, 8.3)	-5.2 (-7.0, -3.2)
Liver Disease	0.85 (0.54, 1.2)	0.69 (0.38, 1)	-2.5 (-5.7, 0.3)	0.63 (0.42, 0.83)	0.95 (0.64, 1.3)	2.4 (-2.7, 4.7)	0.68 (0.38, 0.99)	0.65 (0.34, 0.96)	-0.9 (-4.6, 2.5)	1.1 (0.39, 1.88)	1.2 (0.58, 1.8)	-2.5 (-6, 5.4)
Obesity-Related Cancers	3.8 (3.3, 4.3)	2.2 (1.8, 2.7)	-3.7 (-5.5, -2.2)	2.5 (2.1, 2.8)	2.1 (1.7, 2.5)	-1.4 (-2.6, -0.3)	2.2 (1.7, 2.7)	1.7 (1.2, 2.2)	0.3 (-1.7, 2.3)	2.05 (1.19, 2.91)	1.7 (0.93, 2.4)	-0.9 (-4.1, 2.2)
Osteoarthritis & Joint Disorders	13.1 (11.9, 14.3)	7.9 (6.8, 9.1)	-3.4 (-4.0, -2.9)	15.5 (14.4, 16.5)	9.4 (8.4, 10.4)	-3.2 (-4.4, -2.4)	19 (17.3, 20.8)	11.3 (9.7, 12.9)	-3.8 (-5, -2.8)	24.9 (21.8, 28.1)	13.4 (10.7, 16.1)	-4.9 (-6.2, -3.8)
Renal Failure*	9.5 (8.9, 10.1)	3.6 (2.9, 4.3)	-8.5 (-11.7, -5.3)	11.6 (11.1, 12.1)	5.0 (4.3, 5.7)	-5.7 (-10.7, -2.1)	13.8 (12.9, 14.7)	5.3 (4.3, 6.3)	-6 (-10.6, -2.8)	16.5 (14.8, 18.2)	7.8 (5.9, 9.7)	-4.8 (-11.8, -0.6)
Sleep Apnoea	0.36 (0.16, 0.56)	0.53 (0.26, 0.8)	2.2 (0, 4.3)	1.1 (0.8, 1.5)	1 (0.76, 1.3)	-0.4 (-2.2, 1.3)	3.2 (2.5, 3.9)	3.4 (2.6, 4.2)	0.8 (-1.7, 3.1)	8.4 (6.7, 10.1)	14.0 (11.5, 16.5)	4.3 (0.9, 8.1)
Type 2 Diabetes^	5.5 (4.9, 6)	2.2 (1.7, 2.8)	-6.1 (-7.9, -3.8)	9.5 (9, 10.1)	5.7 (4.9, 6.4)	-3.1 (-5.1, -1.6)	19.1 (17.9, 20.3)	10.1 (8.7, 11.5)	-4.8 (-6.4, -3.5)	39.5 (36.5, 42.6)	25.7 (22, 29.4)	-2.6 (-3.8, -1.6)
Ulcers	2.7 (2.2, 3.2)	0.57 (0.32, 0.83)	-6.7 (-9.7, -4.3)	1.5 (1.2, 1.8)	0.50 (0.30, 0.71)	-5.1 (-7.4, -3.1)	1.4 (1, 1.7)	0.61 (0.29, 0.93)	-5.5 (-8.7, -2.7)	0.96 (0.46, 1.5)	0.68 (0.14, 1.22)	-1.5 (-7, 2.1)
FEMALES												
Alzheimer Disease & Dementia	1.7 (1.4, 1.9)	2.5 (2.1, 3)	3.1 (1.6, 4.3)	0.72 (0.54, 0.9)	2.1 (1.7, 2.5)	4.6 (0.7, 8.5)	0.69 (0.43, 0.96)	1.6 (1.1, 2.1)	6.1 (2.7, 9.6)	0.18 (-0.024, 0.38)	1.9 (1.1, 2.7)	8.7 (2.2, 20.8)
Atrial Fibrillation	2.6 (2.3, 3)	2.4 (1.9, 2.8)	-0.9 (-1.6, -0.2)	2.7 (2.3, 3.1)	2.6 (2.1, 3.1)	-0.5 (-1.1, 0.1)	3.7 (3.1, 4.3)	3.2 (2.5, 4)	-0.4 (-1.3, 0.4)	5.2 (4.2, 6.1)	5.6 (4.3, 6.9)	1.1 (-0.6, 2.7)
Cerebrovascular Disease	2.9 (2.6, 3.3)	2.1 (1.7, 2.4)	-2.2 (-3.8, -1)	2.8 (2.4, 3.2)	2 (1.6, 2.4)	-1.4 (-2.7, -0.3)	2.6 (2.1, 3.1)	2.4 (1.7, 3)	-0.6 (-1.9, 0.6)	2.4 (1.7, 3.1)	2.3 (1.5, 3.1)	-0.5 (-3, 1.8)
COPD	4.5 (4, 5)	2.3 (1.9, 2.8)	-4.6 (-5.7, -2.8)	3.6 (3.2, 4)	1.5 (1.1, 1.8)	-4.3 (-5.7, -2.6)	3.8 (3.2, 4.4)	2.2 (1.6, 2.7)	-3.5 (-4.8, -2.4)	4.7 (3.8, 5.6)	3.3 (2.4, 4.2)	-2.7 (-4.7, -0.9)
Depression	17.6 (16.4, 18.7)	7.9 (7, 8.9)	-6.0 (-7.5, -4.8)	18.1 (16.6, 19.5)	7.3 (6.2, 8.3)	-6.4 (-7.4, -5.5)	21.2 (19.1, 23.4)	8.5 (6.8, 10.2)	-5.6 (-6.8, -4.6)	22.3 (19.7, 24.8)	9.8 (7.8, 11.9)	-4.9 (-6.1, -3.9)
Heart Failure	1.7 (1.45, 2)	1.4 (1.1, 1.7)	-2.3 (-3.9, -0.4)	1.9 (1.6, 2.3)	1.6 (1.2, 1.9)	-1.6 (-2.5, 0)	2.8 (2.2, 3.3)	2.6 (2, 3.3)	-0.9 (-1.9, 0.5)	4.8 (3.8, 5.7)	3.1 (2.2, 4.1)	-1.1 (-5, 1.6)
Ischaemic Heart Disease	6.5 (5.9, 7.1)	2.1 (1.7, 2.5)	-8.1 (-9.9, -5.7)	8.2 (7.5, 8.9)	2.2 (1.8, 2.7)	-8.4 (-9.6, -6.9)	9.2 (8.2, 10.3)	2.6 (1.9, 3.2)	-8 (-9.1, -6.3)	9.5 (8.1, 10.9)	2.8 (1.9, 3.6)	-7.6 (-9.1, -5.7)
Liver Disease	0.53 (0.35, 0.7)	0.29 (0.14, 0.44)	-0.7 (-2.4, 0.9)	0.32 (0.19, 0.45)	0.51 (0.3, 0.71)	0.9 (-1.9, 3.5)	0.56 (0.3, 0.82)	0.61 (0.29, 0.94)	1.2 (-2.8, 5)	0.36 (0.14, 0.58)	0.39 (0.1, 0.68)	3.5 (0.2, 7.1)

Obesity-Related Cancers	3.7 (3.3, 4.2)	4 (3.5, 4.6)	-0.1 (-0.9, 0.7)	3.5 (3.1, 4)	4.2 (3.6, 4.8)	0 (-1.1, 1)	3.2 (2.7, 3.8)	4.7 (3.8, 5.5)	0 (-1.8, 1.7)	3.79 (3, 4.59)	4.2 (3.2, 5.1)	0.8 (-1.6, 2.4)
Osteoarthritis & Joint Disorders	14.9 (13.9, 16)	9 (8, 9.9)	-3.0 (-3.7, -2.4)	21.3 (20, 22.6)	11.7 (10.5, 12.9)	-3.7 (-4.2, -2.9)	24.3 (22.4, 26.2)	15.6 (13.6, 17.6)	-3.2 (-3.8, -2.7)	32.2 (29.4, 35)	19.8 (17.1, 22.5)	-2.6 (-3.9, -1.9)
Renal Failure*	10.1 (9.6, 10.6)	5.1 (4.4, 5.8)	-5.6 (-9.6, -2.6)	14.2 (13.6, 14.8)	5.6 (4.8, 6.4)	-6.9 (-12.2, -3.5)	16.5 (15.5, 17.4)	9.1 (7.8, 10.5)	-5.5 (-8.4, -3.3)	21.2 (19.8, 22.7)	8.7 (6.9, 10.4)	-6.6 (-10.1, -4.4)
Sleep Apnoea	0.1 (0, 0.1)	0.2 (0.1, 0.4)	2 (-3.6, 7.4)	0.2 (0.1, 0.3)	0.3 (0.1, 0.5)	3.1 (0.3, 5.9)	0.4 (0.2, 0.6)	1.2 (0.7, 1.6)	6.3 (4.2, 8.5)	1.6 (1.1, 2)	3.9 (3, 4.8)	4.9 (2.3, 7.5)
Type 2 Diabetes^	2.5 (2.3, 2.8)	1.1 (0.82, 1.4)	-6.0 (-8.4, -4.0)	6 (5.6, 6.4)	2.7 (2.2, 3.2)	-5.3 (-6.3, -4)	11.8 (10.9, 12.6)	7.2 (6.1, 8.4)	-3.8 (-5, -2.3)	22.5 (20.9, 24.1)	13.7 (11.8, 15.6)	-3.1 (-4.6, -1.8)
Ulcers	1.2 (0.94, 1.4)	0.55 (0.35, 0.76)	-4.8 (-6, -3.2)	1 (0.81, 1.3)	0.51 (0.3, 0.72)	-3.5 (-5.2, -2.1)	1.1 (0.74, 1.4)	0.65 (0.33, 0.97)	-2.7 (-5.1, -0.5)	1.3 (0.85, 1.75)	0.85 (0.44, 1.3)	-3 (-5.5, -0.8)

*Renal failure start of follow up was 2009; ^Type 2 diabetes start of follow up was 2006

Table 20. Summary of joinpoint regression results, indicating an increase (↑), decrease (↓), or no change (-) in prevalence or incidence rates on average per year between 2004 and 2019, by sex

	Normal weight		Overweight		Obese class I		Obese class II+	
	Prevalence	Incidence	Prevalence	Incidence	Prevalence	Incidence	Prevalence	Incidence
Males								
Alzheimer Disease & Dementia	↑	↑	↑	↑	↑	-	↑	↑
Atrial Fibrillation	↑	-	↑	-	↑	-	↑	-
Cerebrovascular Disease	↑	↓	↑	↓	↑	-	↑	-
COPD	↑	↓	↑	↓	↑	↓	↑	↓
Depression	↑	↓	↑	↓	↑	↓	↑	↓
Heart Failure	↓	↓	↓	↓	↓	↓	↓	-
Ischaemic Heart Disease	↓	↓	↓	↓	↓	↓	↓	↓
Liver Disease	↑	-	↑	-	↑	-	↑	-
Obesity-Related Cancers	↑	↓	↑	↓	↑	-	↑	-
Osteoarthritis & Joint Disorders	↑	↓	↑	↓	↑	↓	↑	↓
Renal Failure	↓	↓	-	↓	↓	↓	↓	↓
Sleep Apnoea	↑	↑	↑	-	↑	-	↑	↑
Type 2 Diabetes	-	↓	-	↓	↑	↓	↑	↓
Ulcers	-	↓	↑	↓	↑	↓	-	-
Females								
Alzheimer Disease & Dementia	↑	↑	↑	↑	↑	↑	↑	↑
Atrial Fibrillation	↑	↓	↑	-	↑	-	↑	-
Cerebrovascular Disease	↑	↓	↑	↓	↑	-	↑	-
COPD	↑	↓	↑	↓	↑	↓	↑	↓
Depression	↑	↓	↑	↓	↑	↓	↑	↓
Heart Failure	↓	↓	↓	↓	-	-	↓	-
Ischaemic Heart Disease	↓	↓	↓	↓	↓	↓	↓	↓
Liver Disease	↑	-	↑	-	↑	-	↑	↑
Obesity-Related Cancers	↑	-	↑	-	↑	-	↑	-
Osteoarthritis & Joint Disorders	↑	↓	↑	↓	↑	↓	↑	↓
Renal Failure	↑	↓	↑	↓	↑	↓	-	↓
Sleep Apnoea	↑	-	↑	↑	↑	↑	↑	↑
Type 2 Diabetes	↓	↓	-	↓	↑	↓	↑	↓
Ulcers	↑	↓	↑	↓	↑	↓	↑	↓

5.3.3 Age-stratified analyses

In age-stratified analyses, there were instances when the prevalence and incidence rates were <0.0001 per 1000 person years, due too few cases and a smaller sample size, and the joinpoint regression could not run or estimate 95% confidence intervals. As rates were very low, in this section I only present the joinpoint results. This primarily affected the youngest age group (<44 years old).

In both males and females, there were very few differences observed for prevalence or incidence trends were the same when comparing specific age groups to the aggregate results, yet some changes did occur by age group and BMI category.

5.3.3.1 Age-stratified prevalence trends

In males <44, prevalence declined in the obese class II+ category COPD by 6% per year (95% CI: -10.0%, -3.4%) (Table 21). Type 2 diabetes prevalence rates also declined by 1-2% per year in the normal weight (95% CI: -2.7%, -1.8%), overweight (95% CI: -2.6%, -0.2%), and obese class II+ (95% CI: -2.6%, -1.6%) categories, and no change in the obese class I. Prevalence rates increased for heart failure by 4% (95% CI: 2.1%, 6.5%) per year in overweight. In the 45-64 category, type 2 diabetes declined by 1% (95% CI: -1.7, -0.8) in overweight and by 0.7% in obese class II+ (95% CI: -1.0%, -0.8%) (Table 20).

In females <44, type 2 diabetes declined by <1% (95% CI: -1.1%, -0.3%) in obese class II+ (Table 22). In females 45-64, there were no significant changes observed that were not already occurring in the age-adjusted models. In females 65+, declines occurred for renal failure, wherein normal weight prevalence rates declined by 2% (95% CI: -2.9%, -1.2%) per year and overweight and both obese categories declined by <1% per year.

Table 21. Age-stratified rates and average percent change of prevalence rates in males

	Normal weight	Overweight	Obese class I	Obese class II+
	Average % change per year (%)	Average % change per year (%)	Average % change per year (%)	Average % change per year (%)
MALES				
<44				
Alzheimer Disease & Dementia	2 (-4.9, 7.3)	8.5 (0.8, 18.5)	14.8 (6.3, 20.4)	-33.1 (-37.4, -28.3)
Atrial Fibrillation	6.7 (2.1, 11.6)	5.6 (2.3, 9.5)	-0.7 (-4.6, 2.6)	6.7 (2.1, 11.6)
Cerebrovascular Disease	4.9 (3.2, 6.1)	3.8 (2.2, 5.5)	4.1 (2.7, 5.5)	3 (1.7, 4.3)
COPD	3.4 (2.1, 4.8)	3.4 (2, 4.8)	1 (-2.1, 4)	-6 (-10, -3.4)
Depression	1.9 (1.6, 2.2)	1.9 (1.6, 2.2)	1.8 (1.5, 2.2)	2.1 (1.8, 2.4)
Heart Failure	2 (-0.1, 4.7)	4.0 (2.1, 6.5)	-2.8 (-6.4, 0.5)	1.5 (-0.6, 4.7)
Ischaemic Heart Disease	-2.7 (-3.4, -2.1)	-4.3 (-5.2, -3.2)	-5.7 (-6.4, -4.9)	-6.6 (-7.5, -5.5)
Liver Disease	1.1 (-0.2, 2)	2.4 (1.1, 3.7)	4.6 (2.1, 7.2)	2.7 (1, 5.1)
Obesity-Related Cancers	1.1 (-3.2, 5.1)	8.4 (4.6, 10.7)	6.5 (3.3, 9.9)	5 (0.4, 14.9)
Osteoarthritis & Joint Disorders	4.5 (4, 5)	3.7 (3.2, 4.2)	3.2 (2.5, 3.7)	2.1 (1.7, 2.5)
Renal Failure*	3.8 (3, 4.3)	4.6 (3.7, 5.2)	-0.3 (-3.6, 1.4)	5.2 (2.8, 6.3)
Sleep Apnoea	3.5 (-0.2, 8)	-10.4 (-16, -7.4)	3 (1.1, 4.7)	-4 (-6.4, -1.8)
Type 2 Diabetes^	-2.3 (-2.7, -1.8)	-1.2 (-2.6, -0.2)	-0.3 (-1.6, 0.5)	-2 (-2.6, -1.6)
Ulcers	0.4 (-0.5, 1.4)	-2.7 (-3.8, -1.2)	-2.2 (-4.5, -0.6)	-6.2 (-11.2, -3.7)
45-64				
Alzheimer Disease & Dementia	8.9 (6, 12.5)	3.8 (-0.7, 9.1)	4.3 (2.3, 6.3)	9.4 (3.8, 16.6)
Atrial Fibrillation	-3.3 (-6.4, -1.4)	2.5 (-0.2, 4.8)	-1.9 (-4, -0.2)	2.3 (0.4, 3.9)
Cerebrovascular Disease	0.4 (0.1, 0.8)	-0.3 (-0.7, 0.2)	2.3 (1.5, 3)	2.1 (1.4, 2.8)
COPD	-1.4 (-1.9, -1)	0.3 (-1, 1.2)	0.5 (-0.2, 1)	1 (0.2, 1.9)
Depression	1.4 (1.2, 1.6)	2.2 (1.9, 2.5)	3.2 (3, 3.4)	3.9 (3.5, 4.4)
Heart Failure	-1.5 (-1.9, -1)	-2.5 (-3.2, -1.9)	-1.1 (-2, -0.3)	-1.9 (-2.3, -1.5)
Ischaemic Heart Disease	-6 (-6.4, -5.6)	-6.1 (-6.3, -5.8)	-4.4 (-4.8, -4)	-3 (-3.3, -2.7)
Liver Disease	2.5 (1.6, 3.4)	3.6 (2.5, 4.7)	2.8 (0.8, 6.3)	6.7 (4.5, 8)
Obesity-Related Cancers	0.1 (-1, 1.2)	3.2 (2.4, 4)	5.1 (4.5, 5.8)	3.7 (1.6, 6.3)
Osteoarthritis & Joint Disorders	1.6 (1.4, 1.7)	1.9 (1.6, 2.1)	1.5 (1.3, 1.7)	1.8 (1.6, 2)
Renal Failure*	-0.3 (-1.5, 0.6)	-0.5 (-1.4, 0.3)	-0.2 (-1.4, 0.6)	-0.1 (-0.5, 0.2)
Sleep Apnoea	-2.4 (-4.5, -0.8)	1.8 (-1, 3.9)	1.1 (-1.6, 3.8)	2.5 (-0.1, 4.4)
Type 2 Diabetes^	0 (-1, 0.9)	-1.2 (-1.7, -0.8)	-0.7 (-1, -0.4)	-0.1 (-0.4, 0.1)
Ulcers	-1.6 (-2.1, -1.1)	-0.2 (-0.9, 0.5)	-0.4 (-1.1, 0.2)	0 (-1, 0.8)
65+				
Alzheimer Disease & Dementia	9 (8.3, 9.9)	9.4 (8.9, 10)	9.2 (7.4, 11.1)	14.1 (12.4, 16.4)
Atrial Fibrillation	-3 (-5.1, -1.3)	6.4 (4.2, 8.5)	-2.4 (-4.7, -0.7)	7 (5.1, 8.8)
Cerebrovascular Disease	1.7 (1.2, 2)	1.9 (1.6, 2.2)	2.2 (1.7, 2.9)	2.2 (1.4, 2.9)
COPD	0.7 (0.4, 1)	1.7 (1.5, 1.9)	2.5 (2, 3.1)	2.6 (2.1, 3.2)
Depression	2.7 (2.3, 3)	4 (3.7, 4.3)	5.1 (4.6, 5.6)	6.4 (5.3, 7.3)
Heart Failure	-0.7 (-1.1, -0.3)	-0.3 (-0.6, -0.1)	-0.7 (-1.1, -0.4)	-0.7 (-1.2, -0.3)
Ischaemic Heart Disease	-2.7 (-3, -2.6)	-2.7 (-2.8, -2.4)	-2.2 (-2.4, -2)	-1.5 (-1.7, -1.2)
Liver Disease	6.3 (5.3, 7.5)	6.3 (5.7, 7.2)	6.6 (5.1, 8.1)	7 (5, 9.3)
Obesity-Related Cancers	3 (2.5, 3.4)	4.5 (3.9, 5.1)	5.8 (5.1, 6.5)	5.7 (5, 6.5)
Osteoarthritis & Joint Disorders	3.4 (3.2, 3.7)	3.1 (2.9, 3.2)	2.9 (2.7, 3.1)	2.4 (2.1, 2.6)
Renal Failure*	-1.6 (-2.6, -1.2)	-1 (-1.8, -0.5)	-1.2 (-2.1, -0.7)	-1.5 (-2, -1.1)
Sleep Apnoea	-0.9 (-3.7, 1.3)	7.2 (6, 8.7)	1.1 (-1.2, 3.3)	7.2 (5, 9.9)
Type 2 Diabetes^	1.2 (1, 1.5)	0.7 (0.5, 0.9)	0.8 (0.5, 0.9)	0.7 (0.5, 0.8)
Ulcers	0.4 (-0.4, 1)	1.4 (0.9, 1.9)	1 (0.1, 1.9)	1.9 (0.9, 3.1)

*Renal failure start of follow up was 2009; ^Type 2 diabetes start of follow up was 2006

Table 22. Age-stratified rates and average percent change of prevalence rates in females

	Normal weight Average % change per year (%)	Overweight Average % change per year (%)	Obese class I Average % change per year (%)	Obese class II+ Average % change per year (%)
FEMALES				
<44				
Alzheimer Disease & Dementia	3.2 (-6, 12.3)	9.3 (0.4, 19.1)	6.3 (-2.1, 14.7)	14 (3.2, 27.1)
Atrial Fibrillation	6.8 (5.1, 8.6)	10.8 (8.2, 13.6)	1.6 (-1.9, 4.5)	6.4 (2.8, 11.5)
Cerebrovascular Disease	8.4 (6.2, 11.6)	6.4 (5, 8.4)	0.3 (-2.1, 2.6)	4.6 (2.9, 6.4)
COPD	5.6 (3.8, 7.9)	1.9 (-0.5, 3.8)	-0.7 (-5, 3.1)	-0.4 (-2.4, 1.4)
Depression	1 (0.8, 1.3)	1 (0.7, 1.3)	1 (0.9, 1.2)	1.2 (1, 1.4)
Heart Failure	3.6 (-1.9, 9.1)	2.7 (-1, 6.5)	4.2 (-0.5, 9.3)	4 (0.9, 7.1)
Ischaemic Heart Disease	1.3 (-0.6, 2.7)	-0.6 (-2.3, 0.8)	-4.9 (-6.8, -3.2)	-5 (-6.4, -3.6)
Liver Disease	6.2 (4.8, 7.7)	6.7 (3.9, 9.2)	6.5 (3.3, 9.5)	11.3 (8.8, 15.3)
Obesity-Related Cancers	7 (6.4, 7.7)	7.1 (4.7, 9.2)	4 (1.9, 5.9)	3.3 (2, 4.5)
Osteoarthritis & Joint Disorders	4.6 (4.3, 5)	2.6 (2.1, 2.9)	3.2 (2.8, 3.6)	1.3 (0.6, 2)
Renal Failure*	6.2 (5.5, 6.9)	6.5 (6, 7)	6.3 (5.1, 7.1)	5.4 (4.7, 6)
Sleep Apnoea	10.1 (8.6, 11.7)	12.1 (10, 14.4)	12.8 (9, 16.4)	11.8 (10.5, 13)
Type 2 Diabetes^	1.1 (0.1, 1.6)	0.9 (0.2, 1.7)	0.3 (-0.8, 1.3)	-0.7 (-1.1, -0.3)
Ulcers	1 (-0.1, 1.9)	-0.1 (-3.1, 2.4)	-2 (-4.5, -0.1)	2.6 (-1.1, 5.7)
45-64				
Alzheimer Disease & Dementia	3.3 (0.9, 5.6)	5.6 (1.5, 10.7)	7.6 (0.2, 19)	8.4 (5.3, 12.1)
Atrial Fibrillation	-0.9 (-2.1, 0.4)	2 (1.2, 2.8)	2.2 (1.3, 3.1)	2.7 (1.6, 3.5)
Cerebrovascular Disease	0.1 (-0.4, 0.6)	1.5 (1.1, 2)	0.1 (-0.4, 1.1)	2.3 (1.6, 3.3)
COPD	0 (-0.8, 0.6)	0.6 (0.3, 0.9)	0.4 (-0.2, 0.9)	0.7 (-0.3, 1.5)
Depression	2.2 (2, 2.5)	2.5 (2.4, 2.6)	3.1 (2.9, 3.2)	3.9 (3.7, 4.1)
Heart Failure	-0.8 (-1.7, 0.4)	-0.4 (-0.9, 0.1)	0.5 (-1, 1.5)	0.4 (-0.4, 1.3)
Ischaemic Heart Disease	-6.3 (-6.8, -5.5)	-5.9 (-6.8, -5.3)	-5.7 (-6.2, -5.2)	-5.9 (-6.1, -5.6)
Liver Disease	2.9 (2, 3.6)	5.2 (4, 6.7)	4.7 (2.9, 6.6)	3.9 (2.7, 5)
Obesity-Related Cancers	4 (3.8, 4.3)	3.7 (3.3, 4.1)	5.5 (5, 6.1)	4.7 (4, 5.5)
Osteoarthritis & Joint Disorders	1.9 (1.7, 2.1)	1.5 (1.3, 1.7)	1.4 (1.2, 1.7)	1.5 (1.3, 1.7)
Renal Failure*	2.4 (1.8, 2.8)	1.7 (1.1, 2.1)	1.7 (0.9, 2.3)	0.8 (0.4, 1.1)
Sleep Apnoea	7.9 (5.6, 11.3)	11.4 (10.1, 13.5)	12.2 (11.3, 13.7)	11.8 (11.2, 12.6)
Type 2 Diabetes^	0.2 (-0.6, 0.9)	-0.3 (-0.9, 0.2)	0.3 (-0.3, 0.7)	0.2 (-0.1, 0.4)
Ulcers	0.3 (-0.3, 1.2)	0.7 (0.1, 1.1)	-0.2 (-1.4, 0.7)	2.1 (1.5, 2.6)
65+				
Alzheimer Disease & Dementia	6.8 (6, 7.6)	11.2 (10, 12.6)	10.1 (9.4, 11.3)	13.9 (11.4, 17.1)
Atrial Fibrillation	1.2 (1, 1.3)	2.7 (2.4, 3)	3.9 (3.6, 4.3)	4.1 (3.2, 5.1)
Cerebrovascular Disease	1.4 (1, 1.7)	2.1 (1.7, 2.4)	2.5 (2, 2.9)	2.2 (1.8, 2.9)
COPD	1.9 (1.6, 2.2)	2.9 (2.1, 3.4)	3.6 (3, 4.1)	4.2 (3.6, 5.2)
Depression	1.4 (1.2, 1.6)	2.9 (2.4, 3.3)	4.1 (3.8, 4.4)	4.6 (4.1, 4.9)
Heart Failure	-1.3 (-1.9, -1)	-0.8 (-1.4, -0.2)	-0.3 (-0.7, 0)	-0.7 (-1.2, -0.3)
Ischaemic Heart Disease	-4.6 (-5, -4.3)	-4.1 (-4.3, -4)	-3.8 (-4.3, -3.4)	-3.5 (-3.7, -3.3)
Liver Disease	4.6 (4, 5.2)	4.8 (3.9, 5.7)	7.1 (5.5, 8.1)	12.1 (4.5, 19.2)
Obesity-Related Cancers	5 (4.8, 5.3)	6 (5.7, 6.4)	6 (5.7, 6.4)	7.2 (6.8, 7.6)
Osteoarthritis & Joint Disorders	3.3 (3.1, 3.4)	2.7 (2.4, 2.9)	3 (2.8, 3.1)	2.8 (2.6, 2.9)
Renal Failure*	-2 (-2.9, -1.2)	-0.6 (-1.7, -0.1)	-0.7 (-1.6, -0.2)	-0.7 (-1.4, -0.3)
Sleep Apnoea	15.6 (13.8, 18)	14.8 (12.3, 18.7)	16.1 (15, 17.5)	16.3 (14.9, 18.5)
Type 2 Diabetes^	-0.6 (-1, -0.3)	0.2 (-0.1, 0.4)	0.6 (0.3, 0.8)	0.5 (0.2, 0.7)
Ulcers	1.5 (1.2, 1.9)	2.3 (1.8, 2.8)	2.9 (1.6, 4.1)	-0.5 (-1.6, 0.4)

*Renal failure start of follow up was 2009; ^Type 2 diabetes start of follow up was 2006

5.3.3.2 Age-stratified incidence trends

Compared to the age-adjusted model, incidence rates in males <44 showed no differences in trends, but heart failure and renal disease did have differing trends in the older age groups in males (Table 23). For females, the only differences between the age-stratified analysis and age-adjusted analysis occurred in the younger age groups (Table 24).

In males 45-64, cerebrovascular disease declined by 3% in obese class I (95% CI: -4.5%, -0.2%) and heart failure declined by 5% (95% CI: -8.8%, -0.2%) per year in obese class II+. In males 65+ renal failure declined by 5.4% (95% CI: -9.5, -1.1) per year. Heart failure incidence also had a borderline decline in the 65+ age group, by about 3% (95% CI: -4.7%, 0.0%) per year in the obese class II+ category.

In females <44, incidence rates for obesity-related cancers increased in the normal weight category by 3% (95% CI: 0.1%, 5.5%) per year. Also in the <44 age group, renal failure incidence increased in the obese class I category by 7% (95% CI: 2.5%, 10.7%) per year and in the normal weight category by 5% (95% CI: 0.5%, 7.9%) per year. Otherwise, there were no other differences between the age-stratified and non-age stratified models in the 45-64 or 65+ category.

Table 23. Age-stratified rates and average percent change of incidence rates in males

	Normal weight	Overweight	Obese class I	Obese class II+
	Average % change per year (%)	Average % change per year (%)	Average % change per year (%)	Average % change per year (%)
<44				
Alzheimer Disease & Dementia	-11.2 (-22, 0.3)	-3.9 (,) ‡	8.8 (-11, 26.8)	NA†
Atrial Fibrillation	-0.1 (-4.4, 4.2)	-3.2 (-6.7, 1.8)	NA†	NA†
Cerebrovascular Disease	1.6 (-4.9, 6)	-0.6 (-6, 4.8)	-2 (-9.8, 4.7)	-2.3 (-9.6, 4.7)
COPD	-2.2 (-7.1, 2.3)	-0.1 (-5, 4.6)	-4.6 (-11.5, 1.4)	-2.6 (-13.7, 11.1)
Depression	-5.7 (-7.4, -3.6)	-3.5 (-5.7, -2.5)	-3.9 (-5.8, -2.1)	-3 (-6, -0.3)
Heart Failure	-2.4 (-11.4, 6.1)	-2.4 (-9.1, 9.3)	-3.6 (-13.5, 5.1)	4.1 (-4, 13.5)
Ischaemic Heart Disease	-6.4 (-10.4, -2.6)	-8.8 (-10.7, -5.8)	-9.5 (-12.5, -5.1)	-7.7 (-12.3, -3.5)
Liver Disease	-3.9 (-9.7, 1.1)	-1.3 (-10.7, 7.7)	1 (-5.7, 7.8)	-6.9 (-14.1, 1.3)
Obesity-Related Cancers	-1.8 (-9.4, 5.3)	-0.9 (-12.5, 11.4)	0 (-8.8, 8.7)	-2.1 (-14.9, 11.8)
Osteoarthritis & Joint Disorders	-1.8 (-3.9, 0.1)	-1.5 (-4.7, 1)	-3 (-5.1, -1.2)	-4.7 (-8.5, -1.4)
Renal Failure*	4.6 (-0.5, 9.4)	0.6 (-3.5, 4)	-4.6 (-19.4, 4.8)	-1.4 (-19, 13.4)
Sleep Apnoea	4.7 (0.5, 9.2)	-1.2 (-3.8, 1.2)	1 (-2.5, 4.2)	6 (3, 9.1)
Type 2 Diabetes^	-6.2 (-12.8, -0.9)	-3.4 (-6.4, -0.4)	-2.2 (-4.9, -0.7)	-2.2 (-4.8, -0.5)
Ulcers	-6.2 (-12.7, -0.1)	-6.3 (-12.5, -0.8)	-3.7 (-13.8, 6.6)	0.3 (-5.8, 6.9)
45-64				
Alzheimer Disease & Dementia	2 (-3.7, 8)	7.9 (2.9, 13.4)	-0.7 (-9.6, 8.3)	1.3 (-8.7, 12.9)
Atrial Fibrillation	-1.8 (-4.4, 0.5)	-3.1 (-4.3, -1)	-3.1 (-4.2, -1)	-0.7 (-3.2, 1.7)
Cerebrovascular Disease	-4.1 (-7.1, -2.7)	-4.1 (-5.2, -2)	-3 (-4.5, -0.2)	-1.5 (-5.1, 2)
COPD	-6 (-7.9, -4.2)	-6.2 (-7.4, -4.5)	-5.3 (-7.6, -3.2)	-3.9 (-5.9, -2.1)
Depression	-5.4 (-7.8, -3.5)	-6.2 (-8.2, -4.7)	-4.8 (-6.3, -3.5)	-4.5 (-7, -2.4)
Heart Failure	-3.9 (-6.7, -1.1)	-6.9 (-8.9, -4.2)	-4.9 (-8.8, -0.2)	-5.4 (-7.5, -1.7)
Ischaemic Heart Disease	-8.9 (-10.4, -6.5)	-8.5 (-9.9, -6.6)	-7.5 (-8.7, -5.3)	-7.1 (-8.4, -5.2)
Liver Disease	-3.8 (-6.3, -1.5)	-1.3 (-4.2, 1.5)	-2.6 (-6.1, 0.7)	3.6 (-0.6, 8.1)
Obesity-Related Cancers	-6.1 (-9.7, -3.1)	-2.4 (-4.1, -0.9)	0.5 (-2, 2.9)	0.6 (-3.7, 4.9)
Osteoarthritis & Joint Disorders	-4.1 (-5.4, -2.9)	-4 (-5.1, -3)	-4.3 (-5.2, -3.5)	-4.6 (-6.5, -3)
Renal Failure*	-8.3 (-15.4, -3.5)	-6.8 (-10.2, -3.5)	-6.1 (-10.5, -3.1)	-5.5 (-10.5, -1.4)
Sleep Apnoea	6.2 (-4.1, 14.2)	-0.3 (-2.8, 1.9)	0.1 (-2, 2.1)	1.2 (-1.8, 4)
Type 2 Diabetes^	-6.2 (-8.2, -3.8)	-5.8 (-8.7, -3.6)	-5.2 (-6.6, -4.1)	-3 (-4.1, -2.3)
Ulcers	-7.4 (-11, -4.4)	-5.3 (-7.8, -3)	-6.6 (-9.3, -4.4)	-5.4 (-11.7, 0.3)
65+				
Alzheimer Disease & Dementia	3.7 (2, 5.3)	5.9 (3.9, 8)	3.8 (-0.8, 10.1)	10.8 (6.9, 15.8)
Atrial Fibrillation	-0.5 (-1.8, 0.6)	1 (-1.2, 2.1)	0.7 (-0.6, 2)	0.9 (-0.6, 2.4)
Cerebrovascular Disease	-2.2 (-3.7, -1)	-2.6 (-4.1, -1.2)	-1.2 (-2.4, 0)	-3 (-5.5, -0.6)
COPD	-5.2 (-6.4, -4.2)	-4.3 (-5.5, -3.3)	-3.9 (-5.3, -2.6)	-4.1 (-6.4, -2.1)
Depression	-7.1 (-8.2, -6.2)	-5.5 (-8.4, -3.1)	-0.6 (-3.2, 1.8)	-7 (-10.1, -4.4)
Heart Failure	-3.5 (-4.5, -1.8)	-2.9 (-3.6, -1.8)	-2.7 (-3.4, -1.7)	-2.9 (-4.7, 0)
Ischaemic Heart Disease	-7.4 (-8.4, -5.9)	-5.9 (-7.6, -4.7)	-7.5 (-8.6, -5.7)	-5.1 (-7.1, -2.7)
Liver Disease	2.9 (-1, 6.7)	0.8 (-2.9, 4.2)	2.3 (-0.7, 5.4)	4.9 (-3, 13.6)
Obesity-Related Cancers	-2.9 (-4.2, -1.8)	-1.2 (-2.7, 0.1)	0.1 (-2.2, 2.2)	-1.2 (-8.5, 6.9)
Osteoarthritis & Joint Disorders	-3.7 (-4.6, -3)	-2.7 (-3.7, -2.1)	-3.8 (-5.1, -2.6)	-4.9 (-6.6, -3.3)
Renal Failure*	-10.3 (-16.6, -6.7)	-6.5 (-12.2, -2.6)	-6.8 (-10.8, -3.9)	-5.3 (-9.9, -2.1)
Sleep Apnoea	4.9 (0.1, 9.8)	4.2 (0.9, 7.5)	4.3 (1.3, 7.5)	1.7 (-1.7, 5)
Type 2 Diabetes^	-2.7 (-5.5, -1.3)	-5.2 (-6.8, -4)	-5.1 (-6.4, -4.1)	-3.5 (-5.2, -2.1)
Ulcers	-5.9 (-8.2, -3.9)	-5.4 (-7.1, -3.9)	-3.6 (-6.8, -1.1)	-3.5 (-5.2, -2.1)

*Renal failure start of follow up was 2009; ^Type 2 diabetes start of follow up was 2006; †NAs indicate there were not enough incident cases throughout the study period to analyse the trends; ‡Empty confidence intervals (,) indicate there were incidence cases, but not enough to properly estimate confidence intervals

Table 24. Age-stratified rates and average percent change of incidence rates in females

	Normal weight	Overweight	Obese class I	Obese class II+
	Average % change per year (%)	Average % change per year (%)	Average % change per year (%)	Average % change per year (%)
<44				
Alzheimer Disease & Dementia	NA†	NA†	5.7 (-5.3, 17.7)	7.8 (,)‡
Atrial Fibrillation	-33.2 (-77.2, 71.3)	1.2 (-5.8, 7.6)	-49.5 (-81.1, 20.2)	-30.4 (-71, 52.9)
Cerebrovascular Disease	0.3 (-6, 6)	-0.4 (-6.3, 4.9)	-3.2 (-9.8, 4.2)	0.9 (-4.1, 5.9)
COPD	-1 (-5, 2.7)	-1.9 (-7.7, 3.6)	-4.1 (-12, 2.6)	3.2 (-19.7, 22.7)
Depression	-5.3 (-6.7, -4.2)	-6.1 (-7.2, -5.1)	-5.2 (-6.6, -4)	-4.3 (-5.5, -3.3)
Heart Failure	-0.2 (-13.4, 12)	7.2 (-2.7, 18.5)	-5.1 (-15.8, 3.5)	3.5 (-2.8, 9.5)
Ischaemic Heart Disease	-1.7 (-7.4, 3.3)	-8.1 (-11.7, -3.9)	-2 (-7.8, 2.4)	-9.7 (-17.8, -3.5)
Liver Disease	-2.2 (-6.5, 1.8)	1.1 (-7.7, 9.1)	3.4 (-3.4, 10.1)	2.8 (-4.1, 9.6)
Obesity-Related Cancers	2.9 (0.1, 5.5)	2.6 (-0.3, 5.5)	2.8 (-2, 7.5)	2.3 (-1.2, 5.7)
Osteoarthritis & Joint Disorders	-0.2 (-2.3, 1.7)	-1.4 (-2.5, -0.5)	-1 (-2.4, 0.3)	-2.5 (-4.1, -1.1)
Renal Failure*	4.5 (0.5, 7.9)	1.2 (-2.8, 4.6)	7.2 (2.5, 10.7)	1.5 (-8.7, 10.1)
Sleep Apnoea	3.7 (-6.9, 13.7)	2.8 (-3.7, 8.6)	3.9 (-1.8, 9.4)	3.7 (-0.8, 7.6)
Type 2 Diabetes^	0.4 (-5.4, 5.2)	0 (-3, 2.7)	0.7 (-4.3, 3.7)	-1.3 (-2.5, -0.2)
Ulcers	-3.2 (-8.8, 1.7)	-0.1 (-6.3, 6)	-4 (-9.2, 3.8)	-0.3 (-9.8, 9.2)
45-64				
Alzheimer Disease & Dementia	1.4 (-25.2, 20.2)	0.6 (-4.2, 5.3)	4.4 (-3.9, 14)	2.9 (-13.2, 20.1)
Atrial Fibrillation	-3.4 (-8, 0.8)	-1.8 (-5.2, 1.1)	-3.5 (-5.9, -1.3)	-0.6 (-3.1, 1.8)
Cerebrovascular Disease	-0.8 (-3.5, 1.8)	-2.2 (-4.1, -0.5)	-1.6 (-4.9, 1.6)	0.9 (-2.6, 4.3)
COPD	-4 (-5.9, -2.2)	-4.6 (-6.8, -2.6)	-3.4 (-5.7, -1.3)	-3.4 (-5.7, -1.3)
Depression	-6.7 (-8.9, -4.9)	-6.9 (-9.2, -5.1)	-5.6 (-7.2, -4.2)	-6 (-8.1, -4.2)
Heart Failure	-0.7 (-5.7, 4.2)	-5.6 (-7.9, -1.5)	-3.9 (-8.6, 1.8)	-2.5 (-6.7, 1.8)
Ischaemic Heart Disease	-9.5 (-11.1, -6.9)	-7.3 (-11.3, -4.9)	-8.6 (-9.9, -6.7)	-7.3 (-9.9, -4.1)
Liver Disease	-0.1 (-4.1, 3.6)	1.3 (-2.6, 5.1)	0.7 (-3.8, 5)	2 (-3.6, 7.8)
Obesity-Related Cancers	0.5 (-1, 1.6)	-0.3 (-1.3, 0.7)	0.1 (-2.2, 2.2)	0.3 (-1.7, 2.2)
Osteoarthritis & Joint Disorders	-3.3 (-3.9, -2.6)	-4.3 (-4.9, -3.2)	-3.8 (-4.6, -3.1)	-2.8 (-4.4, -1.8)
Renal Failure*	-6.4 (-9.9, -3.6)	-5.7 (-12.1, -1.5)	-4.1 (-9, -1.2)	-6 (-10.7, -2.9)
Sleep Apnoea	-1.0 (-8, 5.5)	1.3 (-4.3, 6.3)	9.2 (0.6, 14)	5.2 (1.8, 8.4)
Type 2 Diabetes^	-5.7 (-10, -2.3)	-5.4 (-6.4, -4)	-3.4 (-5.2, -1.5)	-3.2 (-4.9, -1.8)
Ulcers	-3.9 (-6.7, -1.3)	-5.1 (-8.3, -2.4)	-4.9 (-8.2, -1.9)	-2.1 (-7, 2.4)
65+				
Alzheimer Disease & Dementia	2.1 (0.3, 3.5)	4.1 (-0.3, 8.7)	6.1 (2.9, 9.2)	9.1 (5.3, 14.9)
Atrial Fibrillation	-1.1 (-1.9, -0.5)	-0.4 (-2, 0.5)	-0.4 (-1.2, 0.4)	0.9 (-0.9, 2.5)
Cerebrovascular Disease	-3.1 (-4.1, -2.3)	-1.9 (-4.4, -0.2)	0.8 (-3.1, 3.2)	-1.3 (-4.4, 1.6)
COPD	-4.2 (-5.2, -2.8)	-4.1 (-5.1, -2.7)	-3.7 (-5, -2.6)	-2.6 (-5.7, -0.3)
Depression	-7.8 (-9.5, -6.4)	-6.9 (-9.2, -5)	-7.1 (-10.4, -4.5)	-6.9 (-11.3, -3.4)
Heart Failure	-2 (-3.3, -0.8)	-0.1 (-2.6, 1.2)	-0.6 (-1.9, 1.4)	-2 (-4, 0.1)
Ischaemic Heart Disease	-7.9 (-10.5, -5.7)	-8.7 (-10, -6.7)	-8 (-9.4, -6.1)	-7.7 (-11.4, -5.3)
Liver Disease	0 (-3.2, 3)	-0.2 (-2.2, 1.8)	2.3 (-2.6, 7.3)	-1.2 (-7.8, 3.6)
Obesity-Related Cancers	-0.7 (-1.4, 0.1)	-0.4 (-1.8, 0.9)	-0.7 (-2.7, 1)	-1.5 (-3.9, 0.6)
Osteoarthritis & Joint Disorders	-3.8 (-4.8, -2.9)	-4 (-4.7, -3.4)	-4.1 (-4.8, -3.4)	-3.1 (-5.7, -1.8)
Renal Failure*	-8.6 (-12.4, -6)	-9.2 (-14.9, -5.7)	-8 (-10.9, -5.9)	-8.9 (-13.9, -5.8)
Sleep Apnoea	282.5 (75.5, 531.3)	303.9 (95, 570.2)	7.1 (2.7, 11.2)	6.3 (2.6, 10)
Type 2 Diabetes^	-7.1 (-9.7, -5)	-6.3 (-8.1, -4.2)	-5.3 (-7.4, -3.5)	-4.5 (-8.1, -2)
Ulcers	-4.7 (-6.5, -3.2)	-3.1 (-5.9, -1.2)	-2.2 (-4.3, -0.1)	-4.5 (-9.5, 0)

*Renal failure start of follow up was 2009; ^Type 2 diabetes start of follow up was 2006; †NAs indicate there were not enough incident cases throughout the study period to analyse the trends; ‡Empty confidence intervals (,) indicate there were incidence cases, but not enough to properly estimate confidence intervals

5.3.4 Evaluating potential for reverse causality

After excluding individuals with less than five years follow up, the incidence rates were numerically lower over the study period, but the trends did not represent significant reductions (Table 25). The increase in Alzheimer's and dementia previously observed remained for each BMI category (with the exception of obese class II+ in males, which was not significant), but there was no difference in the magnitude of change between BMI categories. In males, COPD increased by 3.7% (95% CI: 0.4%, 6.2%) per year in normal weight, liver disease increased by 4.2% (95% CI: 0.9%, 7.3%) per year in overweight, and heart failure increased by 2.7% (95% CI: 0.4%, 4.7%) per year in obese class I.

In females, obesity-related cancers increased in the overweight category by 6.1% (95% CI: 2.6%, 9.4%) per year only (Table 25). Increases also occurred for cerebrovascular disease by 3.7% (95% CI: 1.0, 6.4%) per year, liver disease by 7.9% (95% CI: 1.9%, 14.0%) per year, and by 2.8% (95% CI: 0.6%, 4.8%) per year in the normal weight category.

Table 25. Sensitivity analysis using a five-year exclusion period for obesity-related morbidities in 2004 and 2019 per 1000 person years and average percent change of incidence rate, by sex

	Normal Weight			Overweight			Obese Class I			Obese Class II+		
	2009 rate	2019 rate	Average % change per year (%)	2009 rate	2019 rate	Average % change per year (%)	2009 rate	2019 rate	Average % change per year (%)	2009 rate	2019 rate	Average % change per year (%)
MALES												
Alzheimer Disease & Dementia	2.1 (1.6, 2.6)	4.4 (3.4, 5.5)	7.5 (4.3, 10.7)	1.8 (1.4, 2.2)	4.3 (3.5, 5.2)	8.6 (6.0, 11.5)	2.3 (1.4, 3.1)	6 (4.3, 7.7)	9.1 (1.0, 18.5)	1.5 (0.03, 3)	4.5 (1.9, 7)	9.2 (-1.2, 20.7)
Atrial Fibrillation	2.9 (2.3, 3.5)	6.5 (5.2, 7.8)	5.9 (2.2, 8.4)	4.2 (3.6, 4.8)	9.2 (8, 10.5)	5.6 (-0.2, 9.7)	5.4 (4.3, 6.4)	12.2 (9.9, 14.5)	6.7 (-5, 15.1)	7.2 (4.7, 9.6)	21.1 (15.7, 26.6)	7.4 (4.1, 10.6)
Cerebrovascular Disease	3.2 (2.5, 3.8)	4 (3, 5.1)	3.2 (-0.5, 5.8)	2.8 (2.3, 3.3)	5.7 (4.7, 6.6)	3.7 (-0.7, 6.9)	4.1 (3.2, 5)	5.7 (4.2, 7.1)	2.4 (-2.5, 5.4)	2.4 (1.4, 3.4)	5.3 (3.2, 7.4)	9.3 (-1.9, 18.7)
COPD	2.1 (1.6, 2.7)	3.4 (2.5, 4.3)	3.7 (0.4, 6.2)	2.1 (1.7, 2.4)	3 (2.4, 3.6)	-0.2 (-11.7, 7.6)	2.8 (2.1, 3.5)	4.1 (2.9, 5.3)	0.9 (-3.7, 5)	4.1 (2.4, 5.9)	6.4 (3.6, 9.1)	-0.7 (-11.8, 9.7)
Depression	3.1 (2.3, 4)	5.7 (4.4, 7)	0 (-4.6, 4)	3.3 (2.7, 4)	3.4 (2.7, 4.2)	-0.5 (-5.8, 2.6)	3.3 (2.5, 4.2)	5 (3.7, 6.3)	2.3 (-0.6, 4.9)	4.4 (2.8, 6.1)	5.7 (3.4, 8)	-1.1 (-9.4, 4.1)
Heart Failure	1.9 (1.4, 2.4)	3.3 (2.4, 4.2)	4.7 (-3.9, 9.6)	3.2 (2.6, 3.7)	4.6 (3.7, 5.5)	3.3 (-0.5, 6.2)	5.6 (4.5, 6.8)	8.7 (6.7, 10.6)	2.7 (0.4, 4.7)	6.1 (3.8, 8.4)	14.1 (9.4, 18.7)	4.4 (-3.8, 12.3)
Ischaemic Heart Disease	4.4 (3.6, 5.3)	4.9 (3.8, 6.1)	0.5 (-6.6, 4.9)	5.2 (4.5, 6)	6.9 (5.8, 8)	1.1 (-2.4, 4)	6.6 (5.3, 7.9)	8.4 (6.6, 10.1)	0.3 (-3.6, 3.6)	5.8 (3.9, 7.6)	13.5 (9.2, 17.9)	1.3 (-3.5, 5.8)
Liver Disease	0.23 (0.047, 0.42)	0.8 (0.4, 1.2)	0.2 (-6.8, 6.3)	0.42 (0.24, 0.59)	0.63 (0.35, 0.92)	4.2 (0.9, 7.3)	0.43 (0.15, 0.72)	0.79 (0.38, 1.2)	4.1 (-7.2, 14.2)	0.56 (0.14, 0.97)	1.5 (0.6, 2.3)	4.4 (-0.7, 9.8)
Obesity-Related Cancers	1.8 (1.3, 2.2)	2.3 (1.6, 3.1)	1 (-1.3, 3.2)	1.9 (1.5, 2.2)	3.2 (2.5, 3.8)	2.3 (-1.4, 5.6)	3.1 (2.3, 3.9)	3.2 (2.2, 4.1)	2.9 (-3, 7)	4 (2.4, 5.7)	5.2 (3.1, 7.2)	0.5 (-9.5, 9.8)
Osteoarthritis & Joint Disorders	6.6 (5.5, 7.7)	10.2 (8.4, 12)	2.3 (-2.8, 5.4)	9.3 (8.3, 10.3)	12.8 (11.2, 14.3)	2.1 (-1.6, 4.7)	13.1 (11.3, 14.9)	13.2 (10.9, 15.5)	-0.8 (-8.9, 5.2)	15 (11.6, 18.4)	20.5 (15.6, 25.5)	1.1 (-4, 5.7)
Renal Failure	7.1 (6.1, 8.2)	5.8 (4.4, 7.2)	-3.4 (-8.9, 1.1)	12.1 (10.9, 13.2)	9.7 (8.2, 11.2)	-2.1 (-6.6, 2.4)	16.2 (13.9, 18.4)	8.3 (6.5, 10.2)	-5 (-9.5, -1.2)	23.1 (18.3, 28)	9.6 (6.4, 12.7)	-6.4 (-11.4, -2.1)
Sleep Apnoea	0.36 (0.14, 0.59)	0.56 (0.23, 0.9)	5.6 (-2.2, 13.4)	0.63 (0.39, 0.87)	1.3 (0.9, 1.6)	1.6 (-4.8, 7.4)	2.2 (1.5, 2.9)	2.8 (2, 3.7)	2.3 (-2.1, 6.5)	4.9 (3.3, 6.5)	8.4 (6.1, 10.7)	2.0 (-4.5, 8.1)
Type 2 Diabetes	1.3 (0.9, 1.8)	2.4 (1.6, 3.2)	5.4 (-4, 11.6)	4.3 (3.6, 4.9)	5.9 (5, 6.8)	1.2 (-5.6, 5.5)	10.2 (8.6, 11.9)	11 (9.1, 12.9)	-0.2 (-4, 3.2)	19.5 (15.4, 23.6)	24.5 (19.4, 29.6)	1.1 (-2.9, 4.3)
Ulcers	0.8 (0.48, 1.1)	0.47 (0.16, 0.77)	-9.5 (-23.9, 4.1)	0.88 (0.61, 1.2)	0.79 (0.46, 1.1)	-1 (-8, 5.1)	0.78 (0.41, 1.2)	1.2 (0.58, 1.9)	-0.5 (-11.1, 9.4)	3.1 (1.5, 4.7)	1.4 (0.17, 2.6)	-1.9 (-12.9, 9.3)
FEMALES												
Alzheimer Disease & Dementia	2.1 (1.7, 2.5)	4.7 (3.8, 5.6)	5.8 (0.6, 10.4)	1.8 (1.4, 2.2)	4.5 (3.7, 5.4)	7.9 (4.0, 12.7)	1.5 (1.0, 2.0)	4.2 (3, 5.4)	5.3 (0.6, 9.7)	1.4 (0.63, 2.1)	4.3 (2.5, 6.2)	12.6 (4.1, 20.8)
Atrial Fibrillation	2 (1.6, 2.4)	3.6 (2.9, 4.4)	5.6 (3.3, 7.8)	2.6 (2.2, 3.1)	5 (4.1, 6)	5.2 (2, 7.6)	3.5 (2.7, 4.3)	5.2 (3.9, 6.4)	4.3 (-0.5, 8.4)	7 (5.4, 8.6)	12.5 (9.6, 15.5)	4.3 (-0.2, 8.6)
Cerebrovascular Disease	2 (1.6, 2.3)	3.3 (2.6, 4)	3.7 (1, 6.4)	2.2 (1.8, 2.6)	3.4 (2.6, 4.1)	2.6 (-7.2, 8.2)	2.9 (2.2, 3.6)	3.6 (2.6, 4.7)	0.4 (-3.2, 4.3)	4.5 (3.3, 5.8)	6.9 (4.7, 9.2)	3.4 (-2, 8.5)
COPD	1.8 (1.4, 2.2)	2.9 (2.3, 3.6)	2.4 (-1.1, 6.7)	1.4 (1.1, 1.7)	2 (1.5, 2.5)	3.1 (-6.1, 9.6)	1.7 (1.2, 2.2)	2 (1.3, 2.8)	0.8 (-5, 5.9)	2.9 (2, 3.7)	4.7 (3.2, 6.2)	-1 (-7.5, 4.6)
Depression	6.2 (5.3, 7)	5.4 (4.5, 6.3)	-2.4 (-5.1, -0.5)	6.7 (5.7, 7.7)	5.6 (4.5, 6.7)	-2.6 (-6.1, -0.6)	5.3 (4.2, 6.5)	6.5 (4.8, 8.1)	-4 (-8.8, 0.1)	9.1 (7.3, 10.9)	6.8 (4.7, 8.8)	-3.2 (-6.2, -0.7)
Heart Failure	1.2 (0.88, 1.5)	1.7 (1.2, 2.2)	4.3 (-4.5, 10.6)	1.6 (1.2, 1.9)	3.3 (2.5, 4)	3.9 (-1.2, 8.5)	2.3 (1.7, 3)	5 (3.8, 6.3)	3.6 (-0.4, 7.2)	5.7 (4.1, 7.3)	6.7 (4.6, 8.8)	4 (-3.4, 11.2)

Ischaemic Heart Disease	2 (1.6, 2.4)	3.1 (2.4, 3.8)	1.3 (-6.8, 6.3)	3 (2.4, 3.5)	3.2 (2.5, 3.9)	-1 (-5, 2.5)	3.8 (3, 4.7)	3.6 (2.7, 4.6)	-1.7 (-5.9, 2)	5 (3.7, 6.3)	5.7 (3.9, 7.4)	0.8 (-2.7, 3.8)
Liver Disease	0.16 (0.056, 0.27)	0.35 (0.14, 0.56)	7.9 (1.9, 14)	0.34 (0.17, 0.51)	0.63 (0.35, 0.9)	4.2 (-0.8, 9.1)	0.52 (0.26, 0.78)	0.62 (0.24, 1)	2.3 (-3.3, 8.2)	0.47 (0.0095, 0.94)	0.4 (0.05, 0.76)	3.6 (-12.2, 19.4)
Obesity-Related Cancers	2.32 (1.9, 2.7)	5.1 (4.2, 5.9)	4.9 (-3.4, 10.5)	2.6 (2.2, 3)	5.3 (4.5, 6.2)	6.1 (2.6, 9.4)	2.4 (1.8, 3)	6.2 (4.9, 7.4)	2.9 (-1.7, 7)	3.7 (2.7, 4.8)	6.5 (5, 8.1)	2.4 (-4.3, 8.8)
Osteoarthritis & Joint Disorders	9.3 (8.3, 10.4)	12.7 (11.1, 14.3)	2.8 (0.6, 4.8)	11.8 (10.6, 13)	14.6 (12.8, 16.4)	2.1 (-0.1, 3.8)	14 (12.1, 15.8)	18.8 (15.8, 21.8)	1.8 (-5, 5.7)	22 (19.1, 25)	25.7 (21.6, 29.9)	1.8 (-1.7, 3.9)
Renal Failure	7.4 (6.6, 8.3)	6.8 (5.7, 7.9)	-0.6 (-7.4, 2.7)	11.4 (10.3, 12.4)	10 (8.5, 11.5)	-1.7 (-8.3, 1.6)	14.7 (12.9, 16.6)	10.6 (8.5, 12.6)	-5.6 (-10, -1.9)	21.4 (18.3, 24.5)	13.7 (10.4, 17)	-4.7 (-8, -1.8)
Sleep Apnoea	0.18 (0.06, 0.29)	0.26 (0.09, 0.42)	1.2 (-7.5, 9.5)	0.28 (0.12, 0.43)	0.26 (0.09, 0.42)	5.3 (1, 9.8)	0.33 (0.13, 0.54)	1.3 (0.7, 1.8)	8.7 (4.8, 12.8)	1.4 (0.8, 1.9)	3.5 (2.4, 4.5)	3.9 (-4.2, 12)
Type 2 Diabetes	1.1 (0.79, 1.4)	0.93 (0.59, 1.3)	1.3 (-5.8, 7.2)	2.8 (2.3, 3.3)	3.5 (2.8, 4.2)	1.2 (-5.8, 6.8)	5.8 (4.7, 6.8)	7.9 (6.4, 9.4)	2.7 (-0.6, 5.6)	10.9 (9, 12.7)	13.6 (11, 16.1)	2.5 (-5.6, 7.6)
Ulcers	0.48 (0.29, 0.66)	0.49 (0.24, 0.74)	0.2 (-4.2, 4)	0.68 (0.46, 0.89)	0.71 (0.4, 1)	0.8 (-3.4, 4.5)	0.57 (0.28, 0.85)	0.65 (0.25, 1)	1.3 (-7.2, 8.8)	0.94 (0.36, 1.5)	1.3 (0.64, 2)	-2.3 (-5.9, 0.6)

5.4 Discussion

5.4.1 Summary of findings

In this chapter, I found four main findings: 1) the prevalence of certain conditions—notably type 2 diabetes, heart failure, depression, osteoarthritis and renal failure—were more strongly associated with a higher BMI level; 2) the prevalence difference for two conditions—COPD and liver disease—in particular was increasing; 3) differences across BMI categories were less pronounced when assessing incidence rates compared to prevalence; and 4) there was no differentiation between obesity-related cancer for prevalence or incidence across the BMI categories.

Type 2 diabetes had the strongest association to a higher BMI level with a 5-fold prevalence difference in the obese class II+ compared to normal weight in males and females. There was also a greater prevalence difference between normal weight and obese class II+ for renal failure, depression, heart failure, and osteoarthritis and joint disorders than for other conditions. For COPD and liver disease – the prevalence difference increased, from relatively similar levels across BMI groups at baseline to 1.2-1.5-fold difference at the end of the period.

These differences in prevalence between obese class II+ and normal weight were less pronounced for incidence rates, but were still observed for heart failure, osteoarthritis, renal failure, and type 2 diabetes in males and females. Some similarities to prevalence include the incidence rates of type 2 diabetes having the largest association to a higher BMI level. The prevalence and incidence rates for Alzheimer's and dementia to be greater in normal weight than obese class II+.

At the beginning of the study, we found IHD was the most prevalent condition in normal weight and overweight categories in males only, and due to the declines in IHD prevalence in both

males and females in all BMI categories, this shifted musculoskeletal and depression to the become the most prevalent condition in males and females. Overall, the rate of increase in prevalence was greatest in obese class II+ compared to normal weight.

When considering incidence, despite a 3% decline per year in the obese class II+ category, type 2 diabetes had the largest incidence rates in males throughout the study period. Otherwise, in 2004 and 2019 the largest incidence rates across the BMI categories occurred for osteoarthritis and joint disorders. Whilst incidence rates declined for the majority of conditions, there was very little difference between the rate of decline in the obese class II+ category compared to normal weight category for males and females. In males there was a borderline greater rate of decline in type 2 diabetes incidence in normal weight compared to obese class II+. Finally, both males and females had increases in Alzheimer's and dementia incidence, which was the only increasing incident condition. In males, the rate of increase was greater in the obese class II+ than normal weight, which was not observed for females.

5.4.2 Interpretation of findings

The association between type 2 diabetes, heart failure, renal failure, depression, and osteoarthritis and BMI are well known, with obese males having twice the risk of heart failure compared to normal weight (179). Those with obese class II+ had three times the risk of advanced chronic kidney disease, and there is a positive association between obesity and increased depression risk (180, 181). Obese class II+ individuals also had an increased risk of hip, knee, and hand osteoarthritis, with the risk of knee osteoarthritis five times higher in obese class II+ compared to normal weight (182). And finally, in England, the risk of diabetes is five times higher among obese individuals compared to normal weight (84).

However, there was little difference in the association of cerebrovascular morbidity across the BMI categories, which was unexpected. Literature states there is an increased risk of stroke as BMI increases, but there is also evidence that risk can vary depending on the type of stroke (ischemic or haemorrhagic) (183-186). For instance in a study including both males and females, overweight and obesity are shown to increase the risk of ischaemic stroke (185). This is also confirmed in a systematic review and meta-analysis showing overweight and obese males have a higher risk of ischaemic stroke than females and ischaemic strokes are more highly associated with obesity than haemorrhagic stroke (183). However, the risk of haemorrhagic stroke is still prominent, with a study of US males showed with each 1 kg/m² increase in BMI, both ischaemic and haemorrhagic stroke risk increased 6% (184); and a study in Korean males showed a 11% and 6% increased risk for ischaemic and haemorrhagic stroke risk, respectively, with each 1 kg/m² increase in BMI (187). However, whilst the ischaemic stroke risk is also associated with obesity in females, in the Million Women Study, for every 5 kg/m² increase in BMI ischemic stroke risk increases 21% and haemorrhagic stroke risk declined by 12% (188). Not having separated ischaemic stroke and haemorrhagic stroke could explain why I did not observe any difference in cerebrovascular disease prevalence or incidence by BMI in my results.

A study utilising 39 cohort studies found that survival bias may underestimate the association between Alzheimer's and dementia and BMI as those who were obese were less likely to live long enough to develop neurological conditions compared to normal weight individuals (189). In my results I observed a nearly three times greater increase in incidence rates per year in the obese class II+ category compared to the normal weight category, suggesting those who were originally at risk of CVD mortality, for instance, are living longer and developing long-term chronic conditions such as Alzheimer's and dementia. However, whether this is due to true

increases, or because of changes in how causes of death are coded is unclear (176, 177). Another consideration is when a BMI exposure is defined and an incident neurological outcome occurs. Excess adiposity is a consistent exposure, with the potential to cause vascular and non-vascular problems, which may contribute to neurological degeneration as early as midlife (190, 191). This is further investigated in the context of an individual's BMI trends in mid- to late-life and their risk of dementia later in life. Specifically, an increase in BMI in early mid-life, followed by a decline in BMI in late-life is associated with an increase in dementia risk, as found in the Framingham Offspring Study among others (190-192). This gives rise to the potential of reverse causality, where the impact of excess adiposity on neurological health occurs years before a diagnosis of Alzheimer's disease or dementia (193).

After having applied a 5-year exclusion period for the incidence of obesity-related morbidities I did observe a greater incidence in Alzheimer's and dementia compared to no exclusion period. However based on the literature, using a 5-year exclusion may not be long enough to properly correct for reverse causality and the impact of obesity on Alzheimer's and dementia risk, indicating a need for a more in depth study investigating BMI trajectory and Alzheimer's and dementia.

This Chapter's findings are consistent with other literature, as the prevalence of people living with disease is expected to increase by 37% between 2019 and 2040, with diabetes, depression, and chronic pain as the main contributors to this increase (194). Overall, morbidity prevalence rates are increasing, and incidence rates are declining, with exceptions. There are many factors which contribute to the increasing prevalence rates (declining mortality rates) and declining incidence rates (improved prevention strategies) (195).

For a 5 kg/m² increase in BMI, studies found a 23-29% increased risk of IHD, yet IHD prevalence consistently declined in all BMIs and both genders in my analysis (196, 197). One study using hospital admission data in the UK found a slight decline in IHD prevalence in England from 2003 to 2013 and between 2019 and 2040 is expected to decline (132, 194). A study using HSE data from 2017 found that the prevalence of IHD fell in males and females between 1998 and 2011, but rates did not change from 2011 to 2017 (198). There is no clear explanation for the decrease in IHD prevalence, but one study does indicate because of incidence declines and improved case fatality, there is a potential that the incidence declines have offset the increase in prevalence (132).

The increasing prevalence of osteoarthritis and joint disorders is consistent with other CPRD data, in which a 1.5% increase per year in prevalence and a 1.6% decline in incidence per year occurred among English adults in the general population between 1998 and 2017 (199). Another finding in this Chapter was that osteoarthritis and depression had similar prevalence rates by the end of the study, which is consistent with the prevalence rates in England, showing people with musculoskeletal conditions have almost a two times higher risk of depression or anxiety (139). This was most prominent in females and the obese class II+, which had the highest prevalence rates, but was still observed for males and the other BMI categories.

Finally, one study, using HSE data between 2003 and 2018 found prevalence trends similar to my results, wherein there was no change in prevalence of type 2 diabetes for males and females in the normal weight category, but the prevalence increased in males and females in the overweight and obese categories (195). There is a slight difference between my findings and the HSE study as I did not observe a change in prevalence for females in the overweight category or for males in the obese class II+ category.

5.4.3 Strengths and limitations

The primary strength of this aim is being able to utilise a large amount of data for BMI and morbidity diagnosis. Similar to Chapter 4, the ability to use BMI as a time-dependent variable ensures the most updated BMI measurement is assessed at the time of diagnosis. With the amount of data available I was also able to include two different obese categories for a more granular analysis of prevalence and incidence rates, which illustrated the obese class II+ (and to a lesser extent obese class I) category often had a higher prevalence difference compared to normal weight categories. Further, I was able to utilise ICD-10 codes from the HES outpatient and inpatient data, but also GP diagnostic information from read codes, providing the most detailed diagnostic information available. However, similarly to Chapter 4, I could not account for any changes in coding practices which could inflate the incidence of certain conditions.

Another limitation of this study includes how prevalent conditions were defined. I defined prevalence as those who had a diagnosis five years prior to a BMI measurement, which assumes the individual had the same BMI at the time of diagnosis. This was an arbitrary decision, but I wanted to ensure the prevalence of conditions was up to date but also accounted for the fact that numerous comorbidities of interest are long-term conditions, where remission is not often achieved. However, it also assumes that the diagnosis of the condition five years ago is still prevalent. Multiple conditions can be recurrent, such as a stroke or cancer, but I only counted the first occurrence to ensure we were not overestimating the incidence rates of an event which was referring to a past diagnosis.

Despite concerns of overestimating prevalence, there is also the possibility that the diagnostic coding is incorrect or missing, which could also result in an underestimation prevalence and incidence rates. As new QOF policies were implemented during my study period, which resulted in an increase in screening for renal failure and diabetes, I excluded the years prior to

the implementation and a year after as prevalence and incidence rates had drastically changed as a result of the new guidelines, rather than true changes in incidence and prevalence. Thus, fewer years of trend analysis was available for these morbidities.

Reverse causality was a concern when assessing incidence rates as an individual could lose weight as a result of a condition, prior to diagnosis. For a secondary analysis, I performed a lag analysis excluding individuals who did not have five years follow-up after their BMI measurement. After this exclusion, the incidence rates did not change significantly across the study period for the majority of comorbidities. One reason for performing this secondary analysis was because of how similar obesity-related cancer incidence rates were by BMI category. After applying the exclusion period, the obese categories showed only a small incidence difference when comparing females in the obese class II+ category to the normal weight category. Females in the overweight category was the only group to have an increase in obesity-related cancer incidence per year. As my study period began in 2004 to account for QOF, it may be the case the sample size is not powerful enough to identify differences by BMI across the comorbidities.

5.5 Summary

In summary, in males in the obese categories, type 2 diabetes remains the primary contributor to both prevalence and incidence rates throughout the study. Conditions such as osteoporosis and joint disorders and depression are the most prevalent co-morbidities in males in the overweight and normal weight categories and females in all BMI categories. Prevalence rates are increasing at a greater rate in obese class II+ individuals than normal weight individuals, indicating a greater need for care, treatment, and management for disease maintenance in the obese categories. Meanwhile, incidence rates are declining, but with no difference in the rate

of change between normal weight and obese class II+. As obese individuals have worse health outcomes than normal weight, preventing illness is a key strategy to improve the overall burden of disease and to relieve the demand on the healthcare system.

6. Clinical obesity

6.1 Background

The *Lancet Diabetes & Endocrinology* Obesity Commission is a new consensus report to define the circumstances wherein obesity should be considered a disease, as opposed to a risk factor. The definition depends on information on at least two measurements of adiposity as well as information about co-occurring prevalent conditions. The aim of the Obesity Commission is to reframe the definition of obesity and provide some resolution to the longstanding debate in the clinical and public health community of obesity as a disease. A clinical definition of obesity—considered clinical obesity—would provide a crucial tool to define and treat obesity in a timely and effective manner (146). Implementing these criteria will guide clinical and public health practices, as well as improve economic and societal costs for those living with obesity (146). My analytic objective was to assess the prevalence and implications of these new definitions. This chapter will evaluate the prevalence of clinical obesity, the primary conditions that contribute to cases of clinical obesity, hospitalisation and mortality rates of clinical obesity and other adiposity categories, using a subset of the CPRD dataset among English adults.

6.2 Methods

The Commission utilised the Delphi method for decision making, wherein a panel of clinical and epidemiological experts were surveyed to come to a consensus on how to define clinical obesity. The first criterium assessed was the adiposity measures to diagnose obesity and the second criterium decided the list of prevalent diseases/conditions to include which occur independently of other obesity-related morbidities. Thus, the diagnosis of clinical obesity requires 1) a clinical diagnosis of obesity by assessing excess and/or abnormal adiposity and 2) at least one diagnosis of reduced organ/tissue function due to obesity or limitations in ADL.

(Operational definitions for these conditions for the present analyses are described below.) The definition of clinical obesity was inherently subjective and determined by expert opinion, thus the contribution of specific conditions to the prevalence was not known. I adjusted certain aspects of the definitions, when necessary, but both criteria were pre-determined by the Commission. However, this is a preliminary definition and is subject to change, provided by members of the Commission (EWG, JV, DC, FR).

6.2.1 Defining clinical obesity

6.2.1.1 *Assessing adiposity*

The Commission indicated multiple options on how to define obesity, including direct measures of body fat (i.e., Dual-energy X-ray absorptiometry or bioimpedance); at least one anthropometric measure (WC, waist-to-hip ratio, or waist-to-height ratio) and BMI; or at least two anthropometric measures (WC, waist-to-hip ratio, or waist-to-height ratio) regardless of BMI.

Due to CPRD capabilities, I defined levels of adiposity using BMI and WC measurements and extracted data from individuals who had both measures to clinically assess obesity and excess adiposity. Obesity was defined by a BMI ≥ 30 kg/m² and a WC >120 cm in males and > 88 cm in females (as specified by the British Heart Foundation). If an individual had an obese BMI but not an obese WC or vice versa, they would be considered pre-obese. Defining the levels of adiposity according to these definitions are shown in Table 26.

Table 26. Defining adiposity levels with BMI and WC

Classification	Measurement
Underweight	<18.5 kg/m ²
Normal Weight	18.5-24.9 kg/m ²
Overweight	25-29.9 kg/m ²
Pre-obese	BMI ≥ 30 kg/m ² OR WC ≥ 102 cm (MALES) BMI ≥ 30 kg/m ² OR WC ≥ 88 cm (FEMALES)
Obese	BMI ≥ 30 kg/m ² & WC ≥ 102 cm (MALES) BMI ≥ 30 kg/m ² & WC ≥ 88 cm (FEMALES)

WC was only available in a subset of the participants, whereas BMIs were available for all participants. If a participant had a BMI and WC measured on the same day, that measurement was used, but in instances the BMI and WC were not taken on the same day, an individual's BMI and WC measurement dates had to be within a year of each other to be included. If a participant had multiple BMI and WC measures taken on different days, the two separate measures within the closest period of each other were selected.

6.2.1.2 Diagnoses of diseases and conditions

The next criteria to estimate clinical obesity is the presence of at least one disease and/or condition, defined by the Commission. Diagnostic information was extracted from read codes directly through CPRD and ICD-10 codes from outpatient and inpatient HES data, linked to the participant. As some of the diagnoses are quite specific and not likely to be the main reason an individual is seeking care, any diagnosis which occurred as an outpatient or inpatient in HES was extracted and used to diagnose the respective condition. ICD-10 codes and GP read codes were selected based on the conditions of interest and sent to members of the Commission to ensure proper diagnostic codes were used.

To determine the prevalence of clinical obesity and the diseases and conditions which contribute to clinical obesity, the prevalence estimates were separated into different tiers. The first tier is the overall prevalence of having any condition; the second tier is the prevalence of the overall system which is being impacted (i.e., central nervous system (CNS) or musculoskeletal system); and the third tier is the prevalence of a specific disease within the system (i.e., recurrent headaches or joint pain). Within the third tier, some of the specific conditions comprised the entire system (for example, joint pain was the only condition included within the musculoskeletal system) thus, the prevalence of the disease is the same as the whole system prevalence. The prevalence when assessing the specific condition within tier 3 is not mutually exclusive, so an individual could be diagnosed with multiple diseases within each system, meaning a person could be diagnosed with raised blood pressure, chronic atrial fibrillation, and joint pain.

There were some diseases which the Commission indicated as recurrent but did not define what a recurrent condition was. In these cases, I applied my own arbitrary definition depending on the disease. For instance, recurrent headache was a condition of interest to define clinical obesity. In this scenario, a migraine was automatically determined to be recurrent. Otherwise, I defined recurrent as having a headache coded in the read codes or ICD-10 codes at least three times within one year. There were also instances, such as the definition for the metabolic system, where I used measured biomarkers and/or diagnostic codes. The diseases and conditions specified to define clinical obesity, and the definitions I used to determine and extract these diagnoses, are shown in Table 27. A disease was considered prevalent if diagnosis occurred five years prior to and six months after the adiposity measurements.

Table 27. Diseases and conditions included in the Obesity Commission’s definition of clinical obesity

System	Commission’s Terminology	Marisa’s Terminology	ICD/read code/biomarker	ICD Code	Notes
ADL	Limitations of mobility and/or basic activities of daily living (bathing, dressing, toileting, continence, eating)	Limitations in ADL	ICD & read code	Z73.6 Limitation of activities due to disability	
CNS	Raised intracranial pressure	Raised Intracranial Pressure	ICD & read code	G93.2 Benign intracranial hypertension	
	Recurrent headaches	Recurrent headaches	ICD & read code	G43. Migraine	Assuming recurrent
				G44.0 Cluster headache syndrome	Recurrent: at least 3 headache codes within 1 year
				G44.1 Vascular headache, not elsewhere classified	
				G44.2 Tension-type headache	
				R51 Headache	
	Vision loss	Vision Loss	ICD & read code	H53.1 Subjective visual disturbances	
				H54.1 Severe visual impairment, binocular	
				H54.5 Severe visual impairment, monocular	
				H54.9 Unspecified visual impairment (binocular)	
CVD	Chronic/recurrent atrial fibrillation	Chronic/recurrent atrial fibrillation	ICD & read code	I48 Atrial fibrillation and flutter (inc. paroxysmal, persistent and chronic)	Recurrent: atrial fibrillation read code at least 3 times in 5 years; ICD: I48
	Reduced left ventricular systolic function (heart failure with reduced ejection fraction)	Left Ventricular Heart Failure	ICD & read code	I50.3 Left ventricular failure	Read terms are available for this, but not ICD 10 codes.
	Chronic fatigue, lower limb oedema due to impaired diastolic dysfunction (heart failure with preserved ejection fraction)				
	Pulmonary Arterial Hypertension	Pulmonary Arterial Hypertension	ICD & read code	I27.0 Primary pulmonary hypertension	
				I27.2 Other secondary pulmonary hypertension	

	Raised blood pressure	Raised Blood Pressure	ICD, read code, register	I10 Essential (primary) hypertension	Also using CPRD hypertension register
	Recurrent DVT and/or pulmonary thromboembolic disease	Recurrent DVT and/or pulmonary thromboembolic disease	ICD & read code	I80.2 Phlebitis and thrombophlebitis of other deep vessels of lower extremities I26.0 Pulmonary embolism with mention of acute cor pulmonale	Recurrent: DVT read code or ICD 10 code at least 3 times in 5 years
Liver	NAFLD with hepatic fibrosis	Hepatic fibrosis	ICD & read code	K74.0 Hepatic fibrosis	
		NAFLD with hepatic fibrosis	ICD & read code	K76.0 Fatty (change of) liver, not elsewhere classified	
				K74.0 Hepatic fibrosis	
Lymphatic	Lower limbs lymphedema causing chronic pain and/or range of motion	Lower limb lymphedema	ICD & read code	I89.0 Lymphoedema, not elsewhere classified	
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	Cluster of hyperglycaemia, high triglycerides, low HDL	ICD, read code, & biomarker	R73.9 Hyperglycaemia, unspecified E78.1 Pure hyperglyceridaemia E78.6 Lipoprotein deficiency	Hyperglycaemia: HbA1C >6.5%; FPG >7 mmol/L High triglycerides: >4.5 mmol/L Low HDL: <1 (males); <1.2 (females) mmol/L
Musculoskeletal	Chronic, severe knee or hip pain associated with joint stiffness and reduced range of joint motion	Joint pain	ICD & read code	M25.5 Pain in joint	
				M25.6 Stiffness of joint, not elsewhere classified	
Renal	Microalbuminuria with reduced eGFR	Microalbuminuria with reduced eGFR	Read code & biomarker	NA	Albumin creatinine ratio/urine microalbumin: >3 mg/mmol eGFR: < 60 ml/min
Reproductive	Male hypogonadism	Male hypogonadism		E29.1 Testicular hypofunction	
	Anovulation	Anovulation	ICD & read code	N97.0 Female infertility associated with anovulation	
	Oligomenorrhea	Oligomenorrhea	ICD & read code	N91.3 Primary oligomenorrhoea	
				N91.4 Secondary oligomenorrhoea	
				N91.5 Oligomenorrhoea, unspecified	

	Polycystic ovary syndrome	Polycystic ovary syndrome	ICD & read code	E28.2 Polycystic ovary syndrome	
Respiratory	Breathlessness	Breathlessness	ICD & read code	R06.0 Dyspnoea	
	Diaphragmatic Compliance	Diaphragmatic Compliance	ICD & read code	J98.6 Disorders of diaphragm	
	Hypoventilation	Hypoventilation	ICD & read code	E66.2 Extreme obesity with alveolar hypoventilation	
	Wheezing	Wheezing	ICD & read code	R06.2 Wheezing	
Upper Airways	Apnoeas/hypopneas during sleep	Apnoeas/hypopneas during sleep	ICD & read code	G47.3 Sleep apnoea	
Urinary	Recurrent/chronic urinary incontinence	Recurrent/chronic urinary incontinence	ICD & read code	N39.4 Other specified urinary incontinence	Assuming recurrent
				R32 Unspecified urinary incontinence	

ADL: activities of daily living; CNS: central nervous system; CVD: cardiovascular disease; NAFLD: non-alcoholic fatty liver disease; HDL: high-density lipoprotein; eGFR: estimated glomerular filtration rate

6.2.2 Prevalence of clinical obesity

To obtain the most up to date prevalence of clinical obesity, I examined the sample of individuals with a BMI and WC measurement between January 1, 2015, and December 31, 2019, extracted from CPRD. The study cohort for determining clinical obesity prevalence consisted of 35,667 participants with BMI and WC measurements. As period prevalence rates were estimated, only the most recent BMI and WC measurements were utilised.

I first estimated the distribution of individuals according to their adiposity levels (i.e., underweight, normal weight, overweight, pre-obese, and obese) and the proportion of individuals with at least one prevalent condition, from the list of conditions provided by the Commission to define clinical obesity. This initial analysis includes all individuals with a BMI and WC measurement.

My secondary analysis only includes individuals with clinical obesity to explore the prevalence estimates by: 1) system, and 2) by specific conditions within each system. There were 6,251 individuals with clinical obesity who were included in these estimates to understand the burden of clinical obesity and the diseases which contribute most to clinical obesity. The prevalence of clinical obesity is presented as the proportion of individuals with a diagnosis for each aspect of clinical obesity being examined (i.e., the overall prevalence, prevalence of the system, or prevalence of a specific disease within the system). The crude prevalence was assessed for this aim. I also stratified by age groups < 44, 45-64, and 65+.

6.2.3 Assessing individuals who have a WC measurement

As measuring for WC is not standard practice when visiting the GP, I conducted several secondary analyses to examine potential differences between those who have a WC and those

who do not. To do this, I extracted the last BMI measurement available from the entire CPRD dataset, which was described in Chapter 3 (referred to as ‘the entire dataset’). I also extracted individuals who had both a BMI and WC measurement but only utilised the BMI measurement for comparability between datasets (referred to as ‘the BMI-WC subset’). I assessed descriptive statistics between the two datasets between 2005 and 2019. I also applied the Commission’s diagnostic criteria of comorbidities of interest to both datasets to illustrate the distribution of BMI level and prevalence of disease in each population between 2005 and 2019. For the final assessment, I compared HSE to the BMI-WC subset of CPRD, plotting the proportion of individuals with a BMI greater than 25 kg/m² (i.e., were overweight or obese) and a WC >120 cm in males or > 88 cm in females (i.e., very high WC) between 2005 and 2019 (200).

6.2.4 Hospitalisation rates by adiposity level

I assessed both the hospitalisation rates and mortality rates by adiposity levels. For these aims, the study period was from 1 January 2005 through 31 December 2019.

Poisson regression models were utilised for both hospitalisation rate and mortality rate analyses. Follow-up began at the date of the first BMI and WC measurement in the study period and continued until death or end of follow-up (end of study period, last collection date of the GP, or transferring out of CPRD), whichever occurred first. In other chapters, each year had its own exposure length as the analyses were discretised by calendar year. However, in this analysis, the total time spent in the study was the exposure length for each individual and was the offset for the Poisson model. Models were stratified by gender, included interaction terms between adiposity level and age, and the predicted hospitalisation and mortality rates were age-adjusted using ONS mid-year population data.

Hospitalisation data was extracted from HES outpatient and inpatient linkage data and included 132,207 individuals in the analysis. Hospitalisations after a BMI and WC measurement were utilised and any hospitalisation—until the end of follow-up—after these measures were included in the regression. An individual was able to have multiple hospitalisations throughout the study period. As a secondary analysis, I also excluded individuals who did not have at least 5-years follow up after their BMI measurement.

6.2.5 Mortality rate by adiposity level

For mortality rates, I accounted for reverse causality to ensure weight loss did not overestimate the mortality risks of lower BMI categories by excluding participants who died within five years after their BMI and WC measurements. This resulted in a final study analysis including 61,404 individuals. In the models, the last available BMI and WC measurement after accounting for the 5-year survival period was the adiposity category utilised in the model to ensure the most recent estimate the association between adiposity levels and mortality.

I conducted further analyses for all-cause mortality rates, wherein I tested the association of WC, BMI, and the inclusion of a prevalent condition which indicates clinical obesity. In these analyses, I run Poisson regressions as described above, but with different independent variables consisting of 1) BMI with prevalent disease status, 2) BMI only, 3) WC with prevalent disease status, and 4) WC only.

6.3 Results

6.3.1 Descriptive statistics, comparing datasets

Descriptive statistics were calculated for individuals in the datasets from 2005 to 2019, which compared the BMI-WC subset to the entire dataset (individuals with at least one BMI

measurement) at the time of their last BMI measurement (Table 28). In the BMI-WC subset, there was also a higher proportion of individuals overweight (37% vs 34%) and obese (34% vs 28%) compared to the entire dataset. Overall, there was a smaller proportion of individuals aged <44 years in the BMI-WC subset (15%) compared to the entire dataset (33%) and a higher proportion were 45-64 (47% vs 35%) and 65-74 (23% vs 16%) in the BMI-WC subset compared to the entire dataset.

Whilst there was still a higher proportion of females than males in both datasets, the proportion of males was higher in the BMI-WC subset compared to the entire dataset (48% vs 43%). Further, the distribution of IMD quintiles was similar, but in the BMI-WC subset, there was a greater proportion of individuals with missing IMD data. The BMI-WC subset also had a lower proportion of current smokers (14% vs 18%) and a higher proportion of ex-smokers (32% vs 27%) compared to the entire dataset. Finally, the BMI-WC subset had a higher proportion of individuals who are current drinkers compared to the entire dataset (79% vs 71%).

Table 28. Descriptive statistics of the entire CPRD and the subset of data at the time of the most recent BMI measurement

	Entire Dataset	BMI-WC Subset
	N = 1,356,452	N = 132,207
Age (Years)		
<44	441,529 (33%)	20,482 (15%)
45-64	468,333 (35%)	62,265 (47%)
65-74	211,538 (16%)	30,898 (23%)
75+	235,052 (17%)	18,562 (14%)
Median (IQR)	54 (40, 69)	59 (49, 69)
BMI (kg/m²)		
Underweight	39,540 (2.9%)	1,274 (1.0%)
Normal weight	477,590 (35%)	36,409 (28%)
Overweight	465,971 (34%)	49,567 (37%)
Obese	373,351 (28%)	44,957 (34%)
Median (IQR)	26.5 (23.2, 30.4)	27.6 (24.5, 31.5)
Gender		
Male	577,000 (43%)	63,774 (48%)
Female	779,452 (57%)	68,433 (52%)
Ethnicity		
Asian	46,302 (3.4%)	5,049 (3.8%)
Black	28,434 (2.1%)	2,559 (1.9%)
Mixed	8,840 (0.7%)	712 (0.5%)
Other	23,515 (1.7%)	2,368 (1.8%)
White	1,145,369 (84%)	113,483 (86%)
Missing	103,992 (7.7%)	8,036 (6.1%)
Index of Multiple Deprivation		
Quintile 1 (Least deprived)	305,472 (23%)	31,045 (23%)
Quintile 2	307,333 (23%)	31,483 (24%)
Quintile 3	269,777 (20%)	25,058 (19%)
Quintile 4	258,512 (19%)	22,889 (17%)
Quintile 5 (Most Deprived)	210,840 (16%)	20,070 (15%)
Missing	4,518 (0.3%)	1,662 (1.3%)
Smoking Status		
Current	245,581 (18%)	19,024 (14%)
Never	736,474 (54%)	70,125 (53%)
Ex	366,507 (27%)	42,157 (32%)
Missing	7,890 (0.6%)	901 (0.7%)
Drinking Status		
Current	962,418 (71%)	104,243 (79%)
Never	235,568 (17%)	20,115 (15%)
Ex	42,044 (3.1%)	3,993 (3.0%)
Missing	116,422 (8.6%)	3,856 (2.9%)

Unless otherwise stated, estimates are reported as median (IQR) or number (%).

6.3.1.1 Prevalence of disease by BMI status

When comparing the prevalence of clinical obesity in the BMI-WC subset to the entire dataset, the proportion of individuals who were obese was greater in the WC-BMI subset, accounting for 34% of the population compared to 27.5% between 2005 and 2019 (Figure 16). Further, 18.6% (95% CI: 18.4%, 18.9%) of individuals in the WC-BMI subset had clinical obesity compared to 13.5% (95% CI: 13.4, 13.6%) in the entire dataset. Within the obese category, about 54% of individuals had clinical obesity in the BMI-WC subset, compared to 49% in the entire dataset.

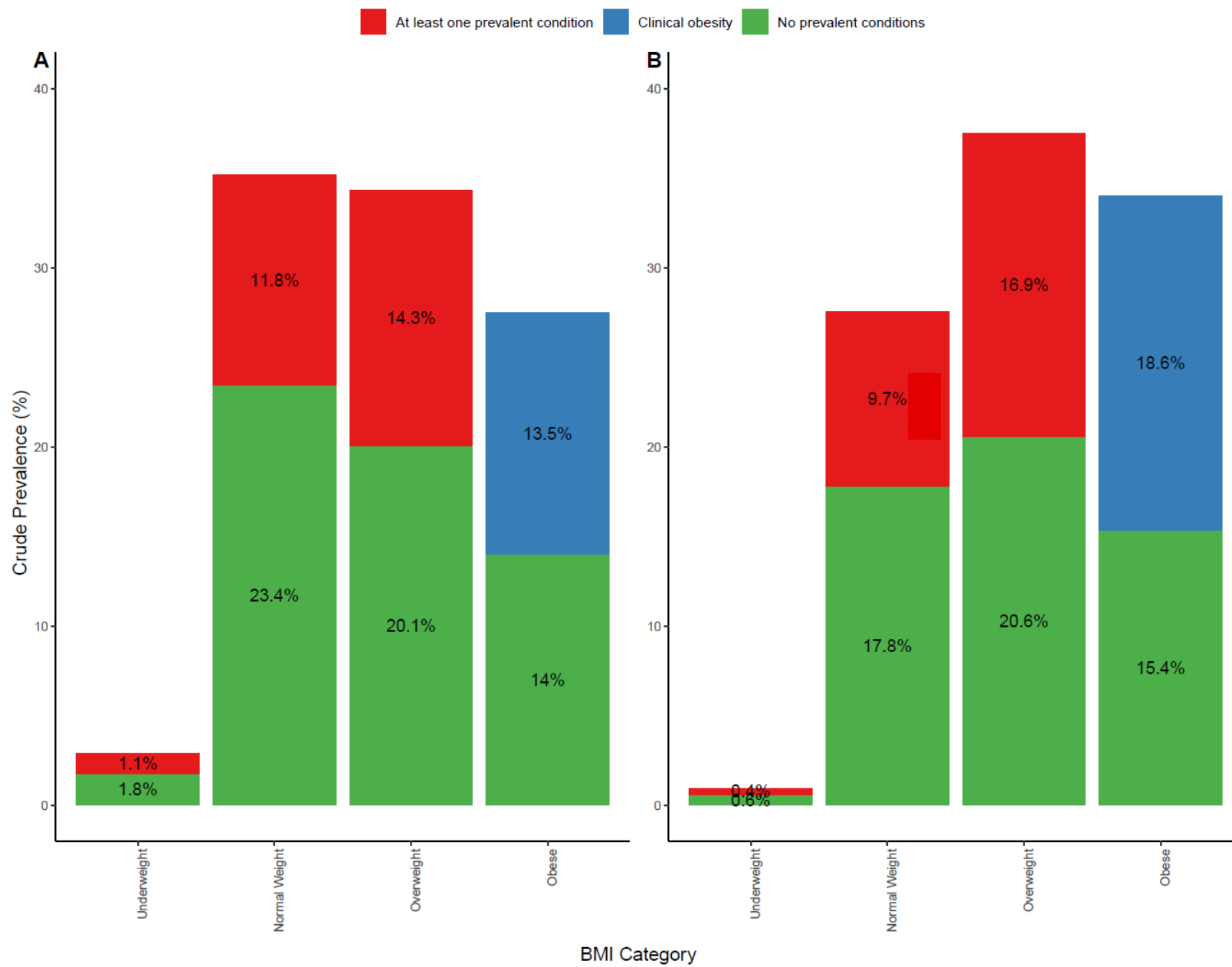


Figure 16. Crude prevalence (%) of BMI with prevalent disease status across the study population in A) the entire CPRD dataset and B) the subset with BMI and WC

6.3.1.2 BMI-WC subset and HSE comparisons

Compared to HSE, the BMI-WC subset had a higher proportion of males and females with an overweight or obese BMI and a very high WC measurement (200). As the study period continues, the proportion of individuals with either an overweight or obese BMI or a very high WC begin to converge, with prevalence becoming more similar between the two datasets (Figure 17, Figure 18). By 2019, the proportion of females with an overweight or obese BMI was the same in both CPRD and HSE at 60%. In males, by 2019 the BMI-WC subset still had a larger proportion of individuals with an overweight or obese BMI compared to HSE. When assessing the prevalence of a very high WC, CPRD had a higher proportion of both males (by four percentage points) and females (by two percentage points) with a very high WC.

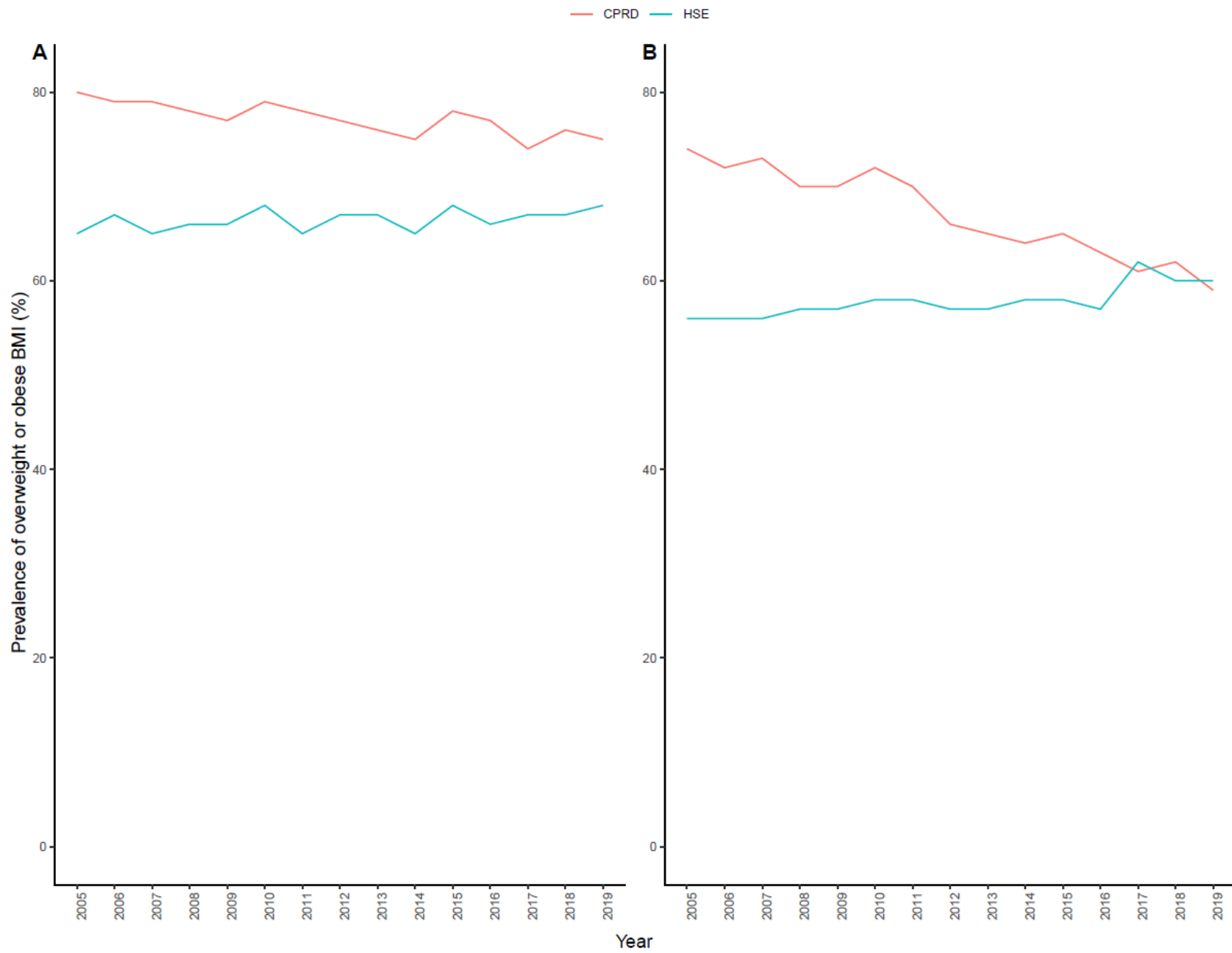


Figure 17. Comparing the prevalence of an overweight or obese BMI in CPRD and HSE 2005-2019 in A) males and B) females

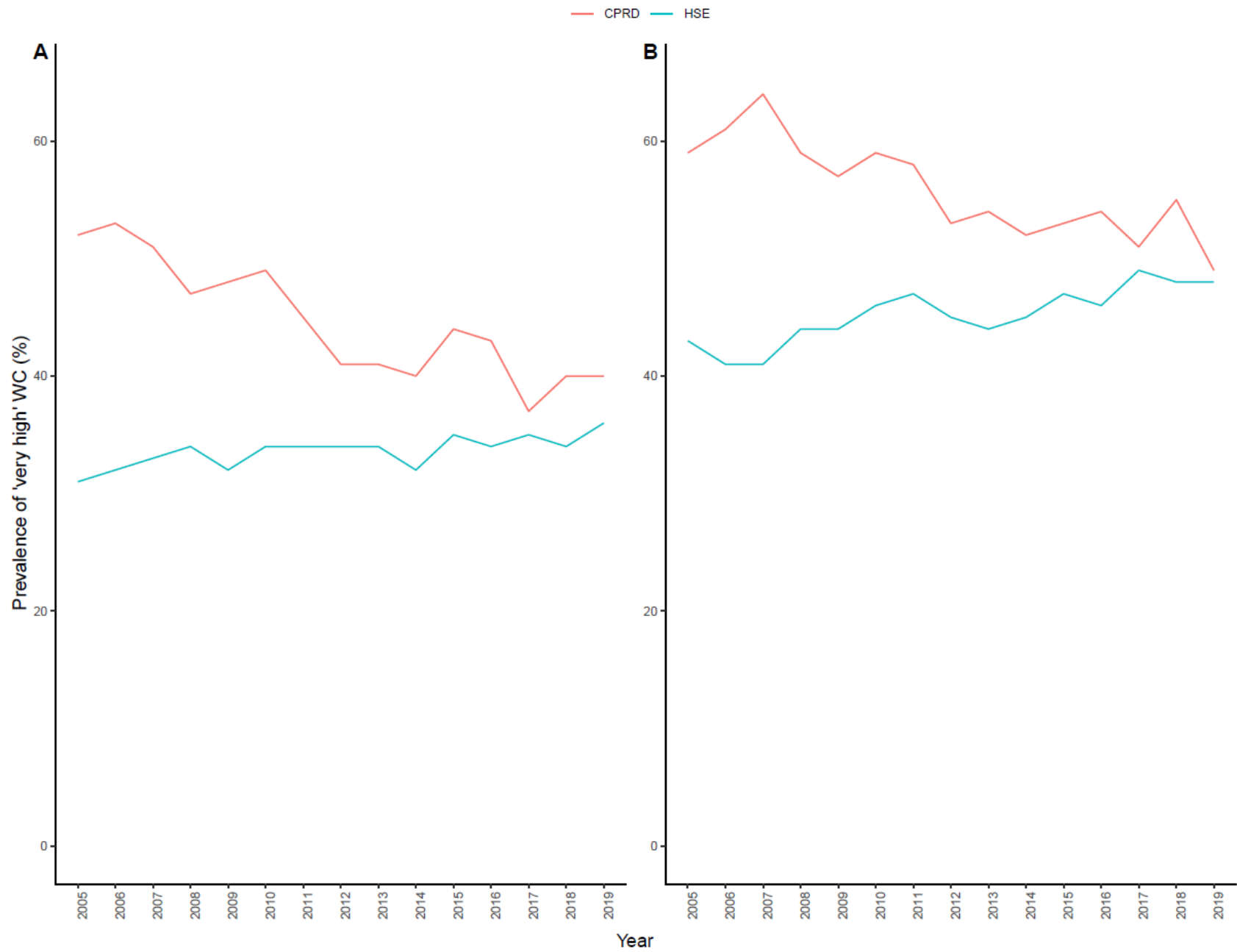


Figure 18. Comparing the prevalence of a ‘very high’ WC in the BMI-WC subset and HSE 2005-2019 in A) males and B) females

6.3.2 Adiposity and prevalence of disease

6.3.2.1 Overall prevalence of adiposity levels and clinical obesity

The prevalence of at least one condition across the respective male and female study populations is shown in Figure 19. About 27% of males had obese adiposity levels (defined in Table 26), with 17.0% (95% CI: 16.4%, 17.6%) having at least one prevalent condition, thus meeting the clinical obesity definition. For females, 29% had an obese adiposity level, and 18.1% (95% CI: 17.4%, 18.7%) had clinical obesity. Thus, about two-thirds of persons with obesity met the definition of clinical obesity. For additional perspective, we show that among adults with normal weight, overweight, and pre-obesity, roughly 40% have additional conditions.

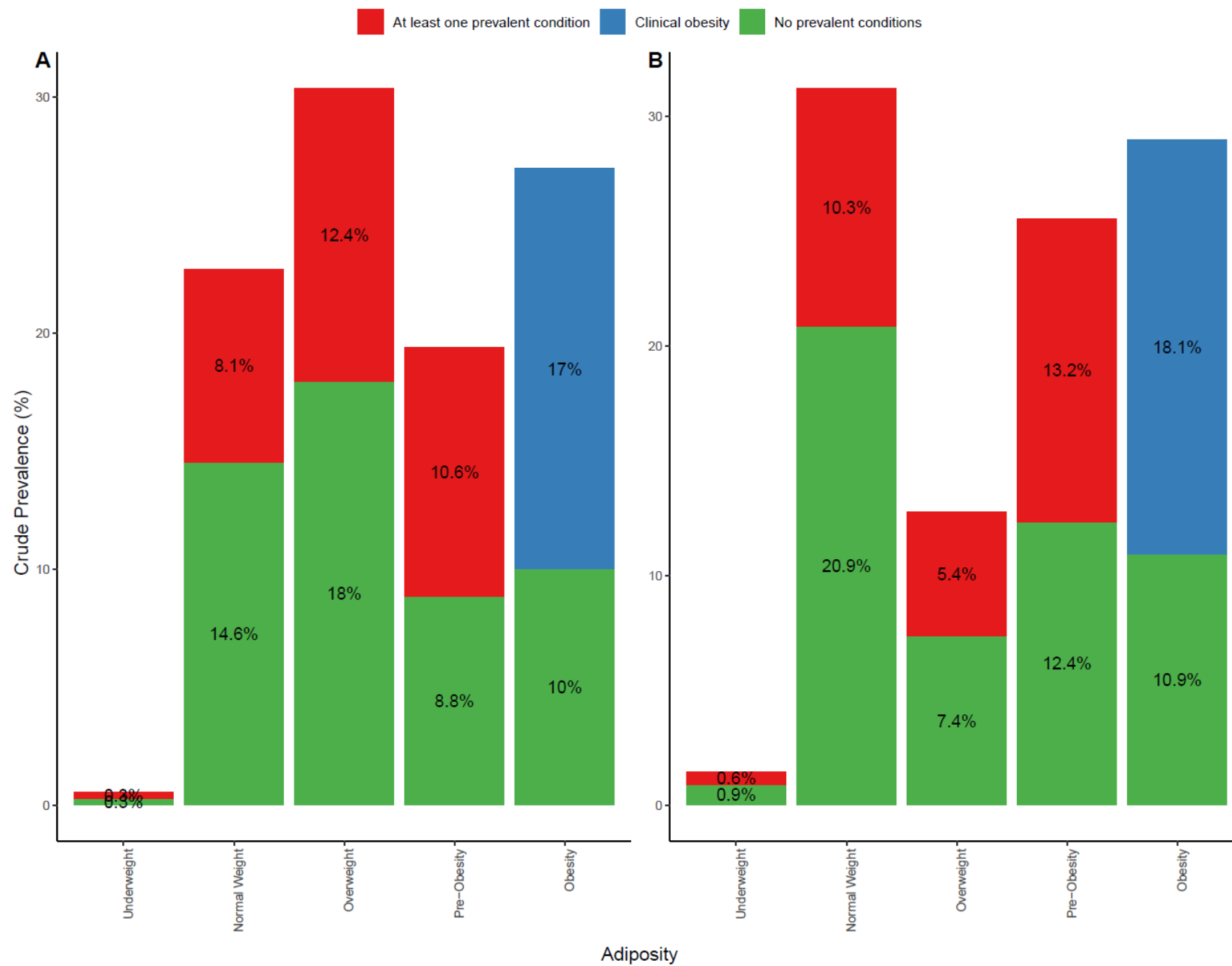


Figure 19. Crude prevalence (%) of adiposity levels across the entire BMI-WC subset in A) males and B) females

6.3.2.2 Prevalence of contributors to clinical obesity, by system

Among males with clinical obesity, 71.1% (95% CI: 68.1%, 74.2%) had a CVD diagnosis (Figure 20A). The next highest contributors to disease prevalence were musculoskeletal conditions and respiratory conditions, wherein 33.7% (95% CI: 31.6%, 35.8%) and 15.7% (95% CI: 14.3%, 17.2%) of males had these diagnoses, respectively.

In females with clinical obesity, 57.4% (95% CI: 54.8%, 59.9%) had a CVD, accounting for the highest contributor to prevalent conditions (Figure 20B). Musculoskeletal conditions were the next highest contributor, wherein 43.8% (95% CI: 41.6%, 46.1%) of females with clinical obesity had a prevalent musculoskeletal diagnosis, followed by respiratory diseases with 16.6% (95% CI: 15.3%, 18.0%) of females with clinical obesity having a diagnosis. Limitations in ADL and conditions of the central nervous, renal, and urinary systems each contributed to 8-11% of prevalent conditions among females with clinical obesity.

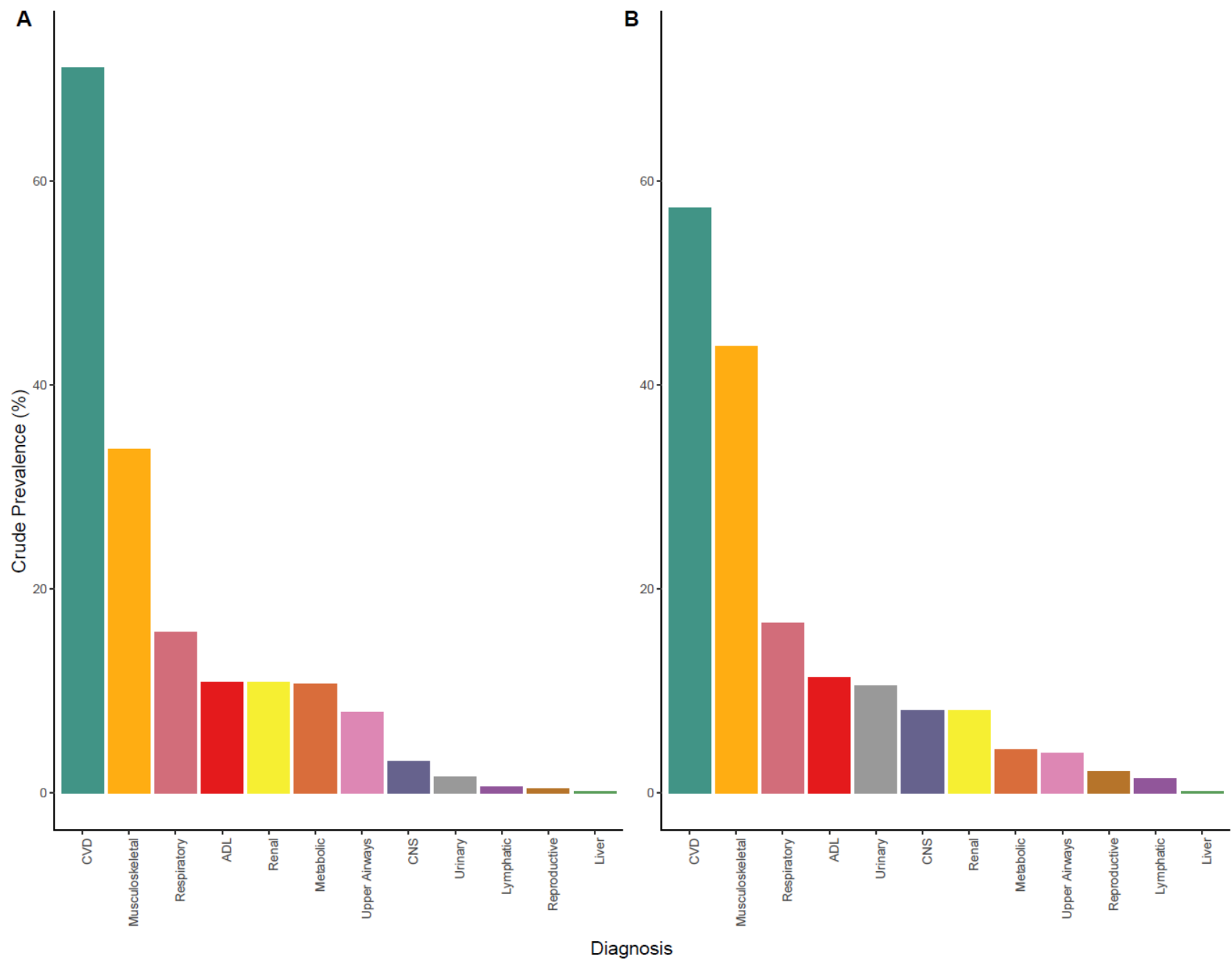


Figure 20. Crude prevalence (%) of conditions/diseases by system in clinically obese A) males and B) females

6.3.2.3 Prevalence of contributors to clinical obesity, by disease/condition

When assessing the prevalence of specific diseases and conditions contributing to clinical obesity, 69.0% (95% CI: 66.0%, 72.0%) of males had raised blood pressure, accounting for the largest contributor to the prevalence (Table 29). This is followed by joint pain which affects 33.7% (95% CI: 31.6%, 35.8%) of males with clinical obesity. Breathlessness within the respiratory system contributed to 13.8% (95% CI: 12.5%, 15.2%) of the prevalence within the clinically obese.

Raised blood pressure was the largest contributor to prevalence with 55.5% (95% CI: 52.9%, 58.0%) of females with clinical obesity with a diagnosis (Table 29). This was followed by raised joint pain affecting 43.8% (95% CI: 41.6%, 46.1%) of females with clinical obesity. Breathlessness contributed to 13.7% (95% CI: 12.4%, 14.9%) of prevalent conditions among females with clinical obesity. About 7-8% of females with clinical obesity had diagnoses for recurrent headaches within CNS and chronic atrial fibrillation within CVD.

Table 29. Crude prevalence (%) of specific diseases contributing to clinical obesity in males and females

System	Prevalence (%)	Condition	Prevalence (%)
MALES			
ADL	10.9 (9.7, 12.1)	Limitations in ADL	10.9 (9.7, 12.1)
CNS	3.1 (2.5, 3.7)	Raised intracranial pressure	0
		Recurrent headache	2.3 (1.7, 2.8)
		Vision loss	0.88 (0.5, 1.2)
CVD	71.1 (68.1, 74.2)	Chronic atrial fibrillation	8.8 (7.7, 9.9)
		Chronic DVT or thromboembolism	1 (0.6, 1.3)
		Left ventricular heart failure	3.9 (3.2, 4.7)
		Pulmonary arterial hypertension	0.34 (0.1, 0.55)
		Raised blood pressure	69 (66, 72)
Liver	0.17 (0.021, 0.32)	Hepatic fibrosis	0.034 (-0.033, 0.1)
		NAFLD with hepatic fibrosis	0.14 (0.003, 0.27)
Lymphatic	0.61 (0.33, 0.9)	Lymphedema	0.61 (0.3, 0.9)
Metabolic	10.7 (9.5, 11.9)	High triglycerides, glycemia, and low HDL	10.7 (9.5, 11.9)
Musculoskeletal	33.7 (31.6, 35.8)	Joint pain	33.7 (31.6, 35.8)
Renal	10.9 (9.7, 12.1)	Microalbuminuria with reduced eGFR	11 (9.8, 12.1)
Reproductive	0.41 (0.18, 0.64)	Male hypogonadism	0.41 (0.2, 0.64)
		Oligomenorrhea	NA
		Polycystic ovary syndrome	NA
Respiratory	15.7 (14.3, 17.2)	Breathlessness	13.8 (12.5, 15.2)
		Diaphragmatic compliance	0.034 (-0.033, 0.1)
		Hypoventilation	0.2 (0.041, 0.37)
		Wheezing	2.7 (2.1, 3.2)
Upper Airways	8 (6.9, 9)	Sleep apnoea	8 (6.9, 9)
Urinary	1.6 (1.1, 2.1)	Chronic urinary incontinence	1.6 (1.1, 2.1)
FEMALES			
ADL	11.3 (10.2, 12.4)	Limitations in ADL	11.3 (10.2, 12.4)
CNS	8.1 (7.1, 9.1)	Raised intracranial pressure	0.091 (-0.012, 0.19)
		Recurrent headache	7.1 (6.2, 8)
		Vision loss	1.1 (0.7, 1.4)
CVD	57.4 (54.8, 59.9)	Chronic atrial fibrillation	5.9 (5.1, 6.8)
		Chronic DVT or thromboembolism	0.91 (0.6, 1.2)
		Left ventricular heart failure	1.9 (1.4, 2.3)
		Pulmonary arterial hypertension	0.63 (0.4, 0.91)
		Raised blood pressure	55.5 (52.9, 58)
Liver	0.15 (0.019, 0.28)	Hepatic fibrosis	0.06 (-0.023, 0.14)
		NAFLD with hepatic fibrosis	0.12 (0.002, 0.24)
Lymphatic	1.4 (1, 1.8)	Lymphedema	1.4 (1, 1.8)
Metabolic	4.2 (3.5, 4.9)	High triglycerides, glycemia, and low HDL	4.2 (3.5, 4.9)
Musculoskeletal	43.8 (41.6, 46.1)	Joint pain	43.8 (41.6, 46.1)
Renal	8.1 (7.1, 9.1)	Microalbuminuria with reduced eGFR	8.1 (7.2, 9.1)
Reproductive	2.1 (1.6, 2.6)	Male hypogonadism	NA
		Oligomenorrhea	0.42 (0.2, 0.64)
		Polycystic ovary syndrome	1.8 (1.4, 2.3)
Respiratory	16.6 (15.3, 18)	Breathlessness	13.7 (12.4, 14.9)
		Diaphragmatic compliance	0.06 (-0.023, 0.14)
		Hypoventilation	0.33 (0.1, 0.53)
		Wheezing	3.7 (3, 4.3)
Upper Airways	3.9 (3.3, 4.6)	Sleep apnoea	3.9 (3.3, 4.6)
Urinary	10.5 (9.4, 11.6)	Chronic urinary incontinence	10.5 (9.4, 11.6)

NAs indicate the diagnosis was gender-specific, thus was not available in a certain gender; ADL: activities of daily living; CNS: central nervous system; CVD: cardiovascular disease; NAFLD: non-alcoholic fatty liver disease; HDL: high density lipoprotein; eGFR: estimated glomerular filtration rate

6.3.3 Age-stratified analyses of clinical obesity

6.3.3.1 Overall prevalence of age-stratified adiposity levels and clinical obesity

In the age-stratified analysis, a larger proportion of older individuals were obese and had clinical obesity. About 28% of males in the 65+ age group were in the obese category, of which 22.2% (95% CI: 21.0%, 23.3%) had clinical obesity (Figure 21A). In the 45-64 age group 15.7% (95% CI: 14.8%, 16.5%) were clinically obese and 7.8% (95% CI: 6.7%, 9.0%) in the <44 age group had clinical obesity.

In females, of those in the 65+ age group, about 30% were in the obese category of which 23.7% (95% CI: 22.5%, 25.0%) were clinically obese (Figure 21B). In the 45-64 age group, 16.2% (95% CI: 15.4%, 17.0%) were clinically obese and 12.1% (95% CI: 10.8%, 13.4%) of females in the <44 age group were clinically obese.

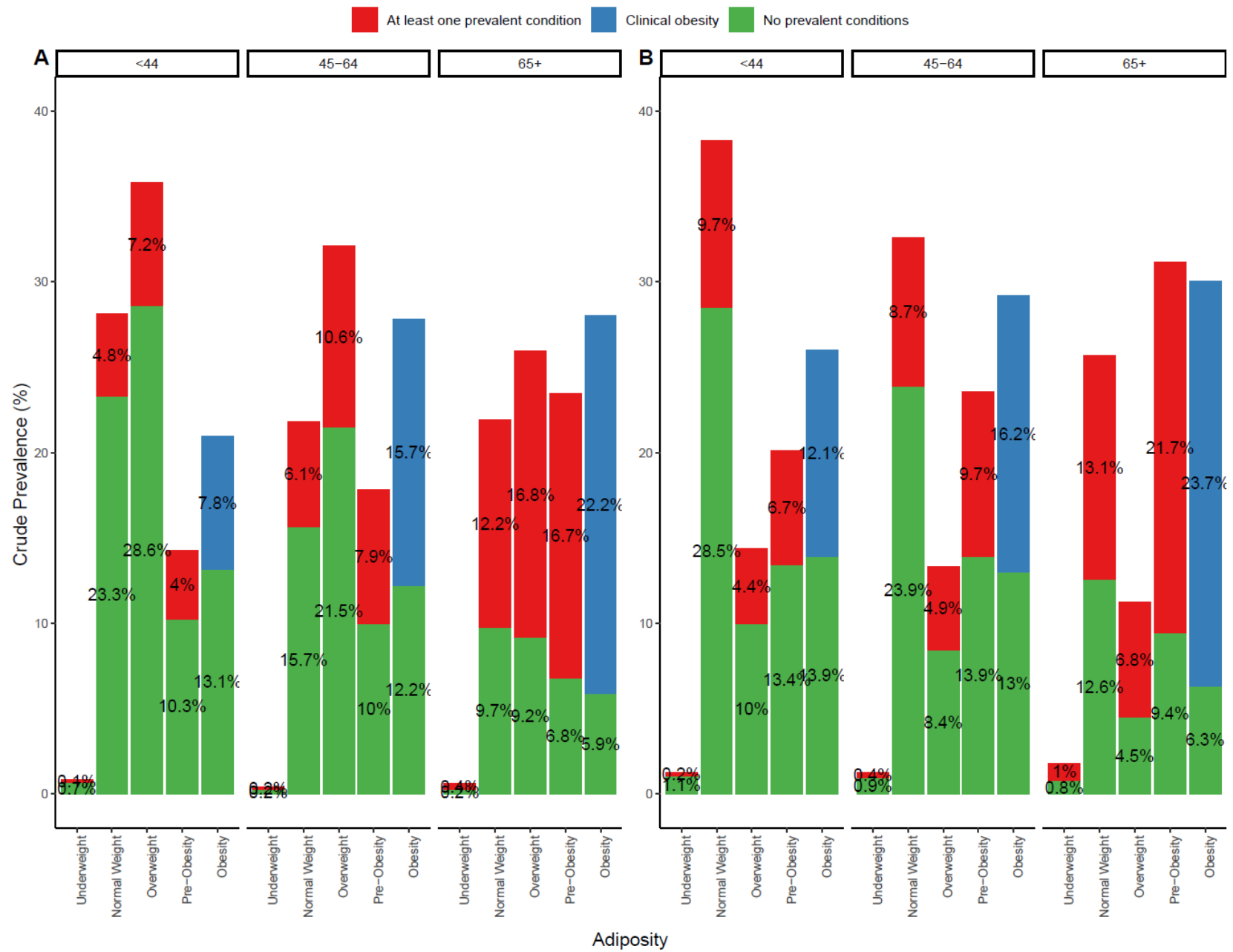


Figure 21. Age-stratified prevalence (%) of adiposity levels across BMI-WC subset in A) males and B) females

6.3.3.2 Prevalence of age-stratified contributors to clinical obesity, by system

Among males with clinical obesity, CVD remained the greatest contributor to clinical obesity prevalence across all age groups, whereas in females it was the most prominent condition in the older age groups. Of males aged 65+ years with clinical obesity, 44.3% (95% CI: 41.7%, 46.9%) had CVD, followed by 16.9% (95% CI: 15.3%, 18.5%) with musculoskeletal disorders and about 10% with renal (95% CI: 9.4%, 11.9%) or respiratory (95% CI: 8.9%, 11.4%) conditions (Figure 22A, Table 30). In males 45-64 years old with clinical obesity, 42.3% (95% CI: 39.5%, 45.0%) had a CVD condition and 23.5% (95% CI: 21.5%, 25.6%) had a musculoskeletal condition. About 5-8% of males with clinical obesity in this age group had a prevalent respiratory, metabolic, ADL, or upper airways condition. Finally, 28.4% (95% CI: 21.8%, 35.0%) of males with clinical obesity <44 years old had a CVD condition, followed by 26.4% (95% CI: 20.0%, 32.8%) with a musculoskeletal condition and 13.6% (95% CI: 9.0%, 18.2%) a respiratory condition.

Among females aged 65+ with clinical obesity, 40.8% (95% CI: 38.4%, 43.2%) had CVD and 22.3% (95% CI: 20.5%, 24.1%) had a musculoskeletal condition (Figure 22B, Table 31). About 10.1% (95% CI: 8.9%, 11.3%) of females with clinical obesity in this age group had a respiratory condition, and 7-8% had renal and limitations in activities of daily living (ADL) diagnoses. In the 45-64 age group, CVD and musculoskeletal conditions had a similar prevalence among females with clinical obesity, with a prevalence of 30.7% (95% CI: 28.5%, 33.0%), and 29.7% (95% CI: 27.5%, 31.9%), respectively. In contrast, in the <44 age group, the prevalence of musculoskeletal conditions in females with clinical obesity was highest accounting for 30.1% (95% CI: 25.3%, 34.9%), followed by CVD and CNS which had a prevalence of 14.9% (95% CI: 11.6%, 18.3%) and 13.9% (95% CI: 10.7%, 17.2%), respectively. The prevalence of reproductive and respiratory conditions was both 10.4% (95% CI: 7.5%, 13.2%).

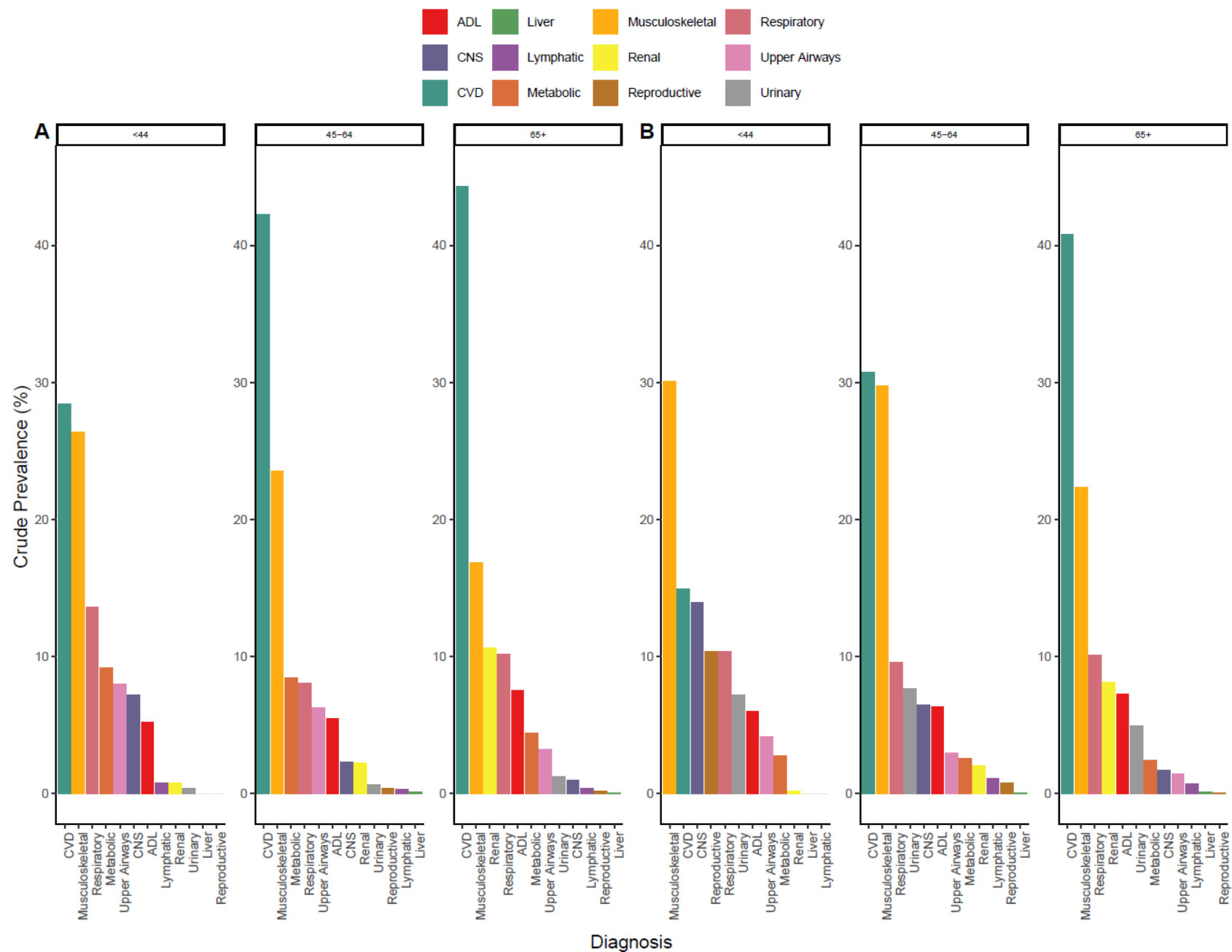


Figure 22. Age-stratified prevalence (%) of conditions/diseases by system in clinically obese A) males and B) females

6.3.3.3 Prevalence of age-stratified contributors to clinical obesity, by disease/condition

When considering the specific diseases and conditions contributing to clinical obesity prevalence, 38.6% (95% CI: 36.3%, 40.9%) of males with clinical obesity had raised blood pressure in the 65+ group. Joint pain followed within this group at 15.2% (95% CI: 8.5%, 16.7%) and microalbuminuria with reduced estimated glomerular filtration rate (eGFR) at 9.7% (95% CI: 8.5%, 10.8%) (Table 30). About 8.3% (95% CI: 7.3%, 9.4%) of males 65+ with clinical obesity had breathlessness, and about 7% had limitations in ADL (95% CI: 5.8%, 7.8%), and chronic atrial fibrillation (95% CI: 5.8%, 7.7%). In males with clinical obesity 45-64, 39.3% (95% CI: 36.7%, 41.9%) had raised blood pressure, followed by 22.4% (95% CI: 20.4%, 24.4%) with joint pain. Between 5-8% had high triglycerides, high glycemia, and low high-density lipoprotein (HDL), breathlessness, sleep apnoea, and limitations in ADL. Finally, across males with clinical obesity <44, 26.9% (95% CI: 20.5%, 33.3%) had had raised blood pressure and 26.1% (95% CI: 19.8%, 32.4%) had joint pain. About 9% of males with clinical obesity had breathlessness (95% CI: 5.7%, 13.3%) and high triglycerides, high glycemia, and low HDL (95% CI: 5.4%, 12.8%).

In females with clinical obesity aged 65+, 36.6% (95% CI: 34.4%, 38.8%) had raised blood pressure and 20.6% (95% CI: 19.0%, 22.3%) had joint pain (Table 31). About 5-8% of females with clinical obesity in this age group had breathlessness, microalbuminuria with reduced eGFR, limitations in ADL, chronic atrial fibrillation, and chronic urinary incontinence. In females 45-64 with clinical obesity, about 29.0% had joint pain and raised blood pressure. (95% CI: 26.8, 31.1%). About 7% of females with clinical obesity in this age group had chronic urinary incontinence (95% CI: 6.4%, 8.5%), breathlessness (95% CI: 6.1%, 8.2%), and about 6% had limitations in ADL (95% CI: 5.2%, 7.2%) and recurrent headaches (95%CI: 4.7%, 6.6%). Finally, 29.4% (95% CI: 24.7%, 34.1%) of females <44 with clinical obesity had joint pain, about 13% had raised blood pressure (95% CI: 10.1%, 16.4%) and recurrent headaches

(95% CI: 9.6%, 15.7%), and 9.3% had (95% CI: 6.7%, 15.7%) polycystic ovary syndrome (PCOS).

Table 30. Age-stratified prevalence (%) of specific diseases contributing to clinical obesity in males, by age

System	<44	45-64	65+	Diagnosis	<44	45-64	65+
ADL	5.2 (2.4, 8)	5.4 (4.4, 6.4)	7.5 (6.5, 8.6)	Limitations in ADL	5.1 (2.3, 7.9)	5.2 (4.2, 6.1)	6.8 (5.8, 7.8)
CNS	7.2 (3.9, 10.5)	2.3 (1.6, 2.9)	1 (0.6, 1.4)	Raised intracranial pressure	0 (0, 0)	0 (0, 0)	0 (0, 0)
				Recurrent headache	6.7 (3.5, 9.9)	1.6 (1.1, 2.2)	0.5 (0.24, 0.76)
				Vision loss	0.79 (-0.31, 1.9)	0.54 (0.24, 0.85)	0.43 (0.18, 0.67)
CVD	28.4 (21.8, 35)	42.3 (39.5, 45)	44.3 (41.7, 46.9)	Chronic atrial fibrillation	0 (0, 0)	3.1 (2.4, 3.8)	6.7 (5.8, 7.7)
				Chronic DVT or thromboembolism	1.2 (-0.16, 2.5)	0.45 (0.17, 0.73)	0.53 (0.26, 0.8)
				Left ventricular heart failure	0.79 (-0.31, 1.9)	1.3 (0.83, 1.8)	3 (2.4, 3.7)
				Pulmonary arterial hypertension	0 (0, 0)	0.18 (0.004, 0.36)	0.21 (0.04, 0.38)
				Raised blood pressure	26.9 (20.5, 33.3)	39.3 (36.7, 41.9)	38.6 (36.3, 40.9)
Liver	0 (0, 0)	0.14 (-0.019, 0.3)	0.079 (-0.03, 0.19)	Hepatic fibrosis	0 (0, 0)	0.045 (-0.043, 0.13)	0 (0, 0)
				NAFLD with hepatic fibrosis	0 (0, 0)	0.09 (-0.035, 0.22)	0.07 (-0.027, 0.17)
Lymphatic	0.8 (-0.31, 1.9)	0.33 (0.09, 0.58)	0.35 (0.12, 0.58)	Lymphedema	0.79 (-0.31, 1.9)	0.32 (0.08, 0.55)	0.32 (0.11, 0.53)
Metabolic	9.2 (5.4, 13)	8.5 (7.2, 9.7)	4.4 (3.6, 5.2)	High triglycerides, glycemia, and low HDL	9.1 (5.4, 12.8)	8.1 (6.9, 9.3)	4 (3.2, 4.7)
Musculoskeletal	26.4 (20, 32.8)	23.5 (21.5, 25.6)	16.9 (15.3, 18.5)	Joint pain	26.1 (19.8, 32.4)	22.4 (20.4, 24.4)	15.2 (13.8, 16.7)
Renal	0.8 (-0.31, 1.9)	2.2 (1.6, 2.9)	10.7 (9.4, 11.9)	Microalbuminuria with reduced eGFR	0.79 (-0.31, 1.9)	2.1 (1.5, 2.7)	9.7 (8.5, 10.8)
Reproductive	0	0.38 (0.12, 0.64)	0.16 (0.003, 0.31)	Male hypogonadism	0 (0, 0)	0.36 (0.11, 0.61)	0.14 (0.003, 0.28)
				Oligomenorrhea	0 (0, 0)	0 (0, 0)	0 (0, 0)
				Polycystic ovary syndrome	0 (0, 0)	0 (0, 0)	0 (0, 0)
Respiratory	13.6 (9, 18.2)	8 (6.8, 9.3)	10.2 (8.9, 11.4)	Breathlessness	9.5 (5.7, 13.3)	6.6 (5.6, 7.7)	8.3 (7.3, 9.4)
				Diaphragmatic compliance	0 (0, 0)	0.045 (-0.043, 0.13)	0 (0, 0)
				Hypoventilation	0.4 (-0.38, 1.2)	0.14 (-0.018, 0.29)	0.07 (-0.027, 0.17)
				Wheezing	3.6 (1.2, 5.9)	1.4 (0.94, 1.9)	1.3 (0.89, 1.7)
Upper Airways	8 (4.5, 11.5)	6.2 (5.2, 7.3)	3.2 (2.5, 3.9)	Sleep apnoea	7.9 (4.4, 11.4)	6 (4.9, 7)	2.9 (2.3, 3.5)
Urinary	0.4 (-0.38, 1.2)	0.66 (0.32, 1)	1.3 (0.82, 1.7)	Chronic urinary incontinence	0.4 (-0.38, 1.2)	0.63 (0.3, 0.96)	1.1 (0.74, 1.5)

ADL: activities of daily living; CNS: central nervous system; CVD: cardiovascular disease; DVT: deep vein thrombosis; NAFLD: Non-alcoholic fatty liver disease; HDL: High-density lipoprotein; eGFR: estimated glomerular filtration rate

Table 31. Age-stratified prevalence (%) of specific diseases contributing to clinical obesity in females, by age

System	<44	45-64	65+	Diagnosis	<44	45-64	65+
ADL	6 (3.8, 8.1)	6.3 (5.3, 7.3)	7.2 (6.2, 8.3)	Limitations in ADL	5.8 (3.7, 7.9)	6.2 (5.2, 7.2)	6.7 (5.8, 7.6)
CNS	13.9 (10.7, 17.2)	6.4 (5.4, 7.5)	1.7 (1.2, 2.2)	Raised intracranial pressure	0.19 (-0.19, 0.58)	0.08 (-0.032, 0.2)	0 (0, 0)
				Recurrent headache	12.6 (9.6, 15.7)	5.6 (4.7, 6.6)	1.2 (0.83, 1.6)
				Vision loss	1.4 (0.35, 2.4)	0.67 (0.34, 0.99)	0.44 (0.2, 0.68)
CVD	14.9 (11.6, 18.3)	30.7 (28.5, 33)	40.8 (38.4, 43.2)	Chronic atrial fibrillation	0.19 (-0.19, 0.58)	1.5 (1, 2)	5.4 (4.6, 6.3)
				Chronic DVT or thromboembolism	0.97 (0.12, 1.8)	0.46 (0.19, 0.73)	0.48 (0.23, 0.73)
				Left ventricular heart failure	0.19 (-0.19, 0.58)	0.37 (0.13, 0.62)	1.8 (1.3, 2.3)
				Pulmonary arterial hypertension	0.19 (-0.19, 0.58)	0.25 (0.05, 0.45)	0.48 (0.23, 0.73)
				Raised blood pressure	13.2 (10.1, 16.4)	28.9 (26.8, 31.1)	36.6 (34.4, 38.8)
Liver	0 (0, 0)	0.043 (-0.041, 0.13)	0.15 (0.003, 0.29)	Hepatic fibrosis	0 (0, 0)	0 (0, 0)	0.07 (-0.026, 0.16)
				NAFLD with hepatic fibrosis	0 (0, 0)	0.042 (-0.04, 0.12)	0.1 (-0.013, 0.22)
Lymphatic	0 (0, 0)	1.1 (0.68, 1.5)	0.74 (0.42, 1.1)	Lymphedema	0 (0, 0)	1.1 (0.67, 1.5)	0.68 (0.38, 0.98)
Metabolic	2.8 (1.3, 4.2)	2.6 (1.9, 3.2)	2.4 (1.8, 3)	High triglycerides, glycemia, and low HDL	2.7 (1.3, 4.2)	2.5 (1.9, 3.1)	2.3 (1.7, 2.8)
Musculoskeletal	30.1 (25.3, 34.9)	29.7 (27.5, 31.9)	22.3 (20.5, 24.1)	Joint pain	29.4 (24.7, 34.1)	29 (26.8, 31.1)	20.6 (19, 22.3)
Renal	0.2 (-0.19, 0.59)	2 (1.5, 2.6)	8.1 (7, 9.2)	Microalbuminuria with reduced eGFR	0.19 (-0.19, 0.58)	2 (1.5, 2.6)	7.5 (6.5, 8.5)
Reproductive	10.4 (7.5, 13.2)	0.77 (0.41, 1.1)	0.037 (-0.035, 0.11)	Male hypogonadism	0 (0, 0)	0 (0, 0)	0 (0, 0)
				Oligomenorrhea	1.4 (0.35, 2.4)	0.29 (0.08, 0.51)	0 (0, 0)
				Polycystic ovary syndrome	9.3 (6.7, 12)	0.46 (0.19, 0.73)	0.034 (-0.033, 0.1)
Respiratory	10.4 (7.5, 13.2)	9.6 (8.4, 10.9)	10.1 (8.9, 11.3)	Breathlessness	7.2 (4.9, 9.5)	7.2 (6.1, 8.2)	8.3 (7.3, 9.4)
				Diaphragmatic compliance	0 (0, 0)	0 (0, 0)	0.07 (-0.026, 0.16)
				Hypoventilation	0 (0, 0)	0.25 (0.05, 0.45)	0.17 (0.021, 0.32)
				Wheezing	3.9 (2.2, 5.6)	2.8 (2.1, 3.5)	1.2 (0.8, 1.6)
Upper Airways	4.2 (2.4, 6)	3 (2.3, 3.7)	1.4 (1, 1.9)	Sleep apnoea	4.1 (2.3, 5.8)	2.9 (2.2, 3.6)	1.3 (0.91, 1.7)
Urinary	7.2 (4.8, 9.5)	7.6 (6.5, 8.8)	4.9 (4.1, 5.7)	Chronic urinary incontinence	7 (4.7, 9.3)	7.4 (6.4, 8.5)	4.5 (3.8, 5.3)

ADL: activities of daily living; CNS: central nervous system; CVD: cardiovascular disease; DVT: deep vein thrombosis; NAFLD: Non-alcoholic fatty liver disease; HDL: High-density lipoprotein; eGFR: estimated glomerular filtration rate

6.3.4 Multimorbidity prevalence

Out of the 6,251 individuals with clinical obesity, approximately two-thirds had only one diagnosis of a condition of interest. There were 2,894 individuals with more than one prevalent condition, with 27.1% having two conditions, 11.2% having three, 4.8% with four, and less than 2.1% with five, and less than 1% having six to nine conditions (Figure 23). Of those with more than one condition, the largest proportion of individuals had a combination of a CVD and musculoskeletal disorder.

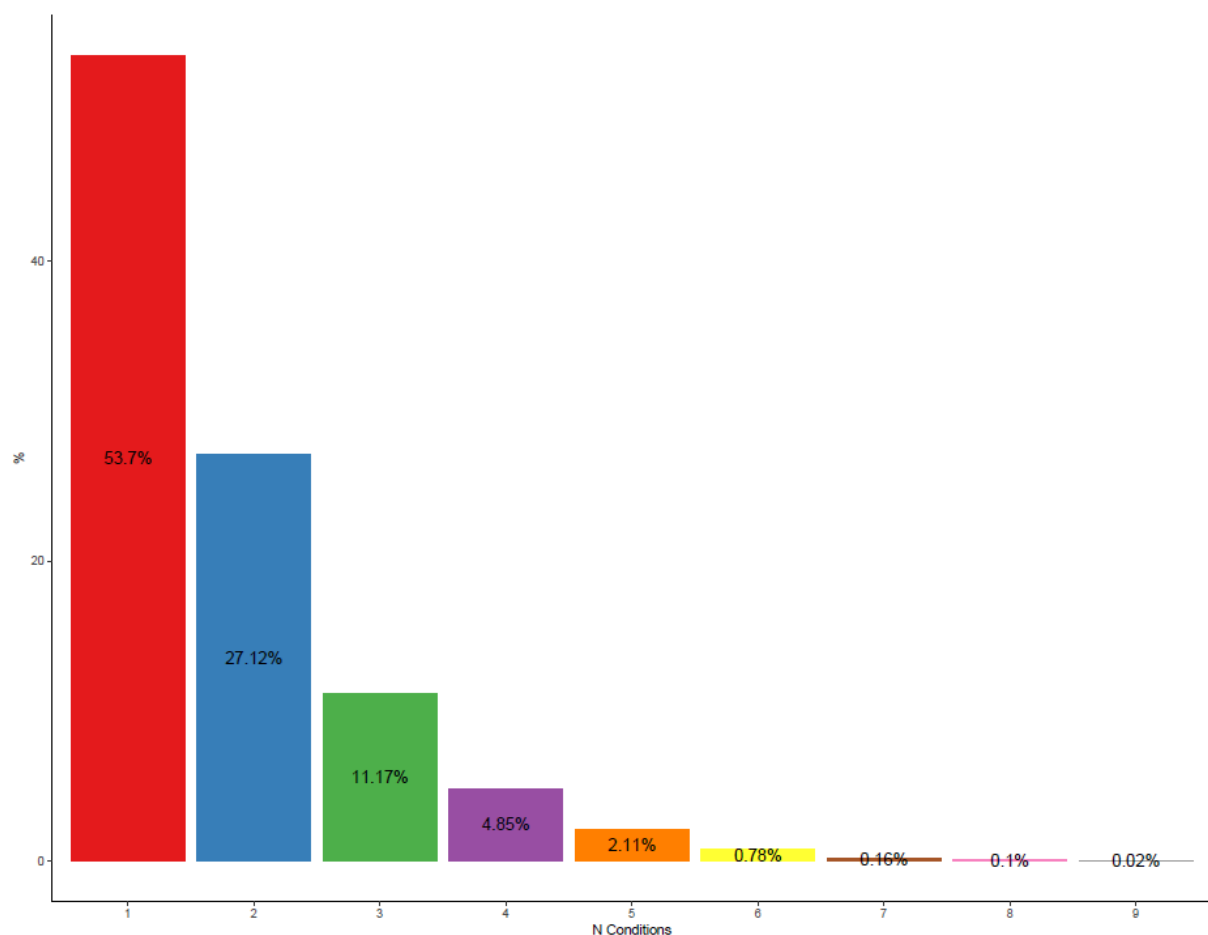


Figure 23. Proportion of individuals with clinical obesity with a specific number of conditions

6.3.5 Hospitalisations

Compared to males with normal weight, overweight, pre-obesity, and pre-clinical obesity, males with clinical obesity had the highest hospitalisation rate, at 168 hospitalisations per 1000 people per year (Table 32). This was followed by males with normal weight with a hospitalisation rate of 159 hospitalisations per 1000 people and overweight, pre-obese, and pre-clinical obese with about between 145-150 hospitalisations per 1000 people.

Females in the normal weight category had the highest hospitalisation rate of 166 hospitalisations per 1000 people compared to the other adiposity levels (Table 32). Those in the overweight category had 155 hospitalisations per 1000 people, followed by pre-clinical obesity with 149 hospitalisations per 1000. The lowest hospitalisation rate was in the pre-obese and clinical obese categories, accounting for about 142 hospitalisations per 1000 people.

Table 32. Age-adjusted hospitalisation rate per 1000 person years by adiposity level in males and females

Adiposity	Males	Females
Normal weight	159.0 (158.7, 159.4)	165.6 (165.2, 166)
Overweight	147.8 (147.6, 148.1)	155.1 (154.6, 155.5)
Pre-Obese	149.8 (149.5, 150)	142.3 (142, 142.5)
Pre-Clinical Obesity	144.8 (144.5, 145)	149.3 (149, 149.5)
Clinical Obesity	168.2 (167.9, 168.6)	142.6 (142.3, 143)

6.3.5.1 Hospitalisations, secondary analysis

A secondary analysis for hospitalisations excluded individuals with less than 5 years follow up after their BMI and WC measurement (Table 33). This resulted in clinical obesity having the lowest hospitalisation rate in males accounting for 90 hospitalisations per 1000 person years, with pre-clinical obesity having the highest hospitalisation rate at 107 hospitalisations per 1000 person years. In females, those with clinical obesity had penultimate lowest hospitalisation rate,

accounting for 103 hospitalisations per 1000 person years. Pre-clinical obesity had the highest hospitalisation rate at 111 hospitalisations per 1000 person years (Table 33).

Table 33. Sensitivity analysis using a five-year exclusion period for age-adjusted hospitalisation rate per 1000 person years by adiposity level in males and females

	Males	Females
Normal weight	103.9 (103.6, 104.3)	110 (109.7, 110.4)
Overweight	97.1 (96.9, 97.4)	108.5 (108.1, 109)
Pre-Obese	91 (90.8, 91.2)	97.1 (96.9, 97.4)
Pre-Clinical Obesity	107.3 (107.1, 107.6)	111.1 (110.9, 111.4)
Clinical Obesity	89.6 (89.3, 89.8)	103.1 (102.8, 103.5)

6.3.5.2 Age-stratified hospitalisations

Males with clinical obesity aged <44 had the highest hospitalisation rate at about 149 hospitalisations per 1000 person years, followed by 137 hospitalisations per 1000 person years in the normal weight group (Table 34). Males 45-64 years old had the second lowest hospitalisation rate in the clinically obese category, with 105 hospitalisations per 1000 person years, compared to the highest hospitalisation rate in the normal weight category accounting for 143 hospitalisations per 1000 person years. In the 65+ age group in males, those with pre-clinical obesity had the highest hospitalisation rate of 249 hospitalisations per 1000 person years, followed by overweight, clinical obesity, and normal weight with about 232 hospitalisations per 1000 person years.

In females <44, those with clinical obesity had the lowest hospitalisation rate accounting for 86 hospitalisations per 1000 person years (Table 34). In the 45-64 age group and the 65+ age group, clinical obesity had the third highest hospitalisation rate at 141 hospitalisations per 1000 person years and 225 hospitalisations per 1000 person years, respectively. In the normal weight category, there were the highest hospitalisation rates across all age groups ranging from 137

hospitalisations per 1000 person years in the <44 age group to 246 hospitalisations per 1000 person years in the 65+ age group.

Table 34. Age-stratified hospitalisation rate per 1000 person years by adiposity level in males and females

	<44	45-64	65+
MALES			
Normal	136.9 (131.1, 142.7)	143.4 (139, 147.8)	231.7 (226.6, 236.8)
Overweight	101.5 (100.3, 102.6)	122.3 (121.8, 122.7)	232.1 (231.6, 232.6)
Pre-Obese	120 (118.3, 121.7)	112.1 (111.6, 112.5)	220.3 (219.9, 220.8)
Pre-Clinical Obesity	91.3 (90.4, 92.1)	103 (102.6, 103.3)	249.7 (249.2, 250.2)
Clinical Obesity	149.3 (146.4, 152.1)	104.8 (104.3, 105.3)	232 (231.4, 232.5)
FEMALES			
Normal	136.9 (132.2, 141.7)	149.6 (146.4, 152.8)	246.4 (243.4, 249.4)
Overweight	120.8 (119.5, 122)	145.6 (144.8, 146.4)	221.8 (221, 222.6)
Pre-Obese	105.1 (104.2, 106)	127.6 (127.1, 128.1)	217.7 (217.2, 218.1)
Pre-Clinical Obesity	100 (99.4, 100.6)	128.1 (127.7, 128.4)	229.7 (229.2, 230.2)
Clinical Obesity	86.8 (85.7, 87.9)	141.5 (140.9, 142.1)	224.6 (224, 225.2)

6.3.6 Mortality rates

Males with clinical obesity had the lowest mortality rates at 4.5 deaths per 1000 person years.

The highest mortality rate was in the pre-clinical obese category, at 8.6 deaths per 1000 person years (Table 35). The next highest rates occurred in normal weight, overweight, and pre-obese, accounting for 5.2-5.7 deaths per 1000 and 5.2 deaths per 1000 person years.

For females, clinical obesity had the lowest mortality rates at 2.7 deaths per 1000 person years.

The pre-clinical obese category had the highest mortality rates at 5 deaths per 1000 (Table 35).

This was followed by normal weight at 3.6 deaths per 1000 person years and pre-obese at 3.4 deaths per 1000 person years. Overweight mortality rates were 2.8 per 1000 person years.

Table 35. Age-adjusted mortality rate per 1000 person years by adiposity level in males and females

	Males	Females
Normal weight	5.7 (5.1, 6.3)	3.6 (3.4, 3.8)
Overweight	5.2 (4.6, 5.8)	2.8 (2.7, 3)
Pre-Obese	5.2 (4.7, 5.8)	3.4 (3.2, 3.7)
Pre-Clinical Obesity	8.6 (7.8, 9.4)	5.0 (4.7, 5.3)
Clinical Obesity	4.5 (2.7, 6.2)	2.7 (2.5, 2.9)

6.3.7 Sensitivity analyses

6.3.7.1 Mortality rates with and without prevalence of clinical obesity

When assessing the mortality rates when only using BMI and a prevalent condition to define clinical obesity, pre-clinical obesity had the highest mortality rate compared to normal weight, overweight, and males and females with clinical obesity (Table 36). This was also the case when using WC and prevalence status.

However, when only using BMI or WC as the independent variable for mortality rate, including a BMI measurement only resulted in the obese category to have the highest mortality rate with 7.8 deaths per 1000 person years for males and 4.7 deaths per 1000 person years for females (Table 36). Similarly, using only WC, the highest mortality rates occurred in individuals with a very high WC at 6.7 deaths per 1000 person years for males and 4.1 deaths per 1000 person years for females.

Table 36. Age-adjusted mortality rate per 1000 person years by adiposity level in males and females, using BMI and prevalence status; BMI only; WC and prevalence status; and WC only

		Males	Females
BMI with prevalence			
	Normal weight	5.6 (5.3, 5.9)	3.6 (3.4, 3.8)
	Overweight	5.2 (5, 5.5)	3.2 (3, 3.4)
	Pre-clinical obesity	8.2 (7.8, 8.6)	4.8 (4.5, 5.1)
	Clinical obesity	4.6 (4.4, 4.8)	2.6 (2.5, 2.8)
BMI only			
	Normal weight	5.6 (5.3, 5.9)	3.6 (3.4, 3.8)
	Overweight	5.2 (5, 5.5)	3.2 (3, 3.4)
	Obese	7.8 (7.4, 8.2)	4.7 (4.4, 4.9)
WC with prevalence			
	Low risk	5.5 (5.2, 5.7)	3.5 (3.3, 3.7)
	High risk	5.4 (5.2, 5.7)	3.3 (3.1, 3.5)
	Pre-clinical obesity	7 (6.6, 7.3)	4.3 (4, 4.5)
	Clinical obesity	3.9 (3.7, 4.1)	1.8 (1.7, 2)
WC only			
	Low risk	5.5 (5.2, 5.7)	3.5 (3.3, 3.7)
	High risk	5.4 (5.2, 5.7)	3.3 (3.1, 3.5)
	Very high risk	6.7 (6.3, 7)	4.1 (3.8, 4.3)

6.4 Discussion

In this chapter, I applied the novel definition of clinical obesity to a subset of individuals with a BMI and WC within my CPRD dataset, providing insight on the public health implications of clinical obesity and the most prominent conditions contributing to obesity as a disease. Over 35,000 individuals were included in the BMI-WC subset and between 2015 and 2019, about 27% of males were obese, of which 17% were clinically obese; 29% of females were obese, and 18% were clinically obese. When assessing the main contributors to clinical obesity, CVD, musculoskeletal conditions, and respiratory conditions were the top three most prevalent conditions in males and females.

6.4.1 Key points

In the analysis including individuals with clinical obesity in males and females, CVD was the most common contributor to clinical obesity, followed by musculoskeletal conditions, and

respiratory conditions. Musculoskeletal conditions only consisted of joint pain, whilst raised blood pressure was the primary contributor to CVD morbidity in males and females with clinical obesity. Across both sexes, respiratory conditions were the third largest contributor to clinical obesity, wherein breathlessness was the largest contributor.

Conditions such as microalbuminuria with reduced eGFR, and high triglycerides, high glycemia, and low HDL, chronic atrial fibrillation, and sleep apnoea were more prevalent in males than females with clinical obesity, whereas conditions such as urinary incontinence, recurrent headaches, and reproductive conditions were more prevalent in females. About half of the disease-specific conditions had a prevalence of <1% in both males and females.

After age-stratifying, raised blood pressure was the most prevalent condition for clinical obesity in males for all age groups and 65+ females. In females with clinical obesity 45-64, the prevalence of joint pain and raised blood pressure was about the same and joint pain was the most prominent condition in females <44 with clinical obesity.

When assessing hospitalisation rates, males in the clinical obese category had the highest rate, at 168 hospitalisations per 1000 person years. In females, normal weight had the highest rate at 165 hospitalisations per 1000 person years and the pre-obese and clinical obese categories had the lowest hospitalisation rates at 142 hospitalisations per 1000 person years. When assessing hospitalisation in those who were still being followed up five years after a BMI and WC measurement, five-year follow up males and females with pre-clinical obesity had the highest hospitalisation rate, indicating an exclusion period for hospitalisations may not properly identify those with increased hospitalisation as they have not yet been diagnosed with a prevalent condition of interest.

Mortality rates were highest in the pre-clinical obese category for both males and females, and lowest in the clinical obesity category. This was an unexpected result therefore multiple sensitivity analyses were conducted to analyse the mortality rates by adiposity level—using BMI and WC separately—with and without a prevalent condition. Considering the mortality rates were highest for those with either an obese BMI or a very high WC but lowest when including a prevalent condition illustrate the diseases and conditions utilised to define clinical obesity are not necessarily indicative of increased mortality.

6.4.2 Comparison with the literature

Out of the CVDs included to define clinical obesity, raised blood pressure was the main contributor in our study. The association between obesity and hypertension is well established, and both BMI and WC are highly correlated to hypertension in a variety of populations (201-204). Hypertension was the leading risk factor for morbidity and mortality globally, according to the GBD 2017 Risk Factor Collaboration and The Framingham Offspring Study, and obesity is accountable for 65% of hypertension cases in females and 78% in males (205, 206).

In the age-stratified analysis, the main contributor for individuals 65+ remained high blood pressure in both males and females. This is consistent with previous findings as high blood pressure and hypertension increase with age for both males and females in high income countries (207, 208). In our study, we also found males had a higher prevalence of hypertension in the 45-64 age group, consistent with research indicating males having higher prevalence of high blood pressure at younger ages compared to females (207). By aged 60 and over, females were shown to have a higher hypertension prevalence than males, however, in this Chapter, we found the prevalence rates for hypertension were about the same for males and females with clinical obesity (207).

Research shows that women have a higher prevalence of diseases and conditions that are not life threatening but are debilitating (209). This is observed for conditions such as joint pain (which is also prominent in males, but remains higher in females), PCOS (which is not a male condition, but in comparison the prevalence of reproductive conditions was small in males), urinary incontinence, and recurrent headaches. In contrast, males had a higher prevalence of primarily metabolic conditions, but also renal conditions.

Obesity and age are both consistently cited as a major risk factor for the development and progression of osteoarthritis, and this study identified joint pain as the second most prominent contributor to clinical obesity in the crude and age-stratified analyses (210, 211). Further, joint pain was highly prevalent for both males and females, consistent with a meta-analysis which found an increase in adiposity was predictive of future musculoskeletal pain and an increase in adiposity resulted in an increase in incidence or worsening joint pain (212). Whilst our study combines all areas of joint pain, studies indicate those with higher adiposity levels risk development of foot, knee, hip, and lower back pain (210, 212).

The high prevalence of musculoskeletal pain is often accompanied with a high prevalence of limitations of ADL considering musculoskeletal pain is associated with a four times greater risk of work-restricting pain (210). After age-stratifying the prevalence rates, the prevalence of both joint pain and limitations of ADL increased with increasing age groups. There is a clear positive association with functional limitations in older ages and limitations of ADL in obese women in the US, with a stronger association in females than males (213).

An expected result in this study was that males with clinical obesity had the highest hospitalisation rate, but unexpectedly the highest hospitalisation rate in females was in the normal weight category. This is particularly unexpected considering data in England and Wales shows females have a consistently higher hospitalisation rate than males, accounting for about 56% of hospital admissions (214). Further, the Million Women Study, which includes females 50-64 years old at baseline, found hospital admission rates were significantly higher for females in the overweight and obese categories, compared to females in the normal weight category which was not the case in our study (215). Even when hospitalisations were age-stratified and a five-year survival period was applied, females with clinical obesity had some of the lowest hospitalisation rates.

6.4.3 Strengths and limitations

Utilising the CPRD database is the main strength of this study. I was able to extract WC for over 100,000 participants between 2005 and 2010 and over 35,000 participants between 2015 and 2019 to assess adiposity levels. As the use of WC was not an original aspect of my research, having the ability to extract a subset data to include individuals with WC in the same year as a BMI measurement was imperative to achieve this aim according to the Obesity Commission's requirements.

Further, having HES data linked and the GP diagnostic read codes allowed for defining the prevalence of conditions to define clinical obesity in the dataset. The HES data allowed for all diagnoses whilst an individual was hospitalised, which was key in this aim as some of the conditions to define clinical obesity are not common conditions to be diagnosed with at the GP. Finally, ONS linked data provided accurate mortality data to analyse the mortality rates, but also ensuring the follow-up period was correctly determined.

Limitations of this study include the very few numbers of individuals in the cohort who had both a BMI and WC within a year. Out of the 1.4 million individuals in the overall CPRD dataset, only about 7% had both measurements within the specified period between 2005 and 2015, which was even smaller when excluding a five-year survival period for the mortality rates, and the prevalence estimates between 2015 and 2019. In 2005, the prevalence of overweight and obesity and a very high WC were highest in CPRD, indicating bias. This was confirmed when comparing the most recent BMI measurement in the entire dataset to the BMI-WC subset considering the proportion of obese individuals in the BMI-WC subset was higher than the entire dataset, and of the obese individuals a higher proportion had clinical obesity. This was also illustrated when comparing the BMI-WC subset to HSE. At the start of the study, there is an over-representation of those with a high BMI or WC, but by 2019, the prevalence of both a high BMI and WC in CPRD is more similar to the results in HSE, indicating a more representative population of individuals with multiple anthropometric measurements.

These differences in the subsample of individuals who have a WC and BMI measurement in my CPRD dataset indicates a sampling bias. In the UK, NICE guidelines specify WC should be a secondary measurement to BMI (72). Further, NICE guidelines also suggest a BMI measurement, a supplementary WC measurement, and recognising co-morbidities in order to appropriately recommend medical interventions needed for the patient. Thus, those who get both WC and BMI measurements are more likely to have a prevalent health condition, resulting in an inflation of the prevalence of individuals with a ‘very high’ WC and obese BMI.

Similarly to a limitation in Chapter 5, we do not know if a diagnosis was correctly defined in the CPRD GP read codes. Further, defining prevalence as a diagnosis five years prior to a WC

and BMI measurement assumes the individual had the same adiposity levels at the time of diagnosis. As the number of BMI and WC measurements were limited, and I defined the prevalence of a disease five years prior to a BMI and WC measurement, we do not know whether a prevalent condition was caused by obesity or obesity caused the condition. For example, if an individual had joint pain, it could be that the excess adiposity resulted in joint pain or joint pain limited activity and resulted in obesity. There were conditions which do require biopsies and more in-depth diagnostic criteria, such as hepatic failure, thus it is probably these individuals were not identified in the study. There were also conditions which were defined as 'chronic' or 'recurrent' which did not have a formal definition.

6.5 Summary

In this analysis, I found that the main contributors to clinical obesity were CVD, musculoskeletal, and respiratory conditions in both males and females. The primary conditions which contributed to the prevalence include raised blood pressure, joint pain, and breathlessness, which increased with increasing age. Further, whilst clinical obesity may be a good indicator for hospitalisation, it is not necessarily a good indicator for mortality. These results show the conditions that primarily affect those with clinical obesity and provide insight to clinicians and public health professionals on the appropriate measures to increase access to care and appropriate treatments, interventions, and health strategies for individuals with clinical obesity in mind.

7. Discussion

7.1 Summary

In this thesis I used CPRD, a longitudinal database representative of the English population between 2004 and 2019. I have assessed the trends and diverse burden of mortality and morbidity by BMI, through mortality rates, incidence and prevalence rates, and prevalent conditions associated with a newly-developed definition of clinical obesity.

The main findings in this thesis are: 1) all-cause mortality is declining across all BMI categories in males and in females with obesity as a result of declining CVD mortality; 2) the proportional burden of mortality is broadening, with cancer as the largest contributor to mortality in males and females in the overweight category, with increases in mortality burden from neurological and respiratory conditions; 3) with few exceptions, the prevalence of obesity-related comorbidities is increasing and incidence rates are declining; 4) there is a shift in comorbidity prevalence and incidence from IHD and type 2 diabetes in the obese categories to conditions such as depression and musculoskeletal conditions; 5) about two-thirds of individuals with obesity have clinical obesity, with high blood pressure, joint pain, and breathlessness as the main contributors to clinical obesity prevalence.

Prior to this work, research on mortality and morbidity by BMI categories was primarily conducted through association studies over single periods of time (75). Further, studies investigating the trends of mortality and morbidity would focus on one specific cause of death or diagnosis in the overall population, rather than by BMI or multiple obesity-related diseases and conditions. To our knowledge, this is the first study that has examined the trends in the broad and diverse spectrum of obesity related to mortality and morbidity by BMI. This is also the first study to examine the implications of *The Lancet Diabetes and Endocrinology* Obesity

Commission's preliminary definition of clinical obesity and the prevalence of the diseases and conditions which make up clinical obesity.

My results for mortality in the overall population are largely consistent with previous research, indicating all-cause mortality is declining. Although some previous studies indicate a stagnation or slowing of improvements in all-cause mortality, we found a general continuation of reduction in mortality rates (123, 133-135). This decline is occurring for all BMI categories in males, declining by 3% on average per year. Whilst all-cause mortality declined by 2% per year in females in the obese category, this was the only BMI group with significant changes in the study period. These declines in all-cause mortality are largely driven by declines in CVD mortality wherein the obese category had declined 7% on average per year in males and 4% per year in females.

As a result of declining mortality rates, I observed a diversification of the diseases which contribute to the proportional mortality burden. In males, cancers have become the largest contributor to mortality across all BMI categories and in overweight women. This indicates the changes in CVD mortality in females is slower than in males and may require more focus on improvements in survival. For males, the proportion of deaths from cancers was greater in the overweight and obese categories compared to the normal weight category, but there was no discernible difference between overweight and obese categories.

Further consistencies with prior research include the divergence between incidence and prevalence trends, wherein prevalence increased but incidence decreased for most conditions across BMI categories. This is likely attributed to improved disease prevention and survival and care after diagnosis (141, 142). As mortality rates declined for life threatening conditions

such as CVD, there is a higher risk of developing long-term diseases and conditions such as Alzheimer's and dementia, osteoarthritis and joint disorders, and depression. Alzheimer's and dementia had larger increases per year the obese categories than the normal weight category for both males and females, whereas incidence rates increased at a similar magnitude across all BMIs. Both depression and osteoarthritis and joint disorders had some of the highest prevalence and incidence rates in males and females by 2019, with rates increasing with higher BMI categories, despite declines in incidence rates throughout the study period.

The non-vascular comorbidities of obesity also had a large effect on the prevalence of clinical obesity, wherein joint pain was one of the most prevalent conditions amongst males and females with clinical obesity. The greatest contributing disease/condition to clinical obesity was raised blood pressure in males, but joint pain in females. However, joint pain in males was still a prominent contributor to clinical obesity prevalence. Whilst pre-clinical obesity had the greatest mortality rates in both males and females, I was not expecting clinical obesity to have the lowest. Upon further investigation, I found that using clinical obesity is not indicative to a higher mortality rate, despite clinical obesity contributing to ill health.

7.2 Public health and policy implications

Throughout this research, I have observed large CVD improvements. CVD mortality and incidence rates declined, and prevalence increased for cerebrovascular disease, indicating better survival, whilst heart failure and IHD declined, in response to mortality and declining incidence rates. The impact of these improvements was the most prominent for CVD mortality and prevalence in the obese category, whereas the improvements in incidence rates were minimal in the obese category compared to normal weight.

A major factor contributing to the improvements in CVD outcomes includes better treatment and management of risk factors such as high blood pressure and high cholesterol. Between 1991 and 2014, CVD prescriptions increased by 78%; further, between 1980 and 2013, the number of surgical interventions increased sevenfold (132). Specifically, there have been sustained increases in antihypertensive drugs, heart failure drugs, and lipid lowering drugs (166). The decline in IHD prevalence and incidence is largely attributed to the increase in preventative prescribing of lipid lowering medications (166). However, whilst these medications are necessary for CVD maintenance, there is still a large gap in treatment and prevention considering in England, 40% of individuals are undiagnosed with high blood pressure and those with diagnosed high blood pressure, only 67% have it controlled (216). This is particularly concerning as I observed in Chapter 6, those with clinical obesity had the highest prevalence of high blood pressure, indicating individuals will need proper care through treatment and management—in addition to those in the pre-clinical obese category to receive monitoring and prevention—to limit incident disease and mortality.

Further, CVDPREVENT, a part of the NHS Long Term Plan which aims to improve pressures of the NHS and improve patient care for future needs—has shown that initiatives are needed to improve the management of multiple CVDs (i.e., atrial fibrillation, lipid lowering therapy) specifically in females (217, 218). This would be beneficial as I found females had slower rate of improvement for CVD mortality across all BMI categories.

The improvement in CVD outcomes are also a result of long-term reductions in smoking in the population, which is another explanation for the declines in IHD prevalence and incidence in Chapter 5 (194). Since the 1970s, England has implemented population tax and regulatory policies on smoking as well as implementing anti-smoking and cessation campaigns. Policies

are continuously being updated, and as of 2022 England had the lowest proportion of smokers ever, accounting for about 13% of the population, compared to 20% of the population in 2011, which was a statistically significant decline (219). With improvements in health outcomes due to smoking cessation, UK Biobank, Tromsø Study, and the Framingham Heart Study found smoking cessation has contributed to weight gain. (220-222). Little information is available regarding further plans to reduce tobacco use and smoking rates, though these studies suggest weight management and obesity prevention strategies should be used in conjunction with smoking cessation interventions (220-223). The improvements in smoking, cholesterol, and blood pressure risk factors are the primary reasons for declining CVD outcomes, but these improvements are now being counteracted as a result of the obesity epidemic (194, 224).

As CVD mortality and incidence declined, there were no changes in cancer mortality or incidence rates throughout the study at any BMI level. As all cancers were aggregated for this analysis, differential trends may have been obscured, considering each type of cancer has differing mortality and incidence trends. For instance, incidence rates for stomach, bladder, and lung (males only) cancers declined in, whereas thyroid, liver, prostate (males only), lung (females only), and breast (females only) increased (92). Whilst I did not observe any changes for cancer mortality in Chapter 4 or incidence in Chapter 5, research indicates cancer mortality is declining, and incidence is increasing. However, when excluding prostate cancer from incidence rates in males, the increase in incidence rates was no longer present, but, when excluding breast cancer for female incidence rates, the increase remained, largely because of increases in uterine cancer (225).

Cancer mortality improvements observed in literature and prevalence increases in Chapter 5 are due to a variety of factors, such as changes in lifestyle from reduced smoking rates (lung

and stomach cancers), increased detection (breast and cervical cancers), and improved treatment (breast and bowel cancers) (225). On the other hand, pancreatic, oesophageal, and gallbladder cancers—which are obesity-related cancers—have no national screening program in place, and are some of the hardest to treat, resulting in low survival (89). There are only three national screening programs for cancer in the UK, which includes breast, cervical, and bowel cancer (226). The importance of successful screening programs, with bowel cancer as the example, is clear. Since the introduction of a screening program in 2006, bowel cancer incidence rates increased, but because of early detection and treatment, mortality declined by 2019 (225). In the UK, a targeted screening program is now recommended for lung cancer, and research is continuously being conducted for prostate cancer and ovary cancer screening where tests are available, but they are not reliable detecting all cancers (226). Thus, further research to improve screening capabilities, ensuring the programs will be more beneficial than harmful, is necessary for continued improvements for survival.

I observed that for the vast majority of morbidities, prevalence was increasing and at a greater magnitude in the obese class II+ category compared to the normal weight category, particularly for conditions such as Alzheimer's and dementia, depression, and liver disease (females only). I also observed that obese individuals had the highest proportion of having at least one prevalent condition, indicating clinical obesity, with high blood pressure, joint pain, and limitations in ADL as some of the most prevalent contributors to clinical obesity. Further, with improvements in mortality and medical advancements, more people are living with obesity and have a greater risk of developing long-term conditions, meaning people are living longer, but in ill health (194). The demand in health care is only increasing, with nearly 20% of individuals aged 20 and older projected to have a major illness by 2040 (194). This information is vital for health care planning, to ensure health care services have the ability to maintain treatment for

consistently prevalent conditions such as diabetes in obese classes and high blood pressure for clinical obesity but also have the capacity to increase care for individuals with increasing prevalence of COPD, depression, Alzheimer's and dementia, and osteoarthritis and joint disorders.

7.3 Policies addressing the obesity epidemic

Addressing the rising obesity prevalence and implementing successful policies to reduce the prevalence and mitigate the risk of ill health associated to obesity is imperative. A successful policy was a tax on sugar-sweetened beverages, which led to manufacturers reducing the sugar content of drinks. As a result, low- and zero-sugar drink purchases rose by 40% and full sugar drinks purchases fell by 50% (227). Yet, research shows that about 43% of food and drinks in the more prominent areas of a grocery store (i.e., the entrance, checkout, and end of aisles) were dense in sugar content and calories (228). Other regulations introduced include restricting marketing of foods high in fat, salt, or sugar on television before 9pm and online. However, the regulations do not apply if an advertisement occurs on radio or podcasts, is from companies which are small/medium in size, and if a brand does not show any unhealthy food and drinks in the advert (229).

Since 1991, the UK has released 14 government strategies (with a total of 689 proposed policies within the 14 strategies) which were dedicated to tackling obesity in England (230). Of the 14 strategies the report assessed, the majority were focused on diet and were similar to strategies proposed in prior years that were not successfully implemented. When considering physical activity, healthcare professionals have been advised to discuss the benefits of physical activity and risks of inactivity and prescribe activity in areas with poor health and low physical activity (231). Active travel, which is meant to promote walking or cycling as a way to modify the built

environment and increase activity, is highly promoted from the Department of Travel, with an investment in improving the walking and cycling infrastructure (194, 232). However, there has been little research on the impact of the campaigns which limit advertisements for unhealthy foods on television and promote activity through active travel or from advice from healthcare professionals.

Of the 14 strategies which were examined, 13 did state the need to reduce inequalities, but only 19% of the policies were likely to reduce inequalities (230). Obesity prevalence is highest in the most deprived areas at 34% and lowest in the least deprived areas at 20% (174). Mortality rates amongst the poorest areas in England were 1.3-1.4 times higher than the richest areas of England in 2003, which increased to 1.5-1.6 times higher by 2017 (233). Whilst life expectancy was increasing in the English population, albeit at a slower rate than observed prior to 2011, life expectancy in males in the most deprived IMD quintiles was declining (233). Smoking prevalence is also higher in the most deprived IMD quintile, with a prevalence of 19% compared to 6% in the least deprived quintile (234).

The changes in mortality from CVDs to cancer, and an increase in people living with chronic diseases such as type 2 diabetes, osteoporosis, and depression, there is a clear increase in long-term debilitating diseases and conditions, particularly in individuals with obesity (178, 194). Maintaining improvements in risk factors and treatment has been major contributors to my results, but reducing the burden of obesity is the priority for these improvements to continue and to reduce the burden of ill health (141, 143, 144). Further, delaying the onset of disease through primary prevention will increase the length and quality of life, thus there is a significant need for more effective disease prevention and better support for promoting healthy behaviours to reduce inequalities and the prevalence of obesity (230, 235).

The purpose of the Lancet Diabetes & Endocrinology's Obesity Commission was to inform clinical and public health practice. In Chapter 6, I applied the clinical obesity definition to understand the prevalence amongst the obese population, but also the main contributors to clinical obesity. Having this knowledge helps inform clinical practice by identifying priorities for care, ensuring blood pressure control is maintained, for example, but also interventions to prevent clinical obesity in individuals with pre-clinical obesity. The policies and practice which could be implemented as a result of this knowledge would ensure improvement in care and allow for greater attention to be paid to individuals with clinical obesity, through treatment, management, and prevention (146).

7.4 Future work

One of the main strengths of my thesis is the use of a vast database to assess the trends of mortality and morbidity outcomes by BMI, with access to linked data. Nonetheless, a continue effort is necessary to support my findings in a clinical and public health setting, but also with further epidemiological work on the subject.

One of the main factors cited for the slowdown in mortality improvements is the widening gap of health inequalities, where the least deprived IMD quintiles are observing improved outcomes, but the most deprived IMDs are not, especially when obesity is considered (174, 233). I was able to stratify my all-cause mortality outcomes by IMD in Chapter 4, but the sample size was not large enough to conduct cause-specific outcomes. Conducting this analysis with a larger sample would be impactful to identify which diseases and conditions were changing by IMD and BMI and what needs to be focused on to ensure in prevention, management, and care can improve.

Both Chapters 4 and 5 indicate that little improvement in cancers have occurred for mortality or morbidity outcomes. Thus, a more granular analysis would be beneficial to identify which cancers are driving these trends and are more associated to BMI level for mortality and morbidity. It was an unexpected result that obesity-related cancer prevalence and incidence were not different across the BMI categories in Chapter 5, so a more thorough investigation into this would provide insight on cancer diagnosis data for screening and management in those groups.

Also observed in Chapters 4 and 5 were significant increases in neurological mortality burden and Alzheimer's and dementia prevalence and incidence. Research has suggested that mortality trends have increased due to changes in policy where neurological mortality is listed as the underlying cause of death, and as a result CVD mortality declines as it is not the underlying cause (177). Conducting a study which looks at underlying cause of death in addition to the other conditions listed on the death registration data would be interesting to determine if the declines in CVD mortality are due to improvements in survival, changes in policy, or a combination of both.

In Chapter 6, I observed mortality rates across clinical obesity were lower than pre-clinical obesity. Whilst the diseases and conditions used to define clinical obesity are subject to change as it is a preliminary definition, looking into medications, for example for high blood pressure, to determine treatment and control would provide an additional explanation if those with clinical obesity have better care or if the diseases which define clinical obesity are not ideal indicators for mortality risk. Utilising a dataset which includes a BMI and WC measurement, with no missing measurement data, would also provide a larger sample size than I had access to, as not

every visit to the GP includes a BMI, and even less often a WC, which could provide more accurate estimates of clinical obesity and the diseases and conditions which contribute to clinical obesity.

Future work which was out of the scope of this PhD includes research on the access to and uptake of weight management interventions for individuals with overweight and obesity. CPRD could provide data on individuals who receive referrals to these specific types of care and utilised them, or prescribed medication. However, previous research using CPRD data has shown primary care and surgical interventions are underutilised amongst individuals with obesity (236). There are regional inequalities regarding access to care, which is necessary to consider from a policy standpoint to ensure resources are not only available, but also accessible for individuals throughout the UK (237). The availability of new drug classes approved in the UK and targeted to those with obesity may be one factor which lessens the obesity epidemic. However, considering access and utilisation are already impacted by regional disparities, clinical and public health systems need to account for these factors, ensuring the disparities don't widen even further for those who are able to access and maintain weight management treatments.

Whilst policy is improving to reduce the prevalence of obesity, further evidence is needed to determine if implemented strategies are successful. For instance, if the bans on fast food advertising is actually reducing consumption and the obesity prevalence.

7.5 Conclusion

All-cause mortality, primarily from declining CVD mortality rates, is improving in English adults, with the most prominent declining trends occurring in the obese population. Throughout

the study period, the trends in mortality rates from cancers or non-cancer, non-CVD NCDs had changed little, apart neurological mortality in the obese category for males and females. As a result of improved treatment and management in CVD outcomes, in addition to policy changes (i.e., how primary cause of death is recorded), a shift in the proportional burden of cause-specific mortality occurred. A diversification in causes of death indicated as CVD mortality declines, the proportion of deaths from cancer, respiratory, neurological conditions increased. These results are prominently affecting the obese population as the prevalence of disease is increasing at a greater rate in obese class II+ than normal weight. Individuals who are clinically obese or pre-clinically obese require the maintenance and treatment to continue the observed declines in incidence and improved survival as seen in the increasing prevalence. Adjusting clinical and public health strategies to prevent, screen, and manage those with obesity for a broader set of diseases, in addition to focusing on reducing the prevalence of obesity, is necessary to continue the improvement of health and survival in the obese population.

8. References

1. World Health Organization. Age-standardized prevalence of obesity among adults (18+ years) 2023 [Available from: <https://data.who.int/indicators/i/BEFA58B>.
2. Chong B, Jayabaskaran J, Kong G, Chan YH, Chin YH, Goh R, et al. Trends and predictions of malnutrition and obesity in 204 countries and territories: an analysis of the Global Burden of Disease Study 2019. *EClinicalMedicine*. 2023;57:101850.
3. Federation. WO. Economic impact of overweight and obesity to surpass \$4 trillion by 2035 2023 [Available from: [https://www.worldobesity.org/news/economic-impact-of-overweight-and-obesity-to-surpass-4-trillion-by-2035#:~:text=The%20majority%20of%20the%20global,2%20billion\)%20will%20have%20obesity.](https://www.worldobesity.org/news/economic-impact-of-overweight-and-obesity-to-surpass-4-trillion-by-2035#:~:text=The%20majority%20of%20the%20global,2%20billion)%20will%20have%20obesity.)
4. NHS Digital. Statistics on Obesity, Physical Activity and Diet, England, 2020 2020 [Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/england-2020/part-3-adult-obesity-copy>.
5. World Health Organization. Obesity and overweight 2021 [updated 9 June 2021. Available from: <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>.
6. Ferris WF, Crowther NJ. Once fat was fat and that was that: our changing perspectives on adipose tissue. *Cardiovasc J Afr*. 2011;22(3):147-54.
7. Tipton CM. Susruta of India, an unrecognized contributor to the history of exercise physiology. *J Appl Physiol* (1985). 2008;104(6):1553-6.
8. Haslam DW, James WPT. Obesity. *The Lancet*. 2005;366(9492):1197-209.
9. Christopoulou-Aletra H, Papavramidou N. Methods used by the hippocratic physicians for weight reduction. *World J Surg*. 2004;28(5):513-7.
10. Sumińska M, Podgórski R, Bogusz-Górna K, Skowrońska B, Mazur A, Fichna M. Historical and cultural aspects of obesity: From a symbol of wealth and prosperity to the epidemic of the 21st century. *Obes Rev*. 2022;23(6):e13440.
11. Eknayan G. A History of Obesity, or How What Was Good Became Ugly and Then Bad. *Advances in Chronic Kidney Disease*. 2006;13(4):421-7.
12. Komaroff M. For Researchers on Obesity: Historical Review of Extra Body Weight Definitions. *J Obes*. 2016;2016:2460285.
13. Sorkin JD. BMI, age, and mortality: the slaying of a beautiful hypothesis by an ugly fact. *Am J Clin Nutr*. 2014;99(4):759-60.
14. Fletcher I. Defining an epidemic: the body mass index in British and US obesity research 1960-2000. *Sociol Health Illn*. 2014;36(3):338-53.
15. Blackburn H, Jacobs D, Jr. Commentary: Origins and evolution of body mass index (BMI): continuing saga. *Int J Epidemiol*. 2014;43(3):665-9.
16. World Health Organization. A healthy lifestyle - WHO recommendations 2010 [Available from: <https://www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle---who-recommendations>.
17. Keys A, Fidanza F, Karvonen MJ, Kimura N, Taylor HL. Indices of relative weight and obesity. *Int J Epidemiol*. 2014;43(3):655-65.
18. Hall DM, Cole TJ. What use is the BMI? *Arch Dis Child*. 2006;91(4):283-6.
19. Deurenberg P. Universal cut-off BMI points for obesity are not appropriate. *Br J Nutr*. 2001;85(2):135-6.
20. U.S. Preventive Services Task Force. Screening for obesity in adults: recommendations and rationale. *Ann Intern Med*. 2003;139(11):930-2.
21. Wormser D, Kaptoge S, Di Angelantonio E, Wood AM, Pennells L, Thompson A, et al. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. *Lancet*. 2011;377(9771):1085-95.
22. Shi W, Neubeck L, Gallagher R. Measurement matters: A systematic review of waist measurement sites for determining central adiposity. *Collegian*. 2017;24(5):513-23.
23. Mason C, Katzmarzyk PT. Variability in Waist Circumference Measurements According to Anatomic Measurement Site. *Obesity*. 2009;17(9):1789-95.
24. Sebo P, Beer-Borst S, Haller DM, Bovier PA. Reliability of doctors' anthropometric measurements to detect obesity. *Preventive Medicine*. 2008;47(4):389-93.

25. Verweij LM, Terwee CB, Proper KI, Hulshof CT, van Mechelen W. Measurement error of waist circumference: gaps in knowledge. *Public Health Nutr.* 2013;16(2):281-8.
26. Sebo P, Herrmann FR, Haller DM. Accuracy of anthropometric measurements by general practitioners in overweight and obese patients. *BMC Obesity.* 2017;4(1):23.
27. James WP. WHO recognition of the global obesity epidemic. *Int J Obes (Lond).* 2008;32 Suppl 7:S120-6.
28. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. *Lancet.* 2017;390(10113):2627-42.
29. World Obesity Federation. *World Obesity Atlas 2023.* 2023.
30. Regional Office for the Americas of the World Health Organization. *Overweight and Obesity.* 2016.
31. World Health Organization. *WHO European Regional Obesity Report 2022.* 2022.
32. Baker C. Obesity statistics. House of Commons Library; 2023.
33. Centers for Disease Control and Prevention. *Adult Obesity Facts 2022* [Available from: <https://www.cdc.gov/obesity/data/adult.html>].
34. Janssen F, Bardoutsos A, Vidra N. Obesity Prevalence in the Long-Term Future in 18 European Countries and in the USA. *Obes Facts.* 2020;13(5):514-27.
35. Schneider H, Dietrich ES, Venetz WP. Trends and stabilization up to 2022 in overweight and obesity in Switzerland, comparison to France, UK, US and Australia. *Int J Environ Res Public Health.* 2010;7(2):460-72.
36. Metcalfe SS, Tom. *Tackling obesity: Improving policy making on food and health.* Institute for Government; 2023.
37. Speakman JR, Elmquist JK. Obesity: an evolutionary context. *Life Metab.* 2022;1(1):10-24.
38. Speakman JR. The evolution of body fatness: trading off disease and predation risk. *J Exp Biol.* 2018;221(Pt Suppl 1).
39. Obradovic M, Sudar-Milovanovic E, Soskic S, Essack M, Arya S, Stewart AJ, et al. Leptin and Obesity: Role and Clinical Implication. *Front Endocrinol (Lausanne).* 2021;12:585887.
40. Izquierdo AG, Crujeiras AB, Casanueva FF, Carreira MC. Leptin, Obesity, and Leptin Resistance: Where Are We 25 Years Later? *Nutrients.* 2019;11(11).
41. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. *Nature.* 1994;372(6505):425-32.
42. Lakdawalla D, Philipson T. The growth of obesity and technological change. *Econ Hum Biol.* 2009;7(3):283-93.
43. Blüher M. Obesity: global epidemiology and pathogenesis. *Nat Rev Endocrinol.* 2019;15(5):288-98.
44. Frayling TM, Timpson NJ, Weedon MN, Zeggini E, Freathy RM, Lindgren CM, et al. A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. *Science.* 2007;316(5826):889-94.
45. Swinburn B, Egger G, Raza F. Dissecting obesogenic environments: the development and application of a framework for identifying and prioritizing environmental interventions for obesity. *Prev Med.* 1999;29(6 Pt 1):563-70.
46. Swinburn BA, Sacks G, Hall KD, McPherson K, Finegood DT, Moodie ML, et al. The global obesity pandemic: shaped by global drivers and local environments. *Lancet.* 2011;378(9793):804-14.
47. Heymsfield SB, Wadden TA. Mechanisms, Pathophysiology, and Management of Obesity. *N Engl J Med.* 2017;376(3):254-66.
48. Moellering DR, Smith DL, Jr. Ambient Temperature and Obesity. *Curr Obes Rep.* 2012;1(1):26-34.
49. Kanter R, Caballero B. Global gender disparities in obesity: a review. *Adv Nutr.* 2012;3(4):491-8.
50. Kapoor N, Arora S, Kalra S. Gender Disparities in People Living with Obesity - An Uncharted Territory. *J Midlife Health.* 2021;12(2):103-7.
51. Bennett E, Peters SAE, Woodward M. Sex differences in macronutrient intake and adherence to dietary recommendations: findings from the UK Biobank. *BMJ Open.* 2018;8(4):e020017.

52. Mizuno T, Shu IW, Makimura H, Mobbs C. Obesity over the life course. *Sci Aging Knowledge Environ.* 2004;2004(24):re4.
53. Santilli V, Bernetti A, Mangone M, Paoloni M. Clinical definition of sarcopenia. *Clin Cases Miner Bone Metab.* 2014;11(3):177-80.
54. Baumgartner RN, Stauber PM, McHugh D, Koehler KM, Garry PJ. Cross-sectional Age Differences in Body Composition in Persons 60 + Years of Age. *The Journals of Gerontology: Series A.* 1995;50A(6):M307-M16.
55. Beaufrère B, Morio B. Fat and protein redistribution with aging: metabolic considerations. *Eur J Clin Nutr.* 2000;54 Suppl 3:S48-53.
56. Villareal DT, Apovian CM, Kushner RF, Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *Obes Res.* 2005;13(11):1849-63.
57. McKee AMM, John E. Obesity in the Elderly. In: Feingold KR AB, Blackman MR, et al., editors., editor. *Endotext*2021.
58. Evans WJ. What Is Sarcopenia? *The Journals of Gerontology: Series A.* 1995;50A(Special_Issue):5-8.
59. Prado CM, Batsis JA, Donini LM, Gonzalez MC, Siervo M. Sarcopenic obesity in older adults: a clinical overview. *Nature Reviews Endocrinology.* 2024;20(5):261-77.
60. Batsis JA, Villareal DT. Sarcopenic obesity in older adults: aetiology, epidemiology and treatment strategies. *Nature Reviews Endocrinology.* 2018;14(9):513-37.
61. Gao Q, Mei F, Shang Y, Hu K, Chen F, Zhao L, et al. Global prevalence of sarcopenic obesity in older adults: A systematic review and meta-analysis. *Clinical Nutrition.* 2021;40(7):4633-41.
62. Roubenoff R. Sarcopenic obesity: the confluence of two epidemics. *Obes Res.* 2004;12(6):887-8.
63. Ameye H, Swinnen J. Obesity, income and gender: The changing global relationship. *Global Food Security.* 2019;23:267-81.
64. Templin T, Cravo Oliveira Hashiguchi T, Thomson B, Dieleman J, Bendavid E. The overweight and obesity transition from the wealthy to the poor in low- and middle-income countries: A survey of household data from 103 countries. *PLoS Med.* 2019;16(11):e1002968.
65. NHS Digital. Health Survey for England 2018 [NS]. 2020.
66. National Institute for Health and Care Excellence. NICE health inequalities briefing: obesity and weight management (draft for consultation) 2023 [Available from: <https://www.nice.org.uk/guidance/cg189/documents/health-inequalities-briefing-2>].
67. Office for Health Improvement & Disparities. Overweight Adults 2023 [Available from: <https://www.ethnicity-facts-figures.service.gov.uk/health/diet-and-exercise/overweight-adults/latest>].
68. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet.* 2004;363(9403):157-63.
69. Caleyachetty R, Barber TM, Mohammed NI, Cappuccio FP, Hardy R, Mathur R, et al. Ethnicity-specific BMI cutoffs for obesity based on type 2 diabetes risk in England: a population-based cohort study. *Lancet Diabetes Endocrinol.* 2021;9(7):419-26.
70. Chooi YC, Ding C, Magkos F. The epidemiology of obesity. *Metabolism.* 2019;92:6-10.
71. Deurenberg P, Deurenberg-Yap M, Guricci S. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. *Obes Rev.* 2002;3(3):141-6.
72. NHS Digital. Health Survey England Additional Analyses, Ethnicity and Health, 2011-2019 Experimental statistics 2022 [Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-england-additional-analyses/ethnicity-and-health-2011-2019-experimental-statistics>].
73. National Institute for Health and Care Excellence. Obesity: identification, assessment and management 2014 [Available from: <https://www.nice.org.uk/guidance/cg189/chapter/Recommendations>].
74. Hossain P, Kavar B, El Nahas M. Obesity and diabetes in the developing world--a growing challenge. *N Engl J Med.* 2007;356(3):213-5.
75. Bhaskaran K, Dos-Santos-Silva I, Leon DA, Douglas IJ, Smeeth L. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK. *Lancet Diabetes Endocrinol.* 2018;6(12):944-53.

76. Cercato C, Fonseca FA. Cardiovascular risk and obesity. *Diabetology & Metabolic Syndrome*. 2019;11(1):74.
77. World Health Organization. Hypertension 2023 [Available from: <https://www.who.int/news-room/fact-sheets/detail/hypertension#:~:text=If%20hypertension%20isn't%20treated,dizziness.>
78. Akil L, Ahmad HA. Relationships between obesity and cardiovascular diseases in four southern states and Colorado. *J Health Care Poor Underserved*. 2011;22(4 Suppl):61-72.
79. Office for National Statistics. Death registration summary statistics, England and Wales: 2022 [Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/deathregistrationsummarystatisticsenglandandwales/2022#:~:text=In%20England%2C%20540%2C333%20deaths%20were,above%20the%20five%2Dyear%20average.>
80. Lassale C, Tzoulaki I, Moons KGM, Sweeting M, Boer J, Johnson L, et al. Separate and combined associations of obesity and metabolic health with coronary heart disease: a pan-European case-cohort analysis. *European Heart Journal*. 2017;39(5):397-406.
81. World Stroke Organization. Understanding Weight and Stroke.
82. Sims EA, Danforth E, Jr., Horton ES, Bray GA, Glennon JA, Salans LB. Endocrine and metabolic effects of experimental obesity in man. *Recent Prog Horm Res*. 1973;29:457-96.
83. Michaelidou M, Pappachan JM, Jeeyavudeen MS. Management of diabetes: Current concepts. *World J Diabetes*. 2023;14(4):396-411.
84. Public Health England. Adult obesity and type 2 diabetes. 2014.
85. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. *Diabetes Res Clin Pract*. 2010;89(3):309-19.
86. Parkin DM, Boyd L. 8. Cancers attributable to overweight and obesity in the UK in 2010. *Br J Cancer*. 2011;105 Suppl 2(Suppl 2):S34-7.
87. Petrelli F, Cortellini A, Indini A, Tomasello G, Ghidini M, Nigro O, et al. Association of Obesity With Survival Outcomes in Patients With Cancer: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2021;4(3):e213520.
88. Cancer Research UK. How does obesity cause cancer? 2023 [Available from: <https://www.cancerresearchuk.org/about-cancer/causes-of-cancer/bodyweight-and-cancer/how-does-obesity-cause-cancer.>
89. Pati S, Irfan W, Jameel A, Ahmed S, Shahid RK. Obesity and Cancer: A Current Overview of Epidemiology, Pathogenesis, Outcomes, and Management. *Cancers (Basel)*. 2023;15(2).
90. Pischon T, Nimsch K. Obesity and Risk of Cancer: An Introductory Overview. *Recent Results Cancer Res*. 2016;208:1-15.
91. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med*. 2003;348(17):1625-38.
92. Cancer Research UK. Cancer incidence for common cancers [Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/common-cancers-compared#heading-Zero.>
93. Agnew HJ, Kitson SJ, Crosbie EJ. Gynecological malignancies and obesity. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2023;88:102337.
94. Bhaskaran K, Forbes HJ, Douglas I, Leon DA, Smeeth L. Representativeness and optimal use of body mass index (BMI) in the UK Clinical Practice Research Datalink (CPRD). *BMJ Open*. 2013;3(9):e003389.
95. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *The Lancet*. 2008;371(9612):569-78.
96. Luo J, Hendryx M, Manson JE, Figueiredo JC, LeBlanc ES, Barrington W, et al. Intentional Weight Loss and Obesity-Related Cancer Risk. *JNCI Cancer Spectrum*. 2019;3(4):pkz054.
97. Zhang X, Rhoades J, Caan BJ, Cohn DE, Salani R, Noria S, et al. Intentional weight loss, weight cycling, and endometrial cancer risk: a systematic review and meta-analysis. *International Journal of Gynecologic Cancer*. 2019;29(9):1361.

98. Olsen CM, Nagle CM, Whiteman DC, Ness R, Pearce CL, Pike MC, et al. Obesity and risk of ovarian cancer subtypes: evidence from the Ovarian Cancer Association Consortium. *Endocr Relat Cancer*. 2013;20(2):251-62.
99. Office for Health Improvement & Disparities. Musculoskeletal health: trends, risk factors and disparities in England 2022 [Available from: <https://www.gov.uk/government/statistics/musculoskeletal-health-trends-risk-factors-and-disparities-in-england-november-2022>].
100. Ells LJ, Lang R, Shield JP, Wilkinson JR, Lidstone JS, Coulton S, et al. Obesity and disability - a short review. *Obes Rev*. 2006;7(4):341-5.
101. Public Health England. Chronic pain in adults 2017. 2017.
102. King LK, March L, Anandacoomarasamy A. Obesity & osteoarthritis. *Indian J Med Res*. 2013;138(2):185-93.
103. Jiang L, Tian W, Wang Y, Rong J, Bao C, Liu Y, et al. Body mass index and susceptibility to knee osteoarthritis: a systematic review and meta-analysis. *Joint Bone Spine*. 2012;79(3):291-7.
104. Jiang L, Rong J, Wang Y, Hu F, Bao C, Li X, et al. The relationship between body mass index and hip osteoarthritis: a systematic review and meta-analysis. *Joint Bone Spine*. 2011;78(2):150-5.
105. World Health Organization. Mental health action plan 2013 - 2020 2013 [Available from: <https://www.who.int/publications/i/item/9789241506021>].
106. Garipey G, Nitka D, Schmitz N. The association between obesity and anxiety disorders in the population: a systematic review and meta-analysis. *Int J Obes (Lond)*. 2010;34(3):407-19.
107. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry*. 2010;67(3):220-9.
108. Elagizi A, Kachur S, Lavie CJ, Carbone S, Pandey A, Ortega FB, et al. An Overview and Update on Obesity and the Obesity Paradox in Cardiovascular Diseases. *Progress in Cardiovascular Diseases*. 2018;61(2):142-50.
109. Lavie CJ, Sharma A, Alpert MA, De Schutter A, Lopez-Jimenez F, Milani RV, et al. Update on Obesity and Obesity Paradox in Heart Failure. *Progress in Cardiovascular Diseases*. 2016;58(4):393-400.
110. Guglin M. The fiction of the obesity paradox. *European Heart Journal*. 2023;44(39):4199-.
111. Ades PA, Savage PD. The obesity paradox: perception vs knowledge. *Mayo Clin Proc*. 2010;85(2):112-4.
112. McAuley PA, Keteyian SJ, Brawner CA, Dardari ZA, Al Rifai M, Ehrman JK, et al. Exercise Capacity and the Obesity Paradox in Heart Failure: The FIT (Henry Ford Exercise Testing) Project. *Mayo Clinic Proceedings*. 2018;93(6):701-8.
113. McAuley PA, Beavers KM. Contribution of Cardiorespiratory Fitness to the Obesity Paradox. *Progress in Cardiovascular Diseases*. 2014;56(4):434-40.
114. Blüher M. Metabolically Healthy Obesity. *Endocrine Reviews*. 2020;41(3):bnaa004.
115. Department of Health and Social Care. Government plans to tackle obesity in England 2024 [Available from: <https://healthmedia.blog.gov.uk/2023/06/07/government-plans-to-tackle-obesity-in-england/>].
116. Public Health England. Health matters: obesity and the food environment 2017 [Available from: <https://www.gov.uk/government/publications/health-matters-obesity-and-the-food-environment/health-matters-obesity-and-the-food-environment--2>].
117. Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M. Health and economic burden of the projected obesity trends in the USA and the UK. *Lancet*. 2011;378(9793):815-25.
118. le Roux CW, Chubb B, Nørtoft E, Borglykke A. Obesity and healthcare resource utilization: results from Clinical Practice Research Database (CPRD). *Obes Sci Pract*. 2018;4(5):409-16.
119. le Roux CW, Hartvig NV, Haase CL, Nordsborg RB, Olsen AH, Satyrganova A. Obesity, cardiovascular risk and healthcare resource utilization in the UK. *European Journal of Preventive Cardiology*. 2021;28(11):1235-41.
120. The GBD 2015 Obesity Collaborators. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. *N Engl J Med*. 2017;377(1):13-27.

121. GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1736-88.
122. Townsend N, Kazakiewicz D, Lucy Wright F, Timmis A, Huculeci R, Torbica A, et al. Epidemiology of cardiovascular disease in Europe. *Nat Rev Cardiol*. 2022;19(2):133-43.
123. Murphy ML, Marc; Torrisi, Orsola. Stalling of mortality in the United Kingdom and Europe: an analytical review of the evidence. 2019 November 2019.
124. Newton JB, Allan; Fitzpatrick, Justine; Ege, Faith. UK Health Security Agency [Internet]2017. [11 December 2023]. Available from: <https://ukhsa.blog.gov.uk/2017/07/20/whats-happening-with-mortality-rates-in-england/>.
125. Leon DA. Trends in European life expectancy: a salutary view. *Int J Epidemiol*. 2011;40(2):271-7.
126. Raleigh V. What is happening to life expectancy in England? 2022 [Available from: <https://www.kingsfund.org.uk/publications/whats-happening-life-expectancy-england#:~:text=However%2C%20the%20Covid%2D19%20pandemic,be%20little%20change%20in%202021.>
127. Leon DA, Jdanov DA, Shkolnikov VM. Trends in life expectancy and age-specific mortality in England and Wales, 1970-2016, in comparison with a set of 22 high-income countries: an analysis of vital statistics data. *Lancet Public Health*. 2019;4(11):e575-e82.
128. Ho JY, Hendi AS. Recent trends in life expectancy across high income countries: retrospective observational study. *Bmj*. 2018;362:k2562.
129. Townsend N, Wilson L, Bhatnagar P, Wickramasinghe K, Rayner M, Nichols M. Cardiovascular disease in Europe: epidemiological update 2016. *Eur Heart J*. 2016;37(42):3232-45.
130. Wilson L, Bhatnagar P, Townsend N. Comparing trends in mortality from cardiovascular disease and cancer in the United Kingdom, 1983-2013: joinpoint regression analysis. *Popul Health Metr*. 2017;15(1):23.
131. Lopez AD, Adair T. Is the long-term decline in cardiovascular-disease mortality in high-income countries over? Evidence from national vital statistics. *Int J Epidemiol*. 2019;48(6):1815-23.
132. Bhatnagar P, Wickramasinghe K, Wilkins E, Townsend N. Trends in the epidemiology of cardiovascular disease in the UK. *Heart*. 2016;102(24):1945-52.
133. Raleigh VS. Stalling life expectancy in the UK. *Bmj*. 2018;362:k4050.
134. Mensah GA, Wei GS, Sorlie PD, Fine LJ, Rosenberg Y, Kaufmann PG, et al. Decline in Cardiovascular Mortality: Possible Causes and Implications. *Circ Res*. 2017;120(2):366-80.
135. Institute for Health Metrics and Evaluation. GBD Compare. 2019.
136. Preston SH, Vierboom YC, Stokes A. The role of obesity in exceptionally slow US mortality improvement. *Proc Natl Acad Sci U S A*. 2018;115(5):957-61.
137. Adair T, Lopez AD. The role of overweight and obesity in adverse cardiovascular disease mortality trends: an analysis of multiple cause of death data from Australia and the USA. *BMC Med*. 2020;18(1):199.
138. Olshansky SJ, Passaro DJ, Hershow RC, Layden J, Carnes BA, Brody J, et al. A potential decline in life expectancy in the United States in the 21st century. *N Engl J Med*. 2005;352(11):1138-45.
139. Public Health England. Chapter 3: trends in morbidity and risk factors 2018 [Available from: <https://www.gov.uk/government/publications/health-profile-for-england-2018/chapter-3-trends-in-morbidity-and-risk-factors>.
140. Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. *Jama*. 2005;293(15):1868-74.
141. Gregg EW, Shaw JE. Global Health Effects of Overweight and Obesity. *N Engl J Med*. 2017;377(1):80-1.
142. Peeters A, Backholer K. Is the health burden associated with obesity changing? *Am J Epidemiol*. 2012;176(10):840-5.
143. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of comorbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC Public Health*. 2009;9:88.

144. Guo F, Garvey WT. Trends in Cardiovascular Health Metrics in Obese Adults: National Health and Nutrition Examination Survey (NHANES), 1988-2014. *J Am Heart Assoc.* 2016;5(7).
145. Luli M, Yeo G, Farrell E, Ogden J, Parretti H, Frew E, et al. The implications of defining obesity as a disease: a report from the Association for the Study of Obesity 2021 annual conference. *EClinicalMedicine.* 2023;58:101962.
146. Rubino F, Batterham RL, Koch M, Mingrone G, le Roux CW, Farooqi IS, et al. Lancet Diabetes & Endocrinology Commission on the Definition and Diagnosis of Clinical Obesity. *Lancet Diabetes Endocrinol.* 2023;11(4):226-8.
147. Jastreboff AM, Kotz CM, Kahan S, Kelly AS, Heymsfield SB. Obesity as a Disease: The Obesity Society 2018 Position Statement. *Obesity (Silver Spring).* 2019;27(1):7-9.
148. Mathur R, Bhaskaran K, Chaturvedi N, Leon DA, vanStaa T, Grundy E, et al. Completeness and usability of ethnicity data in UK-based primary care and hospital databases. *Journal of Public Health.* 2013;36(4):684-92.
149. Shiekh SI, Harley M, Ghosh RE, Ashworth M, Myles P, Booth HP, et al. Completeness, agreement, and representativeness of ethnicity recording in the United Kingdom's Clinical Practice Research Datalink (CPRD) and linked Hospital Episode Statistics (HES). *Popul Health Metr.* 2023;21(1):3.
150. Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, van Staa T, et al. Data Resource Profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol.* 2015;44(3):827-36.
151. Kousoulis AA, Rafi I, de Lusignan S. The CPRD and the RCGP: building on research success by enhancing benefits for patients and practices. *Br J Gen Pract.* 2015;65(631):54-5.
152. Clinical Practice Research Datalink. CPRD GOLD March 2023 dataset (Version 2023.03.001). In: Clinical Practice Research Datalink, editor. 2023.
153. Clinical Practice Research Datalink. CPRD GOLD Glossary of terms/Data definitions 2023 [Available from: <https://cprd.com/sites/default/files/2023-02/CPRD%20GOLD%20Glossary%20Terms%20v2.pdf>].
154. Chisholm J. The Read clinical classification. *British Medical Journal.* 1990;300(6732):1092-.
155. Clinical Practice Research Datalink. Defining your study population 2023 [Available from: <https://cprd.com/defining-your-study-population>].
156. NHS Health Research Authority. Clinical Practice Research Datalink (CPRD) Research Database 2022 [Available from: <https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/clinical-practice-research-datalink-cprd-research-database/>].
157. Clinical Practice Research Datalink. Safeguarding patient data 2024 [Available from: <https://www.cprd.com/safeguarding-patient-data>].
158. Clinical Practice Research Datalink. Data Access 2024 [Available from: <https://cprd.com/data-access>].
159. Ministry of Housing Communities and Local Government. The English Indices of Deprivation 2010 2011.
160. Health Data Research UK. Phenotype Library [Available from: <https://phenotypes.healthdatagateway.org/>].
161. Nicholson BD, Aveyard P, Bankhead CR, Hamilton W, Hobbs FDR, Lay-Flurrie S. Determinants and extent of weight recording in UK primary care: an analysis of 5 million adults' electronic health records from 2000 to 2017. *BMC Medicine.* 2019;17(1):222.
162. McLaughlin JC, Hamilton K, Kipping R. Epidemiology of adult overweight recording and management by UK GPs: a systematic review. *Br J Gen Pract.* 2017;67(663):e676-e83.
163. World Health Organization. A healthy lifestyle - WHO recommendations 2010 [Available from: <https://www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle---who-recommendations>].
164. ONS Mid-Year Population Estimates [Internet]. [cited 23 October 2023]. Available from: <https://data.london.gov.uk/dataset/ons-mid-year-population-estimates-custom-age-tables>.
165. National Cancer Institute. Joinpoint Trend Analysis Software 2023 [Available from: <https://surveillance.cancer.gov/joinpoint/>].
166. Cheema KM, Dicks E, Pearson J, Samani NJ. Long-term trends in the epidemiology of cardiovascular diseases in the UK: insights from the British Heart Foundation statistical compendium. *Cardiovasc Res.* 2022;118(10):2267-80.

167. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: epidemiological update. *Eur Heart J*. 2014;35(42):2950-9.
168. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: epidemiological update. *Eur Heart J*. 2014;35(42):2929.
169. Baker C, Mansfield Z. Cancer statistics for England. 2023 7 February 2023.
170. Cancer Research UK. Cancer mortality for all cancers combined 2023 [Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/mortality/all-cancers-combined#heading-Four>.
171. Garcia-Ptacek S, Faxen-Irving G, Cermakova P, Eriksdotter M, Religa D. Body mass index in dementia. *Eur J Clin Nutr*. 2014;68(11):1204-9.
172. GBD Chronic Respiratory Disease Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Respir Med*. 2020;8(6):585-96.
173. Saliccioli JD, Marshall DC, Shalhoub J, Maruthappu M, De Carlo G, Chung KF. Respiratory disease mortality in the United Kingdom compared with EU15+ countries in 1985-2015: observational study. *Bmj*. 2018;363:k4680.
174. Health Survey for England. Part 2: Overweight and obesity; Overweight and obesity, by age and sex. 2022 15 December 2022.
175. Doran T, Kontopantelis E, Reeves D, Sutton M, Ryan AM. Setting performance targets in pay for performance programmes: what can we learn from QOF? *Bmj*. 2014;348:g1595.
176. Office for National Statistics. Dementia and Alzheimer's disease deaths including comorbidities, England and Wales: 2019 registrations. 2020 2 December 2020.
177. Adair T, Temple J, Anstey KJ, Lopez AD. Is the Rise in Reported Dementia Mortality Real? Analysis of Multiple-Cause-of-Death Data for Australia and the United States. *Am J Epidemiol*. 2022;191(7):1270-9.
178. Prince MJ, Wu F, Guo Y, Gutierrez Robledo LM, O'Donnell M, Sullivan R, et al. The burden of disease in older people and implications for health policy and practice. *Lancet*. 2015;385(9967):549-62.
179. Kenchaiah S, Sesso HD, Gaziano JM. Body mass index and vigorous physical activity and the risk of heart failure among men. *Circulation*. 2009;119(1):44-52.
180. Herrington WG, Smith M, Bankhead C, Matsushita K, Stevens S, Holt T, et al. Body-mass index and risk of advanced chronic kidney disease: Prospective analyses from a primary care cohort of 1.4 million adults in England. *PLoS One*. 2017;12(3):e0173515.
181. Amiri S, Behnezhad S, Nadinlui KB. Body Mass Index (BMI) and risk of depression in adults: A systematic review and meta-analysis of longitudinal studies. *Obesity Medicine*. 2018;12:1-12.
182. Reyes C, Leyland KM, Peat G, Cooper C, Arden NK, Prieto-Alhambra D. Association Between Overweight and Obesity and Risk of Clinically Diagnosed Knee, Hip, and Hand Osteoarthritis: A Population-Based Cohort Study. *Arthritis Rheumatol*. 2016;68(8):1869-75.
183. Wang X, Huang Y, Chen Y, Yang T, Su W, Chen X, et al. The relationship between body mass index and stroke: a systemic review and meta-analysis. *J Neurol*. 2022;269(12):6279-89.
184. Kurth T, Gaziano JM, Berger K, Kase CS, Rexrode KM, Cook NR, et al. Body mass index and the risk of stroke in men. *Arch Intern Med*. 2002;162(22):2557-62.
185. Shiozawa M, Kaneko H, Itoh H, Morita K, Okada A, Matsuoka S, et al. Association of Body Mass Index with Ischemic and Hemorrhagic Stroke. *Nutrients*. 2021;13(7).
186. Kurth T, Gaziano JM, Rexrode KM, Kase CS, Cook NR, Manson JE, et al. Prospective study of body mass index and risk of stroke in apparently healthy women. *Circulation*. 2005;111(15):1992-8.
187. Song Y-M, Sung J, Smith GD, Ebrahim S. Body Mass Index and Ischemic and Hemorrhagic Stroke. *Stroke*. 2004;35(4):831-6.
188. Kroll ME, Green J, Beral V, Sudlow CL, Brown A, Kirichek O, et al. Adiposity and ischemic and hemorrhagic stroke: Prospective study in women and meta-analysis. *Neurology*. 2016;87(14):1473-81.
189. Kivimäki M, Luukkonen R, Batty GD, Ferrie JE, Pentti J, Nyberg ST, et al. Body mass index and risk of dementia: Analysis of individual-level data from 1.3 million individuals. *Alzheimers Dement*. 2018;14(5):601-9.
190. Gustafson D. Adiposity indices and dementia. *The Lancet Neurology*. 2006;5(8):713-20.

191. Qin Z, Liu Z, Li R, Luo Y, Wei Z, He L, et al. Association between BMI trajectories in late-middle age and subsequent dementia risk in older age: a 26-year population-based cohort study. *BMC Geriatr.* 2023;23(1):773.
192. Li J, Liu C, Ang TFA, Au R. BMI decline patterns and relation to dementia risk across four decades of follow-up in the Framingham Study. *Alzheimers Dement.* 2023;19(6):2520-7.
193. Albanese E, Launer LJ, Egger M, Prince MJ, Giannakopoulos P, Wolters FJ, et al. 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.* 2017;8:165-78.
194. Watt T, Raymond A, Rachet-Jacquet L, Head A, Kypridemos C, Kelly E, et al. Health in 2040: projected patterns of illness in England. The Health Foundation; 2023.
195. Scholes S, Fat LN, Mindell JS. Trends in cardiovascular disease risk factors by BMI category among adults in England, 2003-2018. *Obesity (Silver Spring).* 2021;29(8):1347-62.
196. Bogers RP, Bemelmans WJ, Hoogenveen RT, Boshuizen HC, Woodward M, Knekt P, et al. Association of overweight with increased risk of coronary heart disease partly independent of blood pressure and cholesterol levels: a meta-analysis of 21 cohort studies including more than 300 000 persons. *Arch Intern Med.* 2007;167(16):1720-8.
197. Canoy D, Cairns BJ, Balkwill A, Wright FL, Green J, Reeves G, et al. Body mass index and incident coronary heart disease in women: a population-based prospective study. *BMC Med.* 2013;11:87.
198. Scholes S, Mindell JS. Health Survey for England 2017: Cardiovascular diseases. 2018.
199. Swain S, Sarmanova A, Mallen C, Kuo CF, Coupland C, Doherty M, et al. Trends in incidence and prevalence of osteoarthritis in the United Kingdom: findings from the Clinical Practice Research Datalink (CPRD). *Osteoarthritis Cartilage.* 2020;28(6):792-801.
200. NHS Digital. Weight Health and Social Care Information Centre2020 [Available from: <http://healthsurvey.hscic.gov.uk/data-visualisation/data-visualisation/explore-the-trends/weight.aspx>.
201. Zhang M, Zhao Y, Wang G, Zhang H, Ren Y, Wang B, et al. Body mass index and waist circumference combined predicts obesity-related hypertension better than either alone in a rural Chinese population. *Sci Rep.* 2016;6:31935.
202. Obesity in Asia Collaboration. Is central obesity a better discriminator of the risk of hypertension than body mass index in ethnically diverse populations? *J Hypertens.* 2008;26(2):169-77.
203. Sarno F, Monteiro CA. [Relative importance of body mass index and waist circumference for hypertension in adults]. *Rev Saude Publica.* 2007;41(5):788-96.
204. Dalton M, Cameron AJ, Zimmet PZ, Shaw JE, Jolley D, Dunstan DW, et al. Waist circumference, waist-hip ratio and body mass index and their correlation with cardiovascular disease risk factors in Australian adults. *J Intern Med.* 2003;254(6):555-63.
205. GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet.* 2018;392(10159):1923-94.
206. Garrison RJ, Kannel WB, Stokes J, 3rd, Castelli WP. Incidence and precursors of hypertension in young adults: the Framingham Offspring Study. *Prev Med.* 1987;16(2):235-51.
207. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, et al. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. *Circulation.* 2016;134(6):441-50.
208. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. *Nat Rev Nephrol.* 2020;16(4):223-37.
209. Crimmins EM, Kim JK, Solé-Auró A. Gender differences in health: results from SHARE, ELSA and HRS. *Eur J Public Health.* 2011;21(1):81-91.
210. Wearing SC, Hennig EM, Byrne NM, Steele JR, Hills AP. Musculoskeletal disorders associated with obesity: a biomechanical perspective. *Obes Rev.* 2006;7(3):239-50.
211. Briggs AM, Cross MJ, Hoy DG, Sánchez-Riera L, Blyth FM, Woolf AD, et al. Musculoskeletal Health Conditions Represent a Global Threat to Healthy Aging: A Report for the 2015 World Health Organization World Report on Ageing and Health. *Gerontologist.* 2016;56 Suppl 2:S243-55.

212. Walsh TP, Arnold JB, Evans AM, Yaxley A, Damarell RA, Shanahan EM. The association between body fat and musculoskeletal pain: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2018;19(1):233.
213. Vásquez E, Batsis JA, Germain CM, Shaw BA. Impact of obesity and physical activity on functional outcomes in the elderly: data from NHANES 2005-2010. *J Aging Health*. 2014;26(6):1032-46.
214. Naser AY. Hospitalisation profile in England and Wales, 1999 to 2019: an ecological study. *BMJ Open*. 2023;13(4):e068393.
215. Reeves GK, Balkwill A, Cairns BJ, Green J, Beral V. Hospital admissions in relation to body mass index in UK women: a prospective cohort study. *BMC Med*. 2014;12:45.
216. Office for Health Improvement & Disparities. Cardiovascular disease prevention: applying All Our Health 2022 [Available from: <https://www.gov.uk/government/publications/cardiovascular-disease-prevention-applying-all-our-health/cardiovascular-disease-prevention-applying-all-our-health>.
217. NHS. Overview and summary [Available from: <https://www.longtermplan.nhs.uk/online-version/overview-and-summary/>.
218. Office for Health Improvement & Disparities (OHID) and NHS Benchmarking Network. CVDPREVENT First Annual Audit Report. 2021.
219. Office for National Statistics (ONS). Adult smoking habits in the UK: 2022 2023 [Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandlifeexpectancies/bulletins/adultsmokinghabitsingreatbritain/2022#:~:text=In%20the%20UK%20in%202022%2C%20England%20had%20the%20lowest%20proportion,%2C%20although%20not%20statistically%20significant>.
220. Løvsletten O, Njølstad I, Wilsgaard T, Hopstock LA, Jacobsen BK, Bønaa KH, et al. Is the ongoing obesity epidemic partly explained by concurrent decline in cigarette smoking? Insights from a longitudinal population study. *The Tromsø Study 1994–2016*. *Preventive Medicine*. 2021;147:106533.
221. Dare S, Mackay DF, Pell JP. Relationship between smoking and obesity: a cross-sectional study of 499,504 middle-aged adults in the UK general population. *PLoS One*. 2015;10(4):e0123579.
222. Jain P, Danaei G, Robins JM, Manson JE, Hernán MA. Smoking cessation and long-term weight gain in the Framingham Heart Study: an application of the parametric g-formula for a continuous outcome. *European Journal of Epidemiology*. 2016;31(12):1223-9.
223. Everest G, Marshall L, Fraser C, Briggs A. Addressing the leading risk factors for ill health. 2022.
224. Walsh D, Tod E, McCartney G, Levin KA. How much of the stalled mortality trends in Scotland and England can be attributed to obesity? *BMJ Open*. 2022;12(12):e067310.
225. Shelton J, Zotow E, Smith L, Johnson SA, Thomson CS, Ahmad A, et al. 25 year trends in cancer incidence and mortality among adults aged 35-69 years in the UK, 1993-2018: retrospective secondary analysis. *BMJ*. 2024;384:e076962.
226. Cancer Research UK. What is Cancer Screening? 2022 [Available from: <https://www.cancerresearchuk.org/about-cancer/cancer-symptoms/spot-cancer-early/screening/what-is-cancer-screening#screening20>.
227. Bandy LK, Scarborough P, Harrington RA, Rayner M, Jebb SA. Reductions in sugar sales from soft drinks in the UK from 2015 to 2018. *BMC Medicine*. 2020;18(1):20.
228. The Obesity Health Alliance. Out of place. The extent of unhealthy foods in prime locations in supermarkets. 2018.
229. Care DoHS. Health and Care Bill: advertising of less healthy food and drink 2022 [Available from: <https://www.gov.uk/government/publications/health-and-care-bill-factsheets/health-and-care-bill-advertising-of-less-healthy-food-and-drink>.
230. Theis DRZ, White M. Is Obesity Policy in England Fit for Purpose? Analysis of Government Strategies and Policies, 1992-2020. *Milbank Q*. 2021;99(1):126-70.
231. Disparities OfHI. Physical activity: applying All Our Health 2022 [Available from: <https://www.gov.uk/government/publications/physical-activity-applying-all-our-health#:~:text=The%20UK%20Chief%20Medical%20Officers,reducing%20extended%20periods%20of%20sitting>.

232. Department for Transport. Gear Change: A bold vision for cycling and walking. 2020.
233. Kraftman L, Hardelid P, Banks J. Age specific trends in mortality disparities by socio-economic deprivation in small geographical areas of England, 2002-2018: A retrospective registry study. *Lancet Reg Health Eur*. 2021;7:100136.
234. NHS Digital. Health Survey for England, 2021 part 1: Smoking 2022 [Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-for-england/2021/part-1-smoking>].
235. Lewis T, Buck D, Wenzel L. Equity and endurance: how can we tackle health inequalities this time? 2022 [Available from: <https://www.kingsfund.org.uk/insight-and-analysis/long-reads/how-can-we-tackle-health-inequalities#:~:text=to%20sustain%20success,-,The%20worst%20health%20outcomes,nd%20poor%20experiences%20of%20care>].
236. Booth HP, Prevost AT, Gulliford MC. Access to weight reduction interventions for overweight and obese patients in UK primary care: population-based cohort study. *BMJ Open*. 2015;5(1):e006642.
237. Coulman KD, Margelyte R, Jones T, Blazeby JM, Macleod J, Owen-Smith A, et al. Access to publicly funded weight management services in England using routine data from primary and secondary care (2007-2020): An observational cohort study. *PLoS Med*. 2023;20(9):e1004282.

9. Appendix

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<https://cprd.com/home>

eRAP

Menu

Application #21_000310

▼ [Administrator comments](#)

2021-04-15 08:47: **Study feedback:** **Approved**

Comments:

The below comment is a discretionary comment provided for the applicant's information:

Recording of diagnoses in HES OP data is not mandatory and therefore likely poor. The specialty of the consultant will be available, but this data source may not be particularly valuable for identifying diagnoses.

▼ [General information](#)

Study title

Characterizing the changing morbidity and cause-specific mortality burden of the obesity epidemic in England and the UK

Research area

Disease Epidemiology, Health Services Delivery

Does this protocol describe an observational study using purely CPRD data? Yes

Does this protocol involve requesting any additional information from GPs, or contact with patients? No

▼ [Research team](#)

Applicant's role

Role: Corresponding applicant

Email: marisa.sophiea16@imperial.ac.uk

Name: Miss Marisa Sophiea

Statistical experience: Yes

Experience of handling large datasets: Yes *Experience of practicing in UK primary care:* No

Will the applicant be analysing the data? Yes

Chief investigator

- **Chief investigator's email:** e.gregg@imperial.ac.uk **Will this person be analysing the data?:** No **Status:**

Confirmed

Name: Professor Edward Gregg

Statistical experience: No

Experience of handling large datasets: Yes

Experience of practicing in UK primary care: No

Collaborators

- **Collaborator's email:** j.pearson-stuttard@imperial.ac.uk **Will this person be analysing the data?:** No **Status:** **Confirmed** **Name:** Dr Jonathan Pearson-Stuttard *Statistical experience:* No *Experience of handling large datasets:* Yes *Experience of practicing in UK primary care:* No
- **Collaborator's email:** fz43@leicester.ac.uk **Will this person be analysing the data?:** No

Status: Confirmed**Name:** Dr Francesco Zaccardi*Statistical experience:* Yes*Experience of handling large datasets:* Yes*Experience of practicing in UK primary care:* No▼ [Access to data](#)**Sponsor****Sponsor:** Imperial College London

(Sponsor information is retrieved automatically as the chief investigator's affiliation)

Funding source for the study

Is the funding source for the study the same as Chief Investigator's affiliation? Yes

Institution conducting the research

Is the institution conducting the research the same as Chief Investigator's affiliation? Yes

Method to access the data

Indicate the method that will be used to access the data

Institutional multi-study licence

Is the institution the same as Chief Investigator's affiliation? Yes

Extraction by CPRD

Will the dataset be extracted by CPRD No

Data processors

- **Data processor is:** Same as the chief investigator's affiliation

Processing: Yes**Accessing:** Yes**Storing:** Yes**Processing area:** UK▼ [Information on data](#)

Primary care data

CPRD GOLD

Do you require data linkages Yes –

I do require data linkages

Patient level data

HES Admitted Patient Care, HES Outpatient, ONS Death Registration Data

Area level data

Do you require area level data? Yes

Practice level (UK)

Practice Level Index of Multiple Deprivation

Patient level (England only)

Patient Level Index of Multiple Deprivation

Withheld concepts

Are withheld concepts required? No

Linkage to a dataset not listed

Are you requesting a linkage to a dataset not listed? No

Patient data privacy

Does any person named in this application already have access to any of these data in a patient identifiable form, or associated with an identifiable patient index?

No

▼ [Protocol information](#)

Lay summary

Obesity is a global public health threat and in the past 40 years, the prevalence of obesity worldwide has nearly tripled. High body mass index (BMI) accounted for 4 million deaths globally in 2015-2016, and it was estimated that 1.9 billion adults were overweight, of which 650 million were obese. If the increase in obesity prevalence continues as expected, by 2025 3.7 billion adults are projected to be overweight.

Obesity increases the risk of a number of diseases and conditions, such as cardiovascular disease (stroke, heart attack, etc.), cancers, mental health, among many others; this also increases the risk of premature death. Deaths due to cardiovascular disease has been decreasing, and considering people are living with obesity for a longer period of time, the risk of death from a wider range of conditions is increasing. Further, although obesity is known to lead to a wide range of conditions, few studies have compared the population disease of obesity across a comprehensive spectrum of its associated conditions. This impacts not only the quality of life of the individual, but also puts more pressure on health services.

This study aims to understand how the cause-of-death and diseases/conditions are changing in those who are overweight and obese in England. This research will provide vital information on the diversity and complexity of obesity-related disease and conditions to support those impacted by the health consequences of obesity but also public policy and interventions.

Technical summary

This study aims to advance our understanding of the heterogeneous and changing impact of overweight and obesity, through morbidity and cause-specific mortality, in UK adults.

This will be a dynamic cohort which will estimate the trends in obesity-related morbidity and mortality among overweight and obese adults. The primary exposures of interest will be BMIs which will use continuous BMI measurements to assess non-linear relationships between BMI and mortality/morbidity and categorised BMI using the WHO definitions. The categories will be defined as: normal weight (<25 kg/m²), overweight (BMI 25-29.9 kg/m²) and obesity is a BMI >30 kg/m², with obesity further sub-categorised to account for its severity (class I: 30 to <35, class II: 35 to <40, and class III: >40).

The primary cohort will be individuals with BMIs measured. The outcomes that will be assessed will include the following diseases and conditions: cardiovascular, cancers, respiratory, musculoskeletal, mental, neurological, and endocrine. How these will be categorised and defined are specified in the Appendices, as detailed in the 'Outcomes to be Measured' section.

The primary analysis will be discrete time-to-event Poisson regression, with age and calendar year as time-dependent covariates. This methodology will show the trends in rates of cause-specific mortality and morbidities, thus the changing rates of mortality from specific causes of death proportional to all-causes in overweight and obese individuals.

Outcomes to be measured

The outcomes to be measured will be stratified into three tiers of complexity for mortality and morbidity. Tier 1 is the broad category of conditions, Tier 2 includes specific categories of non-communicable diseases, and Tier 3 is cause-specific mortality or morbidity from each group of condition. The ICD-10 chapters and codes in addition to the categories for cause-specific mortality are in Appendix 1 and cause-specific morbidities are in Appendix 2.

Objectives, specific aims and rationale

Objective:

To advance our understanding of the heterogeneity and explore the changing impact of overweight and obesity in UK adults.

Aims:

There are two aims to investigate the trends in BMI and related complications and outcomes in England from 2001: 1) Analyse and characterize the trends in proportional mortality and cause-specific mortality associated with obesity; 2) Quantify the incidence and trends in obesity-related morbidity from conditions such as diabetes, vascular disease, gastroesophageal conditions, cancer and other complications.

Rationale:

The analyses that will be conducted will reveal the conditions and diseases overweight and obese individuals are being diagnosed with, but also how the burden of specific diseases have shifted over time. Considering the obesity epidemic is projected to continue to increase, the results will help to understand the diversity and complexity of obesity-related morbidity and mortality.

Study background

The prevalence of obesity in populations is extensively documented through surveys and international pooling studies, such as the Global Burden of Disease Obesity Collaborators, Non-communicable Disease Risk Factor Collaboration, and Public Health England. However, research on the incidence and trends of morbidity among overweight and obese individuals is scarce. In a 2009 meta-analysis investigating the incidence of co-morbidities associated to BMI, there were only a small number of studies researching this topic, but the ones included were in either the US or mainland Europe, with no research in the UK. It observed that overweight and obesity were associated with type II diabetes, cancers and CVD, but most studies focused on individual morbidities, thus lacking a holistic view of the co-morbidities individuals are facing and how that may impact mortality (1).

Multiple studies investigating the association between obesity and mortality, between 1948 and 2011 and primarily in the US, observe declining trends in the association between all-cause mortality and being overweight or obese as well as declines in excess CVD and cancer mortality (1–4). This research is also consistent with previous diabetes research where the magnitude of risk of death from CVD was declining and diabetes-related complications were changing (5). The decrease in obesity-attributed mortality, resulting in mortality improvements, has directly benefitted obese persons which may be attributed to the increase in high cholesterol and high blood pressure treatments for all BMI categories, with the greatest increase observed in the overweight and obese population (6). Despite the decline in mortality, the studies recognise that the obesity prevalence continues to increase (2).

In more recent years, with follow-up until 2017, research exploring the same outcomes shows that the steady decline in CVD mortality rates that were previously observed is slowing down or stopping all together (7–9). These studies indicate that the risk of premature mortality associated with overweight and obesity is rising about 3% per year in both men and women (9). Furthermore, the increasing overweight and obesity prevalence may have been a key driver in the slowing of the decline in mortality rates, considering only declines in obesity-related disease mortality has stagnated, such as heart disease, stroke and diabetes, whereas there has been a continued decline in mortality from all-causes combined and cancers (8–10).

Considering the shift in mortality trends, and the fact that morbidities are often the primary conditions leading to mortality, quantifying the effect of health burdens are pressing to understand the direction in which obesity is evolving in the UK. With the expectation that the obesity epidemic is projected to continue to increase, it is imperative to understand the diversity and complexity of obesity-related morbidity and mortality to support not only public policy and interventions, but also those impacted by the health consequences of obesity.

This study will build on previous research using CPRD data which has assessed the association of cause-specific mortality in UK adults; the association of BMI and site-specific cancers; the association of mental health risks in obese individuals; the risk of dementia in older obese individuals; the association between BMI and multimorbidity; trends in diabetes in obese children and young adults; and trends in childhood obesity (11–17). Specifically, this study will expand on the association studies previously conducted with CPRD and will analyse how the incidence of morbidities and proportional mortality in overweight and obese individuals is shifting in the UK population.

Study type

This is an epidemiological descriptive study.

Study design

Longitudinal dynamic cohort study.

Feasibility counts

Given the data minimisation approach, a sample of 1.5 million participants will be sufficient to identify trends in mortality and morbidity from 1998-2021. After assessing feasibility counts through the Big Data and Analytical Unit at Imperial College London, we are aware there are over 8.4 million individuals who have had a BMI measurement and at least 1 year follow-up, thus a sample of 1.5 million participants will be feasible for the study.

Sample size considerations

The feasibility count conducted for this study indicates over 8.4 million participants fit the inclusion criteria for the present study, with a sample size of 1.5 million participants will be ample for the present study. Based on a previous study in 2016 using CPRD data examining the associations between BMI and cause-specific mortality, there were 3.6 million participants with BMI measurements available, with over 1.5 million and 575,000 overweight and obese individuals included in the study, respectively (11). Using linkage death data, over 367,000 deaths were observed of which about half were deaths in never-smokers. Further, the number of specific causes of death ranged from 200 (aortic dissection in obese individuals) to over 20,000 (ischemic heart disease in overweight individuals). The inclusion requirements, BMI measurement and outcome data (i.e. morbidity and cause-specific mortality), are consistent for both studies, and the previous study had follow-up data until 2016, with the present study having follow-up data until 2021, there is an expected increase in the number of outcomes of interest. We are certain a population of 1.5 million will provide a sufficient number of participants and outcomes of interest to identify any trends in proportional mortality and incidence of morbidity amongst overweight and obese individuals.

Planned use of linked data and/or withheld concepts

The linked data that will be used are as follows:

- 1) ONS Death Registration data will be used to estimate the trends in the cause of death for overweight and obese individuals.
- 2) Hospital Episode Statistics data will allow for the identification of the morbidities overweight and obese patients are being diagnosed with, which will also allow for trends to be estimated to observe the burden of disease.
- 3) Index of Multiple Deprivation data will be used to stratify the analyses by socio-economic data to assess if the incidence of disease and complications is impacted by inequalities patients are facing.

Definition of the study population

- 1) Up-to-standard follow up will only be considered
- 2) Patients with BMI measurements will be included
- 3) The study start date is 1 January 1998 and is through March 2021.
- 4) Individuals 18 or older at index date (i.e. the earliest date that they had a BMI measurement), with at least 1 year follow-up prior to the first BMI measurement will be included in the study, in addition to the date the practice became 'up-to-standard'; this will be an open design study
- 5) Follow-up will end at the individual's date of death or end of study period, the date of transferring from the practice, or last date of data entry.

Selection of comparison group(s) or controls

There will be no control groups used in this study, but trends in morbidity incidence and cause-specific mortality will be compared amongst different BMI categories where normal weight will be used as the reference group for the other BMI categories.

Exposures, outcomes and covariates

The exposure will be a BMI, defined by the WHO as an individual's weight (kg) divided by the square of the individual's height (m). BMI categories are defined as: underweight (<18.5 kg/m²); normal weight (18.5-24.99 kg/m²); overweight (25.0-29.9 kg/m²); or obese (>30 kg/m²). The three classes of obesity will be defined as: 30.0-34.9 kg/m²; 35.0-39.9 kg/m²; >= 40 kg/m².

The specific causes of death will be identified through ONS linked data and grouped in broad categories (i.e. cancer, cardiovascular disease, etc.) and more specific categories (myocardial infarction, kidney cancer, etc.) The causes of death and morbidities have been chosen a priori and are well-known diseases and conditions associated with having an overweight or obese BMI. The specific diseases and conditions by category to be included, in addition to their ICD-10 chapters and codes are found in the Appendix.

The covariates that will be adjusted for include: age, diabetes, alcohol use, smoking status, index of multiple deprivation; the analysis will be stratified by gender and BMI category.

Data/statistical analysis

Linked data from 1998 to 2021 will be included in the analysis. The primary analytic method will be a weighted discrete Poisson regression with age and year as time dependent variables, which will calculate yearly rates to compare causes of death across the indicated time period. The same analytical method will be conducted to examine the trends in incident diseases and complications.

Misclassification of BMI is minimal due to using BMI categories. Two methods will be considered through preliminary analysis to identify the best way to assess BMI measurements in addition to address the issue of reverse causality: 1) either using a single BMI measurement from the participant and excluding the first few years of data or 2) using the maximum BMI measurement of a participant (i.e. their weight history) within a certain period of follow-up time. Using a participant's lifetime maximum BMI, which is not affected by disease-associated weight loss, does not require multiple years of study to be excluded in order to account for weight before disease development (18). However, using maximum BMI may not be feasible or may not be the ideal method of assessing BMI and cause specific-mortality/morbidity; the use of single BMI measurement and excluding the first few years of data (which will be determined by a sensitivity analysis) will be done to account for those will either diagnosed illness or not yet diagnosed illness which impacts BMI will be used instead.

Multiple sensitivity analyses will also be conducted to determine the optimal length of time and follow-up necessary to capture the ideal weight history to identify maximum BMI or the ideal period of exclusion, as well as the potential for bias due to reverse causality (e.g., pre-existing illness affecting body weight). There will be sensitivity analyses which will include an analysis with only never-smokers in addition to an analysis adjusted for those with pre-existing conditions. Confounding and missing data plans are in the sections below.

Plan for addressing confounding

To address for confounding, the analysis will be stratified by gender and BMI category; in the model, age, smoking status, alcohol consumption, index of multiple deprivation will all be adjusted for in order to reduce confounding.

Plans for addressing missing data

Those who have never had a BMI measurement included in the CPRD database, will not be included in the study. Data will be explored for missing data and appropriate statistical techniques such as multiple imputation, will be used to account for missing risk factors as identified.

Patient or user group involvement

Patient or user groups will not be engaged in this research.

Plans for disseminating and communicating study results

At least two papers will be disseminated in an academic publication, with one based on the cause-specific mortality trends and one on incident morbidity. The research may be presented in the appropriate conferences.

Conflict of interest statement

There are no conflicts of interest to report - the corresponding investigator is funded by the Imperial College London President's PhD Scholarship.

Limitations of the study design, data sources, and analytic methods

Limitations to this study include the fact that ascertaining the cause of death is not always objective and is often subject to medical opinion and judgement. This may also be due to the changing of ICD-9 to ICD-10 in addition to cases where it is assumed the cause of death is due to an increased BMI, thus introducing further bias.

Selection bias is likely introduced based on those who did not have BMI measured at GP visits as there may be specific health-related reasons the BMI is (or is not) measured.

Reverse causality is also a limitation considering those who may have an illness (developing or already diagnosed) affecting unintentional weight loss, which may skew the true relationship between BMI and risk of death. Plans to account for this is found in the 'Data/ Statistical Analysis' section.

Findings should be generalisable considering the nature of the primary care practices included in CPRD aim to be representative of the English population.

References

1. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: A systematic review and meta-analysis. BMC Public Health [Internet]. 2009 [cited 2020 Dec 2];9:88. Available from: /pmc/articles/PMC2667420/?report=abstract
2. Vidra N, Bijlsma MJ, Trias-Llimós S, Janssen F. Past trends in obesity-attributable mortality in eight European countries: an application of age-period-cohort analysis. Int J Public Health [Internet]. 2018 Jul 1 [cited 2020 Dec 2];63(6):683–92. Available from: <https://doi.org/10.1007/s00038-018-1126-2>

3. Xu H, Cupples LA, Stokes A, Liu CT. Association of Obesity With Mortality Over 24 Years of Weight History: Findings From the Framingham Heart Study. *JAMA Netw open* [Internet]. 2018 Nov 2 [cited 2020 Dec 2];1(7):e184587. Available from: <https://jamanetwork.com/>

4. Mehta NK, Chang VW. Secular declines in the association between obesity and mortality in the United States. *Popul Dev Rev* [Internet]. 2011 Sep [cited 2020 Dec 2];37(3):435–51. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3220918/>

5. Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. *J Am Med Assoc* [Internet]. 2005 Apr 20 [cited 2020 Dec 23];293(15):1868–74. Available from: <https://jamanetwork.com/>

6. Gregg EW, Cheng YJ, Srinivasan M, Lin J, Geiss LS, Albright AL, et al. Trends in cause-specific mortality among adults with and without diagnosed diabetes in the USA: an epidemiological analysis of linked national survey and vital statistics data. *Lancet* [Internet]. 2018 Jun 16 [cited 2020 Dec 23];391(10138):2430–40. Available from: <https://pubmed.ncbi.nlm.nih.gov/29784146/>

7. Preston SH, Vierboom YC, Stokes A. The role of obesity in exceptionally slow US mortality improvement. [cited 2020 Dec 2]; Available from: www.pnas.org/cgi/doi/10.1073/pnas.1716802115

8. Lahey R, Khan SS. Trends in Obesity and Risk of Cardiovascular Disease. *Curr Epidemiol Reports* [Internet]. 2018 Sep [cited 2020 Dec 2];5(3):243–51. Available from: [/pmc/articles/PMC6349392/?report=abstract](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6349392/?report=abstract)

9. Adair T, Lopez AD. The role of overweight and obesity in adverse cardiovascular disease mortality trends: An analysis of multiple cause of death data from Australia and the USA. *BMC Med* [Internet]. 2020 Aug 4 [cited 2020 Dec 2];18(1):199. Available from: <https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-020-01666-y>

10. Ma J, Ward EM, Siegel RL, Jemal A. Temporal trends in mortality in the United States, 1969–2013. *JAMA - J Am Med Assoc* [Internet]. 2015 Oct 27 [cited 2020 Dec 3];314(16):1731–9. Available from: <https://pubmed.ncbi.nlm.nih.gov/26505597/>

11. Bhaskaran K, dos-Santos-Silva I, Leon DA, Douglas IJ, Smeeth L. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK. *Lancet Diabetes Endocrinol* [Internet]. 2018 Dec 1 [cited 2020 Dec 2];6(12):944–53. Available from: www.thelancet.com/diabetes-endocrinology

12. Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5·24 million UK adults. *Lancet* [Internet]. 2014 [cited 2021 Feb 9];384:755–65. Available from: <http://dx.doi.org/10.1016/>

13. Moussa OM, Ardisino M, Kulatilake P, Faraj A, Muttoni E, Darzi A, et al. Effect of body mass index on depression in a UK cohort of 363 037 obese patients: A longitudinal analysis of transition. *Clin Obes* [Internet]. 2019 Jun 5 [cited 2021 Jan 26];9(3):e12305. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1111/cob.12305>

14. Bowman K, Thambisetty M, Kuchel GA, Ferrucci L, Melzer D. Obesity and Longer Term Risks of Dementia in 65–74 Year Olds. *Age Ageing* [Internet]. 2019 May 1 [cited 2021 Jan 26];48(3):367–73. Available from: <https://academic.oup.com/ageing/article/48/3/367/5307819>

15. Booth HP, Prevost AT, Gulliford MC. Impact of body mass index on prevalence of multimorbidity in primary care: cohort study. *Fam Pract* [Internet]. 2014 Feb 1 [cited 2021 Jan 26];31(1):38–43. Available from: <https://academic.oup.com/fampra/article-lookup/doi/10.1093/fampra/cmt061>

16. Abbasi A, Juszczak D, van Jaarsveld CHM, Gulliford MC. Body Mass Index and Incident Type 1 and Type 2 Diabetes in Children and Young Adults: A Retrospective Cohort Study. *J Endocr Soc* [Internet]. 2017 May 1 [cited 2021 Jan 26];1(5):524–37. Available from: <https://academic.oup.com/jes/article-lookup/doi/10.1210/js.2017-00044>

17. Van Jaarsveld CHM, Gulliford MC. Childhood obesity trends from primary care electronic health records in England between 1994 and 2013: Population-based cohort study. *Arch Dis Child* [Internet]. 2015 Mar 1 [cited 2021 Jan 26];100(3):214–9. Available from: <http://dx.doi.org/10.1136/>

18. Stokes A. Using maximum weight to redefine body mass index categories in studies of the mortality risks of obesity. *Popul Health Metr* [Internet]. 2014 Mar 17 [cited 2021 Feb 10];12(1):6. Available from: [/pmc/articles/PMC3985598/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3985598/)

List of appendices

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Table A1. List of comorbidities and specific diagnoses (read terms) and medcodes

Comorbidity	Read term	Medcode
Alzheimer's and dementia	Alzheimer's disease	16797
Alzheimer's and dementia	Alzheimer's disease with early onset	1917
Alzheimer's and dementia	Alzheimer's disease with late onset	32057
Alzheimer's and dementia	[X] Other Alzheimer's disease	59122
Alzheimer's and dementia	[X]Dementia in Alzheimer's disease	7664
Alzheimer's and dementia	[X]Dementia in Alzheimer's disease with early onset	49263
Alzheimer's and dementia	[X]Presenile dementia,Alzheimer's type	25704
Alzheimer's and dementia	[X]Primary degen dementia, Alzheimer's type, presenile onset	60059
Alzheimer's and dementia	[X]Dementia in Alzheimer's disease with late onset	38678
Alzheimer's and dementia	[X]Senile dementia,Alzheimer's type	11379
Alzheimer's and dementia	[X]Primary degen dementia of Alzheimer's type, senile onset	43346
Alzheimer's and dementia	[X]Dementia in Alzheimer's dis, atypical or mixed type	30706
Alzheimer's and dementia	[X]Dementia in Alzheimer's disease, unspecified	29386
Alzheimer's and dementia	[X]Alzheimer's dementia unspec	8195
Alzheimer's and dementia	Alzheimer's disease	1917
Alzheimer's and dementia	Alzheimer's disease with early onset	16797
Alzheimer's and dementia	Alzheimer's disease with late onset	32057
Alzheimer's and dementia	[X]Other Alzheimer's disease	59122
Alzheimer's and dementia	Arteriosclerotic dementia	19477
Alzheimer's and dementia	Multi infarct dementia	8634
Alzheimer's and dementia	Uncomplicated arteriosclerotic dementia	43089
Alzheimer's and dementia	Arteriosclerotic dementia with delirium	56912
Alzheimer's and dementia	Arteriosclerotic dementia with paranoia	55467
Alzheimer's and dementia	Arteriosclerotic dementia with depression	43292
Alzheimer's and dementia	Arteriosclerotic dementia NOS	42279
Alzheimer's and dementia	[X]Vascular dementia	6578
Alzheimer's and dementia	[X]Arteriosclerotic dementia	9565
Alzheimer's and dementia	[X]Vascular dementia of acute onset	46488
Alzheimer's and dementia	[X]Multi-infarct dementia	11175
Alzheimer's and dementia	[X]Predominantly cortical dementia	55838
Alzheimer's and dementia	[X]Subcortical vascular dementia	8934
Alzheimer's and dementia	[X]Mixed cortical and subcortical vascular dementia	31016
Alzheimer's and dementia	[X]Other vascular dementia	55313
Alzheimer's and dementia	[X]Vascular dementia, unspecified	19393
Alzheimer's and dementia	Other alcoholic dementia	54505
Alzheimer's and dementia	Alcoholic dementia NOS	27342
Alzheimer's and dementia	Drug-induced dementia	62132
Alzheimer's and dementia	Dementia in conditions EC	25386
Alzheimer's and dementia	[X]Dementia in other diseases classified elsewhere	12621
Alzheimer's and dementia	[X]Dementia in Pick's disease	28402
Alzheimer's and dementia	[X]Dementia in Creutzfeldt-Jakob disease	54106
Alzheimer's and dementia	[X]Dementia in Huntington's disease	37014

Alzheimer's and dementia	[X]Dementia in Parkinson's disease	9509
Alzheimer's and dementia	[X]Dementia in human immunodef virus [HIV] disease	41185
Alzheimer's and dementia	[X]Lewy body dementia	26270
Alzheimer's and dementia	[X]Dementia in other specified diseases classif elsewhere	64267
Alzheimer's and dementia	[X]Alcoholic dementia NOS	26323
Alzheimer's and dementia	H/O: dementia	5931
Alzheimer's and dementia	Senile dementia	1916
Alzheimer's and dementia	Senile/presenile dementia	1350
Alzheimer's and dementia	Uncomplicated senile dementia	7323
Alzheimer's and dementia	Presenile dementia	15165
Alzheimer's and dementia	Uncomplicated presenile dementia	42602
Alzheimer's and dementia	Presenile dementia with delirium	49513
Alzheimer's and dementia	Presenile dementia with paranoia	30032
Alzheimer's and dementia	Presenile dementia with depression	27677
Alzheimer's and dementia	Presenile dementia NOS	38438
Alzheimer's and dementia	Senile dementia with depressive or paranoid features	44674
Alzheimer's and dementia	Senile dementia with paranoia	18386
Alzheimer's and dementia	Senile dementia with depression	21887
Alzheimer's and dementia	Senile dementia with depressive or paranoid features NOS	41089
Alzheimer's and dementia	Senile dementia with delirium	37015
Alzheimer's and dementia	[X] Unspecified dementia	4693
Alzheimer's and dementia	[X] Presenile dementia NOS	48501
Alzheimer's and dementia	[X] Primary degenerative dementia NOS	34944
Alzheimer's and dementia	[X] Senile dementia NOS	4357
Alzheimer's and dementia	[X] Senile dementia, depressed or paranoid type	27759
Alzheimer's and dementia	[X]Delirium superimposed on dementia	53446
Alzheimer's and dementia	Language disorder of dementia	55222
Atrial fibrillation	Paroxysmal atrial fibrillation (3)	1268
Atrial fibrillation	Atrial fibrillation, not otherwise specified (5)	1664
Atrial fibrillation	Atrial fibrillation and flutter (6)	2212
Atrial fibrillation	Atrial fibrillation monitoring (2)	18746
Atrial fibrillation	Atrial fibrillation and flutter (6)	23437
Atrial fibrillation	Atrial fibrillation, not otherwise specified (5)	35127
Atrial fibrillation	Persistent or permanent atrial fibrillation (4)	96076
Atrial fibrillation	Persistent or permanent atrial fibrillation (4)	96277
Cerebrovascular disease	Intracerebral haemorrhage	5051
Cerebrovascular disease	CVA - cerebrovascular accid due to intracerebral haemorrhage	6960
Cerebrovascular disease	Stroke due to intracerebral haemorrhage	18604
Cerebrovascular disease	Cortical haemorrhage	31595
Cerebrovascular disease	Internal capsule haemorrhage	40338
Cerebrovascular disease	Basal nucleus haemorrhage	46316
Cerebrovascular disease	Cerebellar haemorrhage	13564
Cerebrovascular disease	Pontine haemorrhage	7912
Cerebrovascular disease	External capsule haemorrhage	30045

Cerebrovascular disease	Intracerebral haemorrhage, intraventricular	30202
Cerebrovascular disease	Intracerebral haemorrhage, multiple localized	57315
Cerebrovascular disease	Intracerebral haemorrhage in hemisphere, unspecified	31060
Cerebrovascular disease	Left sided intracerebral haemorrhage, unspecified	28314
Cerebrovascular disease	Right sided intracerebral haemorrhage, unspecified	19201
Cerebrovascular disease	Intracerebral haemorrhage NOS	3535
Cerebrovascular disease	[X]Other intracerebral haemorrhage	53810
Cerebrovascular disease	[X]Intracerebral haemorrhage in hemisphere, unspecified	96630
Cerebrovascular disease	Subarachnoid haemorrhage from carotid siphon and bifurcation	56007
Cerebrovascular disease	Subarachnoid haemorrhage from middle cerebral artery	19412
Cerebrovascular disease	Subarachnoid haemorrh from intracranial artery, unspecif	17326
Cerebrovascular disease	Evacuation of subdural haematoma	4917
Cerebrovascular disease	Subdural haemorrhage - nontraumatic	4273
Cerebrovascular disease	Subdural haematoma - nontraumatic	17734
Cerebrovascular disease	Subdural haemorrhage NOS	18912
Cerebrovascular disease	Subdural haemorrhage following injury	6569
Cerebrovascular disease	Closed traumatic subdural haemorrhage	2883
Cerebrovascular disease	Open traumatic subdural haemorrhage	94351
Cerebrovascular disease	Traumatic subdural haemorrhage	8181
Cerebrovascular disease	Traumatic subdural haematoma	7862
Cerebrovascular disease	Traumatic subdural haematoma without open intracranial wound	53980
Cerebrovascular disease	Traumatic subdural haematoma with open intracranial wound	96677
Cerebrovascular disease	Evacuation of extradural haematoma	4107
Cerebrovascular disease	Extradural haemorrhage - nontraumatic	36178
Cerebrovascular disease	Extradural haemorrhage following injury	27661
Cerebrovascular disease	Closed traumatic extradural haemorrhage	45421
Cerebrovascular disease	Epidural haematoma following injury	43418
Cerebrovascular disease	Open traumatic extradural haemorrhage	73471
Cerebrovascular disease	Epidural haemorrhage	51504
Cerebrovascular disease	Traumatic extradural haematoma	18411
Cerebrovascular disease	Other and unspecified intracranial haemorrhage	31805
Cerebrovascular disease	Intracranial haemorrhage NOS	20284
Cerebrovascular disease	Rupture of syphilitic cerebral aneurysm	31941
Cerebrovascular disease	Cerebral haemorrhage following injury	5682
Cerebrovascular disease	Traumatic cerebral haemorrhage	28077
Cerebrovascular disease	Cerebral haemorrhage following injury NOS	46545
Cerebrovascular disease	Other cerebral haemorrhage following injury	52968
Cerebrovascular disease	Other cerebral haemorrhage following injury NOS	42283
Cerebrovascular disease	Intracerebral haemorrhage	5051
Cerebrovascular disease	CVA - cerebrovascular accid due to intracerebral haemorrhage	6960
Cerebrovascular disease	Stroke due to intracerebral haemorrhage	18604
Cerebrovascular disease	Cortical haemorrhage	31595
Cerebrovascular disease	Internal capsule haemorrhage	40338
Cerebrovascular disease	Basal nucleus haemorrhage	46316

Cerebrovascular disease	Cerebellar haemorrhage	13564
Cerebrovascular disease	Pontine haemorrhage	7912
Cerebrovascular disease	External capsule haemorrhage	30045
Cerebrovascular disease	Intracerebral haemorrhage, intraventricular	30202
Cerebrovascular disease	Intracerebral haemorrhage, multiple localized	57315
Cerebrovascular disease	Intracerebral haemorrhage in hemisphere, unspecified	31060
Cerebrovascular disease	Left sided intracerebral haemorrhage, unspecified	28314
Cerebrovascular disease	Right sided intracerebral haemorrhage, unspecified	19201
Cerebrovascular disease	Intracerebral haemorrhage NOS	3535
Cerebrovascular disease	[X]Other intracerebral haemorrhage	53810
Cerebrovascular disease	[X]Intracerebral haemorrhage in hemisphere, unspecified	96630
Cerebrovascular disease	Subarachnoid haemorrhage from carotid siphon and bifurcation	56007
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Cerebrovascular disease	Traumatic subdural haemorrhage	8181
Cerebrovascular disease	Traumatic subdural haematoma	7862
Cerebrovascular disease	Traumatic subdural haematoma without open intracranial wound	53980
Cerebrovascular disease	Traumatic subdural haematoma with open intracranial wound	96677
Cerebrovascular disease	Evacuation of extradural haematoma	4107
Cerebrovascular disease	Extradural haemorrhage - nontraumatic	36178
Cerebrovascular disease	Extradural haemorrhage following injury	27661
Cerebrovascular disease	Closed traumatic extradural haemorrhage	45421
Cerebrovascular disease	Epidural haematoma following injury	43418
Cerebrovascular disease	Open traumatic extradural haemorrhage	73471
Cerebrovascular disease	Epidural haemorrhage	51504
Cerebrovascular disease	Traumatic extradural haematoma	18411
Cerebrovascular disease	Other and unspecified intracranial haemorrhage	31805
Cerebrovascular disease	Intracranial haemorrhage NOS	20284
Cerebrovascular disease	Rupture of syphilitic cerebral aneurysm	31941
Cerebrovascular disease	Cerebral haemorrhage following injury	5682
Cerebrovascular disease	Traumatic cerebral haemorrhage	28077
Cerebrovascular disease	Cerebral haemorrhage following injury NOS	46545
Cerebrovascular disease	Other cerebral haemorrhage following injury	52968
Cerebrovascular disease	Other cerebral haemorrhage following injury NOS	42283
Cerebrovascular disease	CVA - cerebral artery occlusion	5363
Cerebrovascular disease	Stroke due to cerebral arterial occlusion	6155
Cerebrovascular disease	Generalised ischaemic cerebrovascular disease NOS	40053

Cerebrovascular disease	Cereb infarct due unsp occlus/stenos precerebr arteries	40758
Cerebrovascular disease	Cerebrl infarctn due/unspcf occlusn or sten/cerebrl artr	33543
Cerebrovascular disease	[X]Cerebrl infarctn due/unspcf occlusn or sten/cerebrl artr	91627
Cerebrovascular disease	[X]Other cerebral infarction	53745
Cerebrovascular disease	[X]Occlusion and stenosis of other precerebral arteries	90572
Cerebrovascular disease	[X]Occlusion and stenosis of other cerebral arteries	92036
Cerebrovascular disease	[X]Cereb infarct due unsp occlus/stenos precerebr arteries	94482
Cerebrovascular disease	[X]Other transnt cerebral ischaemic attacks+related syndroms	63746
Cerebrovascular disease	Transient cerebral ischaemia	504
Cerebrovascular disease	Transient ischaemic attack	1433
Cerebrovascular disease	Other transient cerebral ischaemia	19354
Cerebrovascular disease	Transient cerebral ischaemia NOS	1895
Cerebrovascular disease	Transient cerebral ischaemia NOS	15788
COPD	Chronic obstructive pulmonary disease	1001
COPD	End stage chronic obstructive airways disease	104608
COPD	Eosinophilic bronchitis	106650
COPD	Moderate chronic obstructive pulmonary disease	10802
COPD	Mild chronic obstructive pulmonary disease	10863
COPD	Centrilobular emphysema	10980
COPD	Mucopurulent chronic bronchitis	11150
COPD	Other specified chronic obstructive airways disease	12166
COPD	Acute exacerbation of chronic obstructive airways disease	1446
COPD	Emphysematous bronchitis	14798
COPD	Chronic bronchitis NOS	15157
COPD	Chronic catarrhal bronchitis	15626
COPD	Other emphysema NOS	16410
COPD	Chronic obstruct pulmonary dis with acute lower resp infectn	21061
COPD	Chronic bullous emphysema NOS	23492
COPD	Mixed simple and mucopurulent chronic bronchitis	24248
COPD	Simple chronic bronchitis	25603
COPD	Bronchiolitis obliterans	26125
COPD	Chronic bullous emphysema	26306
COPD	Obstructive chronic bronchitis	27819
COPD	Chronic bronchitis	3243
COPD	Emphysema NOS	33450
COPD	Chronic obstructive pulmonary disease NOS	37247
COPD	Fetid chronic bronchitis	37959
COPD	Purulent chronic bronchitis	40159
COPD	Other emphysema	40788
COPD	Obstructive chronic bronchitis NOS	44525
COPD	Chronic tracheobronchitis	45089
COPD	Panlobular emphysema	46578
COPD	Segmental bullous emphysema	56860
COPD	Chronic obstructive airways disease NOS	5710

COPD	Chronic asthmatic bronchitis	5798
COPD	Chronic wheezy bronchitis	5909
COPD	Acute interstitial emphysema	59263
COPD	Giant bullous emphysema	60188
COPD	Simple chronic bronchitis NOS	61118
COPD	Mucopurulent chronic bronchitis NOS	61513
COPD	Obliterative bronchiolitis due to chemical fumes	63216
COPD	s unilateral emphysema",	63479
COPD	Chronic emphysema due to chemical fumes	64721
COPD	[X]Other specified chronic obstructive pulmonary disease	65733
COPD	Other chronic bronchitis	66043
COPD	[X]Other emphysema	66058
COPD	Other specified chronic obstructive pulmonary disease	67040
COPD	Other chronic bronchitis NOS	68066
COPD	Zonal bullous emphysema	68662
COPD	Atrophic (senile) emphysema	70787
COPD	Chron obstruct pulmonary dis wth acute exacerbation, unspec	7884
COPD	Emphysema	794
COPD	Acute vesicular emphysema	92955
COPD	Very severe chronic obstructive pulmonary disease	93568
COPD	Severe chronic obstructive pulmonary disease	9876
COPD	Bullous emphysema with collapse	99536
COPD	Chronic obstructive airways disease	998
COPD	Chronic obstructive pulmonary disease	1001
COPD	Chronic obstructive airways disease	998
COPD	Chronic bronchitis	3243
COPD	Simple chronic bronchitis	25603
COPD	Chronic catarrhal bronchitis	15626
COPD	Simple chronic bronchitis NOS	61118
COPD	Mucopurulent chronic bronchitis	11150
COPD	Purulent chronic bronchitis	40159
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COPD	Acute vesicular emphysema	92955
COPD	Atrophic (senile) emphysema	70787
COPD	Acute interstitial emphysema	59263
COPD	MacLeod's unilateral emphysema	63479
COPD	Other emphysema NOS	16410
COPD	Emphysema NOS	33450
COPD	Mild chronic obstructive pulmonary disease	10863
COPD	Moderate chronic obstructive pulmonary disease	10802
COPD	Severe chronic obstructive pulmonary disease	9876
COPD	Very severe chronic obstructive pulmonary disease	93568
COPD	End stage chronic obstructive airways disease	104608
COPD	Other specified chronic obstructive airways disease	12166
COPD	Other specified chronic obstructive pulmonary disease	67040
COPD	Chronic obstruct pulmonary dis with acute lower resp infectn	21061
COPD	Chron obstruct pulmonary dis wth acute exacerbation, unspec	7884
COPD	Chronic obstructive airways disease NOS	5710
COPD	Chronic obstructive pulmonary disease NOS	37247
COPD	Chronic emphysema due to chemical fumes	64721
COPD	Obliterative bronchiolitis due to chemical fumes	63216
COPD	Eosinophilic bronchitis	106650
COPD	[X]Other emphysema	66058
COPD	[X]Other specified chronic obstructive pulmonary disease	65733
Depression	Single major depressive episode, mild	16506
Depression	Single major depressive episode, moderate	15155
Depression	[X]Mild depressive episode	11717
Depression	[X]Moderate depressive episode	9211
Depression	[X]Mild depression	10667
Depression	[X]Major depression, mild	98346
Depression	[X]Major depression, moderately severe	98252
Depression	Single major depressive episode, severe, without psychosis	15219
Depression	[X]Major depression, severe without psychotic symptoms	98414
Depression	Depressive psychoses	2560
Depression	Single major depressive episode, severe, with psychosis	32159

Depression	Reactive depressive psychosis	8478
Depression	Psychotic reactive depression	17770
Depression	[X]Single episode of major depression and psychotic symptoms	24117
Depression	[X]Single episode of psychogenic depressive psychosis	52678
Depression	[X]Single episode of psychotic depression	24112
Depression	[X]Single episode of reactive depressive psychosis	28863
Depression	[X]Major depression, severe with psychotic symptoms	98417
Depression	[X]Endogenous depression with psychotic symptoms	23731
Depression	Single major depressive episode	10610
Depression	Single major depressive episode, unspecified	34390
Depression	Single major depressive episode, partial or unspec remission	43324
Depression	Single major depressive episode NOS	7011
Depression	Atypical depressive disorder	27491
Depression	Masked depression	9183
Depression	Neurotic depression reactive type	1131
Depression	Depressive disorder NEC	324
Depression	[X]Depressive episode	4639
Depression	[X]Single episode of depressive reaction	9055
Depression	[X]Single episode of psychogenic depression	18510
Depression	[X]Single episode of reactive depression	7604
Depression	[X]Single episode major depression w/out psychotic symptoms	22806
Depression	[X]Single episode vital depression w/out psychotic symptoms	59386
Depression	[X]Other depressive episodes	6854
Depression	[X]Atypical depression	10720
Depression	[X]Single episode of masked depression NOS	56609
Depression	[X]Depressive episode, unspecified	2970
Depression	[X]Depression NOS	543
Depression	[X]Depressive disorder NOS	3291
Depression	[X]Prolonged single episode of reactive depression	28248
Depression	[X]Reactive depression NOS	5987
Depression	[X]Monopolar depression NOS	36616
Depression	[X]Depressive neurosis	8584
Depression	[X]Neurotic depression	7737
Depression	Endogenous depression first episode	6546
Depression	Endogenous depression first episode	6950
Depression	Endogenous depression	595
Depression	[X]Endogenous depression without psychotic symptoms	11329
Depression	Agitated depression	5879
Depression	Agitated depression	1055
Depression	[X]Single episode agitated depressn w/out psychotic symptoms	41989
Depression	Depressive personality disorder	10455
Depression	[X]Dysthymia	7953
Depression	[X]Depressive personality disorder	10290
Depression	Chronic depression	4323

Depression	Recurrent major depressive episodes, mild	29342
Depression	Recurrent major depressive episodes, moderate	14709
Depression	[X]Recurrent depressive disorder, current episode mild	29784
Depression	[X]Recurrent depressive disorder, current episode moderate	29520
Depression	Recurrent major depressive episodes, severe, no psychosis	25697
Depression	[X]Recurr depress disorder cur epi severe without psyc sympt	33469
Depression	Recurrent major depressive episodes, severe, with psychosis	24171
Depression	[X]Recurrent depress disorder cur epi severe with psyc symp	47009
Depression	[X]Recurr severe episodes/major depression+psychotic symptom	32941
Depression	[X]Recurr severe episodes/psychogenic depressive psychosis	31757
Depression	[X]Recurrent severe episodes of psychotic depression	16861
Depression	[X]Recurrent severe episodes/reactive depressive psychosis	37764
Depression	Recurrent major depressive episode	15099
Depression	Endogenous depression - recurrent	6932
Depression	Recurrent major depressive episodes, unspecified	35671
Depression	Recurrent major depressive episodes,partial/unspec remission	56273
Depression	Recurrent major depressive episodes, in full remission	55384
Depression	Recurrent depression	6482
Depression	Recurrent major depressive episode NOS	25563
Depression	Seasonal affective disorder	10825
Depression	[X]Recurrent depressive disorder	3292
Depression	[X]Recurrent episodes of depressive reaction	8851
Depression	[X]Recurrent episodes of psychogenic depression	19696
Depression	[X]Recurrent episodes of reactive depression	8902
Depression	[X]Seasonal depressive disorder	28756
Depression	[X]SAD - Seasonal affective disorder	8826
Depression	[X]Major depression, recurrent without psychotic symptoms	11252
Depression	[X]Vital depression, recurrent without psychotic symptoms	73991
Depression	[X]Recurrent depressive disorder, currently in remission	22116
Depression	[X]Other recurrent depressive disorders	47731
Depression	[X]Recurrent depressive disorder, unspecified	44300
Depression	[X]Recurrent brief depressive episodes	19054
Depression	Puerperal depression	2923
Depression	Postnatal depression	2639
Depression	Postviral depression	2972
Depression	[X]Postnatal depression NOS	13307
Depression	[X]Postpartum depression NOS	4979
Depression	[D]Postoperative depression	29527
Heart Failure	Congestive heart failure due to valvular disease	94870
Heart Failure	Malignant hypertensive heart disease	50157
Heart Failure	Malignant hypertensive heart disease without CCF	95334
Heart Failure	Malignant hypertensive heart disease with CCF	72668
Heart Failure	Benign hypertensive heart disease with CCF	52127
Heart Failure	Hypertensive heart disease NOS with CCF	62718

Heart Failure	Malignant hypertensive heart and renal disease	67232
Heart Failure	Hypertensive heart&renal dis wth (congestive) heart failure	21837
Heart Failure	Hyperten heart&renal dis+both(congestv)heart and renal fail	57987
Heart Failure	Rheumatic left ventricular failure	22262
Heart Failure	Heart failure confirmed	9913
Heart Failure	Heart failure annual review	30779
Heart Failure	Heart failure 6 month review	83502
Heart Failure	Cardiac failure therapy	24503
Heart Failure	Admit heart failure emergency	32898
Heart Failure	Heart failure review completed	19380
Heart Failure	Acute cor pulmonale	8464
Heart Failure	Chronic cor pulmonale	5695
Heart Failure	Congestive cardiomyopathy	5141
Heart Failure	Congestive obstructive cardiomyopathy	68766
Heart Failure	Heart failure	2062
Heart Failure	Cardiac failure	1223
Heart Failure	Congestive heart failure	398
Heart Failure	Congestive cardiac failure	2906
Heart Failure	Right heart failure	10079
Heart Failure	Right ventricular failure	10154
Heart Failure	Biventricular failure	9524
Heart Failure	Acute congestive heart failure	23707
Heart Failure	Chronic congestive heart failure	32671
Heart Failure	Decompensated cardiac failure	27884
Heart Failure	Compensated cardiac failure	11424
Heart Failure	Left ventricular failure	884
Heart Failure	Asthma - cardiac	23481
Heart Failure	Impaired left ventricular function	5942
Heart Failure	Acute left ventricular failure	5255
Heart Failure	Acute heart failure	27964
Heart Failure	Heart failure NOS	4024
Heart Failure	Cardiac failure NOS	17278
Heart Failure	Left ventricular systolic dysfunction	8966
Heart Failure	Left ventricular diastolic dysfunction	12550
Heart Failure	[D]Cardiorespiratory failure	20324
Heart Failure	Congenital cardiac failure	20822
Ischemic heart disease	Prinzmetal's angina	12986
Ischemic heart disease	Variant angina pectoris	11048
Ischemic heart disease	Coronary artery spasm	36854
Ischemic heart disease	Cardiac syndrome X	8568
Ischemic heart disease	Angina control	13185
Ischemic heart disease	Angina control - good	19542
Ischemic heart disease	Angina control - poor	15373
Ischemic heart disease	Angina control - improving	14782

Ischemic heart disease	Angina control NOS	15349
Ischemic heart disease	Antianginal therapy	45960
Ischemic heart disease	Angina pectoris	1430
Ischemic heart disease	Angina decubitus	20095
Ischemic heart disease	Nocturnal angina	18125
Ischemic heart disease	Angina decubitus NOS	29902
Ischemic heart disease	Angina pectoris NOS	25842
Ischemic heart disease	Stenocardia	54535
Ischemic heart disease	Syncope anginosa	7696
Ischemic heart disease	Angina on effort	1414
Ischemic heart disease	Post infarct angina	9555
Ischemic heart disease	New onset angina	26863
Ischemic heart disease	Stable angina	12804
Ischemic heart disease	Angina pectoris NOS	28554
Ischemic heart disease	Chronic coronary insufficiency	24540
Ischemic heart disease	[X]Other forms of angina pectoris	39546
Ischemic heart disease	Acute coronary syndrome	11983
Ischemic heart disease	Preinfarction syndrome	36523
Ischemic heart disease	Crescendo angina	4656
Ischemic heart disease	Impending infarction	39655
Ischemic heart disease	Unstable angina	1431
Ischemic heart disease	Angina at rest	19655
Ischemic heart disease	Unstable angina	7347
Ischemic heart disease	Angina at rest	17307
Ischemic heart disease	Preinfarction syndrome NOS	54251
Ischemic heart disease	Coronary thrombosis not resulting in myocardial infarction	39449
Ischemic heart disease	Acute coronary insufficiency	9276
Ischemic heart disease	Status anginosus	66388
Ischemic heart disease	ECG: ventricular tachycardia	4924
Ischemic heart disease	Ventricular tachycardia	7794
Ischemic heart disease	ECG: ventricular fibrillation	31286
Ischemic heart disease	Defibrillation	31077
Ischemic heart disease	Ventricular fibrillation and flutter	4374
Ischemic heart disease	Ventricular fibrillation	4827
Ischemic heart disease	Cardiac arrest-ventricular fibrillation	25583
Ischemic heart disease	Ventricular fibrillation and flutter NOS	41916
Ischemic heart disease	Implantation of internal cardiac defibrillator	10160
Ischemic heart disease	Cardioverter defibrillator introduced through the vein	62141
Ischemic heart disease	Implantat cardioverter defibrillator us one electrode lead	88756
Ischemic heart disease	Implant cardioverter defibrillator using two electrode leads	87226
Ischemic heart disease	Implantat cardiovert defibrillator us three electrode leads	98214
Ischemic heart disease	Other specified cardioverter defibrillator intro thr vein	90685
Ischemic heart disease	Cardioverter defibrillator introduced through the vein NOS	91673
Ischemic heart disease	O/E - collapse -cardiac arrest	5925

Ischemic heart disease	Cardiac massage - open	97560
Ischemic heart disease	Advanced cardiopulmonary resuscitation	96801
Ischemic heart disease	Cardiac massage - external	41717
Ischemic heart disease	Closed cardiac massage alone	72762
Ischemic heart disease	Closed cardiac massage+ventil.	60367
Ischemic heart disease	Cardiopulmonary resuscitation	28236
Ischemic heart disease	External cardiac massage NOS	72785
Ischemic heart disease	Cardiac arrest	2099
Ischemic heart disease	Cardio-respiratory arrest	25407
Ischemic heart disease	Asystole	33402
Ischemic heart disease	Cardiac arrest with successful resuscitation	33899
Ischemic heart disease	Electromechanical dissociation with successful resuscitation	51140
Ischemic heart disease	Electromechanical dissociation	7630
Ischemic heart disease	Cardiac arrest, unspecified	49882
Ischemic heart disease	Cardiac arrest as a complication of care	72435
Ischemic heart disease	Diab mellit insulin-glucose infus acute myocardial infarct	61670
Ischemic heart disease	Acute myocardial infarction	241
Ischemic heart disease	Attack - heart	13566
Ischemic heart disease	Coronary thrombosis	2491
Ischemic heart disease	Cardiac rupture following myocardial infarction (MI)	30421
Ischemic heart disease	Heart attack	1204
Ischemic heart disease	MI - acute myocardial infarction	1677
Ischemic heart disease	Thrombosis - coronary	13571
Ischemic heart disease	Silent myocardial infarction	17689
Ischemic heart disease	Acute anterolateral infarction	12139
Ischemic heart disease	Other specified anterior myocardial infarction	5387
Ischemic heart disease	Acute anteroapical infarction	40429
Ischemic heart disease	Acute anteroseptal infarction	17872
Ischemic heart disease	Anterior myocardial infarction NOS	14897
Ischemic heart disease	Acute inferolateral infarction	8935
Ischemic heart disease	Acute inferoposterior infarction	29643
Ischemic heart disease	Posterior myocardial infarction NOS	23892
Ischemic heart disease	Lateral myocardial infarction NOS	14898
Ischemic heart disease	True posterior myocardial infarction	63467
Ischemic heart disease	Acute subendocardial infarction	3704
Ischemic heart disease	Acute non-Q wave infarction	9507
Ischemic heart disease	Inferior myocardial infarction NOS	1678
Ischemic heart disease	Acute Q-wave infarct	30330
Ischemic heart disease	Mural thrombosis	17133
Ischemic heart disease	Acute posterolateral myocardial infarction	32854
Ischemic heart disease	Acute transmural myocardial infarction of unspecif site	29758
Ischemic heart disease	Other acute myocardial infarction	34803
Ischemic heart disease	Acute atrial infarction	28736
Ischemic heart disease	Acute papillary muscle infarction	62626

Ischemic heart disease	Acute septal infarction	41221
Ischemic heart disease	Other acute myocardial infarction NOS	46017
Ischemic heart disease	Acute myocardial infarction NOS	14658
Ischemic heart disease	Dressler's syndrome	15661
Ischemic heart disease	Microinfarction of heart	68357
Ischemic heart disease	Subsequent myocardial infarction	18842
Ischemic heart disease	Subsequent myocardial infarction of anterior wall	45809
Ischemic heart disease	Subsequent myocardial infarction of inferior wall	38609
Ischemic heart disease	Subsequent myocardial infarction of other sites	72562
Ischemic heart disease	Subsequent myocardial infarction of unspecified site	46166
Ischemic heart disease	Certain current complication follow acute myocardial infarct	36423
Ischemic heart disease	Haemopericardium/current comp folow acut myocard infarct	24126
Ischemic heart disease	Atrial septal defect/curr comp folow acut myocardal infarct	23708
Ischemic heart disease	Ventric septal defect/curr comp fol acut myocardal infarctn	37657
Ischemic heart disease	Ruptur cardiac wall w/out haemopericard/cur comp fol ac MI	59189
Ischemic heart disease	Ruptur chordae tendinae/curr comp fol acute myocard infarct	59940
Ischemic heart disease	Rupture papillary muscle/curr comp fol acute myocard infarct	69474
Ischemic heart disease	Thrombosis atrium,auric append&vent/curr comp foll acute MI	29553
Ischemic heart disease	Postoperative myocardial infarction	32272
Ischemic heart disease	Postoperative transmural myocardial infarction anterior wall	46112
Ischemic heart disease	Postoperative transmural myocardial infarction inferior wall	46276
Ischemic heart disease	Postoperative subendocardial myocardial infarction	41835
Ischemic heart disease	Postoperative myocardial infarction, unspecified	68748
Ischemic heart disease	Post infarction pericarditis	35119
Ischemic heart disease	[X]Acute transmural myocardial infarction of unspecif site	96838
Ischemic heart disease	Acute ST segment elevation myocardial infarction	12229
Ischemic heart disease	Acute non-ST segment elevation myocardial infarction	10562
Ischemic heart disease	ECG: myocardial infarction	7783
Ischemic heart disease	ECG: antero-septal infarct.	26975
Ischemic heart disease	ECG:posterior/inferior infarct	26972
Ischemic heart disease	ECG: subendocardial infarct	55401
Ischemic heart disease	ECG: lateral infarction	52705
Ischemic heart disease	ECG: myocardial infarct NOS	59032
Ischemic heart disease	Diab mellit insulin-glucose infus acute myocardial infarct	61670
Ischemic heart disease	Acute myocardial infarction	241
Ischemic heart disease	Coronary thrombosis	2491
Ischemic heart disease	Cardiac rupture following myocardial infarction (MI)	30421
Ischemic heart disease	MI - acute myocardial infarction	1677
Ischemic heart disease	Thrombosis - coronary	13571
Ischemic heart disease	Acute anterolateral infarction	12139
Ischemic heart disease	Other specified anterior myocardial infarction	5387
Ischemic heart disease	Acute anteroapical infarction	40429
Ischemic heart disease	Acute anteroseptal infarction	17872
Ischemic heart disease	Anterior myocardial infarction NOS	14897

Ischemic heart disease	Acute inferolateral infarction	8935
Ischemic heart disease	Acute inferoposterior infarction	29643
Ischemic heart disease	Posterior myocardial infarction NOS	23892
Ischemic heart disease	Lateral myocardial infarction NOS	14898
Ischemic heart disease	True posterior myocardial infarction	63467
Ischemic heart disease	Acute subendocardial infarction	3704
Ischemic heart disease	Acute non-Q wave infarction	9507
Ischemic heart disease	Inferior myocardial infarction NOS	1678
Ischemic heart disease	Acute Q-wave infarct	30330
Ischemic heart disease	Acute posterolateral myocardial infarction	32854
Ischemic heart disease	Acute transmural myocardial infarction of unspecif site	29758
Ischemic heart disease	Other acute myocardial infarction	34803
Ischemic heart disease	Acute atrial infarction	28736
Ischemic heart disease	Acute papillary muscle infarction	62626
Ischemic heart disease	Acute septal infarction	41221
Ischemic heart disease	Other acute myocardial infarction NOS	46017
Ischemic heart disease	Acute myocardial infarction NOS	14658
Ischemic heart disease	Microinfarction of heart	68357
Ischemic heart disease	Postoperative myocardial infarction	32272
Ischemic heart disease	Postoperative transmural myocardial infarction anterior wall	46112
Ischemic heart disease	Postoperative transmural myocardial infarction inferior wall	46276
Ischemic heart disease	Postoperative subendocardial myocardial infarction	41835
Ischemic heart disease	Postoperative myocardial infarction, unspecified	68748
Ischemic heart disease	[X]Acute transmural myocardial infarction of unspecif site	96838
Ischemic heart disease	Subsequent myocardial infarction	18842
Ischemic heart disease	Subsequent myocardial infarction of anterior wall	45809
Ischemic heart disease	Subsequent myocardial infarction of inferior wall	38609
Ischemic heart disease	Subsequent myocardial infarction of other sites	72562
Ischemic heart disease	Subsequent myocardial infarction of unspecified site	46166
Ischemic heart disease	Acute ST segment elevation myocardial infarction	12229
Ischemic heart disease	Acute non-ST segment elevation myocardial infarction	10562
Ischemic heart disease	Atherosclerotic retinopathy	41229
Ischemic heart disease	Atheroscleritic retinopathy	34455
Ischemic heart disease	Atherosclerotic cardiovascular disease	36609
Ischemic heart disease	Cardiovascular arteriosclerosis unspecified	56621
Ischemic heart disease	Atherosclerosis	5640
Ischemic heart disease	Arteriosclerosis	996
Ischemic heart disease	Other specified artery atheroma	5168
Ischemic heart disease	Arteriosclerotic vascular disease NOS	3995
Ischemic heart disease	Coronary heart disease annual review	18135
Ischemic heart disease	Coronary heart disease review	10260
Ischemic heart disease	Coronary heart disease medication review	11648
Ischemic heart disease	Admit ischaemic heart disease emergency	95550
Ischemic heart disease	Ischaemic heart disease	240

Ischemic heart disease	Arteriosclerotic heart disease	24783
Ischemic heart disease	Atherosclerotic heart disease	20416
Ischemic heart disease	IHD - Ischaemic heart disease	1792
Ischemic heart disease	Other acute and subacute ischaemic heart disease	27951
Ischemic heart disease	Myocardial infarction aborted	61072
Ischemic heart disease	MI - myocardial infarction aborted	55137
Ischemic heart disease	Other acute and subacute ischaemic heart disease	9413
Ischemic heart disease	Subendocardial ischaemia	39693
Ischemic heart disease	Transient myocardial ischaemia	21844
Ischemic heart disease	Other acute and subacute ischaemic heart disease NOS	27977
Ischemic heart disease	Other chronic ischaemic heart disease	28138
Ischemic heart disease	Coronary atherosclerosis	5413
Ischemic heart disease	Coronary artery disease	1344
Ischemic heart disease	Ischaemic cardiomyopathy	7320
Ischemic heart disease	Silent myocardial ischaemia	29421
Ischemic heart disease	Other specified chronic ischaemic heart disease	34633
Ischemic heart disease	Chronic myocardial ischaemia	23078
Ischemic heart disease	Other specified chronic ischaemic heart disease NOS	35713
Ischemic heart disease	Other chronic ischaemic heart disease NOS	15754
Ischemic heart disease	Asymptomatic coronary heart disease	18889
Ischemic heart disease	Other specified ischaemic heart disease	22383
Ischemic heart disease	Ischaemic heart disease NOS	1676
Ischemic heart disease	[X]Ischaemic heart diseases	52517
Ischemic heart disease	[X]Other forms of acute ischaemic heart disease	68401
Ischemic heart disease	[X]Other forms of chronic ischaemic heart disease	47637
Liver disease	Chronic hepatitis	1754
Liver disease	Chronic persistent hepatitis	23578
Liver disease	Chronic active hepatitis	9029
Liver disease	Chronic aggressive hepatitis	1755
Liver disease	Chronic lobular hepatitis	66534
Liver disease	Chronic hepatitis unspecified	53877
Liver disease	Chronic hepatitis NOS	15489
Liver disease	Chronic alcoholic hepatitis	7602
Liver disease	Open operations on oesophageal varices	24220
Liver disease	Local ligation of oesophageal varices	43404
Liver disease	Open injection sclerotherapy to oesophageal varices	20912
Liver disease	Open operation on oesophageal varices NOS	20233
Liver disease	Fibreoptic endoscopic banding of oesophageal varices	16759
Liver disease	Rigid oesophagoscopy injection sclerotherapy oesoph varices	47214
Liver disease	Rigid oesophagoscopy banding of oesophageal varices	46647
Liver disease	Oesophageal varices	1641
Liver disease	Oesophageal varices with bleeding	24989
Liver disease	Oesophageal varices without bleeding	30655
Liver disease	Oesophageal varices in diseases EC	44424

Liver disease	Oesophageal varices with bleeding in diseases EC	96756
Liver disease	Oesophageal varices without bleeding in diseases EC	73139
Liver disease	Oesophageal varices in diseases EC NOS	62582
Liver disease	Oesophageal varices NOS	10797
Liver disease	Hepatic coma	23511
Liver disease	Encephalopathy - hepatic	22411
Liver disease	Portal hypertension	5129
Liver disease	Hepatorenal syndrome	10636
Liver disease	[X] Hepatic failure	24901
Liver disease	[X] Liver failure	21769
Liver disease	Hepatic failure NOS	56070
Liver disease	Liver failure NOS	23775
Liver disease	Hepatic failure	16062
Liver disease	Chronic kidney disease stage 1	29013
Liver disease	Chronic kidney disease stage 2	12586
Liver disease	Chronic kidney disease stage 1 with proteinuria	94789
Liver disease	Chronic kidney disease stage 1 without proteinuria	95572
Liver disease	Chronic kidney disease stage 2 with proteinuria	95146
Liver disease	Chronic kidney disease stage 2 without proteinuria	95121
Liver disease	Plasmodium malariae malaria with nephropathy	49046
Liver disease	Acute glomerulonephritis	2088
Liver disease	Acute nephritis	5417
Liver disease	Acute proliferative glomerulonephritis	29384
Liver disease	Acute nephritis with lesions of necrotising glomerulitis	67460
Liver disease	Other acute glomerulonephritis	63599
Liver disease	Acute glomerulonephritis in diseases EC	20027
Liver disease	Acute exudative nephritis	94261
Liver disease	Acute focal nephritis	48261
Liver disease	Acute diffuse nephritis	55100
Liver disease	Other acute glomerulonephritis NOS	47838
Liver disease	Acute glomerulonephritis NOS	20129
Liver disease	Tubulo-interstit nephritis, not specif as acute or chron	23990
Liver disease	Acute renal failure	2266
Liver disease	Acute renal tubular necrosis	10837
Liver disease	Acute renal cortical necrosis	46242
Liver disease	Acute renal medullary necrosis	31369
Liver disease	Acute drug-induced renal failure	57919
Liver disease	Acute renal failure due to urinary obstruction	97198
Liver disease	Other acute renal failure	35235
Liver disease	Acute renal failure NOS	25582
Liver disease	Acute interstitial nephritis	9379
Liver disease	Acute nephritic syndrome	31581
Liver disease	Acute nephritic syndrome, focal+segmental glomerular lesions	66136
Liver disease	Acute nephritic syn, diffuse membranous glomerulonephritis	66503

Liver disease	Acute neph syn, diffuse mesangiocapillary glomerulonephritis	54312
Liver disease	Acute nephrotic syndrm diffuse crescentic glomerulonephritis	61814
Liver disease	Acute pyelonephritis	2546
Liver disease	Acute pyelonephritis without medullary necrosis	64482
Liver disease	Acute pyelonephritis NOS	38698
Liver disease	[X]Other acute renal failure	53945
Liver disease	Acute renal failure following labour and delivery	63277
Liver disease	Post-delivery acute renal failure unspecified	72458
Liver disease	Post-delivery acute renal failure - delivered with p/n prob	96179
Liver disease	Post-delivery acute renal failure with postnatal problem	69433
Liver disease	Renal failure following crush syndrome	15945
Liver disease	Renal failure after crushing	63760
Liver disease	Acute renal failure due to rhabdomyolysis	24676
Liver disease	Post operative renal failure	24292
Liver disease	Chronic renal impairment	12720
Liver disease	Chronic kidney disease stage 3	12566
Liver disease	Chronic kidney disease stage 4	12479
Liver disease	Chronic kidney disease stage 5	12585
Liver disease	Chronic kidney disease stage 3A	94965
Liver disease	Chronic kidney disease stage 3B	95179
Liver disease	Chronic kidney disease stage 3 with proteinuria	94793
Liver disease	Chronic kidney disease stage 3 without proteinuria	95123
Liver disease	Chronic kidney disease stage 3A with proteinuria	95408
Liver disease	Chronic kidney disease stage 3A without proteinuria	95175
Liver disease	Chronic kidney disease stage 3B with proteinuria	95178
Liver disease	Chronic kidney disease stage 3B without proteinuria	95177
Liver disease	Chronic kidney disease stage 4 with proteinuria	95122
Liver disease	Chronic kidney disease stage 4 without proteinuria	95406
Liver disease	Chronic kidney disease stage 5 with proteinuria	95508
Liver disease	Chronic kidney disease stage 5 without proteinuria	95405
Liver disease	Creation of graft fistula for dialysis	60302
Liver disease	Pre-transplantation of kidney work-up, recipient	90952
Liver disease	Compensation for renal failure	31549
Liver disease	Other specified compensation for renal failure	48022
Liver disease	Compensation for renal failure NOS	64636
Liver disease	Placement ambulatory apparatus compensation renal failure	56760
Liver disease	Placement ambulatory apparatus- compensate renal failure OS	59194
Liver disease	Placement other apparatus for compensation for renal failure	83513
Liver disease	Placement other apparatus- compensate for renal failure NOS	65089
Liver disease	Renal transplant planned	17253
Liver disease	Tuberculous nephropathy	52272
Liver disease	Tuberculous pyelonephritis	49235
Liver disease	Haemorrhagic nephrosonephritis	67197
Liver disease	Diabetic nephropathy	2475

Liver disease	Diabetes mellitus with nephropathy NOS	35107
Liver disease	Insulin dependent diabetes mellitus with nephropathy	57621
Liver disease	Type I diabetes mellitus with nephropathy	66872
Liver disease	Non-insulin dependent diabetes mellitus with nephropathy	59365
Liver disease	Type II diabetes mellitus with nephropathy	64571
Liver disease	Type 2 diabetes mellitus with nephropathy	24836
Liver disease	Type 1 diabetes mellitus with nephropathy	10418
Liver disease	Type 2 diabetes mellitus with nephropathy	12640
Liver disease	Gouty nephropathy	52969
Liver disease	Gouty nephropathy NOS	61145
Liver disease	Gout due to impairment of renal function	21687
Liver disease	Nephropathic amyloidosis	68112
Liver disease	Haemolytic-uraemic syndrome	29323
Liver disease	Anaemia secondary to renal failure	16929
Liver disease	Anaemia secondary to chronic renal failure	25394
Liver disease	Henoch-Schonlein nephritis	22897
Liver disease	Polyneuropathy in uraemia	19454
Liver disease	Hypertensive renal disease	4668
Liver disease	Malignant hypertensive renal disease	39649
Liver disease	Benign hypertensive renal disease	43935
Liver disease	Hypertensive renal disease with renal failure	32423
Liver disease	Hypertensive renal disease NOS	15106
Liver disease	Hypertensive heart and renal disease	63466
Liver disease	Malignant hypertensive heart and renal disease	67232
Liver disease	Benign hypertensive heart and renal disease	63000
Liver disease	Hypertensive heart&renal dis wth (congestive) heart failure	21837
Liver disease	Hypertensive heart and renal disease with renal failure	28684
Liver disease	Hypertensive heart and renal disease NOS	68659
Liver disease	Acute pericarditis - uraemic	40956
Liver disease	[X]Hypertension secondary to other renal disorders	97533
Liver disease	Nephritis, nephrosis and nephrotic syndrome	2773
Liver disease	Nephrotic syndrome	2999
Liver disease	Nephrotic syndrome with proliferative glomerulonephritis	9840
Liver disease	Nephrotic syndrome with membranous glomerulonephritis	1803
Liver disease	Nephrotic syndrome with minimal change glomerulonephritis	29634
Liver disease	Steroid sensitive nephrotic syndrome	57926
Liver disease	Nephrotic syndrome, minor glomerular abnormality	23913
Liver disease	Nephrotic syndrome, focal and segmental glomerular lesions	22852
Liver disease	Nephrotic syndrome, diffuse membranous glomerulonephritis	19316
Liver disease	Nephrotic syn difus mesangial proliferativ glomerulonephritis	21947
Liver disease	Nephrotic syn,difus endocapillary prolifv glomerulonephritis	50472
Liver disease	Nephrotic syn,diffuse mesangiocapillary glomerulonephritis	21989
Liver disease	Nephrotic syndrome, dense deposit disease	56987
Liver disease	Nephrotic syndrome, diffuse crescentic glomerulonephritis	17365

Liver disease	Congenital nephrotic syndrome	63786
Liver disease	Nephrotic syndrome in amyloidosis	47922
Liver disease	Nephrotic syndrome in diabetes mellitus	2471
Liver disease	Nephrotic syndrome in polyarteritis nodosa	58750
Liver disease	Nephrotic syndrome in systemic lupus erythematosus	47672
Liver disease	Lupus nephritis	22205
Liver disease	Nephrotic syndrome with other pathological kidney lesions	94373
Liver disease	Nephrotic syndrome NOS	27427
Liver disease	Chronic glomerulonephritis	7804
Liver disease	Nephritis - chronic	10647
Liver disease	Nephropathy - chronic	11875
Liver disease	Chronic proliferative glomerulonephritis	34998
Liver disease	Chronic membranous glomerulonephritis	10809
Liver disease	Chronic membranoproliferative glomerulonephritis	61494
Liver disease	Chronic rapidly progressive glomerulonephritis	65064
Liver disease	Other chronic glomerulonephritis	60960
Liver disease	Chronic glomerulonephritis + diseases EC	97758
Liver disease	Chronic focal glomerulonephritis	4669
Liver disease	Chronic diffuse glomerulonephritis	65400
Liver disease	Other chronic glomerulonephritis NOS	63615
Liver disease	Chronic glomerulonephritis NOS	15097
Liver disease	Nephritis and nephropathy unspecified	33580
Liver disease	Nephritis and nephropathy unspecified	4850
Liver disease	Nephropathy, unspecified	11873
Liver disease	Proliferative nephritis unspecified	16008
Liver disease	Membranous nephritis unspecified	5291
Liver disease	Membranoproliferative nephritis unspecified	12465
Liver disease	Focal membranoproliferative glomerulonephritis	67995
Liver disease	Anaphylactoid glomerulonephritis	62868
Liver disease	Familial glomerulonephritis in Alport's syndrome	24384
Liver disease	Other familial glomerulonephritis	57072
Liver disease	Berger's IgA or IgG nephropathy	21423
Liver disease	Nephritis unsp+OS membranoprolif glomerulonephritis lesion	67193
Liver disease	Hypocomplementaemic persistent glomerulonephritis NEC	50305
Liver disease	Mesangioproliferative glomerulonephritis NEC	36342
Liver disease	Mesangiocapillary glomerulonephritis NEC	41881
Liver disease	Mixed membranous and proliferative glomerulonephritis NEC	97388
Liver disease	Nephritis unsp+membranoprolif glomerulonephritis lesion NOS	94350
Liver disease	Rapidly progressive nephritis unspecified	58164
Liver disease	Renal cortical necrosis unspecified	41676
Liver disease	Renal medullary necrosis unspecified	45867
Liver disease	Unspecif nephr synd, diff concentric glomerulonephritis	36125
Liver disease	Unspecified nephritic syndrome, dense deposit disease	60128
Liver disease	Unsp nephrit synd, diff endocap prolif glomerulonephritis	62520

Liver disease	Unsp nephrit synd, diff mesang prolif glomerulonephritis	30301
Liver disease	Other nephritis and nephrosis unspecified	35065
Liver disease	Other nephritis and nephrosis in diseases EC	27335
Liver disease	Other interstitial nephritis	34669
Liver disease	Other nephritis and nephrosis NOS	44055
Liver disease	Unspecified glomerulonephritis NOS	5182
Liver disease	Chronic renal failure	512
Liver disease	Chronic uraemia	10081
Liver disease	End stage renal failure	53852
Liver disease	End stage renal failure	6712
Liver disease	Renal failure unspecified	350
Liver disease	Uraemia NOS	4809
Liver disease	Renal impairment	11787
Liver disease	Impaired renal function	6842
Liver disease	Impaired renal function disorder	8919
Liver disease	Renal osteodystrophy	29638
Liver disease	Phosphate-losing tubular disorders	68114
Liver disease	Renal dwarfism	34648
Liver disease	Renal infantilism	50728
Liver disease	Renal rickets	66062
Liver disease	Renal osteodystrophy NOS	34637
Liver disease	Nephrogenic diabetes insipidus	30310
Liver disease	Other impaired renal function disorder	39840
Liver disease	Hypokalaemic nephropathy	56939
Liver disease	Renal function impairment with growth failure	41013
Liver disease	Renal tubular acidosis	5072
Liver disease	Other impaired renal function disorder NOS	50804
Liver disease	Renal acidaemia	48475
Liver disease	Impaired renal function disorder NOS	25980
Liver disease	Acut neph syn, diffuse mesangial proliferative glomnephritis	55389
Liver disease	Rapidly progressive nephritic syndrome	71174
Liver disease	Rapid progres nephritic syn focal+segmental glomerulr lesion	97734
Liver disease	Rapid progres neph syn diffuse membranous glomerulonephritis	41285
Liver disease	Rpd prog neph syn df mesangial proliferatv glomerulonephritis	58060
Liver disease	Rapid progressive nephritic syndrome, dense deposit disease	50200
Liver disease	Rapid progres nephritic syn df crescentic glomerulonephritis	62320
Liver disease	Recur+persist haematuria difus membranous glomerulonephritis	61317
Liver disease	Recur+persist haemuria df mesangial prolif glomerulnephritis	49642
Liver disease	Recur+persist hmuria df mesangiocapillary glomerulonephritis	60484
Liver disease	Recur+persist haematuria difus crescentic glomerulonephritis	60856
Liver disease	IgA nephropathy	85659
Liver disease	Chronic nephritic syndrome	21297
Liver disease	Chronic nephritic syndrome, minor glomerular abnormality	66505
Liver disease	Chronic nephritic syndrm focal+segmental glomerular lesions	40413

Liver disease	Chron nephritic syndrom difuse membranous glomerulonephritis	57168
Liver disease	Chron neph syn difus mesangial prolifrtiv glomerulonephritis	56893
Liver disease	Chronic neph syn difus mesangiocapillary glomerulonephritis	73026
Liver disease	Chronic nephritic syndrome, dense deposit disease	60198
Liver disease	Chronic nephritic syn diffuse crescentic glomerulonephritis	60857
Liver disease	Isoltd prteinur+specfd morph les df mesangiocap glomnephrit	61811
Liver disease	Hereditary nephropathy not elsewhere classified	36205
Liver disease	Hereditary nephropathy NEC, minor glomerular abnormality	51113
Liver disease	Hereditary nephropathy NEC,focal+segmnt glomerular lesion	41239
Liver disease	Hereditry nephropathy NEC,difus membran glomerulonephritis	44270
Liver disease	Hereditry nephropathy NEC difus mesangial prolif glomnephrit	58671
Liver disease	Hereditary nephropathy, NEC, dense deposit disease	91738
Liver disease	Hereditary nephropathy, unspecif morphological changes	62980
Liver disease	Renal tubulo-interstitial disorders in diseases EC	45523
Liver disease	Renal tubulo-interstitial disorder/ neoplastic diseases	64622
Liver disease	Renal tubulo-interstitial disorder in SLE	41148
Liver disease	Analgesic nephropathy	8607
Liver disease	Nephropathy induced by other drugs meds and biologl substncs	41159
Liver disease	Nephropathy induced by unspec drug medicament or biol subs	57784
Liver disease	Toxic nephropathy, not elsewhere classified	50893
Liver disease	End-stage renal disease	8330
Liver disease	Other specified nephritis, nephrosis or nephrotic syndrome	49150
Liver disease	Nephritis, nephrosis and nephrotic syndrome NOS	15780
Liver disease	Chronic pyelonephritis	4654
Liver disease	Chronic pyelonephritis with medullary necrosis	57568
Liver disease	Nonobstructive reflux-associated chronic pyelonephritis	35360
Liver disease	Chronic obstructive pyelonephritis	48855
Liver disease	Calculous pyelonephritis	2939
Liver disease	Chronic pyelonephritis NOS	48111
Liver disease	Xanthogranulomatous pyelonephritis	38572
Liver disease	Pyelonephritis and pyonephrosis unspecified	53944
Liver disease	Pyelonephritis unspecified	1899
Liver disease	Pyelonephritis in diseases EC	95710
Liver disease	Unspecified pyelonephritis NOS	59121
Liver disease	Other kidney and ureter disorders	36273
Liver disease	Other kidney disorders	8098
Liver disease	Vascular disorders of kidney	11992
Liver disease	Renal vascular disorders	10460
Liver disease	Renal vascular disorders NOS	15340
Liver disease	Other kidney and ureteric disorders	44657
Liver disease	Other kidney and ureteric disorders NOS	34675
Liver disease	Salt-losing nephritis	20516
Liver disease	Kidney and ureter disease NOS	2991
Liver disease	[X]Unsp nephrit synd, diff mesang prolif glomerulonephritis	71709

Liver disease	[X]Renal tubulo-interstitial diseases	94842
Liver disease	[X]Nephropathy induced by other drugs+biological substances	72478
Liver disease	[X]Renal failure	61930
Liver disease	[X]Other chronic renal failure	53940
Liver disease	[X]Other disorders of kidney and ureter	70157
Liver disease	[X]Other disorders resulting/impaired renal tubular function	96819
Liver disease	[X]Other specified disorders of kidney and ureter	56896
Liver disease	Renal failure following abortive pregnancy	71314
Liver disease	Uraemia following abortive pregnancy	70422
Liver disease	Unspecified renal disease in pregnancy	47080
Liver disease	Nephropathy NOS in pregnancy without hypertension	38312
Liver disease	Uraemia in pregnancy without hypertension	92579
Liver disease	Unspecified renal disease in pregnancy unspecified	54938
Liver disease	Unspecified renal disease in pregnancy - delivered	96724
Liver disease	Congenital cystic kidney disease	15917
Liver disease	Congenital cystic renal disease	20629
Liver disease	Polycystic kidney disease	4503
Liver disease	Polycystic kidney disease NOS	56852
Liver disease	Cystic kidney disease NEC	9240
Liver disease	Other specified congenital cystic kidney disease	59018
Liver disease	Fibrocystic kidney disease	67486
Liver disease	Other congenital cystic kidney disease NOS	59031
Liver disease	Congenital cystic kidney disease NOS	50331
Liver disease	[X]Other cystic kidney diseases	72877
Liver disease	Fetus or neonate affected by maternal renal/urinary disease	73373
Liver disease	Congenital renal failure	47342
Liver disease	Renal failure as a complication of care	11554
Liver disease	Kidney failure as a complication of care	39598
Liver disease	Uraemia - post operative	55858
Liver disease	Haemodialysis training	74905
Liver disease	[V]Preparatory care for dialysis	52088
Obesity-related cancers	Malignant neoplasm of female breast	3968
Obesity-related cancers	Ca female breast	348
Obesity-related cancers	Malignant neoplasm of nipple and areola of female breast	26853
Obesity-related cancers	Malignant neoplasm of nipple of female breast	23380
Obesity-related cancers	Malignant neoplasm of areola of female breast	64686
Obesity-related cancers	Malignant neoplasm of nipple or areola of female breast NOS	59831
Obesity-related cancers	Malignant neoplasm of central part of female breast	31546
Obesity-related cancers	Malignant neoplasm of upper-inner quadrant of female breast	29826
Obesity-related cancers	Malignant neoplasm of lower-inner quadrant of female breast	45222
Obesity-related cancers	Malignant neoplasm of upper-outer quadrant of female breast	23399
Obesity-related cancers	Malignant neoplasm of lower-outer quadrant of female breast	42070
Obesity-related cancers	Malignant neoplasm of axillary tail of female breast	20685
Obesity-related cancers	Malignant neoplasm, overlapping lesion of breast	49148

Obesity-related cancers	Malignant neoplasm of other site of female breast	56715
Obesity-related cancers	Malignant neoplasm of ectopic site of female breast	95057
Obesity-related cancers	Malignant neoplasm of other site of female breast NOS	38475
Obesity-related cancers	Malignant neoplasm of female breast NOS	9470
Obesity-related cancers	Malignant neoplasm of male breast	19423
Obesity-related cancers	Malignant neoplasm of nipple and areola of male breast	54494
Obesity-related cancers	Malignant neoplasm of nipple of male breast	68480
Obesity-related cancers	Malignant neoplasm of areola of male breast	67884
Obesity-related cancers	Malignant neoplasm of other site of male breast	54202
Obesity-related cancers	Malignant neoplasm of ectopic site of male breast	95323
Obesity-related cancers	Malignant neoplasm of male breast NOS	48809
Obesity-related cancers	Carcinoma in situ of breast	7833
Obesity-related cancers	[M]Juvenile breast carcinoma	40359
Obesity-related cancers	[M]Secretory breast carcinoma	67701
Obesity-related cancers	[M]Paget's disease and infiltrating breast duct carcinoma	42542
Obesity-related cancers	[M]Paget's disease and intraductal carcinoma of breast	12480
Obesity-related cancers	[X]Malignant neoplasm of breast	12499
Obesity-related cancers	Secondary malignant neoplasm of breast	16760
Obesity-related cancers	Malignant neoplasm of oesophagus	1062
Obesity-related cancers	Malignant neoplasm of cervical oesophagus	61695
Obesity-related cancers	Malignant neoplasm of thoracic oesophagus	41362
Obesity-related cancers	Malignant neoplasm of abdominal oesophagus	63470
Obesity-related cancers	Malignant neoplasm of upper third of oesophagus	50789
Obesity-related cancers	Malignant neoplasm of middle third of oesophagus	54171
Obesity-related cancers	Malignant neoplasm of lower third of oesophagus	42416
Obesity-related cancers	Malignant neoplasm, overlapping lesion of oesophagus	67497
Obesity-related cancers	Malignant neoplasm of other specified part of oesophagus	53591
Obesity-related cancers	Malignant neoplasm of oesophagus NOS	30700
Obesity-related cancers	Oesophageal cancer	4865
Obesity-related cancers	Malignant neoplasm of cardio-oesophageal junction of stomach	22894
Obesity-related cancers	Malignant neoplasm of gastro-oesophageal junction	94278
Obesity-related cancers	Malignant neoplasm of stomach	8386
Obesity-related cancers	Malignant neoplasm of cardia of stomach	32022
Obesity-related cancers	Malignant neoplasm of cardio-oesophageal junction of stomach	22894
Obesity-related cancers	Malignant neoplasm of cardia of stomach NOS	37859
Obesity-related cancers	Malignant neoplasm of pylorus of stomach	21620
Obesity-related cancers	Malignant neoplasm of prepylorus of stomach	48237
Obesity-related cancers	Malignant neoplasm of pyloric canal of stomach	41215
Obesity-related cancers	Malignant neoplasm of pylorus of stomach NOS	59092
Obesity-related cancers	Malignant neoplasm of pyloric antrum of stomach	19318
Obesity-related cancers	Malignant neoplasm of fundus of stomach	32362
Obesity-related cancers	Malignant neoplasm of body of stomach	43572
Obesity-related cancers	Malignant neoplasm of lesser curve of stomach unspecified	42193
Obesity-related cancers	Malignant neoplasm of greater curve of stomach unspecified	55434

Obesity-related cancers	Malignant neoplasm, overlapping lesion of stomach	51690
Obesity-related cancers	Malignant neoplasm of other specified site of stomach	55019
Obesity-related cancers	Malignant neoplasm of anterior wall of stomach NEC	65312
Obesity-related cancers	Malignant neoplasm of posterior wall of stomach NEC	96802
Obesity-related cancers	Malignant neoplasm of other specified site of stomach NOS	65372
Obesity-related cancers	Malignant neoplasm of stomach NOS	14800
Obesity-related cancers	Malignant neoplasm of colon	1220
Obesity-related cancers	Malignant neoplasm of hepatic flexure of colon	9088
Obesity-related cancers	Malignant neoplasm of transverse colon	6935
Obesity-related cancers	Malignant neoplasm of descending colon	10864
Obesity-related cancers	Malignant neoplasm of sigmoid colon	2815
Obesity-related cancers	Malignant neoplasm of ascending colon	10946
Obesity-related cancers	Malignant neoplasm of splenic flexure of colon	18619
Obesity-related cancers	Malignant neoplasm, overlapping lesion of colon	93478
Obesity-related cancers	Malignant neoplasm of other specified sites of colon	48231
Obesity-related cancers	Malignant neoplasm of colon NOS	28163
Obesity-related cancers	Colonic cancer	9118
Obesity-related cancers	Malignant neoplasm of rectum, rectosigmoid junction and anus	35357
Obesity-related cancers	Malignant neoplasm of anus unspecified	27897
Obesity-related cancers	Malig neop other site rectum, rectosigmoid junction and anus	55659
Obesity-related cancers	Malignant neoplasm rectum,rectosigmoid junction and anus NOS	50974
Obesity-related cancers	[M]Adenomatous and adenocarcinomatous polyps of colon	41702
Obesity-related cancers	[M]Adenomatous or adenocarcinomatous polyps of the colon NOS	39875
Obesity-related cancers	Malignant neoplasm of rectum, rectosigmoid junction and anus	35357
Obesity-related cancers	Malignant neoplasm of rectosigmoid junction	27855
Obesity-related cancers	Malignant neoplasm of rectum	1800
Obesity-related cancers	Carcinoma of rectum	7219
Obesity-related cancers	Rectal carcinoma	5901
Obesity-related cancers	Malig neop other site rectum, rectosigmoid junction and anus	55659
Obesity-related cancers	Malignant neoplasm rectum,rectosigmoid junction and anus NOS	50974
Obesity-related cancers	Malignant neoplasm of mesorectum	30165
Obesity-related cancers	Cancer of bowel	11628
Obesity-related cancers	Malignant neoplasm of caecum	3811
Obesity-related cancers	Carcinoma of caecum	22163
Obesity-related cancers	Malignant neoplasm of retrocaecal tissue	24048
Obesity-related cancers	Malignant neoplasm of mesocaecum	59388
Obesity-related cancers	Secondary malignant neoplasm of colon	28727
Obesity-related cancers	Secondary malignant neoplasm of large intestine and rectum	44529
Obesity-related cancers	Secondary malignant neoplasm of rectum	62909
Obesity-related cancers	Secondary malig neop of large intestine or rectum NOS	36200
Obesity-related cancers	Secondary malignant neoplasm of liver	36147
Obesity-related cancers	Secondary malignant neoplasm of liver	15103
Obesity-related cancers	Liver metastases	4403
Obesity-related cancers	Malignant neoplasm of liver and intrahepatic bile ducts	8918

Obesity-related cancers	Primary malignant neoplasm of liver	25535
Obesity-related cancers	Primary carcinoma of liver	16126
Obesity-related cancers	Hepatoblastoma of liver	31210
Obesity-related cancers	Primary angiosarcoma of liver	68410
Obesity-related cancers	Primary malignant neoplasm of liver NOS	44399
Obesity-related cancers	Malignant neoplasm of liver unspecified	26393
Obesity-related cancers	Malignant neoplasm of liver and intrahepatic bile ducts NOS	38978
Obesity-related cancers	[M]Liver cell carcinoma	25641
Obesity-related cancers	[X]Other specified carcinomas of liver	43490
Obesity-related cancers	Malignant neoplasm gallbladder and extrahepatic bile ducts	54103
Obesity-related cancers	Malignant neoplasm of gallbladder	16105
Obesity-related cancers	Carcinoma gallbladder	31393
Obesity-related cancers	Malignant neoplasm other gallbladder/extrahepatic bile duct	60312
Obesity-related cancers	Malignant neoplasm gallbladder/extrahepatic bile ducts NOS	15907
Obesity-related cancers	Malignant neoplasm of intrahepatic bile ducts	16915
Obesity-related cancers	Malignant neoplasm of interlobular bile ducts	65124
Obesity-related cancers	Malignant neoplasm of intrahepatic bile ducts NOS	61643
Obesity-related cancers	Malignant neoplasm of extrahepatic bile ducts	23433
Obesity-related cancers	Malignant neoplasm of common bile duct	7982
Obesity-related cancers	Carcinoma common bile duct	36495
Obesity-related cancers	Malignant neoplasm of extrahepatic bile ducts NOS	74896
Obesity-related cancers	[M]Bile duct carcinoma	40438
Obesity-related cancers	[M]Bile duct cystadenocarcinoma	41313
Obesity-related cancers	[M]Hepatoblastoma	57677
Obesity-related cancers	Malignant neoplasm of pancreas	8166
Obesity-related cancers	Malignant neoplasm of head of pancreas	8771
Obesity-related cancers	Malignant neoplasm of body of pancreas	40810
Obesity-related cancers	Malignant neoplasm of tail of pancreas	39870
Obesity-related cancers	Malignant neoplasm, overlapping lesion of pancreas	97875
Obesity-related cancers	Malignant neoplasm of other specified sites of pancreas	48537
Obesity-related cancers	Malignant neoplasm of specified site of pancreas NOS	95783
Obesity-related cancers	Malignant neoplasm of pancreas NOS	34388
Obesity-related cancers	Malignant neoplasm of pancreatic duct	35535
Obesity-related cancers	Malignant neoplasm of ectopic pancreatic tissue	96635
Obesity-related cancers	[M]Pancreatic adenomas and carcinomas	8032
Obesity-related cancers	[M]Pancreatic adenoma or carcinoma NOS	21659
Obesity-related cancers	Malignant neoplasm of endometrium of corpus uteri	2890
Obesity-related cancers	Malignant neoplasm of endometrium	49400
Obesity-related cancers	[M]Endometrioid adenomas and carcinomas	8606
Obesity-related cancers	[M]Endometrioid carcinoma	9447
Obesity-related cancers	[M]Endometrioid adenoma or carcinoma NOS	28388
Obesity-related cancers	[M]Endometrial stromal sarcoma	34030
Obesity-related cancers	Secondary malignant neoplasm of ovary	44615
Obesity-related cancers	Malignant neoplasm of ovary and other uterine adnexa	19141

Obesity-related cancers	Malignant neoplasm of ovary	7805
Obesity-related cancers	Cancer of ovary	1986
Obesity-related cancers	[M]Ovarian cystadenoma or carcinoma	17151
Obesity-related cancers	Anaemia in ovarian carcinoma	48145
Obesity-related cancers	Malig neop of kidney and other unspecified urinary organs	13559
Obesity-related cancers	Malignant neoplasm of kidney parenchyma	1599
Obesity-related cancers	Malignant neoplasm of kidney or urinary organs NOS	29462
Obesity-related cancers	[M]Clear cell sarcoma of kidney	18771
Obesity-related cancers	Secondary malignant neoplasm of kidney	1952
Obesity-related cancers	Malignant neoplasm of cerebral meninges	28919
Obesity-related cancers	Malignant neoplasm of cerebral meninges NOS	70104
Obesity-related cancers	Malignant neoplasm of spinal meninges	49714
Obesity-related cancers	Malignant neoplasm of spinal meninges NOS	67211
Obesity-related cancers	Malignant neoplasm of meninges, unspecified	49875
Obesity-related cancers	[X]Malignant neoplasm of meninges, unspecified	63925
Obesity-related cancers	Cerebral meningioma	8672
Obesity-related cancers	Spinal meningioma	9544
Obesity-related cancers	Malignant neoplasm of thyroid cartilage	47862
Obesity-related cancers	Malignant neoplasm of thyroid gland	5637
Obesity-related cancers	[M]Thyroid adenoma and adenocarcinoma	19263
Obesity-related cancers	[M]Thyroid adenoma or adenocarcinoma NOS	38685
Obesity-related cancers	[X]Malignant neoplasm of thyroid and other endocrine glands	40608
Obesity-related cancers	Multiple myeloma	4944
Obesity-related cancers	Myelomatosis	15211
Obesity-related cancers	Solitary myeloma	19028
Obesity-related cancers	Lambda light chain myeloma	46042
Obesity-related cancers	Myeloma - solitary	43312
Obesity-related cancers	[M]Plasma cell myeloma	31671
Obesity-related cancers	[M]Multiple myeloma	18744
Obesity-related cancers	[M]Myeloma NOS	3672
Obesity-related cancers	[M]Myelomatosis	53647
Obesity-related cancers	[M]Plasmacytic myeloma	39490
Obesity-related cancers	[M]Solitary myeloma	73135
Obesity-related cancers	Osteoporosis in multiple myelomatosis	60433
Obesity-related cancers	Malignant plasma cell neoplasm, extramedullary plasmacytoma	22158
Obesity-related cancers	Plasmacytoma NOS	21329
Obesity-related cancers	Plasmacytoma NOS	38321
Obesity-related cancers	[M]Plasmacytoma NOS	63864
Obesity-related cancers	Kahler's disease	43552
Obesity-related cancers	Myelomatosis	15211
Obesity-related cancers	[M]Myelomatosis	53647
Obesity-related cancers	Osteoporosis in multiple myelomatosis	60433
Obesity-related cancers	Malignant plasma cell neoplasm, extramedullary plasmacytoma	22158
Obesity-related cancers	Plasmacytoma NOS	21329

Obesity-related cancers	Plasmacytoma NOS	38321
Obesity-related cancers	[M]Plasmacytoma NOS	63864
Osteoarthritis and joint disorders	O/E - hands - Heberden's nodes	17282
Osteoarthritis and joint disorders	Osteoarthritis and allied disorders	3057
Osteoarthritis and joint disorders	Osteoarthritis	396
Osteoarthritis and joint disorders	Generalised osteoarthritis - OA	4353
Osteoarthritis and joint disorders	Generalised osteoarthritis of unspecified site	38631
Osteoarthritis and joint disorders	Generalised osteoarthritis of the hand	36327
Osteoarthritis and joint disorders	Heberdens' nodes	4015
Osteoarthritis and joint disorders	Bouchards' nodes	35919
Osteoarthritis and joint disorders	Generalised osteoarthritis of multiple sites	23676
Osteoarthritis and joint disorders	Bouchard's nodes with arthropathy	38018
Osteoarthritis and joint disorders	Primary generalized osteoarthritis	23646
Osteoarthritis and joint disorders	Secondary multiple arthrosis	11256
Osteoarthritis and joint disorders	Erosive osteoarthritis	38019
Osteoarthritis and joint disorders	Heberden's nodes with arthropathy	24432
Osteoarthritis and joint disorders	Generalised osteoarthritis NOS	34867
Osteoarthritis and joint disorders	Localised, primary osteoarthritis	32839
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of unspecified site	54224
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of the shoulder region	24022
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of the upper arm	24217
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of the forearm	34806
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of the hand	21350
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of the pelvic region/thigh	15839
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of the lower leg	21159
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of the ankle and foot	25793
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of other specified site	20472
Osteoarthritis and joint disorders	Primary coxarthrosis, bilateral	24287
Osteoarthritis and joint disorders	Coxarthrosis resulting from dysplasia, bilateral	25812
Osteoarthritis and joint disorders	Primary gonarthrosis, bilateral	24146
Osteoarthritis and joint disorders	Primary arthrosis of first carpometacarpal joints, bilateral	36182
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of the wrist	24958
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of toe	28908
Osteoarthritis and joint disorders	Localised, primary osteoarthritis of elbow	18602
Osteoarthritis and joint disorders	Localised, primary osteoarthritis NOS	20660
Osteoarthritis and joint disorders	Localised, secondary osteoarthritis	42045
Osteoarthritis and joint disorders	Localised, secondary osteoarthritis of unspecified site	68712

Osteoarthritis and joint disorders	Localised, secondary osteoarthritis of the shoulder region	33574
Osteoarthritis and joint disorders	Localised, secondary osteoarthritis of the upper arm	41088
Osteoarthritis and joint disorders	Localised, secondary osteoarthritis of the forearm	45815
Osteoarthritis and joint disorders	Localised, secondary osteoarthritis of the hand	23638
Osteoarthritis and joint disorders	Localised, secondary osteoarthritis of pelvic region/thigh	44041
Osteoarthritis and joint disorders	Localised, secondary osteoarthritis of the lower leg	33479
Osteoarthritis and joint disorders	Localised, secondary osteoarthritis of the ankle and foot	34035
Osteoarthritis and joint disorders	Localised, secondary osteoarthritis of other specified site	32891
Osteoarthritis and joint disorders	Post-traumatic coxarthrosis, bilateral	64503
Osteoarthritis and joint disorders	Post-traumatic gonarthrosis, bilateral	24392
Osteoarthritis and joint disorders	Post-traumatic arthrosis of first carpometacarpal jt bilat	60183
Osteoarthritis and joint disorders	Post-traumatic gonarthrosis, unilateral	50470
Osteoarthritis and joint disorders	Localised, secondary osteoarthritis NOS	57912
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified	34122
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified, of unspecified site	49545
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified, of shoulder region	15441
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified, of the upper arm	59637
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified, of the forearm	60537
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified, of the hand	16242
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified, pelvic region/thigh	20626
Osteoarthritis and joint disorders	Hip osteoarthritis NOS	1104
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified, of the lower leg	34804
Osteoarthritis and joint disorders	Patellofemoral osteoarthritis	1296
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified, of the ankle and foot	4461
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified, of other spec site	18112
Osteoarthritis and joint disorders	Arthrosis of first carpometacarpal joint, unspecified	21177
Osteoarthritis and joint disorders	Localised osteoarthritis, unspecified, NOS	31200
Osteoarthritis and joint disorders	Oligoarticular osteoarthritis, unspecified	21528
Osteoarthritis and joint disorders	Oligoarticular osteoarthritis, unspec, of unspecified sites	48214
Osteoarthritis and joint disorders	Oligoarticular osteoarthritis, unspecified, of shoulder	52095
Osteoarthritis and joint disorders	Oligoarticular osteoarthritis, unspecified, of upper arm	97073
Osteoarthritis and joint disorders	Oligoarticular osteoarthritis, unspecified, of hand	59616
Osteoarthritis and joint disorders	Oligoarticular osteoarthritis, unspecified, of pelvis/thigh	68648
Osteoarthritis and joint disorders	Oligoarticular osteoarthritis, unspecified, of lower leg	41090
Osteoarthritis and joint disorders	Oligoarticular osteoarthritis, unspecified, of ankle/foot	72109
Osteoarthritis and joint disorders	Oligoarticular osteoarthritis, unspecified, other spec sites	41985

Osteoarthritis and joint disorders	Oligoarticular osteoarthritis, unspecified, multiple sites	57267
Osteoarthritis and joint disorders	Osteoarthritis of more than one site, unspecified, NOS	53858
Osteoarthritis and joint disorders	Osteoarthritis NOS	5776
Osteoarthritis and joint disorders	Joint degeneration	1509
Osteoarthritis and joint disorders	Osteoarthritis NOS, of unspecified site	35527
Osteoarthritis and joint disorders	Osteoarthritis NOS, of shoulder region	3147
Osteoarthritis and joint disorders	Osteoarthritis NOS, of the upper arm	50848
Osteoarthritis and joint disorders	Elbow osteoarthritis NOS	639
Osteoarthritis and joint disorders	Osteoarthritis NOS, of the forearm	24152
Osteoarthritis and joint disorders	Wrist osteoarthritis NOS	15206
Osteoarthritis and joint disorders	Osteoarthritis NOS, of the hand	658
Osteoarthritis and joint disorders	Finger osteoarthritis NOS	4490
Osteoarthritis and joint disorders	Thumb osteoarthritis NOS	1959
Osteoarthritis and joint disorders	Osteoarthritis NOS, pelvic region/thigh	4967
Osteoarthritis and joint disorders	Hip osteoarthritis NOS	2209
Osteoarthritis and joint disorders	Osteoarthritis NOS, of the lower leg	15144
Osteoarthritis and joint disorders	Knee osteoarthritis NOS	665
Osteoarthritis and joint disorders	Osteoarthritis NOS, of ankle and foot	15447
Osteoarthritis and joint disorders	Ankle osteoarthritis NOS	52897
Osteoarthritis and joint disorders	Foot osteoarthritis NOS	1312
Osteoarthritis and joint disorders	Toe osteoarthritis NOS	4878
Osteoarthritis and joint disorders	Osteoarthritis NOS, other specified site	15052
Osteoarthritis and joint disorders	Osteoarthritis NOS, of shoulder	5802
Osteoarthritis and joint disorders	Osteoarthritis NOS, of sternoclavicular joint	3814
Osteoarthritis and joint disorders	Osteoarthritis NOS, of acromioclavicular joint	2229
Osteoarthritis and joint disorders	Osteoarthritis NOS, of elbow	19713
Osteoarthritis and joint disorders	Osteoarthritis NOS, of distal radio-ulnar joint	65748
Osteoarthritis and joint disorders	Osteoarthritis NOS, of wrist	9649
Osteoarthritis and joint disorders	Osteoarthritis NOS, of MCP joint	7866
Osteoarthritis and joint disorders	Osteoarthritis NOS, of PIP joint of finger	11032
Osteoarthritis and joint disorders	Osteoarthritis NOS, of DIP joint of finger	9681
Osteoarthritis and joint disorders	Osteoarthritis NOS, of hip	6812
Osteoarthritis and joint disorders	Osteoarthritis NOS, of sacro-iliac joint	34023
Osteoarthritis and joint disorders	Osteoarthritis NOS, of knee	2487
Osteoarthritis and joint disorders	Osteoarthritis NOS, of tibio-fibular joint	70425
Osteoarthritis and joint disorders	Osteoarthritis NOS, of ankle	8202

Osteoarthritis and joint disorders	Osteoarthritis NOS, of subtalar joint	40972
Osteoarthritis and joint disorders	Osteoarthritis NOS, of talonavicular joint	55388
Osteoarthritis and joint disorders	Osteoarthritis NOS, of other tarsal joint	54350
Osteoarthritis and joint disorders	Osteoarthritis NOS, of 1st MTP joint	6887
Osteoarthritis and joint disorders	Osteoarthritis NOS, of lesser MTP joint	9010
Osteoarthritis and joint disorders	Osteoarthritis NOS, of IP joint of toe	27834
Osteoarthritis and joint disorders	Osteoarthritis NOS	27972
Osteoarthritis and joint disorders	[X]Arthrosis	18795
Osteoarthritis and joint disorders	[X]Other polyarthrosis	53741
Osteoarthritis and joint disorders	[X]Other primary coxarthrosis	10854
Osteoarthritis and joint disorders	[X]Other secondary coxarthrosis, bilateral	73948
Osteoarthritis and joint disorders	[X]Other primary gonarthrosis	43474
Osteoarthritis and joint disorders	[X] Unilateral primary gonarthrosis	24079
Osteoarthritis and joint disorders	[X]Other secondary gonarthrosis, bilateral	73952
Osteoarthritis and joint disorders	[X]Other secondary gonarthrosis	73930
Osteoarthritis and joint disorders	[X] Unilateral secondary gonarthrosis	24145
Osteoarthritis and joint disorders	[X]Other specified arthrosis	51360
Osteoarthritis and joint disorders	[X] Unilateral secondary coxarthrosis	24326
Osteoarthritis and joint disorders	[X]Post-traumatic arthrosis of other joints	67336
Osteoarthritis and joint disorders	Myelopathy due to spondylosis	8920
Osteoarthritis and joint disorders	Nerve root and plexus compressions in spondylosis	23699
Osteoarthritis and joint disorders	Spondylosis and allied disorders	2001
Osteoarthritis and joint disorders	Arthritis of spine	2294
Osteoarthritis and joint disorders	Osteoarthritis of spine	7429
Osteoarthritis and joint disorders	Cervical spondylosis without myelopathy	2881
Osteoarthritis and joint disorders	Cervical spondylosis	771
Osteoarthritis and joint disorders	Osteoarthritis cervical spine	17092
Osteoarthritis and joint disorders	Single-level cervical spondylosis without myelopathy	38501
Osteoarthritis and joint disorders	Two-level cervical spondylosis without myelopathy	51531
Osteoarthritis and joint disorders	Multiple-level cervical spondylosis without myelopathy	15744
Osteoarthritis and joint disorders	Cervical spondylosis with myelopathy	8208
Osteoarthritis and joint disorders	Single-level cervical spondylosis with myelopathy	27583
Osteoarthritis and joint disorders	Two-level cervical spondylosis with myelopathy	63192
Osteoarthritis and joint disorders	Multiple-level cervical spondylosis with myelopathy	58865
Osteoarthritis and joint disorders	Thoracic spondylosis without myelopathy	18217
Osteoarthritis and joint disorders	Thoracic spondylosis	5183

Osteoarthritis and joint disorders	Single-level thoracic spondylosis without myelopathy	69912
Osteoarthritis and joint disorders	Two-level thoracic spondylosis without myelopathy	62914
Osteoarthritis and joint disorders	Multiple-level thoracic spondylosis without myelopathy	50448
Osteoarthritis and joint disorders	Dorsal spondylosis without myelopathy	18205
Osteoarthritis and joint disorders	Thoracic spondylosis with myelopathy	55628
Osteoarthritis and joint disorders	Single-level thoracic spondylosis with myelopathy	64854
Osteoarthritis and joint disorders	Multiple-level thoracic spondylosis with myelopathy	96103
Osteoarthritis and joint disorders	Lumbosacral spondylosis without myelopathy	15015
Osteoarthritis and joint disorders	Degeneration of lumbar spine	1565
Osteoarthritis and joint disorders	Lumbar spondylosis	1100
Osteoarthritis and joint disorders	Single-level lumbosacral spondylosis without myelopathy	20791
Osteoarthritis and joint disorders	Two-level lumbosacral spondylosis without myelopathy	52991
Osteoarthritis and joint disorders	Multiple-level lumbosacral spondylosis without myelopathy	37097
Osteoarthritis and joint disorders	Lumbosacral spondylosis with myelopathy	11688
Osteoarthritis and joint disorders	Single-level lumbosacral spondylosis with myelopathy	41516
Osteoarthritis and joint disorders	Two-level lumbosacral spondylosis with myelopathy	45730
Osteoarthritis and joint disorders	Multiple-level lumbosacral spondylosis with myelopathy	63578
Osteoarthritis and joint disorders	Cervical spondylosis with radiculopathy	10121
Osteoarthritis and joint disorders	Single-level cervical spondylosis with radiculopathy	55810
Osteoarthritis and joint disorders	Two-level cervical spondylosis with radiculopathy	51318
Osteoarthritis and joint disorders	Multiple-level cervical spondylosis with radiculopathy	56212
Osteoarthritis and joint disorders	Cervical spondylosis with vascular compression	35851
Osteoarthritis and joint disorders	Thoracic spondylosis with radiculopathy	19386
Osteoarthritis and joint disorders	Single-level thoracic spondylosis with radiculopathy	54852
Osteoarthritis and joint disorders	Multiple-level thoracic spondylosis with radiculopathy	93977
Osteoarthritis and joint disorders	Lumbosacral spondylosis with radiculopathy	9834
Osteoarthritis and joint disorders	Single-level lumbosacral spondylosis with radiculopathy	54843
Osteoarthritis and joint disorders	Two-level lumbosacral spondylosis with radiculopathy	65641
Osteoarthritis and joint disorders	Multiple-level lumbosacral spondylosis with radiculopathy	48810
Osteoarthritis and joint disorders	Osteoarthritis of spine	18826
Osteoarthritis and joint disorders	Osteoarthritis of cervical spine	41378
Osteoarthritis and joint disorders	Osteoarthritis of thoracic spine	47024
Osteoarthritis and joint disorders	Osteoarthritis of lumbar spine	22452
Osteoarthritis and joint disorders	Osteoarthritis of spine NOS	53184
Osteoarthritis and joint disorders	Cervical spondylosis	96948
Osteoarthritis and joint disorders	Spondylosis NOS	3447

Osteoarthritis and joint disorders	Osteoarthritis spine	829
Osteoarthritis and joint disorders	Spondylosis without myelopathy, NOS	56594
Osteoarthritis and joint disorders	Spondylosis with myelopathy, NOS	35838
Osteoarthritis and joint disorders	Spondylosis NOS	17766
Osteoarthritis and joint disorders	[X]Other spondylosis with radiculopathy	71477
Osteoarthritis and joint disorders	[X]Other spondylosis	55238
Renal failure	Chronic kidney disease stage 1	29013
Renal failure	Chronic kidney disease stage 2	12586
Renal failure	Chronic kidney disease stage 1 with proteinuria	94789
Renal failure	Chronic kidney disease stage 1 without proteinuria	95572
Renal failure	Chronic kidney disease stage 2 with proteinuria	95146
Renal failure	Chronic kidney disease stage 2 without proteinuria	95121
Renal failure	Plasmodium malariae malaria with nephropathy	49046
Renal failure	Acute glomerulonephritis	2088
Renal failure	Acute nephritis	5417
Renal failure	Acute proliferative glomerulonephritis	29384
Renal failure	Acute nephritis with lesions of necrotising glomerulitis	67460
Renal failure	Other acute glomerulonephritis	63599
Renal failure	Acute glomerulonephritis in diseases EC	20027
Renal failure	Acute exudative nephritis	94261
Renal failure	Acute focal nephritis	48261
Renal failure	Acute diffuse nephritis	55100
Renal failure	Other acute glomerulonephritis NOS	47838
Renal failure	Acute glomerulonephritis NOS	20129
Renal failure	Tubulo-interstit nephritis, not specif as acute or chron	23990
Renal failure	Acute renal failure	2266
Renal failure	Acute renal tubular necrosis	10837
Renal failure	Acute renal cortical necrosis	46242
Renal failure	Acute renal medullary necrosis	31369
Renal failure	Acute drug-induced renal failure	57919
Renal failure	Acute renal failure due to urinary obstruction	97198
Renal failure	Other acute renal failure	35235
Renal failure	Acute renal failure NOS	25582
Renal failure	Acute interstitial nephritis	9379
Renal failure	Acute nephritic syndrome	31581
Renal failure	Acute nephritic syndrome, focal+segmental glomerular lesions	66136
Renal failure	Acute nephritic syn, diffuse membranous glomerulonephritis	66503
Renal failure	Acute neph syn, diffuse mesangiocapillary glomerulonephritis	54312
Renal failure	Acute nephrotic syndrm diffuse crescentic glomerulonephritis	61814
Renal failure	Acute pyelonephritis	2546
Renal failure	Acute pyelonephritis without medullary necrosis	64482
Renal failure	Acute pyelonephritis NOS	38698
Renal failure	[X]Other acute renal failure	53945

Renal failure	Acute renal failure following labour and delivery	63277
Renal failure	Post-delivery acute renal failure unspecified	72458
Renal failure	Post-delivery acute renal failure - delivered with p/n prob	96179
Renal failure	Post-delivery acute renal failure with postnatal problem	69433
Renal failure	Renal failure following crush syndrome	15945
Renal failure	Renal failure after crushing	63760
Renal failure	Acute renal failure due to rhabdomyolysis	24676
Renal failure	Post operative renal failure	24292
Renal failure	Chronic renal impairment	12720
Renal failure	Chronic kidney disease stage 3	12566
Renal failure	Chronic kidney disease stage 4	12479
Renal failure	Chronic kidney disease stage 5	12585
Renal failure	Chronic kidney disease stage 3A	94965
Renal failure	Chronic kidney disease stage 3B	95179
Renal failure	Chronic kidney disease stage 3 with proteinuria	94793
Renal failure	Chronic kidney disease stage 3 without proteinuria	95123
Renal failure	Chronic kidney disease stage 3A with proteinuria	95408
Renal failure	Chronic kidney disease stage 3A without proteinuria	95175
Renal failure	Chronic kidney disease stage 3B with proteinuria	95178
Renal failure	Chronic kidney disease stage 3B without proteinuria	95177
Renal failure	Chronic kidney disease stage 4 with proteinuria	95122
Renal failure	Chronic kidney disease stage 4 without proteinuria	95406
Renal failure	Chronic kidney disease stage 5 with proteinuria	95508
Renal failure	Chronic kidney disease stage 5 without proteinuria	95405
Renal failure	Creation of graft fistula for dialysis	60302
Renal failure	Pre-transplantation of kidney work-up, recipient	90952
Renal failure	Compensation for renal failure	31549
Renal failure	Other specified compensation for renal failure	48022
Renal failure	Compensation for renal failure NOS	64636
Renal failure	Placement ambulatory apparatus compensation renal failure	56760
Renal failure	Placement ambulatory apparatus- compensate renal failure OS	59194
Renal failure	Placement other apparatus for compensation for renal failure	83513
Renal failure	Placement other apparatus- compensate for renal failure NOS	65089
Renal failure	Renal transplant planned	17253
Renal failure	Tuberculous nephropathy	52272
Renal failure	Tuberculous pyelonephritis	49235
Renal failure	Haemorrhagic nephrosonephritis	67197
Renal failure	Diabetic nephropathy	2475
Renal failure	Diabetes mellitus with nephropathy NOS	35107
Renal failure	Insulin dependent diabetes mellitus with nephropathy	57621
Renal failure	Type I diabetes mellitus with nephropathy	66872
Renal failure	Non-insulin dependent diabetes mellitus with nephropathy	59365
Renal failure	Type II diabetes mellitus with nephropathy	64571
Renal failure	Type 2 diabetes mellitus with nephropathy	24836

Renal failure	Type 1 diabetes mellitus with nephropathy	10418
Renal failure	Type 2 diabetes mellitus with nephropathy	12640
Renal failure	Gouty nephropathy	52969
Renal failure	Gouty nephropathy NOS	61145
Renal failure	Gout due to impairment of renal function	21687
Renal failure	Nephropathic amyloidosis	68112
Renal failure	Haemolytic-uraemic syndrome	29323
Renal failure	Anaemia secondary to renal failure	16929
Renal failure	Anaemia secondary to chronic renal failure	25394
Renal failure	Henoch-Schonlein nephritis	22897
Renal failure	Polyneuropathy in uraemia	19454
Renal failure	Hypertensive renal disease	4668
Renal failure	Malignant hypertensive renal disease	39649
Renal failure	Benign hypertensive renal disease	43935
Renal failure	Hypertensive renal disease with renal failure	32423
Renal failure	Hypertensive renal disease NOS	15106
Renal failure	Hypertensive heart and renal disease	63466
Renal failure	Malignant hypertensive heart and renal disease	67232
Renal failure	Benign hypertensive heart and renal disease	63000
Renal failure	Hypertensive heart&renal dis wth (congestive) heart failure	21837
Renal failure	Hypertensive heart and renal disease with renal failure	28684
Renal failure	Hypertensive heart and renal disease NOS	68659
Renal failure	Acute pericarditis - uraemic	40956
Renal failure	[X]Hypertension secondary to other renal disorders	97533
Renal failure	Nephritis, nephrosis and nephrotic syndrome	2773
Renal failure	Nephrotic syndrome	2999
Renal failure	Nephrotic syndrome with proliferative glomerulonephritis	9840
Renal failure	Nephrotic syndrome with membranous glomerulonephritis	1803
Renal failure	Nephrotic syndrome with minimal change glomerulonephritis	29634
Renal failure	Steroid sensitive nephrotic syndrome	57926
Renal failure	Nephrotic syndrome, minor glomerular abnormality	23913
Renal failure	Nephrotic syndrome, focal and segmental glomerular lesions	22852
Renal failure	Nephrotic syndrome, diffuse membranous glomerulonephritis	19316
Renal failure	Nephrotic syn difus mesangial proliferativ glomerulonephritis	21947
Renal failure	Nephrotic syn,difus endocapillary proliferativ glomerulonephritis	50472
Renal failure	Nephrotic syn,difus mesangiocapillary glomerulonephritis	21989
Renal failure	Nephrotic syndrome, dense deposit disease	56987
Renal failure	Nephrotic syndrome, diffuse crescentic glomerulonephritis	17365
Renal failure	Congenital nephrotic syndrome	63786
Renal failure	Nephrotic syndrome in amyloidosis	47922
Renal failure	Nephrotic syndrome in diabetes mellitus	2471
Renal failure	Nephrotic syndrome in polyarteritis nodosa	58750
Renal failure	Nephrotic syndrome in systemic lupus erythematosus	47672
Renal failure	Lupus nephritis	22205

Renal failure	Nephrotic syndrome with other pathological kidney lesions	94373
Renal failure	Nephrotic syndrome NOS	27427
Renal failure	Chronic glomerulonephritis	7804
Renal failure	Nephritis - chronic	10647
Renal failure	Nephropathy - chronic	11875
Renal failure	Chronic proliferative glomerulonephritis	34998
Renal failure	Chronic membranous glomerulonephritis	10809
Renal failure	Chronic membranoproliferative glomerulonephritis	61494
Renal failure	Chronic rapidly progressive glomerulonephritis	65064
Renal failure	Other chronic glomerulonephritis	60960
Renal failure	Chronic glomerulonephritis + diseases EC	97758
Renal failure	Chronic focal glomerulonephritis	4669
Renal failure	Chronic diffuse glomerulonephritis	65400
Renal failure	Other chronic glomerulonephritis NOS	63615
Renal failure	Chronic glomerulonephritis NOS	15097
Renal failure	Nephritis and nephropathy unspecified	33580
Renal failure	Nephritis and nephropathy unspecified	4850
Renal failure	Nephropathy, unspecified	11873
Renal failure	Proliferative nephritis unspecified	16008
Renal failure	Membranous nephritis unspecified	5291
Renal failure	Membranoproliferative nephritis unspecified	12465
Renal failure	Focal membranoproliferative glomerulonephritis	67995
Renal failure	Anaphylactoid glomerulonephritis	62868
Renal failure	Familial glomerulonephritis in Alport's syndrome	24384
Renal failure	Other familial glomerulonephritis	57072
Renal failure	Berger's IgA or IgG nephropathy	21423
Renal failure	Nephritis unsp+OS membranoprolif glomerulonephritis lesion	67193
Renal failure	Hypocomplementaemic persistent glomerulonephritis NEC	50305
Renal failure	Mesangioproliferative glomerulonephritis NEC	36342
Renal failure	Mesangiocapillary glomerulonephritis NEC	41881
Renal failure	Mixed membranous and proliferative glomerulonephritis NEC	97388
Renal failure	Nephritis unsp+membranoprolif glomerulonephritis lesion NOS	94350
Renal failure	Rapidly progressive nephritis unspecified	58164
Renal failure	Renal cortical necrosis unspecified	41676
Renal failure	Renal medullary necrosis unspecified	45867
Renal failure	Unspecif nephr synd, diff concentric glomerulonephritis	36125
Renal failure	Unspecified nephritic syndrome, dense deposit disease	60128
Renal failure	Unsp nephrit synd, diff endocap prolifer glomerulonephritis	62520
Renal failure	Unsp nephrit synd, diff mesang prolifer glomerulonephritis	30301
Renal failure	Other nephritis and nephrosis unspecified	35065
Renal failure	Other nephritis and nephrosis in diseases EC	27335
Renal failure	Other interstitial nephritis	34669
Renal failure	Other nephritis and nephrosis NOS	44055
Renal failure	Unspecified glomerulonephritis NOS	5182

Renal failure	Chronic renal failure	512
Renal failure	Chronic uraemia	10081
Renal failure	End stage renal failure	53852
Renal failure	End stage renal failure	6712
Renal failure	Renal failure unspecified	350
Renal failure	Uraemia NOS	4809
Renal failure	Renal impairment	11787
Renal failure	Impaired renal function	6842
Renal failure	Impaired renal function disorder	8919
Renal failure	Renal osteodystrophy	29638
Renal failure	Phosphate-losing tubular disorders	68114
Renal failure	Renal dwarfism	34648
Renal failure	Renal infantilism	50728
Renal failure	Renal rickets	66062
Renal failure	Renal osteodystrophy NOS	34637
Renal failure	Nephrogenic diabetes insipidus	30310
Renal failure	Other impaired renal function disorder	39840
Renal failure	Hypokalaemic nephropathy	56939
Renal failure	Renal function impairment with growth failure	41013
Renal failure	Renal tubular acidosis	5072
Renal failure	Other impaired renal function disorder NOS	50804
Renal failure	Renal acidaemia	48475
Renal failure	Impaired renal function disorder NOS	25980
Renal failure	Acut neph syn, diffuse mesangial proliferative glomnephritis	55389
Renal failure	Rapidly progressive nephritic syndrome	71174
Renal failure	Rapid progres nephritic syn focal+segmental glomerulr lesion	97734
Renal failure	Rapid progres neph syn diffuse membranous glomerulonephritis	41285
Renal failure	Rpd prog neph syn df mesangial proliferatv glomerulonephritis	58060
Renal failure	Rapid progressive nephritic syndrome, dense deposit disease	50200
Renal failure	Rapid progres nephritic syn df crescentic glomerulonephritis	62320
Renal failure	Recur+persist haematuria difus membranous glomerulonephritis	61317
Renal failure	Recur+persist haemuria df mesangial prolif glomerulnephritis	49642
Renal failure	Recur+persist hmuria df mesangiocapillary glomerulonephritis	60484
Renal failure	Recur+persist haematuria difus crescentic glomerulonephritis	60856
Renal failure	IgA nephropathy	85659
Renal failure	Chronic nephritic syndrome	21297
Renal failure	Chronic nephritic syndrome, minor glomerular abnormality	66505
Renal failure	Chronic nephritic syndrm focal+segmental glomerular lesions	40413
Renal failure	Chron nephritic syndrom difuse membranous glomerulonephritis	57168
Renal failure	Chron neph syn difus mesangial proliftriv glomerulonephritis	56893
Renal failure	Chronic neph syn difus mesangiocapillary glomerulonephritis	73026
Renal failure	Chronic nephritic syndrome, dense deposit disease	60198
Renal failure	Chronic nephritic syn diffuse crescentic glomerulonephritis	60857
Renal failure	Isoltd prteinur+specfd morph les df mesangiocap glomneph	61811

Renal failure	Hereditary nephropathy not elsewhere classified	36205
Renal failure	Hereditary nephropathy NEC, minor glomerular abnormality	51113
Renal failure	Hereditary nephropathy NEC,focal+segmnt glomerular lesion	41239
Renal failure	Hereditry nephropathy NEC,difus membran glomerulnephritis	44270
Renal failure	Hereditry nephropathy NEC difus mesangial prolif glomnephrit	58671
Renal failure	Hereditary nephropathy, NEC, dense deposit disease	91738
Renal failure	Hereditary nephropathy, unspecif morphological changes	62980
Renal failure	Renal tubulo-interstitial disorders in diseases EC	45523
Renal failure	Renal tubulo-interstitial disorder/ neoplastic diseases	64622
Renal failure	Renal tubulo-interstitial disorder in SLE	41148
Renal failure	Analgesic nephropathy	8607
Renal failure	Nephropathy induced by other drugs meds and biologl substncs	41159
Renal failure	Nephropathy induced by unspec drug medicament or biol subs	57784
Renal failure	Toxic nephropathy, not elsewhere classified	50893
Renal failure	End-stage renal disease	8330
Renal failure	Other specified nephritis, nephrosis or nephrotic syndrome	49150
Renal failure	Nephritis, nephrosis and nephrotic syndrome NOS	15780
Renal failure	Chronic pyelonephritis	4654
Renal failure	Chronic pyelonephritis with medullary necrosis	57568
Renal failure	Nonobstructive reflux-associated chronic pyelonephritis	35360
Renal failure	Chronic obstructive pyelonephritis	48855
Renal failure	Calculus pyelonephritis	2939
Renal failure	Chronic pyelonephritis NOS	48111
Renal failure	Xanthogranulomatous pyelonephritis	38572
Renal failure	Pyelonephritis and pyonephrosis unspecified	53944
Renal failure	Pyelonephritis unspecified	1899
Renal failure	Pyelonephritis in diseases EC	95710
Renal failure	Unspecified pyelonephritis NOS	59121
Renal failure	Other kidney and ureter disorders	36273
Renal failure	Other kidney disorders	8098
Renal failure	Vascular disorders of kidney	11992
Renal failure	Renal vascular disorders	10460
Renal failure	Renal vascular disorders NOS	15340
Renal failure	Other kidney and ureteric disorders	44657
Renal failure	Other kidney and ureteric disorders NOS	34675
Renal failure	Salt-losing nephritis	20516
Renal failure	Kidney and ureter disease NOS	2991
Renal failure	[X]Unsp nephrit synd, diff mesang prolif glomerulonephritis	71709
Renal failure	[X]Renal tubulo-interstitial diseases	94842
Renal failure	[X]Nephropathy induced by other drugs+biological substances	72478
Renal failure	[X]Renal failure	61930
Renal failure	[X]Other chronic renal failure	53940
Renal failure	[X]Other disorders of kidney and ureter	70157
Renal failure	[X]Other disorders resulting/impaired renal tubular function	96819

Renal failure	[X]Other specified disorders of kidney and ureter	56896
Renal failure	Renal failure following abortive pregnancy	71314
Renal failure	Uraemia following abortive pregnancy	70422
Renal failure	Unspecified renal disease in pregnancy	47080
Renal failure	Nephropathy NOS in pregnancy without hypertension	38312
Renal failure	Uraemia in pregnancy without hypertension	92579
Renal failure	Unspecified renal disease in pregnancy unspecified	54938
Renal failure	Unspecified renal disease in pregnancy - delivered	96724
Renal failure	Congenital cystic kidney disease	15917
Renal failure	Congenital cystic renal disease	20629
Renal failure	Polycystic kidney disease	4503
Renal failure	Polycystic kidney disease NOS	56852
Renal failure	Cystic kidney disease NEC	9240
Renal failure	Other specified congenital cystic kidney disease	59018
Renal failure	Fibrocystic kidney disease	67486
Renal failure	Other congenital cystic kidney disease NOS	59031
Renal failure	Congenital cystic kidney disease NOS	50331
Renal failure	[X]Other cystic kidney diseases	72877
Renal failure	Fetus or neonate affected by maternal renal/urinary disease	73373
Renal failure	Congenital renal failure	47342
Renal failure	Renal failure as a complication of care	11554
Renal failure	Kidney failure as a complication of care	39598
Renal failure	Uraemia - post operative	55858
Renal failure	Haemodialysis training	74905
Renal failure	[V]Preparatory care for dialysis	52088
Sleep apnoea	[D]Sleep apnoea syndrome	2506
Sleep apnoea	Sleep apnoea	7603
Sleep apnoea	Obstructive sleep apnoea	8148
Sleep apnoea	[D]Syndrome sleep apnoea	20438
Sleep apnoea	Obstructive sleep apnoea	20748
Sleep apnoea	Sleep apnoea	23779
Sleep apnoea	[D]Hypersomnia with sleep apnoea	36301
Sleep apnoea	[D]Insomnia with sleep apnoea	48539
Type 2 diabetes	Diabetes mellitus, adult onset, no mention of complication	14803
Type 2 diabetes	Maturity onset diabetes	14889
Type 2 diabetes	Non-insulin dependent diabetes mellitus	506
Type 2 diabetes	Diabetes mellitus, adult onset, with ketoacidosis	54856
Type 2 diabetes	Diabetes mellitus, adult onset, with hyperosmolar coma	43139
Type 2 diabetes	Diabetes mellitus, adult onset, with ketoacidotic coma	68843
Type 2 diabetes	Diabetes mellitus, adult onset, with renal manifestation	35105
Type 2 diabetes	Diabetes mellitus, adult onset, + ophthalmic manifestation	41389
Type 2 diabetes	Diabetes mellitus, adult onset, + neurological manifestation	39317
Type 2 diabetes	Diabetes mellitus, adult, + peripheral circulatory disorder	63357
Type 2 diabetes	Diabetes mellitus, adult with gangrene	33807

Type 2 diabetes	NIDDM with peripheral circulatory disorder	56803
Type 2 diabetes	Non-insulin dependent diabetes mellitus	4513
Type 2 diabetes	NIDDM - Non-insulin dependent diabetes mellitus	5884
Type 2 diabetes	Type 2 diabetes mellitus	17859
Type 2 diabetes	Type II diabetes mellitus	18219
Type 2 diabetes	Non-insulin-dependent diabetes mellitus with renal comps	52303
Type 2 diabetes	Type II diabetes mellitus with renal complications	50225
Type 2 diabetes	Type 2 diabetes mellitus with renal complications	18209
Type 2 diabetes	Non-insulin-dependent diabetes mellitus with ophthalm comps	50429
Type 2 diabetes	Type II diabetes mellitus with ophthalmic complications	59725
Type 2 diabetes	Type 2 diabetes mellitus with ophthalmic complications	70316
Type 2 diabetes	Non-insulin-dependent diabetes mellitus with neuro comps	55842
Type 2 diabetes	Type II diabetes mellitus with neurological complications	67905
Type 2 diabetes	Type 2 diabetes mellitus with neurological complications	45919
Type 2 diabetes	Non-insulin-dependent diabetes mellitus with multiple comps	62146
Type 2 diabetes	Non-insulin dependent diabetes mellitus with ulcer	34912
Type 2 diabetes	Type II diabetes mellitus with ulcer	55075
Type 2 diabetes	Type 2 diabetes mellitus with ulcer	65704
Type 2 diabetes	Non-insulin dependent diabetes mellitus with gangrene	40401
Type 2 diabetes	Type II diabetes mellitus with gangrene	62107
Type 2 diabetes	Type 2 diabetes mellitus with gangrene	46150
Type 2 diabetes	Non-insulin-dependent diabetes mellitus with retinopathy	17262
Type 2 diabetes	Type II diabetes mellitus with retinopathy	58604
Type 2 diabetes	Type 2 diabetes mellitus with retinopathy	42762
Type 2 diabetes	Non-insulin dependant diabetes mellitus - poor control	8403
Type 2 diabetes	Type II diabetes mellitus - poor control	24458
Type 2 diabetes	Type 2 diabetes mellitus - poor control	45913
Type 2 diabetes	Non-insulin-dependent diabetes mellitus without complication	29979
Type 2 diabetes	Non-insulin dependent diabetes mellitus with mononeuropathy	72320
Type 2 diabetes	Type II diabetes mellitus with mononeuropathy	50813
Type 2 diabetes	Non-insulin dependent diabetes mellitus with polyneuropathy	45467
Type 2 diabetes	Type II diabetes mellitus with polyneuropathy	47409
Type 2 diabetes	Non-insulin dependent diabetes mellitus with nephropathy	59365
Type 2 diabetes	Type II diabetes mellitus with nephropathy	64571
Type 2 diabetes	Type 2 diabetes mellitus with nephropathy	24836
Type 2 diabetes	Non-insulin dependent diabetes mellitus with hypoglyca coma	43785
Type 2 diabetes	Type II diabetes mellitus with hypoglycaemic coma	56268
Type 2 diabetes	Type 2 diabetes mellitus with hypoglycaemic coma	61071
Type 2 diabetes	Non-insulin depend diabetes mellitus with diabetic cataract	69278
Type 2 diabetes	Type II diabetes mellitus with diabetic cataract	48192
Type 2 diabetes	Type 2 diabetes mellitus with diabetic cataract	44779
Type 2 diabetes	Non-insulin-dependent d m with peripheral angiopath	54212
Type 2 diabetes	Type II diabetes mellitus with peripheral angiopathy	54899
Type 2 diabetes	Type 2 diabetes mellitus with peripheral angiopathy	60699

Type 2 diabetes	Non-insulin dependent diabetes mellitus with arthropathy	24693
Type 2 diabetes	Type II diabetes mellitus with arthropathy	18143
Type 2 diabetes	Type 2 diabetes mellitus with arthropathy	49869
Type 2 diabetes	Non-insulin dependent d m with neuropathic arthropathy	40962
Type 2 diabetes	Type II diabetes mellitus with neuropathic arthropathy	47816
Type 2 diabetes	Type 2 diabetes mellitus with neuropathic arthropathy	66965
Type 2 diabetes	Insulin treated Type 2 diabetes mellitus	18278
Type 2 diabetes	Insulin treated non-insulin dependent diabetes mellitus	37648
Type 2 diabetes	Insulin treated Type II diabetes mellitus	18264
Type 2 diabetes	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	36633
Type 2 diabetes	Maturity onset diabetes in youth	46624
Type 2 diabetes	Diabetes mellitus autosomal dominant type 2	36695
Type 2 diabetes	Maturity onset diabetes in youth type 2	59991
Type 2 diabetes	Latent autoimmune diabetes mellitus in adult	95636
Type 2 diabetes	Type 2 diabetes mellitus	758
Type 2 diabetes	Type II diabetes mellitus	22884
Type 2 diabetes	Type 2 diabetes mellitus with renal complications	18777
Type 2 diabetes	Type II diabetes mellitus with renal complications	57278
Type 2 diabetes	Type 2 diabetes mellitus with ophthalmic complications	47321
Type 2 diabetes	Type 2 diabetes mellitus with neurological complications	34268
Type 2 diabetes	Type II diabetes mellitus with neurological complications	98616
Type 2 diabetes	Type 2 diabetes mellitus with multiple complications	65267
Type 2 diabetes	Type II diabetes mellitus with multiple complications	43227
Type 2 diabetes	Type 2 diabetes mellitus with ulcer	49074
Type 2 diabetes	Type II diabetes mellitus with ulcer	91646
Type 2 diabetes	Type 2 diabetes mellitus with gangrene	12736
Type 2 diabetes	Type 2 diabetes mellitus with retinopathy	18496
Type 2 diabetes	Type II diabetes mellitus with retinopathy	49655
Type 2 diabetes	Type 2 diabetes mellitus - poor control	25627
Type 2 diabetes	Type II diabetes mellitus - poor control	47315
Type 2 diabetes	Type 2 diabetes mellitus without complication	47954
Type 2 diabetes	Type II diabetes mellitus without complication	53392
Type 2 diabetes	Type 2 diabetes mellitus with mononeuropathy	62674
Type 2 diabetes	Type II diabetes mellitus with mononeuropathy	95351
Type 2 diabetes	Type 2 diabetes mellitus with polyneuropathy	18425
Type 2 diabetes	Type II diabetes mellitus with polyneuropathy	50527
Type 2 diabetes	Type 2 diabetes mellitus with nephropathy	12640
Type 2 diabetes	Type 2 diabetes mellitus with hypoglycaemic coma	46917
Type 2 diabetes	Type II diabetes mellitus with hypoglycaemic coma	98723
Type 2 diabetes	Type 2 diabetes mellitus with diabetic cataract	44982
Type 2 diabetes	Type II diabetes mellitus with diabetic cataract	93727
Type 2 diabetes	Type 2 diabetes mellitus with peripheral angiopathy	37806
Type 2 diabetes	Type 2 diabetes mellitus with arthropathy	59253
Type 2 diabetes	Type 2 diabetes mellitus with neuropathic arthropathy	35385

Type 2 diabetes	Insulin treated Type 2 diabetes mellitus	1407
Type 2 diabetes	Insulin treated Type II diabetes mellitus	64668
Type 2 diabetes	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	34450
Type 2 diabetes	Type 2 diabetes mellitus with persistent proteinuria	26054
Type 2 diabetes	Type II diabetes mellitus with persistent proteinuria	60796
Type 2 diabetes	Type 2 diabetes mellitus with persistent microalbuminuria	18390
Type 2 diabetes	Type II diabetes mellitus with persistent microalbuminuria	85991
Type 2 diabetes	Type 2 diabetes mellitus with ketoacidosis	32627
Type 2 diabetes	Type 2 diabetes mellitus with ketoacidotic coma	51756
Type 2 diabetes	Type 2 diabetes mellitus with exudative maculopathy	25591
Type 2 diabetes	Type 2 diabetes mellitus with gastroparesis	63690
Type 2 diabetes	Diabetes mellitus, adult, + other specified manifestation	63371
Type 2 diabetes	Diabetes mellitus, adult onset, + unspecified complication	63762
Ulcers	Balfour excision of gastric ulcer	92695
Ulcers	Resection of gastric ulcer by cautery	64710
Ulcers	Endoscopic injection haemostasis of gastric ulcer	63718
Ulcers	Operations on gastric ulcer	23688
Ulcers	Stomach ulcer operations	6865
Ulcers	Closure of perforated gastric ulcer	20677
Ulcers	Closure of gastric ulcer NEC	64014
Ulcers	Suture of ulcer of stomach NEC	70005
Ulcers	Other specified operation on gastric ulcer	94104
Ulcers	Operation on gastric ulcer NOS	33914
Ulcers	Gastric ulcer - (GU)	1262
Ulcers	Prepyloric ulcer	6333
Ulcers	Pyloric ulcer	3101
Ulcers	Acute gastric ulcer	24040
Ulcers	Acute gastric ulcer without mention of complication	64165
Ulcers	Acute gastric ulcer with haemorrhage	30054
Ulcers	Bleeding acute gastric ulcer	11124
Ulcers	Acute gastric ulcer with perforation	14671
Ulcers	Acute gastric ulcer with haemorrhage and perforation	71403
Ulcers	Acute gastric ulcer unspecified	24342
Ulcers	Acute gastric ulcer NOS	44324
Ulcers	Chronic gastric ulcer	18654
Ulcers	Chronic gastric ulcer without mention of complication	48946
Ulcers	Chronic gastric ulcer with haemorrhage	63582
Ulcers	Bleeding chronic gastric ulcer	36583
Ulcers	Chronic gastric ulcer with perforation	53336
Ulcers	Perforated chronic gastric ulcer	11104
Ulcers	Chronic gastric ulcer with haemorrhage and perforation	71897
Ulcers	Chronic gastric ulcer with obstruction	67356
Ulcers	Chronic gastric ulcer unspecified	64556
Ulcers	Chronic gastric ulcer NOS	44309

Ulcers	Anti-platelet induced gastric ulcer	63001
Ulcers	Anti-platelet induced gastric ulcer NOS	89227
Ulcers	Non steroidal anti inflammatory drug induced gastric ulcer	89023
Ulcers	Unspecified gastric ulcer	53081
Ulcers	Unspecified gastric ulcer without mention of complication	73338
Ulcers	Unspecified gastric ulcer with haemorrhage	57958
Ulcers	Unspecified gastric ulcer with perforation	36461
Ulcers	Unspecified gastric ulcer with obstruction	73697
Ulcers	Unspec gastric ulcer; unspec haemorrhage and/or perforation	94397
Ulcers	Unspecified gastric ulcer NOS	44284
Ulcers	Gastric ulcer NOS	29771
Ulcers	Multiple gastric ulcers	52323
Ulcers	Endoscopic injection haemostasis of duodenal ulcer	45981
Ulcers	Operations on duodenal ulcer	5928
Ulcers	Closure of perforated duodenal ulcer	4741
Ulcers	Suture of duodenal ulcer not elsewhere classified	37268
Ulcers	Oversew of blood vessel of duodenal ulcer	55350
Ulcers	Other specified operation on duodenal ulcer	56005
Ulcers	Operation on duodenal ulcer NOS	55933
Ulcers	Duodenal ulcer - (DU)	352
Ulcers	Acute duodenal ulcer	18027
Ulcers	Acute duodenal ulcer without mention of complication	44335
Ulcers	Acute duodenal ulcer with haemorrhage	18001
Ulcers	Acute duodenal ulcer with perforation	18324
Ulcers	Acute duodenal ulcer with haemorrhage and perforation	48730
Ulcers	Acute duodenal ulcer with obstruction	73417
Ulcers	Acute duodenal ulcer unspecified	53822
Ulcers	Acute duodenal ulcer NOS	53797
Ulcers	Chronic duodenal ulcer	9853
Ulcers	Chronic duodenal ulcer without mention of complication	33438
Ulcers	Chronic duodenal ulcer with haemorrhage	48951
Ulcers	Bleeding chronic duodenal ulcer	18625
Ulcers	Chronic duodenal ulcer with perforation	37643
Ulcers	Perforated chronic duodenal ulcer	23087
Ulcers	Chronic duodenal ulcer with haemorrhage and perforation	71881
Ulcers	Chronic duodenal ulcer with obstruction	44073
Ulcers	Chronic duodenal ulcer unspecified	52138
Ulcers	Chronic duodenal ulcer NOS	51406
Ulcers	Duodenal ulcer disease	22918
Ulcers	Recurrent duodenal ulcer	29317
Ulcers	Anti-platelet induced duodenal ulcer	89234
Ulcers	Non steroidal anti inflammatory drug induced duodenal ulcer	85989
Ulcers	Unspecified duodenal ulcer	53669
Ulcers	Unspecified duodenal ulcer without mention of complication	71150

Ulcers	Unspecified duodenal ulcer with haemorrhage	2814
Ulcers	Unspecified duodenal ulcer with perforation	657
Ulcers	Unspecified duodenal ulcer with haemorrhage and perforation	93436
Ulcers	Unspecified duodenal ulcer with obstruction	71904
Ulcers	Unspec duodenal ulcer; unspec haemorrhage and/or perforation	28366
Ulcers	Unspecified duodenal ulcer NOS	65737
Ulcers	Duodenal ulcer NOS	15175
Ulcers	Peptic ulcer - (PU) site unspecified	670
Ulcers	Stress ulcer NOS	15821
Ulcers	Acute peptic ulcer	32856
Ulcers	Acute peptic ulcer without mention of complication	68661
Ulcers	Acute peptic ulcer with haemorrhage	44637
Ulcers	Acute peptic ulcer with perforation	5521
Ulcers	Acute peptic ulcer with haemorrhage and perforation	45304
Ulcers	Acute peptic ulcer unspecified	67711
Ulcers	Acute peptic ulcer NOS	50048
Ulcers	Chronic peptic ulcer	40997
Ulcers	Chronic peptic ulcer with haemorrhage	53126
Ulcers	Chronic peptic ulcer with perforation	37620
Ulcers	Chronic peptic ulcer with obstruction	52313
Ulcers	Chronic peptic ulcer unspecified	70390
Ulcers	Chronic peptic ulcer NOS	69663
Ulcers	Unspecified peptic ulcer	50497
Ulcers	Unspecified peptic ulcer without mention of complication	67082
Ulcers	Unspecified peptic ulcer with haemorrhage	70456
Ulcers	Unspecified peptic ulcer with perforation	64111
Ulcers	Unspecified peptic ulcer with haemorrhage and perforation	96622
Ulcers	Unspecified peptic ulcer NOS	60249
Ulcers	Peptic ulcer NOS	19928
Ulcers	Gastrojejunal ulcer (GJU)	23082
Ulcers	Gastrocolic ulcer	64913
Ulcers	Jejunal ulcer	9981
Ulcers	Acute gastrojejunal ulcer	45184
Ulcers	Acute gastrojejunal ulcer with haemorrhage	96628
Ulcers	Acute gastrojejunal ulcer NOS	42274
Ulcers	Chronic gastrojejunal ulcer	96090
Ulcers	Unspecified gastrojejunal ulcer	63482
Ulcers	Unspecified gastrojejunal ulcer with haemorrhage	60346
Ulcers	Unspecified gastrojejunal ulcer with perforation	15979
Ulcers	Unspecified gastrojejunal ulcer NOS	66092
Ulcers	Gastrojejunal ulcer NOS	15403

Table A2. List of diagnoses to identify clinical obesity, by system, condition, medical terminology, read codes, and medcodes.

System	Disease	Read term	Read Code	Medcode
ADL	Limitations in ADL	Mobility poor	13CE.00	2539
ADL	Limitations in ADL	Short of breath on exertion	173C.00	2575
ADL	Limitations in ADL	Difficulty breathing	1738	2931
ADL	Limitations in ADL	Immobile	13CC.00	4346
ADL	Limitations in ADL	Shortness of breath	1739	4822
ADL	Limitations in ADL	Difficulty in walking	N097.00	6375
ADL	Limitations in ADL	Needs help with dressing	3951	6544
ADL	Limitations in ADL	[V]Dependence on wheelchair	ZV46200	6805
ADL	Limitations in ADL	Mobility very poor	13CD.00	7557
ADL	Limitations in ADL	[V] Poor mobility	ZV4L011	9305
ADL	Limitations in ADL	[V]Reduced mobility	ZV4L000	9458
ADL	Limitations in ADL	Impaired mobility	ZO51.00	9638
ADL	Limitations in ADL	Difficulty mobilising	ZO5..00	10222
ADL	Limitations in ADL	Immobility syndrome	N233100	11292
ADL	Limitations in ADL	Difficulty mobilising using mobility aids	ZO95.00	11448
ADL	Limitations in ADL	Unable to mobilise	ZO2..00	12060
ADL	Limitations in ADL	Impaired mobility	13CP.00	13133
ADL	Limitations in ADL	Difficulty mobilising outside	ZO85.00	19385
ADL	Limitations in ADL	[V]Limitation of activities due to disability	ZV4KA00	21496
ADL	Limitations in ADL	Short of breath dressing/undressing	173F.00	22094
ADL	Limitations in ADL	Unable to perform dressing activity	Z8A2.00	22173
ADL	Limitations in ADL	Unable to prepare food for eating	ZM1B200	24873
ADL	Limitations in ADL	Difficulty bathing self	Z89DG00	25009
ADL	Limitations in ADL	Does not perform personal care activity	Z84..00	25158
ADL	Limitations in ADL	Difficulty performing dressing activity	Z8A5.00	25903
ADL	Limitations in ADL	Difficulty using toilet	Z89A700	26225
ADL	Limitations in ADL	Difficulty in walking NOS	N097z00	28112
ADL	Limitations in ADL	Does not prepare food for eating	ZM1B400	32785
ADL	Limitations in ADL	Unable to perform personal hygiene activity	Z892.00	33614
ADL	Limitations in ADL	Does not perform personal hygiene activity	Z894.00	33649
ADL	Limitations in ADL	Walking difficulty due to lower leg	N097200	36256
ADL	Limitations in ADL	Difficulty performing toileting activities	Z89A200	37563
ADL	Limitations in ADL	Unable to mobilise outside	ZO82.00	38964
ADL	Limitations in ADL	Needs help on stairs	3991	39472
ADL	Limitations in ADL	Unable to walk down stairs	ZOA6B00	39498
ADL	Limitations in ADL	Does not mobilise	ZO4..00	40654
ADL	Limitations in ADL	Needs help with feeding	3911	43142
ADL	Limitations in ADL	Difficulty mobilising using wheelchair	ZO96500	44102
ADL	Limitations in ADL	Difficulty performing personal hygiene activity	Z895.00	44725
ADL	Limitations in ADL	Unable to perform personal care activity	Z82..00	44920
ADL	Limitations in ADL	Does not perform mouthcare activities	Z897400	45764
ADL	Limitations in ADL	Dependent in toilet	3970	46503
ADL	Limitations in ADL	Difficulty walking up stairs	ZOA6900	46866
ADL	Limitations in ADL	Immobile	3980	47491

ADL	Limitations in ADL	Does not mobilise indoors	ZO74.00	50824
ADL	Limitations in ADL	Needs help with cooking	39G0.00	50884
ADL	Limitations in ADL	Difficulty getting on and off toilet	ZO7O.00	51390
ADL	Limitations in ADL	Needs help with housework	39G..00	51467
ADL	Limitations in ADL	Difficulty performing personal care activity	Z85..00	52063
ADL	Limitations in ADL	Unable to get on and off toilet	ZO7L.00	52547
ADL	Limitations in ADL	Unable to mobilise indoors	ZO72.00	54173
ADL	Limitations in ADL	Does not mobilise using mobility aids	ZO94.00	54440
ADL	Limitations in ADL	Difficulty walking up stairs	3993	55875
ADL	Limitations in ADL	Unable to use toilet	Z89A400	56965
ADL	Limitations in ADL	Does not walk up stairs	ZOA6800	57096
ADL	Limitations in ADL	Needs help in toilet	3971	57464
ADL	Limitations in ADL	Unable to mobilise using wheelchair	ZO96200	57762
ADL	Limitations in ADL	Difficulty walking up step	ZOA7A00	59521
ADL	Limitations in ADL	Unable to mobilise using mobility aids	ZO92.00	60130
ADL	Limitations in ADL	Does not perform toileting activities	Z89A100	60557
ADL	Limitations in ADL	Does not walk up step	ZOA7900	60785
ADL	Limitations in ADL	Difficulty mobilising indoors	ZO75.00	61586
ADL	Limitations in ADL	Difficulty walking down step	ZOA7F00	63322
ADL	Limitations in ADL	Unable to walk up step	ZOA7700	66091
ADL	Limitations in ADL	Unable to perform mouthcare activities	Z897200	68059
ADL	Limitations in ADL	Difficulty preparing food for eating	ZM1B500	68331
ADL	Limitations in ADL	Does not walk down step	ZOA7E00	70317
ADL	Limitations in ADL	Difficulty getting off toilet	ZO7Q500	72033
ADL	Limitations in ADL	Difficulty walking down stairs	ZOA6E00	88777
ADL	Limitations in ADL	Difficulty getting on to toilet	ZO7P500	91945
ADL	Limitations in ADL	Unable to get off toilet	ZO7Q200	92343
ADL	Limitations in ADL	Support whilst performing an activity of daily living	Z9M6200	92464
ADL	Limitations in ADL	Does not mobilise using wheelchair	ZO96400	93885
ADL	Limitations in ADL	[X]Difficulty in walking	Ryu3100	95777
ADL	Limitations in ADL	Unable to walk down step	ZOA7C00	97495
ADL	Limitations in ADL	Does not perform dressing activity	Z8A4.00	99438
ADL	Limitations in ADL	At risk of activity intolerance	13Zt.00	102426
ADL	Limitations in ADL	Needs help with shopping	13GE.11	103086
ADL	Limitations in ADL	At high risk of activity intolerance	13Zt000	103211
ADL	Limitations in ADL	Unable to perform personal care activity	1P81.00	104970
ADL	Limitations in ADL	[V]Need for assistance due to reduced mobility	ZV4L300	104984
ADL	Limitations in ADL	Difficulty performing toileting activities	3973	105224
ADL	Limitations in ADL	At moderate risk of activity intolerance	13Zt100	105570
ADL	Limitations in ADL	Difficulty undressing	Z8A7500	107010
ADL	Limitations in ADL	Does not walk down stairs	ZOA6D00	109339
ADL	Limitations in ADL	Unable to perform dressing activity	1P81100	112249
ADL	Limitations in ADL	Difficulty performing personal care activity	1P82.00	112505
ADL	Limitations in ADL	Support whilst performing a functional activity	Z9M6100	114327
ADL	Limitations in ADL	Difficulty walking up stairs	3993	55875
ADL	Limitations in ADL	Difficulty washing self	1P82000	111122
ADL	Limitations in ADL	Difficulty walking up step	ZOA7A00	59521

ADL	Limitations in ADL	Difficulty getting off a bed	ZOCB500	35261
ADL	Limitations in ADL	Difficulty getting into shower	ZO7B500	63686
ADL	Limitations in ADL	Difficulty performing personal care activity	Z85..00	52063
ADL	Limitations in ADL	Difficulty turning over in bed	ZOD6511	61937
ADL	Limitations in ADL	Difficulty using washing facilities	ZM35.00	24987
ADL	Limitations in ADL	Difficulty sitting down on a chair	ZOC7500	57653
ADL	Limitations in ADL	Difficulty getting in bath	ZO7I500	44450
ADL	Limitations in ADL	Difficulty undressing	Z8A7500	107010
ADL	Limitations in ADL	Walking difficulty due to lower leg	N097200	36256
ADL	Limitations in ADL	Difficulty preparing meal	ZM1BZ00	24985
ADL	Limitations in ADL	Difficulty cooking food	ZM1E500	24803
ADL	Limitations in ADL	Difficulty managing stairs	ZOA6500	59773
ADL	Limitations in ADL	Difficulty get on and off a bed	ZOC9500	26315
ADL	Limitations in ADL	Difficulty getting in and out of bath	ZO7H.00	25567
ADL	Limitations in ADL	Difficulty bathing self	Z89DG00	25009
ADL	Limitations in ADL	Difficulty catering for self	ZM16500	24973
ADL	Limitations in ADL	Difficulty with personal care	Z77C.30	68429
ADL	Limitations in ADL	Difficulty using toilet	Z89A700	26225
ADL	Limitations in ADL	Difficulty mobilising outside	ZO85.00	19385
ADL	Limitations in ADL	Difficulty moving up and down bed	ZOD8500	109368
ADL	Limitations in ADL	Difficulty performing personal hygiene activity	Z895.00	44725
ADL	Limitations in ADL	Difficulty washing self	Z89D500	19405
ADL	Limitations in ADL	Difficulty getting on and off toilet	ZO7O.00	51390
ADL	Limitations in ADL	Difficulty turning onto side in bed	ZOD7500	55489
ADL	Limitations in ADL	Difficulty getting in and out of a chair	ZOC6500	19724
ADL	Limitations in ADL	Difficulty getting on and off furniture	ZOC5.00	92049
ADL	Limitations in ADL	Difficulty walking down step	ZOA7F00	63322
ADL	Limitations in ADL	Difficulty in walking NOS	N097z00	28112
ADL	Limitations in ADL	Difficulty preparing food for eating	ZM1B500	68331
ADL	Limitations in ADL	Walking difficulty due to unspecified site	N097000	2537
ADL	Limitations in ADL	Difficulty managing stairs on bottom	ZOA6O00	113698
ADL	Limitations in ADL	Difficulty in walking	N097.00	6375
ADL	Limitations in ADL	Difficulty performing toileting activities	Z89A200	37563
ADL	Limitations in ADL	Difficulty maintaining standard of personal hygiene	Z89C500	66067
ADL	Limitations in ADL	Difficulty performing toileting activities	3973	105224
ADL	Limitations in ADL	Difficulty getting out of shower	ZO7C500	69553
ADL	Limitations in ADL	Difficulty getting on to toilet	ZO7P500	91945
ADL	Limitations in ADL	Difficulty tying shoe laces	3953	105289
ADL	Limitations in ADL	Difficulty using lavatory	Z89A711	54517
ADL	Limitations in ADL	[X]Difficulty in walking, not elsewhere classified	Ryu3100	95777
ADL	Limitations in ADL	Difficulty dressing	Z8A6500	47890
ADL	Limitations in ADL	Difficulty moving around supporting self on furniture	ZO7V.00	59989
ADL	Limitations in ADL	Difficulty mobilising indoors	ZO75.00	61586
ADL	Limitations in ADL	Difficulty walking up stairs	ZOA6900	46866
ADL	Limitations in ADL	Difficulty managing steps and stairs	ZOA5.00	25994
ADL	Limitations in ADL	Difficulty performing personal care activity	1P82.00	112505

ADL	Limitations in ADL	Difficulty getting off toilet	Z07Q500	72033
ADL	Limitations in ADL	Difficulty putting on footwear	Z8A6D00	67595
ADL	Limitations in ADL	Difficulty performing dressing activity	Z8A5.00	25903
ADL	Limitations in ADL	Difficulty walking down stairs	Z0A6E00	88777
ADL	Limitations in ADL	Difficulty travelling on foot	ZN26500	41273
ADL	Limitations in ADL	Difficulty getting in and out of shower	Z07A.00	97402
ADL	Limitations in ADL	Difficulty moving in bed	Z0D5.00	51203
ADL	Limitations in ADL	Difficulty with personal care	Z86..11	38695
ADL	Limitations in ADL	Difficulty climbing stairs	Z0A6911	62765
ADL	Limitations in ADL	Difficulty managing stairs backwards	Z0A6T00	98558
ADL	Limitations in ADL	Difficulty managing stairs on all fours	Z0A6J00	92592
ADL	Limitations in ADL	Does not manage stairs	Z0A6400	100573
ADL	Limitations in ADL	Does not manage stairs on bottom	Z0A6N00	112391
ADL	Limitations in ADL	Does not manage steps and stairs	Z0A4.00	67834
ADL	Limitations in ADL	Does not walk down stairs	Z0A6D00	109339
ADL	Limitations in ADL	Does not walk up stairs	Z0A6800	57096
ADL	Limitations in ADL	Needs help on stairs	3991	39472
ADL	Limitations in ADL	Unable to manage stairs	Z0A6200	71220
ADL	Limitations in ADL	Unable to climb stairs	3990	35002
ADL	Limitations in ADL	Unable to manage steps and stairs	Z0A2.00	26084
ADL	Limitations in ADL	Unable to walk down stairs	Z0A6B00	39498
ADL	Limitations in ADL	ADL - Support whilst performing an activity of daily living	Z9M6211	38127
CNS	Raised Intracranial Pressure	Benign intracranial hypertension	F282.00	5433
CNS	Raised Intracranial Pressure	Benign intracranial hypertension	F282.00	5433
CNS	Recurrent headaches	Headache	1B1G.00	129
CNS	Recurrent headaches	Tension headache	E278100	191
CNS	Recurrent headaches	[D]Headache	R040.00	1197
CNS	Recurrent headaches	Cluster headache	F262000	2554
CNS	Recurrent headaches	Vascular headache	F2X..00	5110
CNS	Recurrent headaches	[X]Tension type headache	F262600	7512
CNS	Recurrent headaches	Generalised headache	1BA2.00	9891
CNS	Recurrent headaches	Headache character NOS	1BBZ.00	29394
CNS	Recurrent headaches	[X]Vascular headache	Fyu5A00	95330
CNS	Recurrent headaches	[X]Chronic headache disorder	Fyu5E00	98205
CNS	Recurrent headaches	Chronic tension-type headache	F262B00	103537
CNS	Recurrent headaches	Bilateral headache	1BA4.00	21663
CNS	Recurrent headaches	Frontal headache	1BA5.00	130
CNS	Recurrent headaches	Occipital headache	1BA6.00	1788
CNS	Recurrent headaches	Parietal headache	1BA7.00	9048
CNS	Recurrent headaches	Unilateral headache	1BA3.00	11321
CNS	Recurrent headaches	Pseudotumour cerebri	F282.11	46041
CNS	Recurrent headaches	[X]Chronic headache disorder	Fyu5E00	98205
CNS	Recurrent headaches	Chronic tension-type headache	F262B00	103537
CNS	Recurrent headaches	[X]Chronic headache disorder	Fyu5E00	98205
CNS	Recurrent headaches	[X]Other migraine	Fyu5300	53813
CNS	Recurrent headaches	Atypical migraine	F261000	9633
CNS	Recurrent headaches	Basilar migraine	F262300	9004
CNS	Recurrent headaches	Chronic tension-type headache	F262B00	103537

CNS	Recurrent headaches	Classical migraine	F260.00	3220
CNS	Recurrent headaches	Common migraine	F261.00	2424
CNS	Recurrent headaches	Common migraine NOS	F261z00	41497
CNS	Recurrent headaches	Complicated migraine	F26y300	27930
CNS	Recurrent headaches	Hemiplegic migraine	F26y000	3658
CNS	Recurrent headaches	Migraine	F26..00	161
CNS	Recurrent headaches	Migraine NOS	F26z.00	14700
CNS	Recurrent headaches	Migraine prophylaxis	8B6N.00	11389
CNS	Recurrent headaches	Migraine variant NOS	F262z00	23621
CNS	Recurrent headaches	Migraine variants	F262.00	5509
CNS	Recurrent headaches	Migraine with aura	F260.11	103502
CNS	Recurrent headaches	Migraine without aura	F261.11	103602
CNS	Recurrent headaches	Moebius' ophthalmoplegic migraine	F26y111	65262
CNS	Recurrent headaches	Ophthalmic migraine	F262400	10583
CNS	Recurrent headaches	Ophthalmoplegic migraine	F26y100	12511
CNS	Recurrent headaches	Other forms of migraine	F26y.00	28031
CNS	Recurrent headaches	Other forms of migraine NOS	F26yz00	28092
CNS	Recurrent headaches	Frequent episodic tension-type headache	F262A00	103755
CNS	Vision Loss	Visual disturbances	F48..00	567
CNS	Vision Loss	Visual loss NOS	F49z.00	1444
CNS	Vision Loss	Subjective visual disturbances	F481.00	11689
CNS	Vision Loss	Visual disturbance NOS	F48z.00	12194
CNS	Vision Loss	Visual loss	F493.00	20256
CNS	Vision Loss	Sudden visual loss	F481100	20736
CNS	Vision Loss	Visual loss	F49y.00	25547
CNS	Vision Loss	Other transient visual loss	F481400	39309
CNS	Vision Loss	Severe visual impairment	F497.00	104853
CNS	Vision Loss	Severe visual impairment	F49B.00	105206
CNS	Vision Loss	Visual impairment	F49D.00	108199
CNS	Vision Loss	Visual disturbances	F48..00	567
CNS	Vision Loss	Visual loss NOS	F49z.00	1444
CNS	Vision Loss	Subjective visual disturbances	F481.00	11689
CNS	Vision Loss	Visual disturbance NOS	F48z.00	12194
CNS	Vision Loss	Visual loss	F493.00	20256
CNS	Vision Loss	Sudden visual loss	F481100	20736
CNS	Vision Loss	Visual loss	F49y.00	25547
CNS	Vision Loss	Other transient visual loss	F481400	39309
CNS	Vision Loss	Severe visual impairment	F497.00	104853
CNS	Vision Loss	Severe visual impairment	F49B.00	105206
CNS	Vision Loss	Visual impairment	F49D.00	108199
CVD	Left Ventricular Heart Failure	HFNEF - heart failure with normal ejection fraction	G583.11	101137
CVD	Left Ventricular Heart Failure	Heart failure with normal ejection fraction	G583.00	101138
CVD	Left Ventricular Heart Failure	Heart failure with preserved ejection fraction	G583.12	106897
CVD	Chronic/recurrent atrial fibrillation	Paroxysmal atrial fibrillation	G573200	1268
CVD	Chronic/recurrent atrial fibrillation	Atrial fibrillation	G573000	1664
CVD	Chronic/recurrent atrial fibrillation	Atrial fibrillation and flutter	G573.00	2212
CVD	Chronic/recurrent atrial fibrillation	Atrial fibrillation and flutter NOS	G573z00	23437

CVD	Chronic/recurrent atrial fibrillation	Persistent atrial fibrillation	G573500	96076
CVD	Chronic/recurrent atrial fibrillation	Permanent atrial fibrillation	G573400	96277
CVD	Raised Blood Pressure	Good hypertension control	6627	16565
CVD	Raised Blood Pressure	Poor hypertension control	6628	27511
CVD	Raised Blood Pressure	Hypertension treatm. started	662F.00	21826
CVD	Raised Blood Pressure	Hypertensive treatm.changed	662G.00	13188
CVD	Raised Blood Pressure	On treatment for hypertension	662O.00	3425
CVD	Raised Blood Pressure	Moderate hypertension control	662b.00	18590
CVD	Raised Blood Pressure	Hypertension six month review	662c.00	18482
CVD	Raised Blood Pressure	Hypertension annual review	662d.00	19070
CVD	Raised Blood Pressure	Trial withdrawal of antihypertensive therapy	662r.00	95359
CVD	Raised Blood Pressure	High cost hypertension drugs	7Q01.00	85944
CVD	Raised Blood Pressure	Antihypertensive therapy	8B26.00	18057
CVD	Raised Blood Pressure	Patient on maximal tolerated antihypertensive therapy	8BL0.00	11056
CVD	Raised Blood Pressure	Hypertension treatment refused	8I3N.00	22333
CVD	Raised Blood Pressure	Blind hypertensive eye	F404200	37086
CVD	Raised Blood Pressure	Hypertensive retinopathy	F421300	6702
CVD	Raised Blood Pressure	Hypertensive disease	G2...00	204
CVD	Raised Blood Pressure	BP - hypertensive disease	G2...11	8732
CVD	Raised Blood Pressure	Essential hypertension	G20..00	799
CVD	Raised Blood Pressure	Malignant essential hypertension	G200.00	15377
CVD	Raised Blood Pressure	Benign essential hypertension	G201.00	1894
CVD	Raised Blood Pressure	Systolic hypertension	G202.00	4372
CVD	Raised Blood Pressure	Diastolic hypertension	G203.00	83473
CVD	Raised Blood Pressure	Essential hypertension NOS	G20z.00	10818
CVD	Raised Blood Pressure	Hypertension NOS	G20z.11	3712
CVD	Raised Blood Pressure	Hypertensive heart disease	G21..00	16292
CVD	Raised Blood Pressure	Malignant hypertensive heart disease	G210.00	50157
CVD	Raised Blood Pressure	Malignant hypertensive heart disease without CCF	G210000	95334
CVD	Raised Blood Pressure	Malignant hypertensive heart disease with CCF	G210100	72668
CVD	Raised Blood Pressure	Benign hypertensive heart disease	G211.00	52427
CVD	Raised Blood Pressure	Benign hypertensive heart disease without CCF	G211000	61660
CVD	Raised Blood Pressure	Benign hypertensive heart disease with CCF	G211100	52127
CVD	Raised Blood Pressure	Hypertensive heart disease NOS	G21z.00	31464
CVD	Raised Blood Pressure	Hypertensive heart disease NOS without CCF	G21z000	61166
CVD	Raised Blood Pressure	Cardiomegaly - hypertensive	G21z011	8857
CVD	Raised Blood Pressure	Hypertensive heart disease NOS with CCF	G21z100	62718
CVD	Raised Blood Pressure	Hypertensive heart disease NOS	G21zz00	16173
CVD	Raised Blood Pressure	Hypertensive renal disease	G22..00	4668
CVD	Raised Blood Pressure	Malignant hypertensive renal disease	G220.00	39649
CVD	Raised Blood Pressure	Benign hypertensive renal disease	G221.00	43935
CVD	Raised Blood Pressure	Hypertensive renal disease with renal failure	G222.00	32423
CVD	Raised Blood Pressure	Hypertensive renal disease NOS	G22z.00	15106
CVD	Raised Blood Pressure	Renal hypertension	G22z.11	29310
CVD	Raised Blood Pressure	Hypertensive heart and renal disease	G23..00	63466

CVD	Raised Blood Pressure	Malignant hypertensive heart and renal disease	G230.00	67232
CVD	Raised Blood Pressure	Benign hypertensive heart and renal disease	G231.00	63000
CVD	Raised Blood Pressure	Hypertensive heart&renal dis with (congestive) heart failure	G232.00	21837
CVD	Raised Blood Pressure	Hypertensive heart and renal disease with renal failure	G233.00	28684
CVD	Raised Blood Pressure	Hyperten heart&renal dis+both(congestv)heart and renal fail	G234.00	57987
CVD	Raised Blood Pressure	Hypertensive heart and renal disease NOS	G23z.00	68659
CVD	Raised Blood Pressure	Other specified hypertensive disease	G2y..00	18765
CVD	Raised Blood Pressure	Hypertensive disease NOS	G2z..00	7057
CVD	Raised Blood Pressure	Hypertensive encephalopathy	G672.00	3979
CVD	Raised Blood Pressure	Hypertensive crisis	G672.11	31816
CVD	Raised Blood Pressure	[X]Hypertensive diseases	Gyu2.00	69753
CVD	Raised Blood Pressure	Adverse reaction to other antihypertensives	TJC7.00	21660
CVD	Raised Blood Pressure	Adverse reaction to antihypertensives NOS	TJC7z00	20497
CVD	Raised Blood Pressure	[X]Oth antihyperten drug caus advers eff in therap use, NEC	U60C500	63164
CVD	Raised Blood Pressure	[X] Adverse reaction to other antihypertensives	U60C511	30770
CVD	Raised Blood Pressure	[X] Adverse reaction to antihypertensives NOS	U60C51A	44350
CVD	Raised Blood Pressure	Hypertension induced by oral contraceptive pill	6146200	32976
CVD	Raised Blood Pressure	Secondary hypertension	G24..00	7329
CVD	Raised Blood Pressure	Secondary malignant hypertension	G240.00	31755
CVD	Raised Blood Pressure	Secondary malignant renovascular hypertension	G240000	59383
CVD	Raised Blood Pressure	Secondary malignant hypertension NOS	G240z00	73293
CVD	Raised Blood Pressure	Secondary benign hypertension	G241.00	57288
CVD	Raised Blood Pressure	Secondary benign renovascular hypertension	G241000	25371
CVD	Raised Blood Pressure	Secondary benign hypertension NOS	G241z00	51635
CVD	Raised Blood Pressure	Hypertension secondary to endocrine disorders	G244.00	34744
CVD	Raised Blood Pressure	Secondary hypertension NOS	G24z.00	16059
CVD	Raised Blood Pressure	Secondary renovascular hypertension NOS	G24z000	31387
CVD	Raised Blood Pressure	Hypertension secondary to drug	G24z100	31341
CVD	Raised Blood Pressure	Secondary hypertension NOS	G24zz00	42229
CVD	Raised Blood Pressure	[X]Hypertension secondary to other renal disorders	Gyu2100	97533
CVD	Pulmonary Arterial Hypertension	Primary pulmonary hypertension	G410.00	245
CVD	Pulmonary Arterial Hypertension	Secondary pulmonary hypertension	G41y000	34065
CVD	Pulmonary Arterial Hypertension	Thromboembolic pulmonary hypertension	G41y100	102444
CVD	Recurrent DVT and/or pulmonary thromboembolic disease	Deep vein thrombosis	G801.11	824
CVD	Recurrent DVT and/or pulmonary thromboembolic disease	DVT - Deep vein thrombosis	G801.13	3392
CVD	Recurrent DVT and/or pulmonary thromboembolic disease	Deep vein phlebitis and thrombophlebitis of the leg	G801.00	3576
CVD	Recurrent DVT and/or pulmonary thromboembolic disease	Deep vein thrombosis of lower limb	G801D00	22038
CVD	Recurrent DVT and/or pulmonary thromboembolic disease	Deep vein thrombosis	G801.12	25478
CVD	Recurrent DVT and/or pulmonary thromboembolic disease	Deep vein phlebitis and thrombophlebitis of the leg NOS	G801z00	27284
CVD	Recurrent DVT and/or pulmonary thromboembolic disease	Deep vein thrombophlebitis of the leg unspecified	G801B00	32002
CVD	Recurrent DVT and/or pulmonary thromboembolic disease	Deep vein phlebitis of the leg unspecified	G801500	42158

CVD	Recurrent DVT and/or pulmonary thromboembolic disease	Recurrent deep vein thrombosis	G801G00	104342
CVD	Left Ventricular Heart Failure	Acute left ventricular failure	G581000	5255
CVD	Left Ventricular Heart Failure	Left ventricular systolic dysfunction	G5yy900	8966
CVD	Left Ventricular Heart Failure	Impaired left ventricular function	G581.13	5942
CVD	Left Ventricular Heart Failure	Impaired left ventricular function	33BA.00	7251
CVD	Left Ventricular Heart Failure	Left ventricular cardiac dysfunction	G5yyD00	107397
CVD	Left Ventricular Heart Failure	Left ventricular failure	G581.00	884
Liver	Hepatic fibrosis	Hepatic fibrosis	J61y400	25383
Liver	Hepatic fibrosis	Hepatic fibrosis	J615z15	71453
Liver	NAFLD with hepatic fibrosis	Non-alcoholic fatty liver	J61y100	10234
Lymphatic	Lower limb lymphedema	Lymphoedema	G86..11	4215
Lymphatic	Lower limb lymphedema	Acquired (chronic) lymphoedema	G861100	31425
Lymphatic	Lower limb lymphedema	Other lymphoedema NOS	G861z00	33331
Lymphatic	Lower limb lymphedema	Other lymphoedema	G861.00	46273
Lymphatic	Lower limb lymphedema	Excision of lymphoedematous tissue of leg NEC	7H66300	60543
Lymphatic	Lower limb lymphedema	Tough excision of lymphoedematous tissue of leg	7H66313	69600
Lymphatic	Lower limb lymphedema	Gibson excision of lymphoedematous tissue of leg	7H66311	98963
Lymphatic	Lower limb lymphedema	Constriction ring of lower limb with lymphoedema	PF6D100	114240
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	Pure hyperglyceridaemia	C321.00	1173
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	[D]Hyperglycaemia	R105712	1789
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	Lipoprotein deficiency NOS	C325z00	1983
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	[X]Hyperglycaemia	Ryu8A00	9310
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	Blood hyperglycaemia NOS	44Uz.11	11050
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	Hypertriglyceridaemia	C321000	12439
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	Lipoprotein deficiencies	C325.00	16306
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	Chronic hyperglycaemia	66AJ000	22959
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	Low density lipoprotein apheresis	7L1j000	105783
Metabolic	Cluster of hyperglycaemia, high triglycerides, low HDL	Serum triglycerides raised	44Q3.00	26941
Musculoskeletal	Joint pain	Hip pain	N094K12	286
Musculoskeletal	Joint pain	Ankle stiff	N095711	2499
Musculoskeletal	Joint pain	Hip stiff	N095511	4460
Musculoskeletal	Joint pain	Anterior knee pain	N094W00	6166
Musculoskeletal	Joint pain	Knee pain	1M10.00	9517
Musculoskeletal	Joint pain	Anterior knee pain	1M12.00	10389
Musculoskeletal	Joint pain	Knee stiff	N095611	15060
Musculoskeletal	Joint pain	Multiple stiff joints	N095900	20449
Musculoskeletal	Joint pain	Stiff knee NEC	N095M00	27535
Musculoskeletal	Joint pain	Stiff joint NEC	N095500	36520
Musculoskeletal	Joint pain	Stiff joint NEC	N095600	41620
Musculoskeletal	Joint pain	Stiff hip NEC	N095K00	42080
Musculoskeletal	Joint pain	Stiff joint NEC	N095700	42709
Musculoskeletal	Joint pain	Stiff joint NEC	N095000	44414
Musculoskeletal	Joint pain	Stiff ankle NEC	N095P00	53837

Renal	Microalbuminuria with reduced eGFR	CKD with GFR category G4 & albuminuria category A2	1Z1b.00	109904
Renal	Microalbuminuria with reduced eGFR	CKD with GFR category G4 & albuminuria category A3	1Z1c.00	110626
Renal	Microalbuminuria with reduced eGFR	CKD with GFR category G5 & albuminuria category A2	1Z1e.00	109981
Renal	Microalbuminuria with reduced eGFR	CKD with GFR category G2 & albuminuria category A2	1Z1R.00	110108
Renal	Microalbuminuria with reduced eGFR	CKD with GFR category G2 & albuminuria category A3	1Z1S.00	110251
Renal	Microalbuminuria with reduced eGFR	CKD with GFR category G3a & albuminuria category A2	1Z1V.00	109805
Renal	Microalbuminuria with reduced eGFR	CKD with GFR category G3a & albuminuria category A3	1Z1W.00	109905
Renal	Microalbuminuria with reduced eGFR	CKD with GFR category G3b & albuminuria category A2	1Z1Y.00	109657
Renal	Microalbuminuria with reduced eGFR	CKD with GFR category G3b & albuminuria category A3	1Z1Z.00	109990
Renal	Microalbuminuria with reduced eGFR	CKD with GFR category G5 & albuminuria category A3	1Z1f.00	110467
Renal	Microalbuminuria with reduced eGFR	[D]Microalbuminuria	R110300	10924
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 1	1Z10.00	29013
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 1	K051.00	105392
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 2	K052.00	105383
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 2	1Z11.00	12586
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 3	K053.00	104619
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 3	1Z12.00	12566
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 3A	1Z15.00	94965
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 3B	1Z16.00	95179
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 4	K054.00	104963
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 4	1Z13.00	12479
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 5	1Z14.00	12585
Renal	Microalbuminuria with reduced eGFR	Chronic kidney disease stage 5	K055.00	105151
Renal	Microalbuminuria with reduced eGFR	Dialysis for renal failure	7L1A.11	11773
Renal	Microalbuminuria with reduced eGFR	Peritoneal dialysis	7L1A100	2994
Renal	Microalbuminuria with reduced eGFR	Renal dialysis	7L1A000	20073
Renal	Microalbuminuria with reduced eGFR	End-stage renal disease	K0D..00	8330
Reproductive	Anovulation	Female infertility of anovulatory origin	K5B0.00	4977
Reproductive	Anovulation	Secondary anovulatory infertility	K5B0100	50116
Reproductive	Anovulation	Primary anovulatory infertility	K5B0000	52132
Reproductive	Anovulation	Female infertility of anovulatory origin NOS	K5B0z00	63421
Reproductive	Male hypogonadism	Other testicular hypofunction	C172.00	16341
Reproductive	Male hypogonadism	Other testicular hypofunction NOS	C172z00	41320
Reproductive	Male hypogonadism	Other specified other testicular hypofunction	C172y00	56431
Reproductive	Male hypogonadism	Testicular hypogonadism	C172.12	9577
Reproductive	Male hypogonadism	Hypogonadotropic hypogonadism	C139.00	98210
Reproductive	Male hypogonadism	Eunuchoidism, hypogonadism	C172.11	70378
Reproductive	Oligomenorrhea	Oligomenorrhoea	K591100	1153
Reproductive	Oligomenorrhea	Primary oligomenorrhoea	K591200	6486
Reproductive	Oligomenorrhea	Secondary oligomenorrhoea	K591300	12100
Reproductive	PCOS	Polycystic ovaries	C164.00	1466
Reproductive	PCOS	Polycystic ovarian syndrome	C165.00	11347
Respiratory	Breathlessness	[D]Breathlessness	R060D00	735
Respiratory	Breathlessness	Breathlessness	173..00	1429

Respiratory	Breathlessness	Difficulty breathing	1738	2931
Respiratory	Breathlessness	[D]Dyspnoea	R060A00	3092
Respiratory	Breathlessness	Shortness of breath	1739	4822
Respiratory	Breathlessness	Breathlessness symptom	173..11	5175
Respiratory	Breathlessness	Dyspnoea - symptom	173..12	5896
Respiratory	Breathlessness	Paroxysmal nocturnal dyspnoea	1736	6434
Respiratory	Breathlessness	O/E - dyspnoea	2322	7000
Respiratory	Breathlessness	Nocturnal dyspnoea	173D.00	18116
Respiratory	Breathlessness	Breathlessness NOS	173Z.00	21801
Respiratory	Breathlessness	Dyspnoea on exertion	173C.11	53771
Respiratory	Diaphragmatic Compliance	Paralysis of diaphragm	H5y4100	10832
Respiratory	Diaphragmatic Compliance	Disorders of diaphragm	H5y4.00	18052
Respiratory	Diaphragmatic Compliance	Disorders of diaphragm NOS	H5y4z00	42188
Respiratory	Diaphragmatic Compliance	Diaphragmatitis	H5y4000	48673
Respiratory	Diaphragmatic Compliance	Relaxation of diaphragm	H5y4200	103136
Respiratory	Hypoventilation	Extreme obesity with alveolar hypoventilation	C380200	38059
Respiratory	Hypoventilation	Obesity hypoventilation syndrome	C38y011	103574
Respiratory	Wheezing	Wheezing	1737	173
Respiratory	Wheezing	[D]Wheezing	R060900	2210
Respiratory	Wheezing	Wheezing symptom	1737.11	2891
Respiratory	Wheezing	[D]Severe wheeze	R060G00	101073
Respiratory	Wheezing	[D]Very severe wheeze	R060H00	101421
Respiratory	Wheezing	Constant wheezing	1737000	107182
Respiratory	Wheezing	Wheezing in absence of colds	1737100	109042
Upper airways	Apnoeas/hypopneas during sleep	[D]Apnoea	R060400	982
Upper airways	Apnoeas/hypopneas during sleep	[D]Sleep apnoea syndrome	R005311	2506
Upper airways	Apnoeas/hypopneas during sleep	Sleep apnoea	Fy03.00	7603
Upper airways	Apnoeas/hypopneas during sleep	Obstructive sleep apnoea	Fy03.11	8148
Upper airways	Apnoeas/hypopneas during sleep	[D]Syndrome sleep apnoea	R005312	20438
Upper airways	Apnoeas/hypopneas during sleep	Obstructive sleep apnoea	H5B0.00	20748
Upper airways	Apnoeas/hypopneas during sleep	Sleep apnoea	H5B..00	23779
Urinary	Recurrent/chronic urinary incontinence	Stress incontinence	1A24.00	1929
Urinary	Recurrent/chronic urinary incontinence	Stress incontinence	K198.00	3182
Urinary	Recurrent/chronic urinary incontinence	[D]Incontinence of urine	R083.00	3283
Urinary	Recurrent/chronic urinary incontinence	Urge incontinence of urine	1A26.00	3887
Urinary	Recurrent/chronic urinary incontinence	Stress incontinence - symptom	1A24.11	5844
Urinary	Recurrent/chronic urinary incontinence	Incontinence of urine	1A23.00	6161
Urinary	Recurrent/chronic urinary incontinence	[D]Incontinence of urine NOS	R083z00	15400
Urinary	Recurrent/chronic urinary incontinence	[D] Urge incontinence	R083200	17320
Urinary	Recurrent/chronic urinary incontinence	[D]Urethral sphincter incontinence	R083100	31220
Urinary	Recurrent/chronic urinary incontinence	[X]Other specified urinary incontinence	Kyu5A00	52763
Urinary	Recurrent/chronic urinary incontinence	Functional urinary incontinence	1A23000	110001