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**Exploring ethnic variations in lifestyle and
diabetes: using evidence from UK Biobank Data**

Uduakobong Efanga Ntuk

B.Sc. (Hons), MPH

**Submitted in fulfilment of the requirements for the
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School of Health and Wellbeing

College of Medicine, Veterinary and Life Sciences

University of Glasgow

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Abstract

Type 2 diabetes mellitus (T2DM) is an important public health problem, with prevalence rapidly rising in the last decade by 65% in the United Kingdom. Those with type 2 diabetes carry twice the risk of developing cardiovascular disease and premature mortality amongst adults. The UK population is now ageing and the number of multi-ethnic populations in UK is increasing, the burden of T2DM is of prime importance.

Improved lifestyle behaviours could significantly prevent the onset and also improve the effect of diabetes disease. However, the underpinning evidences have largely been obtained from studies of populations of white European descent. It is unclear whether these recommendations are appropriate for other ethnic groups. The prevalence of T2DM, its impacts and controls differ between ethnic populations. T2DM is more common, more severe, develops at an earlier age as well as develops at lower obesity levels in the non-white minority population living within the United Kingdom compared with the majority White population. Therefore, more inclusive epidemiological information is critical for effective planning and designing of interventions to improve population health, particularly amongst non-white minority groups.

The aim of this thesis was to assess and analyse epidemiological data on the ethnic differences in sex, adiposity and lifestyle factors on T2DM risk among middle-aged adults in the United Kingdom with focus on European white, South Asians (people originating from India, Pakistan and Bangladesh), Blacks (Black African and Black Caribbean) and Chinese descent populations.

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Author's declaration

This thesis is submitted in fulfilment of the requirement for the degree of Doctor of Philosophy at the University of Glasgow. Unless stated otherwise, the work is that of the author. Parts of the research work included in this thesis has been published with co-authors. The following publications and presentations originated from this thesis.

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Definitions

Acronyms and abbreviations

ARIC = Atherosclerosis Risk in Communities

AusDiab = Australian Diabetes, Obesity, and Lifestyle Study

BF% = Body fat percentage

BME = Black and minority ethnic

BMI = Body mass index

CDC = Centers for Disease Control

CI = Confidence interval

CPRD = Clinical Practice Research Datalink

HbA1c = Glycated haemoglobin

HGS = Hand grip strength

IDF = International diabetes federation

IPAQ = International physical activity questionnaire

MESA = The Multi-Ethnic Study of Atherosclerosis

MVPA = Moderate-to-vigorous physical activity

NICE = The National Institute for Health and Care Excellence

OR = Odds ratio

PA= Physical activity

PURE= Prospective Urban Rural Epidemiology

PAR= Population attributable risk

PAF= Population attributable fraction

SA = South Asians

SABRE = Southall and Brent Revisited

SAT= Subcutaneous adipose tissue

SMD= Standardized mean differences

T1D= Type 1 diabetes

T2D = Type 2 diabetes

UKBB= UK Biobank

VAT= Visceral adipose tissue

WC = Waist circumference

WHO = World health organisation

WHR= Waist-to-hip ratio

1 Introduction

1.1 Overview

This thesis is about how established and emerging risk factors for type 2 diabetes - age, sex, adiposity, muscular strength, physical activity and television viewing - may affect diabetes risk differently in different ethnic groups. Compared with data in populations of White European origin, there is relatively limited data on how these risk factors affect diabetes risk in non-White groups. This may have implications for understanding the relative importance of different aetiological factors across ethnic groups and inform guidelines and the design of future intervention. This chapter provides the background for the work undertaken in this thesis. It starts with an overview of ethnicity, before covering previous diabetes research. The risk factors of diabetes and its impact of diabetes on ethnic minorities in the United Kingdom were also explored. Throughout this chapter key gaps in understanding are highlighted and the chapter concludes with the aims of the thesis which addresses some of the key gaps identified.

1.1 Ethnicity

This section provides an overview of the concepts of ethnicity and race, with an emphasis on the historical exodus of migrants from the British Commonwealth and the multicultural demography of the United Kingdom. In addition, it summarises the development of the collection of data on ethnicity in the UK and the current effect of ethnicity on public health outcomes.

1.1.1 The Concept of Ethnicity

In general terms, ethnicity is a multidimensional concept, used to define a group of people's identities based on shared common ancestry, history, geographical origin, language, religion, nationality and physical features (1-3). Apart from sharing common descent, belonging to an ethnic group includes sharing important segments of common culture and participating in shared activities (4). Therefore, to identify with an ethnic group is mostly dependent on a person's self-perception, and observation by others (5). Williams (6) argues that ethnicity is not so much about belonging to a group but best understood as the 'sense of difference' that

members of a particular cultural, tribal or national group feel when interacting with non-members.

Ethnicity could also be considered fluid and can change over time in response to political and cultural forces as culture is not an autonomous and static feature in an individual's life (7). It is an element of identity whose significance depends on the context within which the individual finds themselves and can evolve over time within individuals and between generations (8,9). This is particularly evident in multicultural countries such as the United Kingdom, where the first-generation migrants may identify ethnically with their foreign country of birth or home country, while their descendants may identify with the country of residence. Subsequently, people with mixed parentage from different ethnic groups may identify with either or create a new identity for themselves (10). As such, ethnicity there is no universally accepted definition of ethnicity as it is related to the cultural, social, and political context in which it is used within a period of time.

1.1.2 Relating Ethnicity and Race

The term 'race' has been used interchangeably with ethnicity, although there is a conceptual distinction between both terms. The traditional concept of 'race' refers to biological differences / homogeneity between groups as defined by a few phenotypical features e.g., hair texture and skin colour, eye colour and physical appearance, etc. (11). In much of the 18th to 20th centuries, it was popular social science practice to see race as an organizing principle social order, and therefore a legitimate criterion for the selection of cases for comparative analyses (12). The utility and value of 'race' as a classificatory concept in scientific studies is losing ground (13). More recently, race as a scientific variable has been shown to be less accurate, given the heterogeneity within a race (14). Therefore, ethnic groups or ethnicity is a more appropriate term used in this thesis to represent cultural and social identities of individuals. UK Biobank is a very large and detailed prospective study including over 500,000 men and women aged mostly between 37 and 73 years old at the time of recruitment between 2006 and 2010. Because of its large sample size, UK Biobank boasts a large ethnic minority sample size, which allows analysis by ethnicity subgroups(15).

1.1.3 Ethnicity as an Epidemiological Variable

As an epidemiological variable, ethnicity reflects self-identification incorporating and measuring the influences of cultural/lifestyle factors on health experience and outcomes that provide strength, meaning and boundaries between groups (16). While ethnicity may not be precisely measured or defined every time, its application in British epidemiological research could still be useful (17).

The lens of ethnicity has been used to understand and investigate diseases (usually chronic diseases), which are typically of high prevalence within the countries of origin of minority ethnic groups e.g., coronary artery disease (CAD) in Pakistani, diabetes in Indians (18) and hypertension in Blacks (19). Ethnicity has also been used to investigate disease which appear to be part of the spectrum of ill health e.g., mental ill-health faced by minorities who have migrated to the UK (20). Thirdly, ethnicity has been used to investigate how risk factors for chronic diseases e.g., obesity(21), physical inactivity(22), sedentary habits (23,24) may differ between populations groups and the potential impact of this on disease prevalence and incidence (25).

1.1.4 Ethnicity in United Kingdom

In the United Kingdom 14% of the population self-identified as non-white and are collectively referred to as being from a minority ethnic group. People from the broad classification of “Asian” ethnic groups made up the second largest percentage of the overall population (at 9.3%), followed by “Black” ethnic groups (at 3.3%), “Mixed/Multiple” ethnic groups (at 4.0%), and “Other” ethnic groups (at 2.0%)(26). The percentage of ethnic minority groups in the UK is set to increase further. Approximately 73% of UK population growth is from the minority ethnic groups. Rees and colleagues estimated that the ethnic minority will increase from 17.5% in 2011 to 32.5% by 2051(27,28). Their prediction was determined by the fertility, mortality and immigration flows from local areas specific to all ethnic groups in the UK according to the 2001 census, survey and administrative data.

1.1.5 Classification of ethnicity

As earlier explained, ethnicity is fluid and subjective to a person's identity and how they are seen by others. Hence, people can identify with groups at different levels, whether as a British (nationality) or Punjabi (culture). Therefore, classification of ethnicity is complex on the basis of the multifaceted and subjective concepts. However, to allow data to be collected and analysed on a large scale in the UK, ethnicity is treated as a fixed variable. In UK, the widely used form of ethnic classification is drawn from the ONS yearly census self-identification questionnaire (29).

1.1.6 Data On Ethnicity Available for Research

Collectively, people from Indian, Pakistani and Bangladeshi background are categorized as 'South Asians'; people from Black Caribbean and African background are categorized as Blacks. The classification of ethnicity is still an ongoing debate based on the recognition that heterogeneity exists among grouped ethnicities despite the socio-cultural overlap (30). It is argued that use of aggregated ethnicity categories, such as South Asian and Blacks, can obscure important differences between smaller groups such as the Indian, Pakistani and Bangladeshi ethnic groups; between Black African and Black Caribbean. Conversely, when ethnic groups are disaggregated, the numbers might be too small to produce robust epidemiological findings. For example, according to the 2011 UK census for England and Wales, the Bangladeshis represent only about 1.1% of the population, Indians 3.1%, and Pakistanis 2.7%, whereas Black African are 2.5% and Black Caribbean 1.0% (29). These small sizes of minority ethnic populations can make study of health disparities challenging as data would be subject to substantial random variation making the true rate of disease prevalence and incidence in the population difficult to calculate (31-33). Therefore, to make meaningful inferences about small groups, aggregation of groups is often applied.

However, the recognition of between-group and within-group diversity has potential impacts on minorities' health and wellbeing, and relationship with disease outcomes (34). The mechanisms driving these associations for different groups merit attention to shed light on the health needs of minority ethnic groups.

Thereby assisting in health-related policymaking and decision-making at all levels (35). Understanding the health needs of minority ethnic groups involves having access to large sample sized data within minority subgroups. In this thesis, I will examine the effect of both the aggregate classification and individual ethnic groups, where it is quantitatively possible.

There are numerous limitations of available data used to investigate difference between disease and risk in ethnic groups. The existing UK-based literature reflects a trend of including only one or two minority groups, rather than the full range of ethnicities, with often very small numbers in research studies. Limited studies have compared health disparities across several groups with a substantial sample size. To address these limitations to the existing body of evidence, in this thesis, I will be using the UK Biobank which contains in-depth health information from half a million UK participants, such that even a small percentage from 500,000 individuals will provide a large number of ethnic minorities in the data sample size therefore providing reliable estimates for lifestyle risk factor levels in UK ethnic minorities (36,37).

1.2 Diabetes Mellitus

Diabetes mellitus often referred to as diabetes is a non-communicable disease (NCD) that refers to several metabolic conditions characterized by raised blood glucose concentrations, also known as chronic hyperglycemia. Its occurrence is because the pancreas cannot produce the hormone, insulin or when the body cannot effectively use or becomes resistant to the effect of the insulin it produces. Diabetes is a major public health concern and represents an ever-rising threat on a global scale. It is estimated that 537 million people between ages of 20-79 years-10.5% of the world population in this age range-living with the condition have diabetes worldwide and is projected to increase to 783 million people by 2045(38). The highest numbers of adults with diabetes are reported in countries where individuals are from non-European White descent, including China, India and Pakistan living in South-East Asia (38). It is a major cause of morbidity including the increased risk of cardiovascular disease, blindness, chronic kidney disease, neurological disorders and peripheral vascular disease in the lower limbs, cancer, pregnancy complications and adverse oral health (38). Diabetes is also a major cause of increased risk of mortality. In 2021, it was estimated that approximately

6.7 million deaths in people aged 20-79 years was attributed to diabetes and its complications. The global cost spent on diabetes-related health expenditure was estimated to be USD 966 billion (11.5%). Diabetes increase is driven by an increasing ageing population (as risk of diabetes increases with age) and increase in the prevalence of lifestyle-related risk factors, mainly high levels of obesity and physical inactivity. This section provides an overview of some key aspects of diabetes with reference to evidence, and gaps in evidence with respect to epidemiology in the context of ethnicity, which is the focus of this thesis.

1.2.1 Definition

Diabetes mellitus is a complex chronic metabolic disorder characterized by hyperglycemia resulting from inadequate insulin secretion from the pancreas, reduced insulin action or both (39). Historically, the role of the pancreas in causing the condition was discovered in late 19th century, by a Dr Oskar Minkowski who experimented on dogs induced diabetes by removing their pancreas. He noticed that the urine from his dog which had undergone pancreatectomy attracted an unusually high number of flies. Curious he tasted the urine and was struck by its sweetness. Based on this observation, he was able to indicate that the pancreas contained regulators for controlling blood sugar level and therefore provided a model for the study of diabetes (40).

The human body is constantly working to maintain homeostasis and the pancreas plays an important role in this by regulating blood glucose levels through the release of two main hormones; insulin (beta cells in the islets of Langerhans) and glucagon (alpha cells) (41,42). When the blood glucose levels are rising too high, the pancreas releases insulin to communicate with the cells to store glucose. On the opposite side, when the blood glucose levels are decreasing too low, the body releases glucagon to tell the cells to release the stored glucose (39,43). The human body's blood glucose level has the potential to rise to unsafe levels that can cause damage to blood vessels and neurons if the body is not able to produce insulin or is insulin resistant. This is clinically known as hyperglycemia (39).

Diabetes is clinically diagnosed by the deterioration of several parameters including fasting plasma glucose (FPG), or from an oral 2-h plasma glucose value during a 75-g oral glucose tolerance test (OGTT) or from the measurement of

glycated haemoglobin-A1C (HbA1c) or postprandial glucose levels. The diagnosis criteria (39,44) are as follows:

- FPG \geq 126 mg/dL (7.0 mmol/L)
- 2-h plasma glucose \geq 200 mg/dL (11.1 mmol/L) during an OGTT (glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water)
- HbA1C \geq 6.5% (48 mmol/mol)⁶⁴
- In a patient with classic symptoms of hyperglycaemia, a random plasma glucose \geq 200 mg/dL (11.1 mmol/L).

1.2.2 Classification and types of diabetes

There are several types of diabetes, but most cases are of one of two forms; type 1 diabetes and type 2 diabetes. However, there are several other forms of the disease including gestational diabetes (diabetes in pregnancy in the absence of a previous history of diabetes), and various relatively uncommon monogenic forms of the disease.

In brief, type 1 diabetes, previously known as insulin-dependent diabetes mellitus (IDDM), is caused by the complete lack of insulin in the body. It is an autoimmune disease where the body attacks the beta-cells which produces insulin leading to the pancreas eventually producing little to no insulin to regulate the blood glucose level in the body (45). Type 1 diabetes accounts for between 5% and 10% of all diabetes cases and onset typically occurs in childhood or young adulthood, though it can occur at any age (38,45). Symptoms include excessive excretion of urine (polyuria), thirst (polydipsia), constant hunger, weight loss, vision changes, and fatigue. These symptoms may occur suddenly. Management of type 1 diabetes requires continuous insulin treatment using an injection or wearing an insulin pump to simulate the function of the beta-cells (39) In contrast to type 2 diabetes, risk of type 1 diabetes is not affected by lifestyle-related factors such as obesity and physical activity.

Type 2 diabetes results from the body's ineffective use of insulin. The disease was formerly called non-insulin dependent diabetes (NIDDM), or sometimes adult-

onset diabetes. Type 2 diabetes is the focus of this thesis and will be discussed in detail in the subsequent sections.

1.3 Type 2 Diabetes

Type 2 diabetes mellitus represents over 90% of all diabetes cases (45) and is recognized as one of the most urgent public health challenges of the 21st Century (45). It is caused by insensitivity of body cells (primarily in skeletal muscle, the liver and adipose tissue), to the actions of insulin, leading to high circulating insulin concentrations needed to maintain euglycemia, and the pancreatic beta cells being unable to produce sufficient insulin to compensate for this insulin resistance (46). This combination can be controlled for several years, but when the beta cells become unable to maintain the high level of insulin secretion needed to compensate for the insulin resistance, the blood glucose levels rise leading to type 2 diabetes (Ryden et al 2013). Notably, normoglycemic insulin resistant and pre-diabetes individuals are at increased risk of macrovascular complications caused by insulin resistance several years prior to the onset of type 2 diabetes. In contrast, risk of microvascular complications only increases substantially with the onset of diabetes. There are several risk factors for type 2 diabetes which will be considered in detail in the sections below.

1.4 Epidemiology of Type 2 Diabetes

1.4.1 Global prevalence of type 2 diabetes

Type 2 diabetes is the most common of diabetes and accounts for over 90% of all diabetes cases worldwide(47). According to the International Diabetes Federation (IDF) in 2021 the prevalence of diabetes amongst adults aged 20-79 years. The prevalence of diabetes is highest in countries with largely non-white populations. Thus, burden of diabetes is largely in non-white groups, but focus of much of the available research about risk of diabetes has been on white groups. This is a gap which this thesis aims to address(38).

1.4.2 Diabetes in the UK

Within the UK, prevalence of diagnosed diabetes has increased dramatically over the past three decades from 1.4 million to 3.8 million (~5.6% of the population) in 2019 (48). In addition, it is estimated that a further 1 million people living with type 2 diabetes and are unaware of their condition, resulting in a true prevalence estimation of 4.7 million (accounting for 7.4% of the population) (48).

1.4.3 Financial Burden of Type 2 Diabetes in the United Kingdom

Expenditure of diabetes management currently accounts for approximately one tenth of NHS total expenditure (48,49). In 2019, it was reported that an estimated £23.7 billion is spent a year on direct and indirect costs associated with diagnosed and undiagnosed diabetes in the UK, including treatment, intervention and complications or adverse events (50). 80% of NHS spending on diabetes goes into managing potentially preventable complications, accordingly the cost of prescribing medication for complications of diabetes is around 3 to 4 times the cost of prescribing diabetes medication. (49,50), This makes it the largest contributor to healthcare cost and reduced life expectancy.

1.4.4 Complications of type 2 diabetes

Complications of type 2 diabetes reduce the quality of life of the patients. Diabetes is a major contributor to kidney failure, amputations and cardiovascular disease, including heart attack and stroke(51). The complications of diabetic disease are caused by high levels of glucose in the blood which damages tissues by altering proteins, the complications of diabetes can be acute or chronic, and chronic is divided into microvascular and macrovascular.

The microvascular complications (neuropathy, nephropathy and retinopathy) occur in the smaller blood vessels, prolonged exposure of high levels of glucose results in progressive narrowing and occlusion of these small blood vessels, reducing perfusion, ischemia and damage to the tissues they supply. Microvascular complications include diabetic peripheral neuropathy; this begins in the extremities of the feet and hands; it is caused by progressive damage to the peripheral nerves as a result of sustained high blood glucose levels. Loss of

peripheral sensation makes people with diabetes particularly susceptible to foot ulcers, which along with other complications of poor blood perfusion and peripheral arterial disease can lead to gangrene and the need for limb amputation. People with peripheral artery disease and diabetes have an eight times greater risk of amputation (45,52,53). Diabetic nephropathy another microvascular complication of diabetes is the world's leading cause of end-stage renal disease in the developed world(39,42). It is characterized by persistent albuminuria (>300mg/24 hours) and a progressive decline in renal function(54). Diabetic retinopathy is the leading cause of blindness, caused by the abnormal growth of blood vessels in the retina. The damages occur in the endothelial cells in the retinal capillaries and causes abnormal vascular permeability, ischemia and retinal neovascularization(55). Studies allude a strong relationship between diabetic nephropathy and diabetic retinopathy(56,57). Therefore, a comprehensive of patients with either complications should include evaluation of the other.

The macrovascular complications of diabetes are related to the larger central and peripheral vessels, there is a two times increased risk factor for ischaemic stroke, ((45)), and for cardiovascular disease when the coronary vessels are involved (45)The increased risk of cardiovascular complications is five times higher in men, and eight times higher in women, who have diabetes (53).

1.5 Diabetes in minority ethnic groups - the scale of the problem

The nature of health disparities of diabetes in minority ethnic groups compared to the majority white Europeans in the United Kingdom makes this one of the most pressing issues facing the health sector and researchers today. Differences in the prevalence, incidence, mortality, adverse health conditions and burden of diabetes is alarming high among minority ethnic groups, in the UK, ranging from three times higher in Black African/Caribbean ethnic groups to five times higher in the South Asian ethnic group than in the White ethnic population ((58). Minority non-white European type 2 diabetes patients tend to also experience significant disparities and higher risk in the incidence of cardiovascular disease than the white European counterparts (59). Ethnic differences in complications caused by diabetes will be discussed in more detail in sections below. The high burden of type 2 diabetes in

minority ethnic groups means that addressing the ethnic disparities in diabetes risk and management is significant public health priority(60-63).

1.5.1 Complications in Ethnic minorities

Ethnic differences exist in the rates of microvascular and macrovascular complications caused by type 2 diabetes(42). In the UK South Asians are likely to have higher rates of nephropathy and end-stage renal disease (64,65), lower rates of retinopathy(64) and lower limb amputation (66), lower/equal rates of cardiovascular complications(67,68) compared to white Europeans while Black African/Caribbean participants had lower risks of lower limb amputation and cardiovascular complications, equal rates of retinopathy, nephropathy and end-stage renal disease compared with European whites(69). Interestingly, the differences ethnic in diabetic complications, particularly for Blacks seem to be distinct in the US. Lanting and colleagues performed a systematic review of 51 US and UK based studies(70) that showed that Blacks-African living in the US had higher risks of mortality, lower limb amputation, retinopathy, nephropathy and end-stage renal disease, compared to Whites (70,71). It is postulated that the differences between Blacks in the UK and US could be attributed to different migration histories influencing culture differences between both cohorts. It is also plausible that difference in healthcare systems, healthcare access and quality of care between both countries could explain the differences- access to care in the UK, with the National Health Service (NHS) being more equal among ethnic groups than in the US which is mostly provided by private sector healthcare services(70). Using the UK THIN database, Adjah et al investigated the ethnic differences in diabetes complications in relation to BMI. 'At diagnosis the rates of comorbidities were 30% in white Europeans compared with 11% of African-Caribbean and South Asian populations (72,73). Clear distinctions in the incidence of chronic kidney disease have been found, which is higher in white Europeans than both African-Caribbean and South Asian populations(72). Ethnic differences in the incidence of major cardiovascular diseases are also apparent; coronary heart disease is highest among South Asians, whereas African-Caribbean people experience significantly lower rates of coronary heart disease compared with white Europeans and South Asians, but rates of stroke do not differ by ethnicity(72,74). Investigations in the SABRE cohort are providing evidence for the mechanisms which may underlie these

ethnic patterns in cardiovascular diseases. For example, arterial stiffness has recently been reported to be more favourable among Black people compared with South Asians, which may explain some of the relative protection from coronary heart disease experienced by UK Black African or Caribbean groups' (75,76). In a focus on coronary heart disease among South Asian people, Park et al. (75) reported the detrimental impact of hyperglycemia on left ventricular failure in South Asians that is not seen in white Europeans.

1.6 Risk factors of diabetes

According to the WHO, any attribute, characteristic or exposure that predisposes an individual to disease is described as a risk factor(77). Risk factors for type 2 diabetes can be classed as modifiable and non-modifiable. Non-modifiable risk factors include age, sex, family history and ethnicity. However, diabetes risk factors are considered largely preventable and associated with lifestyle or behaviour, including obesity, physical inactivity, sedentariness, and poor diet(45).

As earlier discussed, the occurrence of type 2 diabetes is not evenly distributed across populations, particularly in ethnic minorities in UK and other westernized countries(45,47,78). Recognition of significant variability in diabetes prevalence has led to extensive research provides evidence that these disparities are driven by a complex interplay of biological, social healthcare system and lifestyle factors. This section gives an overview of diabetes, primarily focusing on Type 2 diabetes (T2D) and considered with relevance to the growing prevalence in the United Kingdom ethnic minority population. The focus of this thesis is mostly on the lifestyle factors, but I will briefly discuss other factors too.

1.6.1 Non-modifiable Risk Factors

1.6.1.1 Age

Globally, increasing life expectancy has resulted in ageing populations and is one of the main reasons for the upsurge in T2DM. T2D normally occurs from middle-age onwards and the incidence increases markedly with age. According to the International Diabetes Foundation (IDF), the prevalence of T2D is 2.6% in the 25-to-39-year age range, with a gradual increase with increasing age, up to 11% in

the 40-59 age range and 18.6% in the 60 and older age group(79). In the United Kingdom, 21.3% of persons over 60 years have diabetes in comparison to 14.6% in the 40-59 age group(80). Factors that are likely to contribute to the increase in the incidence of T2D with age include reduced insulin secretion and increased insulin resistance which may be due, in part, to age-related changes in the morphology and function of the β -cells in the pancreatic islets and decreased lean muscle mass(81). Age is also associated with changes in lifestyle risk factors such as reduced physical activity, weight gain and changes in dietary habits.

The incidence and prevalence of T2D are generally low before the age of 30 years. However, there has been a progressive increase in the prevalence of early onset T2D in younger adults and even teenagers(82).

Findings from the London Southall and Brent revisited (SABRE) cohort estimates that 40-50% of South Asian and Black men and women had twice prevalence the type 2 diabetes by age 80 years of life, compared to their age-matched white European counterparts in a sample of 4,202 (83). Paul et al conducted a case-control analysis of UK primary care data showed that on average, the age of onset of diabetes diagnosis maybe 10-12 earlier in South Asian (46 +/- 12 years) and Black (48 +/-12 years) population compared with Whites (58 +/-12 years)(73). Additionally, the study showed that a significant greater proportion of people within the minority ethnic population develop Type 2 diabetes before the age of 40 years compared with the predominant White ethnic group(73). The early onset of diabetes among minority ethnic populations is observed in other western countries. In Canada, Tenkorang found that the South Asians, Chinese, Blacks developed diabetes earlier than the Whites(84). Interestingly, the study also found that risk of developing diabetes vanished in Black women after accounting for lifestyle factors(84). To my knowledge, no study has assessed the comparison of age of onset of T2D in Chinese against White populations in the UK. The ethnic differences in the age of onset of diabetes may, in part, be attributed to an earlier decline in metabolic homeostasis and/or a shorter latency to the development of diabetes (84).

1.6.1.2 Sex

The prevalence of diabetes is higher among men than women, with 56% of cases occurring in men and 44% in women in the UK (85,86). However, the prognosis associated with diabetes is worse in women than men(53,87-89). Women with type 2 diabetes tend to have poorer glycaemic control(53,87-89) and women with T2D have a 4-fold increased risk of CVD mortality compared with a 3-fold higher in men(87-93).

However, men tend to develop T2D at a lower BMI than women (86,94-96) (94). However, there is limited research regarding whether the sex differences in diabetes prevalence differ between ethnic groups within the UK and whether it persists after consideration of important differences in BMI, socio-economic status (SES) and lifestyle factors between ethnicities. This is important as the occurrence of diabetes does not occur in isolation of these risk. This will be the focus of **Chapter 3** of this thesis.

1.6.1.3 Family history

Having a first-degree relative (parent or sibling) with diabetes is independently associated with a two-to-six-fold increased risk of T2D compared with individuals with no family history of the disease (97,98). The risk is greatest when there are multiple family members affected or the disease occurred at an early age of onset. The lifetime risk of diabetes is 15% for individuals who have one parent with T2D and 75% when both parents have the condition. This association is consistent across population studies and cultures(99,100).

1.6.2 Modifiable and Lifestyle-related Risk Factors

This section explores the ethnic variations of lifestyle/behavioural factors and components of physical health-related fitness in relation to diabetes health. Thus, the focus of this chapter is to review what is known about the variations in obesity, physical activity, sedentary as television viewing behaviour and muscular strength, in minority ethnic groups from South Asian, Black African/Caribbean and Chinese.

1.6.2.1 Obesity and fat distribution

Obesity is defined as an excessive accumulation of unused energy caused by a combination of excessive energy intake and insufficient energy expenditure. The excess energy is stored as fat in the adipose tissue. It appears to be the most important modifiable risk factor for type 2 diabetes. Abdullah and colleagues conducted a meta-analysis of 18 prospective studies including a total of 590,251 participants, of which 16,107 developed diabetes over follow-up period of 2-27 years, and found that, compared with individuals of normal weight, individuals who were overweight (defined as BMI 25-29.99 kg m⁻² in most of the included studies) had a relative risk of diabetes of 2.99 (95% confidence interval: 2.42 to 3.71), and those who were obese (defined an BMI \geq 30 kg m⁻² in most studies) had a relative risk of 7.19 (95% confidence interval: 5.74 to 9.00)(101). Weight gain in adulthood, particularly early adulthood, is also a strong risk factor for type 2 diabetes, as evidenced by meta-analysis of 15 eligible studies, by Kodama and colleagues, which examined the association between weight gain in early adulthood (aged 18-24 years) and later adulthood (from age 25 onwards) on risk of incident type 2 diabetes. Weight gain corresponding to a 5kg m⁻² increase in BMI in early adulthood was associated with three-fold increase (relative risk 3.07, 95% confidence interval 2.49 to 3.79) in risk of type 2 diabetes, with similar weight gain after age 25 being associated with a doubling of type 2 diabetes risk (relative risk 2.12, 95% confidence interval 1.74 to 2.58) (102).

While BMI has the advantage of being easy to measure, it is criticised as being a relatively crude measure of adiposity, as it does not distinguish between fat and lean mass, neither does it provide information about body fat distribution, distinguishing the amount of subcutaneous adipose tissue from the intra-abdominal or visceral fat, the fat depot that predicts the strongest development of diabetes risk(103). It is however increasingly recognised that other anthropometric measures, particularly ones which specifically provide indices of abdominal obesity (such as waist circumference, waist-to-hip or waist-to-height ratio) may likely confer a better indicator of type 2 diabetes risk(104). A meta-analysis of 15 studies, including 120,012 participants, of which 6,472 developed diabetes over mean follow-up period of six years, compared the strength of association of different anthropometric obesity indicators on risk of type 2

diabetes, finding that the difference of one standard deviation increment in BMI was associated with an increment in the relative risk of diabetes of 1.55 (95% confidence interval 1.43 to 1.69), whereas one standard deviation increments in waist circumference, waist-to-hip ratio and waist-to-height ratio were associated with relative risks of 1.63 (95% confidence interval 1.49 to 1.79), 1.52 (95% confidence interval 1.40 to 1.66), and 1.62 (95% confidence interval 1.48 to 1.78), respectively(105). All studies included in the meta-analysis showed that BMI or WC (or WHR) was strongly associated with type 2 diabetes independently. For any given BMI, the variation in waist circumference is considerable, and adults with higher BMI and higher waist circumference values are at increased risk of type 2 diabetes compared with those with lower BMI or waist circumference(106-108). This interpretation is supported by a study in the Health Professionals Follow-up Study of 27,270 male health professionals who were followed up for 13 years, reported that men who had a high BMI ≥ 25 and high waist circumference ≥ 102 cm had the highest relative risk of 8.7 (95%CI:6.8-11.1) compared to those who had a low BMI and waist circumference(106,109). Moreover, because both overall BMI and waist circumference independently predicted type 2 diabetes risk, it has been advocated that BMI and waist circumference should be used in combination to better assess the associated risk of type 2 diabetes with increased adiposity(104).

The relationship between adiposity and type 2 diabetes is likely to be casual. In the Diabetes Remission Clinical Trial (DiRECT) a randomised controlled trial in 298 patients with type 2 diabetes, who were randomised into 'usual care' or intensive structured weight-management programme involving 12 weeks of an approximately 800 kcal/day total diet replacement intervention, followed by gradual reintroduction over two months and then ongoing weight management support, Lean and colleagues found that at the average weight loss was 10 kg at 12 months and 7.6 kg at 24 months, with more than 45% of patients achieving diabetes remission at 12 months, which persisted until 24 months in more than 35% of patients. Higher levels of weight loss increased the chances of attaining diabetes remission, with 64% of patients maintaining at least 10 kg weight loss at 24 months achieving sustained diabetes remission(110,111).

Obesity plays a major role in the risk of type 2 diabetes across different ethnic groups(112), this means that not everyone with obesity develops the disease, whereas individuals with normal weight develop diabetes. This is especially so

when the excess adiposity is centrally distributed (i.e., have disproportionately large waist circumference). Ectopic fat depots are potential contributing mechanisms. Ectopic fat, defined as the deposition of triglycerides (TG) within cells of non-adipose tissues, is believed to be important to the development of Type 2 diabetes by causing metabolic disturbances in the organ or tissue in which it resides (113). Visceral (abdominal cavity) or truncal subcutaneous or liver and pancreatic fat are important ectopic depots.

It has been hypothesized that one reason for ethnic and sex differences in the association between adiposity and type 2 diabetes relates to the differences in the extent to which weight gain leads to ectopic fat accumulation(113-115) (Sattar and Gill 2014). In White populations, liver fat has been shown to consistently correlate with measure of insulin resistance(113-115). Individuals from South Asian and Chinese descent are at higher risk of diabetes at lower levels of BMI in comparison with White populations, because they have higher visceral (abdominal) deposit compared to Whites such that when there is a small weight gain, the fat is stored in the visceral (abdominal) increases their risk of insulin resistance and then type 2 diabetes (113).

A systematic review using findings from eight published and 3 unpublished datasets, including a total of 1853 South Asians and 5162 European White men and women reported separately that despite South Asian men having a mean BMI approximately 0.5-0.7 kg/m² lower than white European men (depending on the comparison), nine studies showed 0.34 standardized mean differences (SMD) (95% CI 0.12, 0.55; I²=83%) more subcutaneous adipose tissue (SAT) and seven studies showed 0.56 SMD (95% CI 0.14, 0.98; I²=93%) more liver fat, but nine studies had similar VAT (-0.03 SMD; 95% CI -0.24, 0.19; I²=85%) compared with their white European counterparts. South Asian women had an approximately 0.9 kg/m² lower BMI but 0.31 SMD (95% CI 0.14, 0.48; I²=53%) more liver fat than their white European counterparts in five studies. However, in women, Subcutaneous fat levels (0.03 SMD; 95% CI -0.17, 0.23; I²=72%) and visceral adipose tissue (VAT) levels (0.04 SMD; 95% CI -0.16, 0.24; I²=71%) did not differ significantly between ethnic groups in eight studies analysed(116). In Black population, visceral fat, liver and pancreatic fat has been reported to be lower compared with their White counterparts, however, the studies were conducted in mostly women and with a

focus on obese populations without diabetes(97,117). More studies on Blacks are needed to support this hypothesis.

South Asians and Chinese are also more likely to have a higher percentage bodyfat than Whites with the same BMI level(49,118). Huxel et al found that body fat in South Asians is up to 5% higher at any BMI value compared to Whites(119). Using mathematical modelling, Deurenberg predicted that for the same amount of body fat as Whites who have a BMI of 30 kg/m^2 , the BMI cut-off points for obesity would have to be approximately 27 kg/m^2 for people from Chinese descent compared to their White counterparts(118). These findings were consistent in other studies (81,120,121)(122), reported that the cut-off of 25% body fat in white males corresponded to a BMI of 26.2 kg/m^2 in male Chinese adults and the cut-off value of 35% body fat in white female adults corresponded to a BMI of 24.4 kg/m^2 in their Chinese women(108,122). Rush et al showed that BMI of 26 kg/m^2 in Indian Women corresponded to BMI of 30 kg/m^2 at the same BF% value as European white correspondingly (81). This evidence led to proposals that perhaps the thresholds used to measure obesity, which were derived from predominantly white populations, may not be applicable for those from non-white European descent and that the values for adiposity either for whole body (BMI) or abdominal (Waist Circumference) for minority ethnic groups need to be revised (58,123-128). The WHO and IDF recognise this and reviewed the BMI and WC obesity and obese thresholds for diabetes in people from South Asian and Chinese ethnic background. However, whether these values have been based on studies with small numbers of the ethnic minorities and more robust studies are needed to support the recommendations. This thesis aims to contribute to the research using a more robust data and analyses. More details on ethnic specific obesity cut-offs will be discussed later in the thesis.

In contrast, the high susceptibility to type 2 diabetes in Blacks cannot be explained by abdominal visceral fat. Compared with White ethnic groups Blacks have lower quantity of VAT at same BMI, while the corresponding subcutaneous adipose tissue depot (SAT) tends to be the same or greater in Blacks than Whites in both women and men(129-132). In a UK study, Eastwood et al reported higher levels of truncal subcutaneous fat in African/Caribbean subgroup were associated peripheral insulin resistance, which may contribute to their excess diabetes risk in the absence of high levels of estimated VAT(97). It has been suggested that Black's

susceptibility to diabetes may be due to having more intermuscular fat than do whites or Asians even after adjustment for differences in total adiposity, skeletal muscle mass and other potential covariates(61,133). Additionally, studies have found that Blacks have lower body fat and higher lean muscle mass than whites of the same weight and height (81,134). For example, Heymsfield systematically reviewed the magnitude of these ethnic differences across white, Black, and Mexican American adults, using data analyses from the US National Health and Nutrition Examination Survey(134). They found that percent bodyfat was lower in Blacks than whites or Mexicans, even after controlling for BMI, gender and age (63,134). These ethnic differences in body fat-BMI relationships also appear to be more pronounced in women than men (63,134-136).

1.6.2.2 Ethnic-Specific Obesity Thresholds to Predict Diabetes Risk

As previously discussed, studies have suggested the need for ethnic specific obesity cut points related to diabetes risk in Asians (referring to both Chinese and South Asian descent) and Blacks be different from European Whites. Some of these studies were carried out in native countries while others are countries where they are minority populations. Particularly for Indians, Bangladeshis and Chinese descent, research have been carried out in the native countries. However, fewer studies have been conducted for Blacks in western countries and none in Sub-Saharan or Caribbean countries, albeit most studies that have tried to redefine obesity cut offs for Blacks have been on metabolic syndrome. This section would review the studies on ethnicity and type 2 diabetes differences in South Asian, Chinese, and Black ethnic groups, and with which to determine the optimal ethnic-specific obesity thresholds that predicts diabetes equivalent to White European descents.

Caleyachetty and colleagues using the Clinical Practice Research Datalink (CPRD), a general practitioner practice database to determine the risk-equivalent BMI cutoff for obesity in South Asians, Black and Chinese populations. They suggested that the age-sex-adjusted incidence of type 2 diabetes BMI cutoffs in South Asians to be (23.9 kg/m²), Black (28.1 kg/m²), Chinese (26.9 kg/m²)(137). However, in this study the BMI values were opportunistic, that is were only recorded in patients who visited general practice for a clinical problem, maybe not related to diabetes,

findings are therefore biased by incomplete reporting and skewed sampling of data used in the study analysis.

Bodicoat and colleagues conducted in the ADDITION-Leicester, Jaipur Heart Watch and New Delhi study cohort including individuals drawn from UK and Indigenous Indian studies(138). The ADDITION-Leicester study (ADDITION stands for Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen Detected Diabetes in Primary Care) included individuals drawn from the baseline data at the screening phase (2005-2009) who were aged 40-75 years old of White European ethnicity and 25-75 years if of Asian, Black and Chinese ethnicity; who were not previously diagnosed of diabetes, terminal or psychiatric illness, pregnant/lactating or housebound (139) as part of a two-phase UK-based multi-centred randomised controlled trial that screens and evaluated the effectiveness of cardiovascular disease treatments over five years who were invited through the general practices in the Leicestershire and Rutland Strategic Health Authority area. New Delhi cohort conducted between 1998-2003 included individuals who were randomly selected from various residential colonies in New Delhi, aged between 40-75 years The JHW Study was a house-to-house survey conducted in 2001 in Jaipur, Rajasthan, Northern India involving participants aged 20-75 years (128,138). A total of 6998 (4672 whites, 1348 migrant South Asians (MSAs) and 985 Indigenous Indians) participants aged 40-75 years were included in the study. The study applied the fractional polynomial to determine the cut-points of BMI and WC that was equivalent to obesity in Whites, and diabetes was defined on the basis of elevated fasting and elevated post-load 2-hour glucose. From the study, both South Asian groups the cut-points equivalent to 30 kg/m² in the white group were 24.9 kg/m² for MSA and 18.2kg/m² for indigenous Indians based on fasting glucose and 21.1 kg/m² based on 2-hour glucose for migrant South Asians. Likewise, among men, the South Asian groups had a lower cut-point for WC (102 cm in white men) at 90 cm in MSAs and 87.1cm in ISAs based on fasting glucose and 78.8cm based on 2-hour glucose for MSAs. Similarly, South Asian women had a lower cut-point for WC in comparison to 88 cm in white women at 77.1 cm in MSAs and 53.5 cm for ISAs for fasting glucose and 71.7cm for 2-hour glucose in MSA. In this study the model was minimally adjusted for just age. However, by not adjusting for other potential confounding factors such as socio-economic status and smoking habits that are likely to influence the development of diabetes and obesity, their findings

could be under adjusted and biased. Also, there was variation in the data collection methods used to assay glucose tolerance measurements, hence due to these differences, the estimates for migrant SAs might be less precise than those for Indigenous Indians. The body composition of ISA and MSA were different which may have also affected the cut-points as there may be variations depending on the geographic location(128,138), including the environmental and social differences between the study populations in India and the UK, some of which may likely influence the impact of body mass on diabetes and the proposed cut-points(118,140,141). As many important covariates, the analysis model may not have been adequately comparable between the study populations.

The Southall and Brent Revisited (SABRE) study (127) is a prospective investigation of cardiovascular disease and diabetes risk factors among 40 to 69 years old White European, South Asian (93% Indian Asian and Pakistan) and Black (91.5% Caribbean and west African) industrial workers and attendees from general practitioners list living in London which took place between 1998 and 1991. Overall, 6,369 adults took part in the main study, and approximately 2,531 (23.1% women) participated in the follow-up study used to define ethnic risk equivalent of obesity-related diabetes risk using the logistic regression and cubic spline three-knot analysis. The findings from the study, Tillin and colleagues suggested that age-sex adjusted BMI cut-off points of 25.2 kg/m² in South Asians and 27.2 kg/m² in Blacks were equivalent risk for diabetes as with BMI of 30 kg/m² among White Europeans. For central obesity, South Asian and Black men, had almost identical waist circumference cut-points of 90.6 and 90.4cm respectively were equivalent to a value of 102cm in European men. Waist circumference cut-points of 84.0cm in South Asian women and 81.2cm in Black women were associated with diabetes incidence rates equivalent to a value of 88cm in European women. Additional adjustment for years of education, smoking, triglycerides and systolic blood pressure barely altered the ethnicity-specific cut-points for BMI and waist circumference for South Asians and Black populations(142). However, the study was limited by the small sample size which may undermine the precision of the study (143). Secondly, the assumptions are based on a 20-year-old data. In view of the time of the analysis, the demographics and the population distribution within which the data was collected would have changed over the years and may

not well be representative of either the White, South Asian or Black population at present.

Stommel, 2010.(126) in a cohort study from the US National Health Interview Survey (NHIS) aged 18 years and over, in a sample size of 337,375 individuals from white, African, East Asian (Chinese, Japanese, Koreans, and Vietnamese), and Hispanics ethnic groups reported that among the 47,468 participants in the US Black subgroups the prevalence of diabetes was 9.3% and the prevalence of diabetes among 219,521 participants in the White subgroup was 6.1%. The graphical plot of diabetes prevalence against BMI categories in a width of 1-unit kg/m^2 ranged between 20-32 kg/m^2 suggests that prevalence of diabetes is approximately equivalent at a BMI of 26 kg/m^2 among Black participants to the prevalence of 30 kg/m^2 among white participants, a difference of -4 kg/m^2 . At 25 kg/m^2 among white participants the equivalent prevalence is seen at approximately 22 kg/m^2 among Black participants, a difference of about -3 kg/m^2 . However, this study was limited by the use of BMI values based on self-reported height and weight of participants which tend to be overstated and self-reported diabetes status.

Chiu and colleagues(144) conducted a multi-ethnic prospective study using regression and cubic spline analysis compared incident diabetes and derived ethnically appropriate BMI cut-off for obesity associated with diabetes risk across White, South Asian, Chinese and Black ethnic groups aged 30 years and above, living in Ontario, Canada. 57,210 whites, 1,0001 South Asians, 866 Chinese and 747 Black participants were included in the subgroups. Elevated risk of diabetes was evident in both South Asians and Blacks but not in Chinese HR=1.15 (95%CI:0.73-1.6). Compared to the white subgroup, South Asians had a 2.63-fold (2.63, 95%CI 1.99-3.27) increased age-sex-adjusted risk of incident diabetes; the cox proportional hazard ratio for age-sex adjusted diabetes risk for Blacks was 2.04 (95% CI 1.50 to 2.68) compared to whites. Based on the adjusted incidence of diabetes the equivalent BMI values (kg/m^2) for 30 kg/m^2 in Whites was recommended as 24 kg/m^2 in South Asians and 26 kg/m^2 in Blacks, the difference of -6 kg/m^2 and -4 kg/m^2 respectively. The study was limited by the absence of description of the diagnostic criteria used to identify diabetes cases and did not include any confidence intervals to indicate the precision of their cut-off estimates (144). In addition, the study the data collected on body composition

was of questionable accuracy and precision since the BMI was calculated from self-reported height and weight. It has been shown that both male and female participants have a tendency to over report their height and under-report weight, which may consequently affect the result of BMI(145). BMI estimation could also be biased on ethnic perception of body size, some ethnic groups particularly South Asians and Blacks (146) underestimate their weight which could potentially create analytical errors in the study.

Araneta et al (147) combined cross-sectional data from four community-based studies to determine the optimum BMI cut point that might practically identify Asian adults aged 45 year and above across 1,663 Asian Americans from South Asian (N= 609), Filipino, Japanese, Chinese, Korean and mixed Eastern Asia ancestry. Using ROC analysis, they suggest that at BMI of 23.4kg/m² the probability of missing potential cases of type 2 diabetes would be reduced by 15% and a high sensitivity of 84.2% to predict diabetes risk and identify South Asians who should undergo diabetes screening for those aged above 35 years old. The study sample was limited to just 609 South Asian. Although individuals from Chinese descent were recruited in the study, the BMI cut point for Chinese subgroup was not determined and this could have been because of the same size of less than 18 participants.

One of the earlier studies of waist circumference on Asian Indians by Misra et al(148) showed detailed analysis of WC cut-off points using multiple cardiovascular risk factors and BMI.

According to Ramachandran et al(149), in Indians with normal Body Mass Index (BMI), the cut-off values for WC was 85 cm for men and 80 cm for women and for WHR was 0.89 for men and 0.81 for women.

Nyamdorj, et al conducted a review and meta-analysis of pooled data from 30 cross-sectional (DECODA (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Asia) and DECODE (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe) studies including a total of 54,467 participants aged 30 years and older conducted in 11 Asian and European countries from Asian Indian, Mauritian Indian, Chinese and European white descent,(150). Analysis was performed for Asian Indian and Mauritian Indians separately. The

mean baseline BMIs in Indians were: 22.0 to 23.3 kg/m² for males and 23.7 to 24.5 kg/m², 24.3 to 26.6 kg/m² in Chinese males, and 24.3 to 26.3 kg/m² in Chinese females and 25.5 to 27.9 kg/m² among European males and 25.2 to 28.1 kg/m² among European females. The Mean baseline WC ranged from 83.5 to 89.9 cm in Chinese males, 76.6 to 83.4 cm in Chinese females, 91.4 to 98.4 cm in European males and 77.6 to 86.9 cm in European females. At the same BMI or WC levels, undiagnosed diabetes was more prevalent in Indian participants followed by Chinese participants than Europeans. At 30kg/m² in Europeans whites the equivalent prevalence of diabetes was at BMI cut-off of 19.0kg/m² in Indian men and 20 kg/m² in the Indian women, 25 kg/m² for Chinese males and 22 kg/m² in Chinese females. The pooled risk equivalence for undiagnosed diabetes for European men at WC of 102 cm is 73 cm for Indian men and 82 cm for Chinese men. For European women at WC of 88 cm the equivalent undiagnosed diabetes was 67cm in Indian women and 73 cm among Chinese women (150,151).

In a cohort study of 2088 participants who were older than 35 years (152) found that WHR and WC were better adiposity metrics for identifying diabetes risk in a Chinese population in both men and women. In the study, they found that optimal WC cut -off points at 90cm for men and 86cm for women with a sensitivity greater than 70% and specificity greater than 50%.

Pal et al(153) conducted a study in West Bengal, India on 654 subjects aged between 18-60 years using ROC analysis, the researchers determined that appropriate cut-off points of BMI overweight and obesity of 21.87 kg/m² and 24.33kg/m² respectively.

Bhowmik(154) conducted a cross-sectional study in 2293 participants resident in Bangladeshi to evaluate the anthropometric indicators that can predict diabetes and other cardiometabolic risk factors using ROC analysis reported that the optimal cut-off points for diabetes detection were at a BMI of 21.2 kg/m² in men and 21.8 kg/m² in women, WC 82 cm in both men and women, WHR 0.93 and 0.87 and WHR 0.53 and 0.54 respectively. The researchers also found that, the AUC for each of the three central obesity indices were significantly higher than for BMI. In comparison to BMI, WC and WHR measures, WHR had the highest diagnostic values for the detection of diabetes in both sexes. Although the study recommends that cut-off values should be readjusted for different populations, the analyses of cut-

points were unadjusted for confounding variables such as age. Therefore, the relationship between each anthropometric measure and disease risk may underestimate the actual predictive value calculated in ROC analysis in the study.

Hunma et al(155) conducted a cross-sectional study in 175 Mauritius residents to determine the optimal BMI cut-off points for overweight and obese categories in Creole and Indian populations living in Mauritius. The optimal BMI cut-off points for Indian men was 21kg/m² for overweight and 26kg/m² for obese and in Indian women at 22kg/m² was for overweight and 27kg/m² for obese.

Using ROC analysis, Cai and colleagues conducted a cross-sectional study (156) in 3505 among Chinese pulmonary tuberculosis patients aged 18-45 years recruited in a hospital setting found BMI cut-off points at 22.2kg/m² to screen for impaired fasting glucose and 22.3kg/m² to screen for diabetes. However, the study limitation included being conducted in a relatively younger population who were ill and probably had lost weight due to illness as mean BMI of study participants was 21.6-22.6kg/m². Therefore, the accuracy of BMI cut-off point suggested to predict either impaired fasting glucose and diabetes conditions was insufficient.

Using principal components factor analysis to examine associations between body mass index and the prevalence of factors related to glucose metabolism, a Canadian study by Razak et al suggested a BMI cut-off of 21.0 kg/m² in South Asian men and women (124) and Chinese was 20.6 kg/m². Although it was a small sample size 1078 (301 Europeans vs 289 SA vs 281 Chinese).

Gray et al measuring glycaemic risk score, produced BMI cut-offs of 21.5 kg/m² and 22.6 kg/m² for South Asian men and women, respectively, as being equivalent to a BMI of 30.0 kg/m² in whites (123).

In a cohort study by Cameron et al (157) at a WC of 62 cm, South Asian men experience the same diabetes risk as European men exhibit at 102 cm.

1.6.2.3 Policy Context of Obesity Cutoffs

These suggests that conventional clinical thresholds for obesity that were originally derived from populations of white European descent as BMI of ≥ 30 kg/m²

or greater (158), or a waist circumference ≥ 88 cm in women or ≥ 102 cm in men (159), may not be appropriate for non-white groups (117,160).

Based on evidence data experts agreed that due to the heterogeneity of obesity levels in different populations there is need for lower anthropometric measures of obesity to determine diabetes risk in non-white ethnic populations that would potentially reflect the true estimate of risk in these populations. In response to the findings that different criteria for obesity may be needed for Asian populations (primarily South and East Asians), recommendations for BMI and WC cut-off values were made by the World health organisation (WHO), and International Diabetes Federation (IDF) have proposed the development of different thresholds for defining overweight and obesity in Asian populations worldwide, with the WHO Expert consultation on Obesity in Asian and Pacific recommending that overweight should be defined as BMI > 23 kg/m² and obese as BMI > 27.5 kg/m² in Asian populations (WHO Expert Consultation, 2004, 2008). In addition to the WHO definitions, the IDF emphasized on the primary importance of central obesity as assessed by waist circumference with ethnic - specific cut-offs. Therefore, an International Diabetes Federation (IDF) consensus, which was issued in 2005 recommended waist circumference cut-offs of 80 cm for Asian women and 90 cm for Asian men (IDF, 2005) for identifying persons with abdominal obesity. However, the Indian consensus committee argued that the reviewed thresholds were derived from limited data that definition of obesity need to be revised for Asian Indians, therefore suggested that slightly lower cut-offs for BMI of 18.0-22.9 kg/m², 23-24.9kg/m² and 25 kg/m², for normal, overweight and obesity respectively, should be used for Indians (Misra et al., 2009). Additionally, the committee recommended that at WC cut-offs of Men: 78 cm, women: 72 cm for individuals should seek lifestyle interventions to avoid gaining weight and at WC cut-off for Men: 90 cm, women: 80 cm individuals should seek medical interventions for obesity -related risk factor investigation and management. They consented that both BMI and WC are equally important, hence should be used together for population- and clinic-based risk stratification(161). In China, the department of disease control ministry of health guidelines for prevention and control of overweight and obesity define overweight as BMI ≥ 24 kg/m² and obesity as BMI ≥ 28 kg/m² (162,163). Studies in individuals from Black African descent are relatively few and suffer from limitations in methodology, sample size, or design.

Therefore, for the interim IDF and WHO has suggested that the European cut-offs for WC and BMI should be used for Black populations until sufficient data are generated (IDF, 2005(159). At the time, in the UK, the National Institute of Clinical Excellence (NICE) did not adopt these guidelines to the UK health care guidelines as the available evidence were moderately or negligibly applicable to the UK Black and minority ethnic (BME) population and in 2013 during the development of their guidelines for BMI population noted this gap in research and recommend the need for further research on obesity thresholds related to diabetes risk with relevance to the UK population. Currently, in the UK the current guideline recommends the use of lower BMI thresholds of BMI of 23-27.5kg/m² indicating increased risk and a BMI higher than 27.5kg/m² indicates high risk for South Asian and Chinese populations jointly referred to as Asians compared to the equivalent diabetes risk thresholds of BMI higher than 25kg/m² for overweight and BMI higher than 30kg/m² as obese in white populations. The guideline also recommends lower WC thresholds of 94cm in South Asian and Chinese men, while the threshold of 80cm for women which is same value as that for White European women. However, the sensitivity and specificity the thresholds would identify at risk individuals in these groups has yet to be determined. Furthermore, in 2015, the American Diabetes Association recommended the change of the BMI threshold for screening overweight or obese Asian Americans for pre-diabetes and type 2 diabetes from 25 to 23 kg/m² based on evidence shown that this population is at increased risk for diabetes at lower BMI levels relative to the general US population (164). Compared to South Asians and Chinese minority ethnic populations, relatively fewer research have studied obesity cut-points for diabetes risk in those from Black descent, such that the BMI and WC thresholds or cut-points derived from populations of European ancestry are currently recommended for assessing diabetes risk in Black Africans in the absence of sufficient data from African populations(159,165) and NICE recommend the use of Asian BMI thresholds and European WC thresholds for Blacks. However, as ethnic differences in the relationship between adiposity and diabetes are shown to be different in Black populations from those determined by European White and Asian populations, then the optimal obesity threshold indicating increased risk of diabetes will also be different in Black populations juxtaposed to diabetes risk in White, South Asian, or Chinese ethnic population(42). Therefore, the research in this thesis will address this research gap. Since the scope of this research focuses on diabetes, I

have not systematically research on obesity cutoff studies that did not include diabetes in their research.

One limitation of the available data is that most cohorts on adiposity differences between ethnic groups often rely on relatively small numbers of non-white participants within limited geographical locations (127), use of different body composition methods and instruments across the evaluated ethnic groups (138), use body composition methods of questionable accuracy and precision(144) and they include limited demographic descriptions of evaluated subjects, making it difficult to obtain robust estimates of the BMI and waist circumference at which diabetes is prevalence. Furthermore, despite diabetes prevalence differing markedly between South Asians and Chinese populations (166), current proposals for ethnicity-specific obesity cut-offs have generally considered Asians as a single group; and have not evaluated whether obesity thresholds should differ between ethnic groups of Asian origin. Therefore, this thesis aims to address the concerns of the sample and methodology on ethnic differences in obesity-related diabetes, whether the differences still remain after, if so, what is the magnitude (or if so, the magnitude of this effect). It will also add to the existing approaches for developing ethnic-specific determination of obesity classification for White, Black, Chinese and South Asian populations in the UK. This research will evaluate various body measures recommended by previous studies as indicators of obesity such as BMI, waist circumference, waist-to hip ratio (WHR), Body fat percent (BF%) and Waist-to-height ratio (WHR). The thesis would therefore, compare the relationship between adiposity and prevalence of diabetes across ethnic groups in large study (UK Biobank, which is discussed in **chapter 2**) and then determine ethnic specific cut-offs of obesity based on the probability of having obesity-related diabetes risk in Black, Chinese and South Asian ethnic populations that are equivalent to those developed for white populations in terms of diabetes prevalence. Addressing these questions will provide a baseline health policy intervention.

1.6.2.4 Physical Activity

Physical activity is defined as bodily movement produced by skeletal muscles that substantially increases energy expenditure(45) Humans can engage in a range of physical activities that include varying levels of intensities, from light activities

of walking to very high intensity and structured exercise. Physical activity is usually quantified by the time spent in doing all the activities, which is grouped together as total physical activity or grouped together as moderate-to-vigorous physical activity (MVPA). A common approach to epidemiological research and public health guidance is to characterise activity intensities using metabolic equivalents (METs), which measures intensity in multiples of the resting metabolic rate (assumed to correspond to an oxygen uptake of $3.5 \text{ ml kg}^{-1} \text{ min}^{-1}$).

Studies are consistent in reporting physical inactivity as a risk factor for type 2 diabetes. This observation has been confirmed in meta-analyses studies summarising the findings (167-169). Smith and colleagues included 28 eligible cohort studies with a total of 1,261,991 participants and 84,134 incident cases of type 2 diabetes over follow-up periods ranging from 3 to 23 years (168). This analysis revealed a non-linear relationship between level of self-reported leisure-time physical activity and risk of type 2 diabetes with the largest benefit occurring with increments of physical activity at the lower end of the volume range. Compared with those who were inactive, those achieving $11.25 \text{ MET-h week}^{-1}$ of physical activity (equivalent to $150 \text{ min week}^{-1}$ of MVPA) had a 26% lower risk (95% confidence interval 20% to 31%), of developing type 2 diabetes, whereas those achieving twice this amount of physical activity had a 36% lower risk (95% confidence interval 27% to 46%) (168) (Smith et al. 2016). Notably, studies have found that association between physical activity and risk of diabetes is partially independent of or partially mediated by the effects of physical activity on adiposity, mostly BMI. The meta-analysis by Jeon and colleagues, which examined the association between moderate intensity physical activity and risk of type 2 diabetes in 10 prospective cohort studies including 310,221 participants and 9,367 with incident type 2 diabetes, compared risk in those reporting the highest versus lowest levels of moderate-intensity physical activity in analyses with and without adjustment for BMI (167). BMI-adjustment attenuated the risk reduction associated with undertaking a high level of moderate-intensity physical activity from 31% (95% confidence interval 17% to 42%) to 17% (95% confidence interval 10% to 24%), but the association remained statistically significant. These data indicate that the association between physical activity and risk of diabetes is partially independent of, and partially mediated by, the effects of physical activity on BMI. Although, high levels of physical activity can attenuate the excess

risk of type 2 diabetes in overweight and obese individuals, diabetes risk still remains high in active individuals with high BMI. Therefore, encouraging weight loss in addition to adopting a healthy lifestyle is critical for type 2 diabetes prevention(170).

Most studies on physical activity and type 2 diabetes have been performed in participants of white European origin, with relatively few from South Asian and Black African population. Thus, there are limited data examining the dose-response relationship between physical activity and diabetes risk amongst the non-white populations who are at highest risk of type 2 diabetes. Findings from cross-sectional studies comparing the association between physical activity and metabolic risk factors between South Asian and white European adults suggests that for equivalent MVPA of 150min/week in White Europeans, South Asians may require higher MVPA levels of 232- 266 mins/week in South Asian men and women to achieve favourable metabolic profiles for insulin sensitivity and glycaemia (62,171,172), but substantial further work is needed to understand ethnic differences in the association between physical activity and type 2 diabetes risk more fully.

1.6.2.5 Diabetes Lifestyle Intervention Trials

Evidence shows that lifestyle interventions via increased physical activity can improve insulin sensitivity and glucose control, which is likely to be the key mechanism by which activity affects risk of type 2 diabetes. Effects of physical activity on adiposity, particularly on visceral fat and ectopic fat in the liver, are also likely to contribute(173,174). These adiposity changes can occur even in the absence of weight loss(175). Key lifestyle interventions that have focused on diabetes prevention trials include:

In the Da Qing Diabetes Prevention study,(176) Pan et al, recruited 577 Chinese adults with impaired glucose tolerance from 33 clinics, who were originally followed for 6-years from, 1986 to 1992. The participants were randomly assigned to either an information only control group or to one of three intervention groups: diet only, exercise only, or diet plus exercise group. In the diet only group, participants with BMI $<25\text{kg}/\text{m}^2$ were prescribed diet containing 25-30 Kcal per kg body weight, with 55-65% energy from carbohydrate, 10-15% protein, and 25-30%

fat, and encouraged to consume more vegetables, control alcohol intake and reduce sugar intake. Those with BMI ≥ 25 kg/m² was also encouraged to lose weight until they achieved BMI 23 kg/m². Exercise only intervention involved the increased leisure-time exercise by at least 1 unit per day, where 1 unit equated to 30 mins of mild exercise (e.g., slow walking) or 20 mins of moderate exercise (e.g., brisk walking) or 10 mins of strenuous exercise (e.g., slow running or climbing stairs) or 5 mins of very strenuous exercise (e.g., jumping rope, basketball). Meanwhile, participants in both diet plus exercise group were exposed to combined interventions similar to the diet-only and exercise only groups. At the end of the six-year follow-up, the mean cumulative incidence of diabetes over follow-up was 65.9% for control clinics, 47.1% for diet clinics, 44.2% for exercise clinics, and 44.6% for Diet plus Exercise clinics. Compared to the control group, the incidence of diabetes was lower in the intervention groups (Hazard Ratio:31%, 46%, 42% in the diet, exercise and diet-plus-exercise groups respectively(176). Subsequently, after continued follow-up of 94% of the original participants for another 30 years (177), the investigators combined the three active intervention groups into a single group for follow-up analysis of complications. Compared to control, the intervention reduced incidence of diabetes by 39% (Hazard ratio: 0.61; 95%CI: 0.45-0.83). In addition, the 30-year follow-up data showed that participants who were exposed to the lifestyle interventions experienced delayed onset of type 2 diabetes by around 4 years, a lower incidence of diabetes-related complications and a longer life expectancy in comparison to the controls(177). This is one of the first lifestyle randomised controlled trials on physical activity and diabetes to demonstrate interventions can be effective. It is noteworthy to state that the significant effect was observed over a 30-year period (177).

In the Indian Diabetes Prevention Programme (IDDP)(178), Ramachandran and colleagues recruited 531 Asian Indians for three years with impaired glucose randomised to either lifestyle or metformin, as controls and metformin plus lifestyle as intervention group. The intervention involved and increased walking for more than 30mins per day if sedentary or engaged in lifestyle physical activity as baseline; those already involved in physical activity at baseline including walking or cycling more than 30mins per day or any form of physical activity were encouraged to maintain this lifestyle. Dietary advice was given to reduce total

calories, refined sugars and fats, to avoid sugar and increase fibre-rich foods. After 3 years, lifestyle intervention was similarly effective as use of metformin to prevent incidence diabetes, without weight loss or change in waist circumference. The cumulative incidence of diabetes was 55.0%, 39.3%, 40.5% and 39.5% in the control, lifestyle, metformin and lifestyle plus metformin intervention groups. Compared to the control group, incidence of diabetes was 28.5% lower in the lifestyle group, 28.2% lower in the lifestyle plus metformin group and 26.4% lower in the metformin group (178).

In the UK, the English National Diabetes Prevention Programme was launched in 2015 where over 324,699 people were referred to the programme over a period of 3 years, and amongst the 32,665 who had sufficient time to complete the nine-month behaviour change intervention, increased their physical activity levels, lose weight and improved their diet quality. A mean weight loss of 2.3 kg and a reduction in HbA1c of 1.3mmol.mol⁻¹ was observed (179). Notably in this study was the extent of weight loss and HbA1c reduction was strongly associated with attendance of participants to the intervention sessions. In this study it was observed that loss to follow up was highest amongst the South Asians and weight change was lowest (-1.0kg in South Asians vs -2.5kg in Whites)(179).

1.6.2.6 Sedentary Behaviour

The definition of sedentary behaviour has been evolving during the last decade. In past, sedentary behaviour was conceptualized as the absence of moderate-to-vigorous physical activities or not meeting current recommendations for physical activity (180). Indeed, high levels of sedentary behaviours can coexist with high levels of physical activity. However, sedentary behaviour (too much time spent sitting down) is distinct from physical inactivity and it is possible for an individual to be both highly physically active and highly sedentary; for example, an individual can cycle for an hour but spend the whole day sitting down watching television or working. Sedentary behaviour is defined as sitting or reclined posture activities that does not increase energy expenditure above resting levels ≤ 1.5 METs (181), and until recently, sedentary activities typically included only sleeping and lying down (182). Conversely, research has shown that there are other activities that make up sedentary behaviour (183,184). These activities include, but are not limited to, sitting or lying down, watching television, riding in a vehicle, computer

and video game use (or other screen-based behaviour), and workplace sitting (185), although most studies have focused on television watching or screen time, which could alternatively be described as computer and television use as the largest contributing factor to time spent in sedentary behaviour (182,183,186).

Nowadays, there are rapidly evolving innovations that have led to an increase in labour-saving devices and technological advances(187). These technological advances encourage us to spend more time in reclining or sitting positions; thus, sedentary activities have essentially been engineered into our lives across many settings including home, workplace and transportation (188). Sedentary behaviour (SB) is prevalent globally and takes up a substantial proportion of the average adult's day including in both developed and developing countries (186). Studies have shown that adults spend around 9h per day (out of ~16 hours waking hours) in sedentary pursuits (189) such as television viewing, computer use, or driving(187,190-192). Television watching is one of the most prevalent sedentary behaviours to be studied(191,193). Recent government surveys and academic research suggest that Europeans spend approximately 40% of their free time (approximately 4h/day) watching TV(187), while Australians and Americans spend an average of 5 hours per day, sitting in front of a television(194,195). A Public Health England report has shown that more than 40% of men and 35% of women spend more than 6 hours per day sitting still or desk-bound(196), and people are reporting engaging in higher levels of sedentary behaviour than ever before (189). This shift in lifestyles has impacted total daily energy expenditure and overall health and well-being(187,190). Sitting for long periods may have detrimental physiological effects as it reduces the skeletal muscular contractions which consequently leads to peripheral insulin resistance (197) In addition, lipoprotein lipase regulation is linked to local contractile activity and the decreased activity seen during sedentary behaviour leads to increased plasma triacylglycerol and reduced high density lipoprotein levels (198). Non-exercise activity thermogenesis (NEAT) also affects body fat and influences weight gain (199) . Therefore, decreasing time spent in sedentary behaviour is of substantial interest to the field of public health because it is prevalent and is linked with multiple chronic diseases(192).

1.6.2.7 Sedentary Behaviour and Diabetes

Sedentary behaviour, have been found to be associated with an increased risk of diabetes, cardiovascular disease, and total mortality (200-202). Several studies have addressed the association between sitting time during leisure, television viewing or total sedentary time and diabetes or diabetes-related outcomes regardless of physical activity levels (201,203,204). Recently, a 3-year follow-up of the US diabetes prevention programme demonstrated reduced Type 2 diabetes incidence with the lowest sedentary time (205). These observations are all independent of body mass index (BMI), which suggests that the impact of sitting extends beyond the effect on body composition. Despite these results, much of the evidence arises from self-report measures, focusing on television sitting time. Indeed, a recent study which used daily sedentary time with accelerometers demonstrated significant associations with metabolic parameters cross-sectionally, but sedentary time did not predict 5-year diabetes incidence (206). Wilmot et al, in a meta-analysis showed that those in the highest duration sitting group in comparison to those in the lowest had increased risk of diabetes (197).

Television viewing is the predominantly reported sedentary behaviour and has been linked to obesity and more strongly associated with diabetes risk(187). Two of the earliest studies focused on diabetes risk and sitting behaviour were carried out by Hu and colleagues. In this Health Professional's Follow-Up Study (HPFS), each 2 hour/day increase in TV viewing was associated with a 20% increase in the risk for developing diabetes for men (207). In the Nurse's Health Study carried out few years later, similar findings were seen among women(208). Findings from the study showed that each 2 hour/day increase in TV viewing was associated with a 14% increase in risk for developing diabetes (208). Additionally, each 2 hour/day increase in sitting at work was associated with 7% increase risk for developing diabetes(208). In Australia, a cross sectional study by Dunstan and colleagues in 2004 found an association between greater TV viewing time and increased risk of abnormal glucose metabolism in adults. Their findings reported showed the ORs of having abnormal glucose metabolism were 1.16 in men and 1.49 in women who watched TV >14 hours/week compared with those who watched \leq 7 hours/week. Additionally, higher TV viewing (>14 h/week) was associated with an increased risk of new type 2 diabetes cases in men and women (N= 8,299 men and women (209). Similarly, in 2011 a meta-analysis by Grontved et al, reported a dose-

response relationship between TV viewing and type 2 diabetes. They reported a 20% increased risk of diabetes for every increasing 2 hours of television viewing (210). This risk was relatively higher than risk associated with 15% increased risk for cardiovascular disease and 13%. These associations persist when controlling for adiposity (BMI or waist circumferences). Furthermore, a meta-analysis on 47 studies performed by Biswas et al. in 2015 observed that, compared to those with the lowest amount of sedentary time, those with the highest amount of time spent sedentary had an 81% increased risk of type 2 diabetes incidence (211). In majority of these studies, physical activity was included as a controlling variable, and the authors found that the deleterious effects of sedentary behaviour are not mediated through lower amounts of moderate-to-vigorous intensity physical activity. This means that that irrespective of an individual meeting the physical activity recommendation, their health may still be compromised if they sit for long periods of time throughout the day(212). This therefore suggests sedentary behaviour as an important public health concern.

Television viewing per se may have a more deleterious effect on type 2 diabetes compared to total sitting time. Patterson and colleagues conducted a meta-analysis and found that the associated risk of television viewing with diabetes was higher than total sitting time. They analysed four studies using self-reported total sitting (total n = 271,724; 10,246 diabetes cases) and seven studies using television viewing (total n = 182,568; 7,306 diabetes cases) and adjusted for a range of covariates, including physical activity and reported that the risk of type 2 diabetes increased by 1% for every hour per day increase in total sitting (relative risk 1.01 (1.00-1.01)), and by 9% for every hour per day increase in television viewing (1.09 (1.07-1.12)).(213) Furthermore, Patterson et al reported that 29% of diabetes incidence was attributable to television viewing in the study population (PAF 29%; CI: 26%-32%)(213). The stronger association of type 2 diabetes risk observed for television viewing, compared with total sitting may reflect that there is a clustering of several other adverse risk factors around television viewing such as unhealthy diet and lower socio-economic status which may not be fully adjusted for in statistical analyses (212). Therefore, in terms of potential strategies to reduce type 2 diabetes risk, focusing on reducing television viewing may be a stronger target than overall time spent sitting.

Although studies show the relationship between sedentary or television viewing and type 2 diabetes, majority have been conducted in participants from European White descent and relatively little is known about the extent to which ethnic differences in diabetes is associated with sedentary behaviour in the high-risk population of south Asians and Black ethnic groups, which is of concern given the prevalence of type 2 diabetes is substantially higher in non-white populations(45,171). Furthermore, studies have indicated that south Asian women spend more time at sedentary behaviours than other populations (22,214). The Black Women's Health Study (BWHs) reported 1.9-fold risk of diabetes amongst Black women who spent more than 5 hours watching television in a day relative to those who spent less than 1 hour per day of TV viewing (215).

These studies were conducted in US. There are limited data examining the dose-response relationship between television viewing and type 2 diabetes conducted in the UK. No study to my knowledge has examined the differences of television viewing and diabetes in south Asians. This thesis aims to address this gap in the study and to add to understanding the ethnic differences of television viewing as a risk factor for type 2 diabetes.

1.6.2.8 Muscular Strength

Muscular strength is defined as the muscle's ability to generate maximal force (216). Muscular strength is a physiological trait of physical activity which involves muscles contracting against an external resistance. It is a key determinant of quality of life at old age, an established marker for frailty, predictor of functional limitation, predictor of physical decline and loss of dependence in activities of daily living in middle and older age(217).

In recent years it has become clear that muscular strength is associated with risk of a range of health outcomes including type 2 diabetes(218)and all-cause mortality (219). This will be discussed in following sections.

1.6.2.9 Assessment of muscular strength:

Muscular strength is usually measured during a single maximal voluntary contraction under set conditions, varying with movement pattern, muscle contraction type (concentric, isometric, or eccentric) and contraction velocity.

Typically, muscular strength is measured as force registered by a dynamometer or a measurable external load resisted or moved against, using external weights or a weight machine. Its loss is usually associated with substantial decrease of muscle mass that accompanies aging (217).

Muscular strength can be measured by different instrument. There is no single gold-standard measurement. The one repetition maximum (1-RM) which is the maximum of amount of weight that can be lifted for a single repetition or laboratory tests which measures the maximal voluntary isokinetic (constant speed) or isometric (static) strength of major groups could be assessed using a dynamometer, however, these tests are often expensive, have to be done in a laboratory and require specialists to operate the equipment. To assess muscular strength outside of the laboratory, functional measures such as maximal push-up capacity (220), or the sit-to-stand test, which assesses time taken to repeatedly stand up and sit down again on a chair for a set number of repetitions (usually five or ten), or number of repetitions completed in a set period of time (usually 30 seconds) (221-223) can be used. However, in large-scale studies outside of the laboratory, grip strength is usually used as a measure of muscular strength. Handgrip strength (HGS), is common measurement of muscle motion/ strength that measures the maximum voluntary contraction force of the hand. In addition, it is highly correlated to strength levels of other muscle groups including elbow flexion, knee extension, trunk flexion and trunk extension (222-224) using a hand dynamometer (HGS) is characterized by a relatively low implementation cost and by being related to strength levels of other muscle groups (225). For the objective of this thesis, handgrip strength measured using hand dynamometer is the preferred measure of muscular strength based on its advantages for large observational studies.

1.6.2.10 Muscular strength and health

Muscular strength, usually measured as handgrip strength, has been found to be associated with several health outcomes mortality and type 2 diabetes.

1.6.2.11 Handgrip strength and Mortality

In the Prospective Urban-Rural Epidemiology (PURE) Study, a longitudinal study including participants from 17 countries of different income levels, the association

between grip strength and a range of health outcomes were identified. In the study, a 5kg lower grip strength measured at 35-70 years was associated with increased risk of stroke (HR=1.09, 95% CI:1.05-1.15) and myocardial infarction (HR=1.07; 95% CI=1.02-1.11) after a median follow-up of 4 years. These associations were independent of potential confounders physical activity level, diary dietary energy intake, tobacco and alcohol use, and body mass index (BMI). For cancer, grip strength was associated with reduced rates in high-income countries ((HR=0.92, 95% CI=0.88, 0.95), but with higher rates in low-income countries, although the effect was not statistically significant (HR=1.12, 95% CI=0.93, 1.34). (219)

In UK Biobank, 502,293 men and women aged 40-69 from the general UK population had hand-grip strength measured at baseline and were followed up for a mean of 7.1 years, during which 13,322 died (45). After statistical adjustment for a range of confounding variables, the hazard ratio for mortality per 5 kg reduction in grip strength was 1.20 (95% confidence interval 1.17 to 1.23) in women, and 1.16 (95% confidence interval 1.15 to 1.17) in men, a similar magnitude of association to that observed in the PURE study. The same UK Biobank study reported that lower levels of muscular fitness have to be associated with higher rates of cancer mortality, a 5kg lower grip strength was associated with increased rates of mortality from all cancers (females HR=1.17; 95%CI= 1.31-1.21, males: HR=1.10; 95%CI=1.07-1.13), colorectal cancer (females: HR=1.17, 95% CI=1.04, 1.32; males: HR=1.18, 95% CI=1.09, 1.27), lung cancer (females: HR=1.17, 95% CI=1.07, 1.27; males: HR=1.08, 95% CI=1.03-1.13) and breast cancer (females: HR=1.24, 95%CI=1.10-1.39), independent of confounders physical activity, BMI and sedentary time making handgrip strength an important epidemiological tool (226). A key observation in the UK Biobank study was that the addition of grip strength to an established mortality risk prediction score (which included age, sex, diabetes, body mass index, blood pressure and smoking) improved prediction of all-cause (and CVD) mortality, suggesting that measurement of grip strength might become a useful addition to routine risk screening in health-care settings (45). Historically, HGS was developed for the assessment of recovery after trauma or surgery, due to its applicability and prognostic relevance (227).

1.6.2.12 Muscular Strength and Type 2 Diabetes

Until recently, there was scarce evidence on the relationship between handgrip strength and type 2 diabetes. Higher muscular strength is associated with a lower risk of type 2 diabetes.

In a meta-analysis on muscular strength and type 2 diabetes, Tarp et al observed little increase in muscular strength was associated with reductions in type 2 diabetes with clinical importance. Reviewing 13 studies on muscular strength in 39,233 and 1,713,468 participants from 10 cohort studies found that for each 1 SD higher muscular strength was associated with a 13% (95% CI 6%, 19%) lower RR of type 2 diabetes. Nine effect estimates not controlled for adiposity were available and when these were pooled, a one SD increase in muscular strength was associated with a 24% lower risk of type 2 diabetes (RR=0.76, 95% CI=0.64, 0.91)(228). However, in what manner this impacts in ethnic differences in diabetes is still uncertain.

There is little evidence on the association of muscular strength with type 2 diabetes in populations with varying ethnic backgrounds within one setting. Using data from the SABRE study, comprising 708 participants (311 Europeans, 232 South Asians and 165 African Caribbeans), Jones et al identified that elderly South Asians were 3 kilopascals (kpa) lower in grip strength while African-Caribbeans were 7kpa higher in grip strength levels compared to the Whites participants (229). Furthermore, the authors analysed the association between ethnicity with skeletal muscles and suggested that diabetes does not explain the differences in skeletal muscles strength when diabetes was included the model. However, as diabetes was not a primary outcome in their study (229) this gives a paradoxical effect and not a clear understanding of the impact of diabetes risk and muscular strength in ethnic health disparities.

There is need a need to explore whether differences in muscular strength could account for ethnic differences in the prevalence of type 2 diabetes, and if there is, to understand how whether the dose-response relationship between muscular strength and diabetes differ between ethnic groups, which is the aim of this thesis. This is essential as they may differ significantly across ethnic groups and could potentially explain ethnic differences in the prevalence/risk of type 2

diabetes(230). Muscular strength associations with type 2 diabetes in ethnic minorities is the key element of physical fitness in this thesis.

1.7 Objectives and Aims

The aim of this thesis is to assess and analyse epidemiological data to explore whether there are ethnic differences in sex, adiposity, and lifestyle factors on T2DM risk among middle-aged adults in the United Kingdom with focus on European white, South Asians (people originating from India, Pakistan and Bangladesh), Blacks (Black African and Black Caribbean) and Chinese descent populations. This study also identifies opportunities for appropriate prevention and intervention.

Therefore, using the UK Biobank study data, the thesis aims to address separate, but linked, research questions. These questions relate to areas on sex, obesity, muscular strength and television viewing behaviour and how these may elucidate the ethnic disparities in diabetes risk. The research questions to be addressed are:

1. To investigate the ethnic and sex difference of diabetes prevalence using a robust standardization method (Chapter 3).
2. To compare the relationship between adiposity and prevalent diabetes across different ethnic groups and derive robust ethnic-specific obesity cutoffs for Black, Chinese, and South Asian populations that equate to those developed on White populations in terms of diabetes prevalence (Chapter 4).
3. To quantify the extent to which ethnic differences in muscular strength might account for the substantially higher prevalence of diabetes in Black and South-Asian compared with White European adults (Chapter 5).
4. To examine how the association of television viewing and type 2 diabetes varies by ethnicity in South Asian, Black and White middle-aged adults, using the UK Biobank data and to assess the extent/pattern to which this association is based on ethnicity, independent of PA and BMI (Chapter 6).

2 General Methods

2.1 Introduction

In this chapter, the UK Biobank cohort which is the primary data source used in the subsequent chapters of this thesis is described in detail including its creation, and the recruitment of participants. The available data in the UK Biobank including the outcome of interest, diabetes, and the risk factors of interest are described below. Later in the chapter, the derivation of the variables used in the analysis, and the statistical methods are also described.

2.2 UK Biobank

The UK Biobank cohort was established with funding from the Medical Research Council and the Wellcome Trust, with the aim to investigate how the complex interplay between lifestyle, environment and genetics increases the risk of a wide range of diseases(231,232). UK Biobank is a very large and detailed prospective study including over 500,000 men and women aged mostly between 37 and 73 years old at the time of recruitment between 2006 and 2010. This age range was chosen because the chronic diseases such as diabetes, heart diseases, dementia and cancers tend to develop during midlife according to US's CDC(233).

At baseline, participants provided detailed information on their lifestyle, health and environmental factors, completed physical measures and provided biological samples. Participants were followed up via linkage to national electronic health databases such as Hospital Episodes Statistics for England (HES), the National Cancer Registry, primary care, prescriptions data, and death registries to provide comprehensive ascertainment of cases and reduce potential bias in the selection of cases for interventions(234).

A major challenge for the UK public health community is the availability of comparable, ethnic-specific data on the burden of diabetes and other chronic diseases(235). UK Biobank is a large cohort that used a systematic method to collect data including ethnicity. The recruitment process took the ethnic diversity

of the UK into consideration by ensuring the final cohort has the same ethnic proportion as the UK population (236).

In the long term, the purpose is that the unique combination of large size and detailed information means that UK Biobank remains a rich resource for epidemiological research for many years to come and is able to provide valuable insights for public health interventions and make a real difference to the health of future generations(15).

Other large-scale prospective cohorts have been established in recent years with information on lifestyle, environment and genetics including the 500,000 participant China Kadoorie Biobank(237), the 500,000 participant European Prospective Investigation into Cancer and Nutrition(238) and The Million Women Study(239). In comparison to these cohorts, UK Biobank aims to support a much wider range of health-related research and includes detailed information on a wider range of exposures and health related outcomes, especially in relation to ethnicity.

2.3 Initiation

The UK Biobank was first proposed in May 1999, when the Medical Research Council and the Wellcome Trust hosted a workshop to discuss the potential value of establishing a large prospective cohort that would be able to investigate lifestyle, environment and genetic factors in relation to a wide range of complex diseases of adulthood (240). Then, it was known as the UK Biomedical Population Collection, but changed to its current name in April 2002(241). A protocol for the cohort was developed based on wide consultation with specialist experts as well as public consultation. Following positive international peer review from 12 experts, a full protocol for the project was published in February 2002. UK Biobank was initially granted funding of £61 million jointly by the Medical Research Council, Wellcome Trust, Department of Health, Scottish Government, Welsh Government and the British Heart Foundation and received ethical approval from the North West Multicentre Research Ethics Committee (REC reference: 11/NW/03820).

2.4 Pilot Studies

Two pilot studies were conducted before recruitment to the main study began. A small pilot study of around 300 people was carried out in early 2005 across six centres. The principal aim of this initial pilot study was to evaluate the feasibility and suitability of the assessment methods and to identify areas for improvement.

A more comprehensive pilot study was conducted between March and June 2006(235,240). This pilot study assessed about 4,000 people at an assessment centre in Stockport, UK. This time the main aim was to assess the entire recruitment process from invitation to assessment to sample collection and storage at the throughput rate required for the main recruitment. These participants were included in the final UK Biobank cohort.

Names and addresses of people aged 40-69 years living within the vicinity of the assessment centre were sought from four local National Health Service primary care trusts. These people were sent an invitation letter with a provisional appointment plus an information leaflet and a pre-paid reply form. A freephone service was also available for participants to change their appointment or ask any questions. In total 59,383 primary invitation letters were sent(235).

Whilst the requested data was provided rapidly by one trust, data from another trust was delayed by several weeks and data from the other two trusts could not be obtained before the end of the pilot study(235). This presented a number of issues for recruitment. First, it meant that invitation letters were sent only three to four weeks before the provisional appointments instead of the proposed six to eight weeks. The delays in accessing contact details also meant that there was an uneven pattern of invitations which caused large spikes in demand for the call centre staff and increased waiting times which may have negatively affected participation. Furthermore, the two trusts that did not provide data actually covered the area immediately adjacent to the assessment centre which resulted in few people living within two miles being invited who may have been more likely to participate. These problems highlighted the importance of identifying participants from national data sources to ensure smooth operation.

Overall, about 4,000 participants were recruited in the pilot study, giving a response rate of approximately 6.7%. A higher response rate was expected for the main study since the response rate in the pilot study was affected by the difficulties with the primary care trusts. It was also found that the response rate could be improved by sending pre-visit reminders; the non-attendance rate was halved from 20% to 10% using pre-visit reminders (235). Also, a number of people were unable to arrange a convenient appointment at the end of recruitment in the pilot study which negatively affected the response rate; this should have impacted the response rate in the main study less since assessment centres were open longer. Greater promotion of UK Biobank during the main study should also have encouraged greater participation.

A 10% random sample of people who attended the assessment centre were asked to complete an anonymous postal survey about the assessment visit; 65% of people responded(235). Responses showed that participants had a good understanding of what the study would involve and that participants found the amount of information asked and the length of the assessment visit acceptable(242). There was also a good understanding of what they were agreeing to by consenting to take part in the study. One interesting finding was that 29% of participants mentioned “to have a health check” as one of the main reasons for participating in UK Biobank (242). Thus, following the pilot study, the information included in the invitation materials was revised for the main study.

Approximately 10,000 people declined to participate in the pilot study (most people did not respond) using either the pre-paid response form or by phone and approximately 70% of these people were willing to provide reasons. The most common reasons given were too busy (2,166 people), too unwell (935 people) and too far to travel/too inconvenient (531 people)(235).

Following the pilot study, a revised protocol was assessed by the Wellcome Trust’s Study Design Expert Group, the independent Ethics and Governance Council, and a specially convened International Review Panel(240). The panel concluded that “UK Biobank has the potential, in ways that are not currently available elsewhere, to support a wide range of research, particularly investigations into complex interactions of various exposures, including genetic and lifestyle factors in the pathways to disease and health” and unanimously recommended that full scale

recruitment should begin without delay(240,243). In August 2006, the study was approved. Recruitment to the main study began in April 2007 and lasted over three years with the final participant recruited in October 2010.

2.5 Main Recruitment

2.5.1 Identification and Invitation

Within the UK practically all members of the general population are registered with a general practitioner (GP) through the UK National Health Service (NHS). NHS records were used to identify people aged 40-69 years old in order to invite them to participate in UK Biobank(232). It is estimated that over 95% of the population are registered with the NHS, therefore providing a suitable sampling frame of the UK general population within the eligible age range. The data made available to UK Biobank for recruitment of potential participants was restricted to name, address, sex, date of birth and NHS number, and name and address of GP(240). The UK Biobank protocol is summarised in Figure 2-1 below.

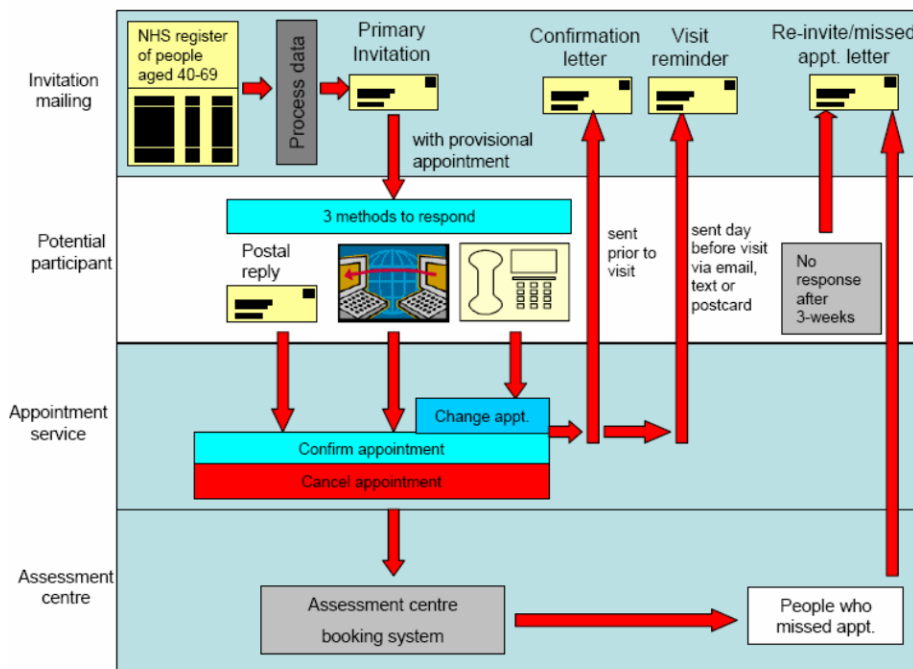


Figure 2-1 Schematic invitation and appointment system (Reproduced from UK Biobank protocol)

People aged 40-69 years old living near to one of the 22 assessment centres were sent an invitation letter with a provisional appointment to participate in UK

Biobank. Invitations were sent at least six to eight weeks before the provisional appointment. With the invitation letter, people also received an information leaflet which gave more detailed information about the purpose of UK Biobank, how people had been identified for invitation, what consenting to take part would mean (including being able to withdraw at any time) and what the assessment visit would involve. People were advised that the assessment visit would last about two to three hours. People who wanted to find out more information were encouraged to telephone the Participant Resource Centre (PRC) free of charge or visit the study website.

To accept the provisional appointment or decline to take part people could phone the PRC, return the reply form using the pre-paid envelope or go to UK Biobank's website. People could change the provisional appointment to a more convenient time by calling the PRC; most assessment centres were open Monday to Friday from 8am to 7pm and Saturday from 8am to 5pm. If people confirmed an appointment, they were asked to provide a telephone number or e-mail address so that they could receive a reminder closer to the date. Also, people who confirmed an appointment were sent written confirmation including a map with directions to the assessment centre and a short pre-visit questionnaire for questions that might be more difficult to answer precisely on the day.

2.5.2 Assessment Centres

The first requirement for establishing an assessment centre was a large number of people aged 40-69 years old (targeting an estimated 150,000 eligible people) living within close proximity in order to maintain a high throughput of participants and reduce recruitment costs(235). Therefore, all assessment centres were generally located in large cities, with a sufficiently large population within a 25 miles radius of the assessment centre. It was also important that assessment centres were conveniently located for public transport links, nearby parking and easy disabled access. UK Biobank ran in a total of 22 assessment centres across Scotland, Wales and England: Edinburgh, Glasgow, Newcastle-upon-Tyne, Middlesbrough, Leeds, Bury, Manchester, Altrincham, Liverpool, Sheffield, Nottingham, Stoke-on-Trent, Birmingham, Oxford, Bristol, Reading, central London, Hounslow, Croydon, Cardiff, Swansea and Wrexham. Figure 2-2 shows a

map of the 22 assessment centres used for recruiting participants and the number of participants recruited at each.

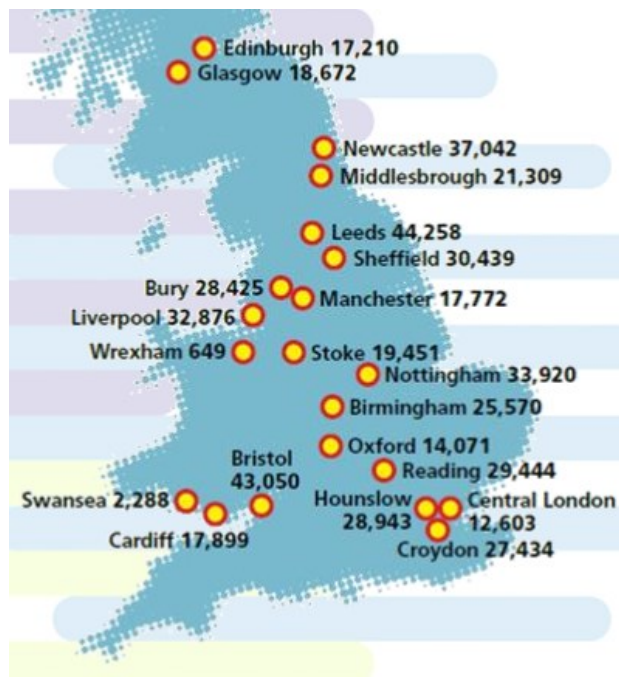


Figure 2-2 Map of UK Biobank's 22 assessment centres

The recruitment process was coordinated centrally with up to six assessment centres open at any time. Each centre recruited around 100 participants per day and most centres were opened for about 6-14 months before it was closed, and a new centre opened in a different part of the UK. Overall, about 9.2 million invitations were batch-mailed to all eligible people in the catchment area of a centre. In total 502,682 participants (5.5% response rate) attended the assessment.

2.5.3 Assessment

The baseline assessment visits consisted of participants being taken through several stations including consent, touchscreen questionnaire, a verbal interview with a trained member of staff and a series of physical measures(235). Participants first provided consent to be part of UK Biobank using the touchscreen and a digital signature pad. Participants were given a physical copy of the consent form. Then participants completed the touchscreen questionnaire which included detailed questions on socio-demographics, lifestyle, environment and health. The touchscreen questionnaire was important in enabling the recruitment of a large

number of participants at a relatively low cost since a number of participants could complete the questionnaire at the same time with minimal supervision from staff. It also meant participants could be guided through the questionnaire in order to only answer the questions pertinent to them and it allowed validity checks for questions e.g., not accepting extreme values or asking participants if, they are sure. The direct data entry by participants maximized efficiency of the data collection process, enhanced privacy and completion rate, even to questions perceived to be sensitive. It also allowed internal consistency checks, automated coding, immediate access and on-going monitoring(240). The full touchscreen questionnaire can be found on the UK Biobank website (www.ukbiobank.ac.uk) and information on each variable can be viewed in the interactive data showcase available on the study website. Figure 2-3 summarises the data collected at the UK Biobank Baseline Assessment(232)

Questionnaire and interview	
Sociodemographic	Social class; ethnicity; employment status; marital status; education; income; car ownership
Family history and early life exposures	Family history of major diseases; birth weight; breast feeding; maternal smoking; childhood body size; residence at birth
Psychosocial factors	Neurosis; depression (including bi-polar spectrum disorder); social support
Environmental factors	Current address; current (or last) occupation; domestic heating and cooking fuel; housing; means of travel; shift work; mobile phone use; sun exposure
Lifestyle	Smoking; alcohol consumption; physical activity; diet; sleep
Health status	Medical history; medications; disability; hearing; sight; sexual and reproductive history
Hearing threshold	Speech reception threshold*
Cognitive function	Pairs matching; reaction time; prospective memory*; fluid intelligence*; numeric memory [†]
Physical measures	
Blood pressure and heart rate	two automated measures, one minute apart
Grip strength	Left- and right-hand grip strength
Anthropometrics	Standing and sitting height; weight and bio-impedance; hip and waist circumference
Spirometry	Up to three measures
Bone density [‡]	Calcaneal ultrasound
Arterial stiffness [¶]	Pulse wave velocity
Eye examination [§]	Refractive index, intraocular pressure; acuity; retinal photograph; optical coherence tomography
Fitness test [§]	Cycle ergometry with electrocardiogram (ECG) heart rate monitoring

* assessed in 170,000 participants;

[†] assessed in 50,000 participants;

[‡]measured in one heel for 170,000 participants and in both heels for 320,000 participants;

[¶] measured in 170,000 participants;

[§] measured in 100,000 participants

doi:10.1371/journal.pmed.1001779.t002

Figure 2-3 Data collected at the UK Biobank Baseline Assessment

Participants were guided through the electronic consent procedure online, with a member of staff present to answer any questions and verify consent before moving onto the next station. The self-completed touchscreen questionnaire station lasted around 40 minutes.

Next, was a 5-minute verbal interview with a member of staff (usually a UK Biobank nurse) which was conducted to obtain more information on early life factors, employment, medications and medical history. This was followed by two blood pressure measurements (one minute apart) using an Omron 705 IT monitor connected directly to the computer. Participants then underwent eye measurements comprising intraocular pressure in both eyes, optical coherence tomography and retinal imaging.

A few physical measures were taken by trained staff, including hand-grip strength using a Jamar J00105 hydraulic hand dynamometer, weight using the Tanita BC-418MA body composition analyser and height using a Seca 202 height measure. Cardiorespiratory fitness was assessed using the bike test procedure where the participants are asked to sit and pedal on a stationary bike in conjunction with an electrocardiograph (ECG) device placed on them to record their ECGs at three stages i.e., a pre-test stage, an activity stage and a recovery stage. Participants unfit, or unable to exercise, had only a resting ECG recorded. A blood collection from the anti-cubital fossa, followed by a urine sample, was provided by the participant.

The final stage at the assessment centre involved a web-based diet questionnaire comprising of food frequency-type questions completed via the touchscreen. These were based on foods commonly eaten by the British population and provided information about common sources of various nutrients (244). At a later date, a sub-set of participants were contacted to complete a validated 24-hour internet-based dietary recall questionnaire.

Upon leaving the assessment centre participants were provided with some basic feedback on their physical measures. While it was important that feedback be kept to a minimum so that participants did not sign up for UK Biobank thinking it was a health check, it was seen as impractical and inappropriate to conceal information on physical measures from participants. Hence, participants received a hard copy of some of the physical measurements such as blood pressure, weight, BMI and heel bone ultrasound along with a simple interpretation (good / borderline / high) and information on seeking further advice. All data provided to users for research were de-identified before they were released for analysis.

2.5.4 Ethnic Recruitment in The UK Biobank Data.

Recruitment and retention of diverse populations are necessary to increase the impact and generalizability of scientific research, and community-engagement strategies are increasingly being incorporated into study design(245). Because of its large sample size, UK Biobank boasts a large ethnic minority sample size, which allows analysis by ethnicity subgroups(15).

Within the UK, UK Biobank data is the latest dataset to boost the ethnic minority sample, with a high-proportion of ethnic minority groups in the cohort, therefore providing reliable estimates for lifestyle risk factor levels in UK ethnic minorities. The rich dataset that results from UK Biobank will enable both top-down (governmental) and bottom-up (community and individual) approaches to improving health outcomes and increasing health equity(246). This approach is particularly vital for ethnic minority populations in the UK. To ensure that sufficient participants were recruited from minority ethnic backgrounds.

UK Biobank decided to generate modestly boosted samples from a small number of selected minority ethnic groups as well as a larger core sample from the UK's majority ethnic population(236). Decisions about including participants from minority ethnic groups were made by calculating the minimum sample size required for analysis using power calculation(246). As such, inclusivity was conceptualised in terms of how the differences between ethnic groups might compromise analytical insights. These were the key justifications for adopting the categories used in UK censuses for the data to be reflective of the proportion of the UK population(247).

2.5.5 Response

The overall response rate for UK Biobank was 5.5%(231). Achieving a high response rate was never an objective of UK Biobank; planning for recruitment was based on a response rate of 10%(240). It is widely accepted that people are generally more reluctant to take part in epidemiological studies nowadays and response rates have been declining for a number of years(242,248). Furthermore, the UK Biobank assessment was particularly demanding; participants were asked to take three hours out of their day to take part in the study.

However, although a low response rate was expected for UK Biobank, it is not clear why the study failed to achieve the projected 10% response or why the response rate was lower than that of the pilot study.

Unfortunately, there is no detailed information available about the recruitment of participants that could possibly explain why the target response rate was not achieved. The pilot report did include some basic information on factors affecting confirmation rates (based on invitation prior to 1st May 2006 to avoid the impact of the assessment centre closure on confirmation rates)(235). For example, younger people and people from more deprived areas were less likely to confirm an appointment. Hence, one possibility for the low response rate would be if these people were under-sampled in recruitment to the pilot study.

There are also other factors that may have contributed to the low response rate. For example, it seems that there was not much local promotion of UK Biobank during recruitment. Hence, the mailed invitation would likely be the first occasion when most people learned of the study and many people may have simply ignored it. The lack of promotion may have been due to constraints on resources i.e., it was more economical to have a low response rate and invite greater numbers of people than to increase the response rate by investing in promotion.

The original protocol mentioned that UK Biobank would recruit participants from 35 assessment centres, each open for about six months(240). In reality, there were fewer assessment centres that were generally open much longer. Again, it is possible that it was decided to keep fewer centres open for longer as it was more economical than establishing new centres though of course this will have negatively affected response rates as more people living further away from the assessment centres would have had to be invited.

Early reports suggested that UK Biobank was achieving a response rate of approximately 10%(249). It is not known whether this does mean that there was a drop-off in response rates in later assessment centres or perhaps response rates were calculated slightly differently. Unfortunately, there is no detailed information about response rates by assessment centre, although it was reported that the response rate achieved in Bristol was much higher than in other assessment centres. Though it cannot be known for certain, this was thought to

be related to the greater awareness of the benefits of cohort studies as a result of the locally-based Avon Longitudinal Study of Parents and Children(250). This is interesting because it indicates that although response rates for epidemiological research are declining, there may be factors that can increase response rates, in particular through increasing awareness of the benefits of such research. Information on the response rate according to ethnicity was not available for UK Biobank.

2.6 Representativeness

The aim of all epidemiological research is to acquire knowledge that can be applied to improve the health of the population. To do this, some form of investigation is undertaken in a sample of the population and it is hoped that the evidence found can be generalised to the population of interest. Investigators must always think carefully about any potential reasons why the results found in the sample may not be generalisable to the larger population. Representativeness of the sample has often been thought of as a crucial component of generalisability but this may not be the case(242,251).

First of all, representativeness is vitally important in certain contexts. The validity of the conclusions from censuses and surveys are completely dependent on the representativeness of the sample used(252). However, cohort studies are used to investigate the magnitude of the associations between risk factors and disease and are not usually used to describe the characteristics of a larger population (e.g., prevalence and absolute risk).

A distinction should first be made between representativeness and response rates. A high response rate obviously signifies that the recruited participants will closely resemble the population of interest, provided that the sample of people approached was adequately drawn. However, a low response rate does not necessarily signify a non-representative sample or cohort. Evaluation of studies have shown that some studies with low response rates as low as 5% are able to yield similar results to studies with higher response rates of up to 70%(242,253,254). A cohort with a low response rate could still be representative if each member of the population of interest had an equal probability of taking

part. In reality though a low response rate generally signifies high levels of self-selection among participants which will result in non-representativeness.

The British Doctors Study is often mentioned when talking about representativeness(255). Male doctors are clearly not representative of the general population. However, the findings of this study on smoking and health have been considered broadly applicable to the general population. In fact, the non-representativeness is often considered as a strength of the study since it meant that smokers and non-smokers were very similar in most regards except for the exposure of interest.

Results from a representative cohort would represent the overall average association in the general population. However, this does not mean that this association applies equally to all sub-groups of the population(251). For example, a hypothetical exposure could be equally harmful to men as it is beneficial to women but this would not mean that the exposure is not associated with the outcome of interest in the general population which comprises both men and women. Furthermore, representativeness is not a static idea. Surveys must be continuously updated. If the proportion of men in the general population were to increase, then the hypothetical exposure would appear to be harmful. However, the association for men and the association for women would not have changed.

Also, the self-selection of participants at baseline may be advantageous if it leads to a more motivated group of participants who are more willing to undergo further measures. Thus, the low response rates at baseline should be balanced against the response rates for follow-up measures.

UK Biobank is not a representative cohort but representativeness was not a priority for UK Biobank and heterogeneity was emphasised over representativeness. UK Biobank is of a sufficient size that it will be possible to obtain reliable estimates of risk factor-disease associations according to a number of subgroups (even though the proportions of people represented in these subgroups may not match those in the general population).

2.7 Further Measurements

A number of further assessments have been carried out (and more will be carried out in the future) in order to enhance the UK Biobank cohort. There are two reasons for conducting further assessments; one is to gain information on changes in participants' exposure over time and the other is to expand the amount of data available in order to enable an even broader scope for research.

The first of these enhancements was the 24-hour recall dietary questionnaire. This web-based questionnaire asked participants about their food and drink intake during the previous 24 hours. It included questions about 200 commonly consumed foods and drinks and took about 15 minutes to complete. This questionnaire was added to the assessment centre towards the end of recruitment. It was later sent out to all participants who provided UK Biobank with an e-mail address (approximately 320,000) on four separate occasions over one year between 2011-2012 in order to account for seasonal variation and gain a more reliable estimate of a participant's average diet. Approximately 210,000 participants completed at least one questionnaire and 80,000 participants completed at least three questionnaires. The data from the 24-hour recall questionnaire was used in the analysis for this thesis.

2.8 Characteristics of UK Biobank Cohort

Baseline data were available for 502,642 participants (229,175 men (46%) and 273,467 women (54%)). Participants were mostly aged 40-69 years at baseline; the age range of the cohort was 37-73 years; seven participants were aged 37-39 years, 2,419 participants were aged 70 years, seven participants were aged 71-73 years; 61% of participants were aged 55 years or over. The age distribution of the cohort is shown in Figure 2-4.

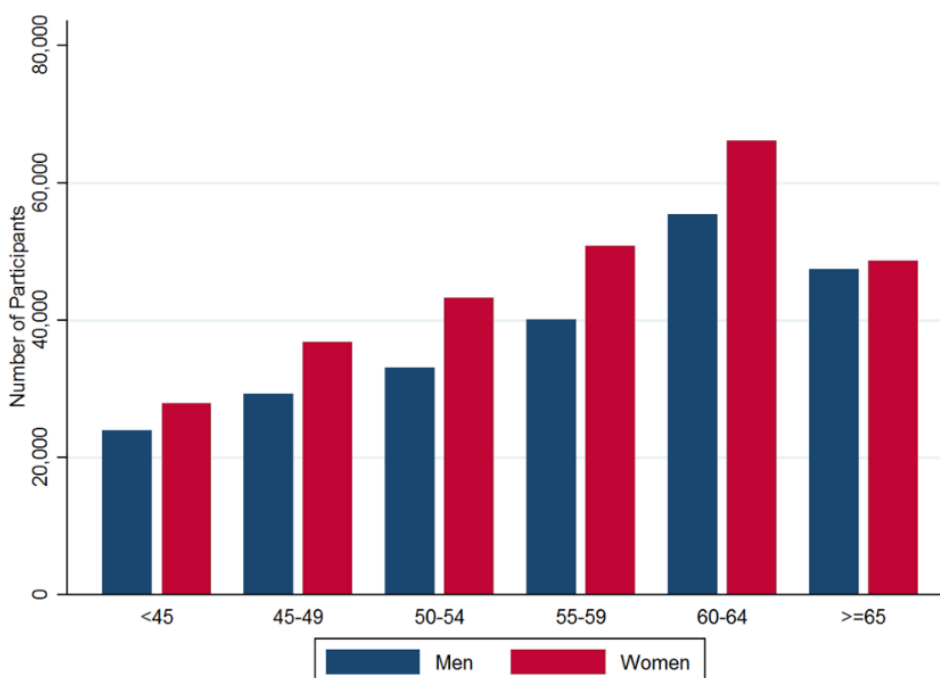


Figure 2-4 Age Distribution of UK Biobank participants by sex

Participation rate was 6.4% in women and 5.1% in men. The ethnic distribution of the UK Biobank cohort was slightly different from the national population of the same age range in the 2021 UK census(29). Table 2-1 shows that in the UK Biobank 94.6% of participants were White (81.7% in Census 2021), 2% were Asian (9.3% Census 2021) and 1.6% were of Black (4.0% in Census 2021).

Ethnic background	Number of Participants	% of Participants
White	472,837	94.6
Asian	9,882	2.0
Black	8,066	1.6
Chinese	1,574	0.3
Mixed	2,958	0.6
Other ethnic groups	4,560	0.9
Do not know	217	0.0
Prefer not to answer	1,662	0.3

Table 2-1 Ethnic Background of UK Biobank Participants

Participants were assigned a Townsend deprivation index score based on data from the 2001 national Census. Participants were assigned the score corresponding to the output area (lowest geographical area for which census data are calculated)

in which their postcode of residence at baseline was located. Townsend deprivation index scores from the 2001 Census for England and Wales by ward are available at census.ukdataservice.ac.uk/get-data/related/deprivation. These data were used to calculate quintiles of Townsend deprivation in the general population. The percentage of UK Biobank participants included in each quintile is shown in Figure 2-5. A higher Townsend score represents a higher level of deprivation. Quintile 1 represents the lowest levels of deprivation and quintile 5 represents the highest levels of deprivation. Thus, 42% of UK Biobank participants lived in areas in the lowest quintile of deprivation.

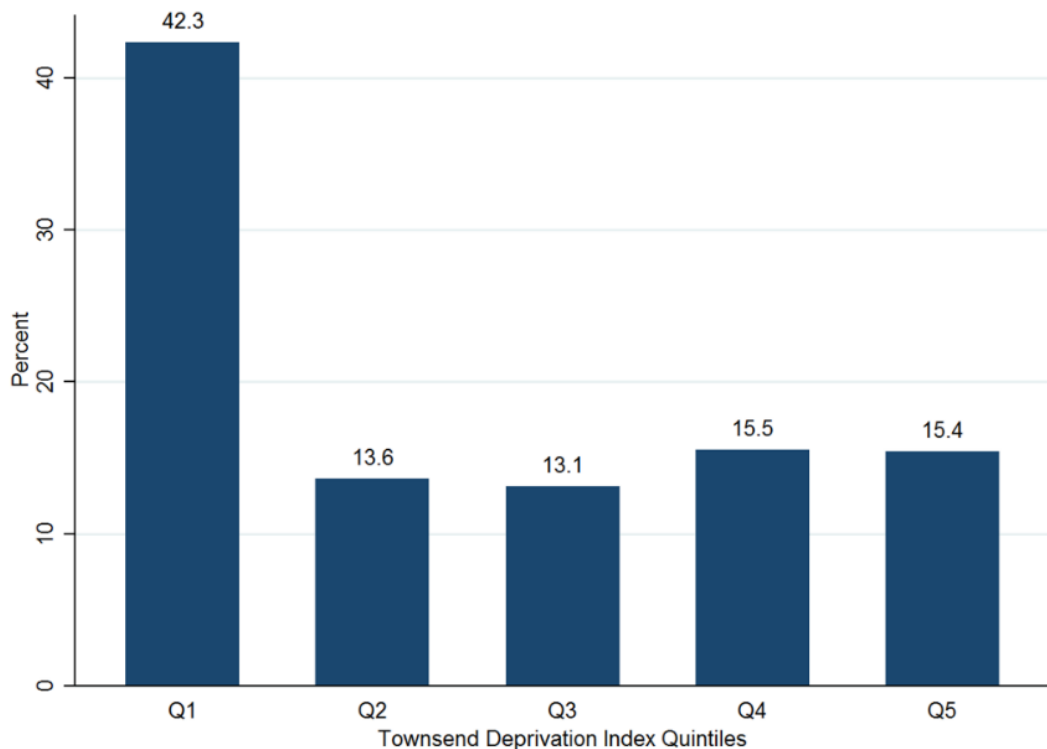


Figure 2-5 Proportion of UK Biobank participants within quintiles of Townsend deprivation index based on national distribution of Townsend scores.

Overall, participants in UK Biobank were more likely to be older and to live in more affluent areas than people in the general population. They were less likely to be obese, smoke, drink alcohol daily and have fewer self-reported health problems. This is consistent with the well-recognised ‘healthy volunteer’ effect ((256)

2.9 Outcome Variables

2.9.1 Diabetes

Diabetes was the main outcome variable of this study. Presence of diabetes (excluding gestational diabetes) was determined from self-report of a physician diagnosis. A participant was categorized as diabetic or non-diabetic based on their answer to the question “has a doctor ever told you that you have diabetes?” The participant’s diabetes status was later confirmed through an interview with a trained member of staff.

At baseline, the number of diabetic participants was 26,999. Fry et al. have shown that, in comparison to the general population, the prevalence of diabetes was lower in participants of the UK Biobank(256). However, a more recent methodological study demonstrated that the estimates of effect sizes obtained from UK Biobank for risk factors and a number of chronic diseases, including diabetes, were comparable to those obtained from 18 nationally representative prospective studies. Suggesting that in spite of its low response rate and lack of representativeness, UK Biobank can produce generalisable results(257).

2.10 Important Independent Variables

2.10.1 Ethnicity

The strength of UK Biobank is in terms of its size and data quality. Detailed classification of ethnicity, geographical national coverage, and comprehensive clinical information make it a valuable data source with significant potential for analysing ethnic disparities in diabetes which this thesis aims to explore. Ethnicity was based on self-classification into the 19 UK Office of National Statistics census categories/groups. This study was restricted to participants who identified themselves as White (British, Irish, and other white), South Asian (Indian, Pakistani and Bangladeshi), Chinese and Black (Black-African, Black-Caribbean and other Black) (258).

The ethnic distribution is heterogenous. The ethnic categorisation codes used in the 2001 Census for England and Wales was used for data analysis in this thesis. Participants self-classified themselves as White, Mixed ethnic group, Asian or Asian British, Black or Black British, Chinese, or Other ethnic groups. Of the 502,682 UK Biobank participants, 491,741 (97.7%) belonged to the eligible ethnic groups. Information on diabetes was missing for 1,453 (0.3%) eligible participants. Of the remainder, 471,174 (96.1%) were white, 9,631 (2.0%) south Asian, 7,949 (1.6%) black and 1,574 (0.3%) Chinese. Of the 38,632 participants who reported immigration to the United Kingdom, 15,271 (39.5%) were from non-white ethnic groups and their median duration of residence in the United Kingdom was 34 years.

In order to maximise statistical power, Indian, Pakistani and Bangladeshi participants were analysed collectively as South Asian, while Black-African and Black-Caribbean participants were grouped together as the Black ethnic. In Chapters 3 and 4, subgroup analysis for Indian and Pakistani participants and obesity cut-offs was considered as their demographic characteristics are known to be heterogenous.

2.10.2 Adiposity Data

This section provides information on the measures of adiposity used in this thesis to investigate the association between adiposity and diabetes by ethnic group and sex. All measures of adiposity were completed by a trained member of staff at the baseline assessment centre. The following measures of adiposity were considered in this thesis: Body Mass Index, Waist Circumference, Waist to Hip Ratio and % body fat.

Body Mass Index (BMI)

BMI is the most commonly used measure of adiposity in the general population. It is defined as the weight in kilograms divided by the square of the height in metres (kg/m^2) and thus provides a very simple measure of weight adjusted for height. In UK Biobank, height and weight were both measured at baseline by the assessment centre staff. Participants were required to stand barefoot for measurements of height and weight. Height was measured to the nearest centimetre, using a wall-mounted SECA 240 height measure. Weight was measured, without shoes and outdoor clothing, using the Tanita BC 418 body

composition analyser to the nearest 100g. A total of 227,529 men and 272,008 women provided height and weight data to calculate BMI.

Waist Circumference (WC)

Waist Circumference was measured to the nearest centimetre by the assessment centre staff using a non-elastic SECA 200 tape measure. The measurement was taken at a point midway between the lowest rib margin and the iliac crest in a horizontal plane. A total of 228,099 men and 272,383 women provided data on waist circumference.

Waist to Hip Ratio (WHR)

Hip circumference was measured to the nearest centimetre by assessment centre staff using a non-elastic SECA 200 tape measure. The waist-to-hip ratio (WHR) was calculated as the ratio between WC and Hip circumference. A total of 228,037 men and 272,340 women provided data on both WC and hip circumference.

Percentage Body Fat (% Body Fat)

Percentage body fat of participants was measured using bioelectrical impedance. Bioelectrical impedance involves sending a low electrical current through the body and then measuring the resistance to this current. Since the current flows more easily through muscle which contains a high proportion of water and less easily through fat tissue, it is possible to estimate body fat. UK Biobank used a Tanita BC418MA body composition analyser to measure % body fat. Data on % body fat was available for 223,889 men and 268,343 women.

2.10.3 Physical Functions and Physical Activity Data

2.10.4 Muscular Strength

The Jamar® J00105 Hydraulic Hand Dynamometer was utilized to assess muscular strength. Participants were instructed by staff how to use the equipment in order to help ensure that maximal effort was obtained. First, they were instructed to adjust the grip bar so that the second joint of their fingers rested over the handle of the handgrip dynamometer. Participants were instructed to hold the dynamometer in their right hand with their elbow flexed at a 90° angle, their forearm and wrist straight pointing forwards and squeeze as strongly as possible

for three seconds. The grip strength measurement was repeated using the left hand and the average value of the right and left arm grip strength values, expressed as kg per kg bodyweight, was used in the analysis.

2.10.5 Physical Activity

Participants gave information on physical activity via the touchscreen questionnaire during the baseline assessment. Physical activity was measured in accordance with the International Physical Activity Questionnaire (IPAQ) scoring protocol (<http://www.ipaq.ki.se/scoring.pdf>) which covers the intensity and duration of walking, moderate and vigorous activity in the past 7 days. Physical activity level was assessed by asking about time typically spent performing light, moderate, and strenuous (vigorous) activities at home and at work, as well as time spent moderately and vigorously exercising/participating in sports. Time spent doing work and home activities was assessed separately for week and weekend days. Exercise and sports participation was assessed for a typical week. Overall physical activity level was estimated as the sum of home activities, work activities, and exercise and sports participation. Time spent walking slowly included moving around, walking at work, walking a dog, and doing light exercise. Walking quickly included going to places, going for exercise and climbing stairs.

The data cleansing process was carried out based on rules published by the IPAQ (IPAQ 2005) which included:

- Only values of 10+ minutes were included, responses of less than 10 minutes (and their associated days) were re-coded to zero.
- All walking, moderate and vigorous time exceeding 180 minutes were truncated to 180 mins.
- For each category (walking, moderate, vigorous), if either days or minutes was recorded as zero and the other was missing, the missing value was recoded to zero.
- Total physical activity was computed as the sum of walking, moderate and vigorous activity.

Time spent walking or in moderate and vigorous activity was measured as metabolic equivalents (MET-minutes per week: MET level x minutes of activity x

events per week) of each category, and the derived measure was analysed as a continuous variable. Each equation was expressed as:

- **Walking METs.min/week** = 3.3 * walking minutes * walking days
- **Moderate METs.min/week** = 4.0 * moderate intensity minutes * moderate days
- **Vigorous METs.min/week** = 8.0 * vigorous intensity minutes * vigorous days
- **Total physical activity METs.min/week** = sum of Walking + Moderate + Vigorous METs.min/week

Participants were excluded if they responded “don’t know” or “prefer not to answer” to any of the questions. Participants were excluded from the analysis if the sum of all walking, moderate and vigorous time was greater than 960 minutes (16 hours). Thus, physical activity was defined for 388,771 participants.

2.10.6 Sedentary Behaviour

In this thesis, hours of television viewing were used as markers of sedentary behaviour. Participants were asked to report the number of hours in a typical day they spent watching television. Self-reported duration of television watching was obtained by using the following question: "In a typical DAY, how many hours do you spend watching TV? (Put 0 if you do not spend any time doing it)".

For all questions, participants provided open-ended duration responses (hours and minutes). Questions were aimed at quantifying the number of hours spent, based on a previous study conducted by Hu and colleagues(207,208). If participants entered data suggesting that they spent greater than 8 hours on television watching they were asked the question a second time to confirm the response. All values exceeding 16 hours were truncated to be equal to 16 hours to allow for 8 hours sleep. A total of 222,873 men and 264,105 women eligible participants provided data on television watching used in this thesis.

2.10.7 Confounder variables

Socioeconomic Status

Socioeconomic status was measured using the Townsend deprivation index score at recruitment. Townsend deprivation score is an area-based measure of material

deprivation based on Census information on housing, employment, overcrowding and car availability. These variables were combined to form an overall score ranking for a particular area relative to others, which was either positive or negative (259). The higher the score, the more deprived the area and the mean is zero. The Townsend deprivation index score is based on questions from the UK Census, hence making it ideal for cross-sectional and longitudinal comparisons of UK population subgroups.

Although the Townsend deprivation index score is continuous, to create the deprivation profile, it was necessary to classify the study population into quintiles of the study population. The least deprived were classified in quintile 1 (Q1) with the most deprived in quintile 5 (Q5). This approach has the advantage of enabling the relationship with deprivation to be explored around the spectrum of deprivation without assuming linearity.

Smoking Status

Participants were classified as 'current smokers' or 'formers smokers' or 'never smokers' based on their responses to the question "Do you smoke tobacco now?" Participants who responded "Yes" were classified as current smokers, while those who responded to "No" were further asked if they smoked in the past. Participants who acknowledged smoking in the past were classified as former smokers and those who neither considered themselves as smokers or former smokers at the time of recruitment were classified as 'never-smokers'.

Alcohol

With regards to alcohol intake, participants were asked about their frequency of alcohol consumption based on six-point scale; never, occasionally, 1 to 3 times per month, once or twice per week, 3 or 4 times per week or daily. Individuals who answered to either question "Do not know" (-1) "Prefer not to answer" (-3) and "None of the above" (-7) were coded as missing.

Age

Age in years was calculated from date of birth and date of baseline assessment.

Sleep duration

Sleep duration was self-reported and obtained by asking the question: “About how many hours sleep do you get in every 24 hours? (please include naps)”. If participants entered data suggesting that they spent less than 3 hours or greater than 12 hours sleeping they were asked the question a second time to confirm the response.

Heart disease and long-standing illnesses

Heart disease and long-standing illnesses were based on self-report of a physician diagnosis and were indicated on the touch screen questionnaire, and then confirmed through a face-to-face interview with a trained member of staff.

2.11 Study Design

The thesis was a cross-sectional study design using the UK Biobank baseline data. Cross-sectional studies are generally designed to describe the distribution of diseases in a population or patterns of associated factors at that point in time(260). My data extract was one of the earliest released by UK Biobank and, at that time, only baseline information was available on the study participants. Therefore, a cross-sectional design was used to address the research questions.

Sex is frequently considered as a confounding variable in public health that distorts the magnitude of an outcome and exposure, since the distribution may differ between men and women. In this thesis, all analyses were stratified by sex and ethnicity to determine the potentially different effects and contribution that sex may have.

2.12 Data Analysis

Statistical analyses for the experimental chapters were performed using Stata (Stata Corporation, College Station, Texas, USA). Participants with missing information on diabetes were excluded, and men and women were analysed separately. The demographic and anthropometric characteristics of each ethnic group were summarised using the median and inter-quartile range for continuous variables, and frequencies and percentages for categorical data. The statistical

significance of differences between ethnic groups was tested using the Kruskal Wallis test for continuous variables and Pearson's chi-squared test for categorical variables. Ordinal variables were tested using a chi-squared test for trend. The p-values for all hypothesis tests were two-sided and $p < 0.05$ was interpreted as statistically significant.

Interactions were assessed both graphically and with formal interaction testing by adding interaction terms to the adjusted models. The p value of interaction term was reported.

2.12.1 Prevalence

Prevalence is the measure of disease frequency used in the thesis. Prevalence quantifies the proportion of individuals in a population who have the disease at a specific instant and provides an estimate of the probability or risk that an individual will be have diabetes at baseline of the study at (a point time).

The formula is:

$$P = \frac{\text{number of existing cases of disease}}{\text{Total population}} \text{ at a given point in time.}$$

2.12.2 Logistic Regression

In this thesis, the accuracy of the risk estimates was optimized by using multivariate regression models to control for potential confounders by including them as covariates in the models. The result of the outcomes is expressed as odds ratios. The major advantage of logistic regression analysis is that it accommodates more than two explanatory variables simultaneously.

All models were tested for interactions of ethnicity and sex with the independent variables. Where there were significant independent x ethnicity x sex interactions with the diabetes outcome, the results meant that the risk differed by ethnicity and between men and women. Hence the models were stratified by ethnicity and sex. Since ethnicity and sex were shown to modify the associations between the variables, hence data from participants were stratified by sex and ethnicity in the research statistical models.

2.12.3 Standardization rates

Standardized rates are a way of comparing the occurrence of a characteristic such as a disease or death across different populations that have different age and other confounding factors. It is hypothesized that some ethnic groups in the UKBiobank data might have a younger population structure compared to others. Similarly, the proportion of women and men; the socioeconomic status and lifestyle characteristics could vary across ethnic groups. For example, an ethnic group might have a younger population on average compared to others. These compositional differences can make it difficult to directly compare the raw diabetes rates and understand the true disparities. Standardized rates address this issue by creating a hypothetical scenario where all populations share the same ethnic distribution, allowing a fairer comparison of the underlying risk of diabetes.

Standardized rates were derived from a weighted average of strata-specific rates, with the weights taken from the standard distribution that represents the reference population. One method of doing this is the Cochran sampling method(261). This method uses an iterative procedure to estimate the standardized rates and their confidence intervals, taking into account the variability of the stratum-specific rates and the standard distribution. The formula for the Cochran method is:

$$\text{Standardized rate} = \frac{\sum(w_i * r_i)}{\sum(w_i)}$$

where w_i is the weight for stratum i , and r_i is the observed rate for stratum i .

The weights can be derived from a standard population, such as the national or regional population, or from a pooled population, which is the combined population of all the groups being compared. The choice of the standard population may affect the magnitude of the standardized rates, but not the relative differences between groups.

The research in chapter 3 will assess diabetes morbidity rates for the four ethnic groups i.e., Whites, South Asians, Blacks and Chinese to determine sex and ethnic specific rates. The morbidity rates took into account the varying effects of age (stratified into 5-year interval) obesity as body mass index, and deprivation using

the Townsend score. The direct standardization method of adjusting for the differences of diabetes rates was employed among the ethnic groups by applying the stratum-specific rates observed in each of the ethnic subpopulations to a single standard population, which in this case was the combined population of all the groups being compared in the research.

The adjusted rates provided a summary value that removed the effect of the differences in population structure to allow for valid comparisons of diabetes prevalence between the ethnic groups that may differ on certain characteristics such as age, sex, deprivation, lifestyle score and obesity.

The following method was used:

- Age was categorised into 5-year bands (40-44, 45-49, 50-54, 55-59, 60-64, >65 years);
- BMI was categorised in accordance with the WHO cut-offs for anthropometry: underweight (<18.5 kg/m²), normal weight (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²), obese (>30kg/m²).
- Townsend score was categorised into five equal sized quintiles: Q1, Q2, Q3, Q4, Q5. The least deprived were classified into quintile 1 (Q1) with the most deprived in quintile 5 (Q5). Other measures of socioeconomic status (SES) measured were household pre-tax income and highest qualification.
- Lifestyle factors including physical activity, TV viewing, fruit and vegetable intake, processed meat, red meat, oily fish, alcohol intake and smoking were collated into a modified lifestyle score of a scale of 0 to 9. 0 represents the highest risk and a score of 9 is associated with the lowest risk. A collective risk score was chosen given that individual lifestyle factors do not occur in isolation but when present together increases the risk of diabetes(262-264).
- A variable 'pop' was created recording the overall population represented by each observation in the Stata. Syntax 'generate pop=1'.

Population and diabetes cases were compiled for each sex, ethnicity, age, BMI and Townsend category. Using the 'collapse' command in Stata, I got the sum of the diabetes counts in each group. This created a new dataset that contained the variables according to sex, ethnicity, deprivation, age, and BMI categories, with

the sum of diabetes cases and population within each category (Figure 2-6).

Data Editor (Browse) - [study_pop_BMI_SES_age.dta]

File Edit View Data Tools

pop[17] 423

	sex	ethnicSABC	townsendqu-e	age_group	BMI_CAT	diabetes_c-s	pop
1	Female	white	1	min-44	Underweight	0	2
2	Female	white	1	min-44	Normal weight	3	260
3	Female	white	1	min-44	Overweight	3	150
4	Female	white	1	min-44	Obese	3	52
5	Female	white	1	min-44	.	0	2
6	Female	white	2	min-44	Underweight	0	4
7	Female	white	2	min-44	Normal weight	5	275
8	Female	white	2	min-44	Overweight	3	162
9	Female	white	2	min-44	Obese	2	82
10	Female	white	2	min-44	.	0	1
11	Female	white	3	min-44	Underweight	0	9
12	Female	white	3	min-44	Normal weight	3	355
13	Female	white	3	min-44	Overweight	4	179
14	Female	white	3	min-44	Obese	6	124
15	Female	white	3	min-44	.	0	2
16	Female	white	4	min-44	Underweight	0	9
17	Female	white	4	min-44	Normal weight	5	423
18	Female	white	4	min-44	Overweight	9	261
19	Female	white	4	min-44	Obese	3	147
20	Female	white	4	min-44	.	0	3
21	Female	white	5	min-44	Underweight	0	14
22	Female	white	5	min-44	Normal weight	6	408
23	Female	white	5	min-44	Overweight	5	255
24	Female	white	5	min-44	Obese	11	196
25	Female	white	5	min-44	.	0	5
26	Female	white	.	min-44	Normal weight	0	3
27	Female	white	.	min-44	Obese	0	4
28	Female	white	1	45-49	Underweight	0	62
29	Female	white	1	45-49	Normal weight	23	2699
30	Female	white	1	45-49	Overweight	22	1541
31	Female	white	1	45-49	Obese	21	722
32	Female	white	1	45-49	.	1	13
33	Female	white	2	45-49	Underweight	0	39

Figure 2-6 Snapshot of variables created for standardization

Using the command 'dstsize diabetes cases pop age-group BMI_CAT, townsendquintile sex if sex==0 | sex==1, by (ethnicSABC) print >level (95)'

2.12.4 Analysis in Chapters

Table 2-2 shows the overview of the study design, study population, exposures, outcomes, sample size and data analysis of each chapter in this thesis.

	Study design and population	Primary Exposures	Outcome	Sample size (n)	Data analysis
Study 1 (Chapter 3)	Cross-sectional White, South Asian, Black and Chinese men and women.	Age, sex, BMI and Deprivation, lifestyle score	Type 2 Diabetes	489,079	Direct standardization
Study 2 (Chapter 4)	Cross-sectional White, South Asian, Black and Chinese men and women	BMI, waist circumference, Body fat %	Type 2 Diabetes	490,288	Multiple logistic regression analysis Restricted Cubic spline
Study 3 (Chapter 5)	Cross-sectional White, South Asian and Black men and women	Grip strength Physical activity	Type 2 Diabetes	418,656	Multiple linear regression analysis Attributable risk ratio
Study 4 (Chapter 6)	Cross sectional White, South Asian and Black men and women	TV viewing Physical activity	Type 2 Diabetes	486,665	Multiple logistic regression analysis.

Table 2-2 Overview of thesis chapter designs

2.12.4.1 Statistical analysis for chapter 3

Diabetes is the disease outcome in the study and uses the following variables:

- Ethnicity measure where each participant identified as 1 of 16 ethnic groups consistent with the UK Office of National Statistics Census categories
- Socioeconomic measures (SES) include individual measures i.e., household, pre-tax income, highest qualification, and the Townsend deprivation score (265).
- Lifestyle factors including physical activity, TV viewing, fruit and vegetable intake, processed meat, red meat, oily fish, alcohol intake and smoking (262-264).
- Other Covariates includes BMI, age and sex.

Crude diabetes prevalence was measured in men and women in each ethnic group using 4 different regression model.

- Model 1 examined ethnic differences in diabetes prevalence standardized by age and sex.
- Model 2 examined the standardized ethnic differences in diabetes prevalence including age, sex and SES.
- Model 3 examined standardized ethnic differences in diabetes prevalence including covariates in models 1 and 2 plus BMI.
- Model 4 tested whether the standardized ethnic differences in diabetes prevalence remains when lifestyle factors was included in the model.

All the analysis was performed using the Stata 14 command ‘dstdize’ with corresponding 95% confidence intervals (CI) (266). The formula used by the Stata’s direct standardization command dstdize is:

$$\text{standardized rate} = I_s = \frac{I_1 T_1 + \dots + I_k T_k}{T_1 + \dots + T_k} = \frac{\sum_{i=1}^k I_i T_i}{\sum_{i=1}^k T_i}$$

Where the I_i are sex, age, BMI, and deprivation-specific proportions used as “standard or weight” for standardization. The weights have been chosen to reflect the age, sex, BMI, lifestyle score and deprivation distribution at diabetes diagnosis of the study’s diabetes population

Furthermore, because of differences in subgroup characteristics within the South Asian population, a subgroup analysis was also performed. Finally, sensitivity analysis was performed excluding individuals with probable Type 1 diabetes by removing those diagnosed with diabetes aged ≤ 30 years(267). All data analyses were undertaken using STATA v14.

2.12.4.2 Statistical analysis for chapter 4

Univariate binary logistic regression models were used to examine the crude association between level of adiposity and diabetes. Separate models were run for each of the anthropometric measures, and all were treated as continuous variables. All ethnic groups were entered into the same model, and the model was stratified by ethnic group with white used as the referent category. All of the models were re-run adjusting for the potential confounding effects of age and Townsend score. Finally, alcohol consumption, physical activity, and presence/absence of heart disease were also added as covariates. Goodness-of-fit of the logistic regression models were assessed using the area under the receiver operating characteristic curve (ROC AUC).

In addition, for non-linear associations the cut-points of obesity were examined by modelling BMI and waist circumference using restricted cubic splines with three knots located at the 30th, 50th and 100th percentiles of the distribution for each ethnic group for prevalence of type 2 diabetes.

2.12.4.3 Statistical analysis for chapter 5

The association of diabetes with grip strength (as a proxy for muscular strength) per unit change with the odds of diabetes was analysed using multiple logistic regression. Firstly, an analysis was carried out adjusting for age at baseline, smoking and socioeconomic status. Further adjustment was done for percentage body fat. All eligible ethnic groups were entered into the models. Participants from the Chinese ethnic group were excluded from the analysis in this chapter due to their small sample size (n=340), and the models were stratified by ethnic group with white used as the referent category.

The attributable risk was determined to estimate the proportions of cases that could be avoided if everyone within their ethnic subpopulation, had strength levels comparable to the highest category in the study population. Population attributable risks (PAR) and 95% confidence intervals (CI) were calculated for muscle strength with diabetes risk in the study using logistic regression(268). The PARs presented were adjusted for confounders in a similar manner to the corresponding logistic regression for odds ratio estimates and, where indicated, were stratified by ethnic subgroups. The PAR estimates were calculated using the interactive risk attributable program in STATA, Using the command 'Regpar' in STATA which is a post-estimation parameter used to estimate the difference between 2 marginal prevalences (PAR)

2.12.4.4 Statistical analysis of chapter 6

Associations of TV viewing was analysed using multivariate logistic regression. Initially, models were adjusted for age, smoking status and alcohol intake. Then analyses with additional adjustment for BMI and physical activity were carried out.

As sedentary time had a non-linear relationship with diabetes risk the data were split using pre-defined thresholds obtained from the literature: <2hr, 2-4 hours and >4 hours.

3 Men across a range of ethnicities have a higher prevalence of diabetes: findings from a cross-sectional study of 500,000 UK Biobank participants

3.1 Introduction

The global diabetes prevalence in adults has increased in the last 40 year, affecting males and females differently. Time trend analysis by Zhou and colleagues reported that, global age-standardised diabetes prevalence increased from 4.3% in men in 1980 to 9.0% in 2014, and from 5.0% in women in 1980 to 7.9% in 2014 (269). This study also revealed that men have higher age-standardized diabetes prevalence compared to women in a few countries. According to the IDF 2021 atlas, the worldwide prevalence of diabetes is 536.6 million out of which 10.8% are in men and 10.2% in women(38). However, there is limited research regarding whether this sex differences occurs across different ethnic groups within the UK, and whether it persists after considering the differences in BMI, socio-economic status (SES) and lifestyle factors between ethnicities.

Using UK Biobank, the prevalence of diabetes differed in men and women across four major ethnic groups: South Asian, Black, Chinese, and White. The differences persisted after standardising for age, BMI, socioeconomic status, and lifestyle factors. Further subgroup analysis revealed that there are sex differences across South Asian subgroups (Indian, Pakistani, and Bangladeshi).

3.2 Research Design and Methods

The method of collection has already been described in detail in Chapter 2 but a brief summary is provided here. UK Biobank is a large, population-based cohort study set up to study lifestyle, environmental and genetic determinants of a range of adulthood diseases (270). Between April 2007 and December 2010, UK Biobank recruited 502 682 participants (5.5% response rate) aged 40-69 years. Overall, participation rates were higher in women (6.4%) than men (5.1%), older age groups (9% in those aged ≥ 60 years and 3% in those aged 40-44 years), and in less socio-economically deprived areas (8.3% in the least deprived areas vs. 3.1% in the most deprived areas) (271). Baseline information was collected via questionnaires and physical measurements.

3.2.1 Data Variables

Disease outcome

Diabetes is the disease outcome in the study and was based on self-report of a physician diagnosis. Participants with type 1 diabetes were excluded from the sensitivity analysis by excluding those first diagnosed with diabetes when they were under 30 years old.

Ethnicity measures

Participants classified themselves into 1 of 16 ethnic groups consistent with the UK Office of National Statistics Census categories. This study was restricted to participants who belonged to one of the following: white, Indian, Pakistani, Bangladeshi, Black African, Black Caribbean or Chinese. To maximize statistical power, Indian, Pakistani and Bangladeshi participants were analysed collectively as South Asian, and Black African and Black Caribbean participants were grouped together as Black for the main analysis.

Socioeconomic measures

The measures of socioeconomic status (SES) measured were household pre-tax income, highest qualification, and the Townsend deprivation score.

The participants' average total income before tax received by their household was categorised into:

- <18,000
- 18,000-30,000
- 31,000-51,000
- 52,000-100,000
- >100,000

The participants' highest qualification acquired at baseline was categorised into:

- Degree
- School (A/O levels, GCSE or equivalent)
- HNC/HND
- Other professional qualifications.

Townsend deprivation score followed standard area of residence-based index of material deprivation derived from census information on housing, employment, social class, and car availability (265).

Lifestyle factors

Lifestyle factors including physical activity, TV viewing, fruit and vegetable intake, processed meat, red meat, oily fish, alcohol intake and smoking were collated into a modified lifestyle score of a scale of 0 to 9. 0 represents the highest risk and a score of 9 is associated with the lowest risk. A collective risk score was chosen given that individual lifestyle factors do not occur in isolation but when present together increases mortality(262-264).

Other Covariates

BMI was calculated as weight divided by the square of height. Age and sex were assessed by self-reports at baseline. Age was calculated as the whole years between date of birth and date of attending the assessment centre at baseline.

3.2.2 Statistical Analyses

Of the 489 079 eligible participants: 471 700 (96.4%) were white, 7871 (1.6%) South Asian, 7974 (1.6%) black and 1534 (0.3%) Chinese. Crude diabetes prevalence was measured in men and women in each ethnic group. The individual measures of SES were analysed in separate models and together standardized in a model to examine how the different SES contributed to the ethnic disparities in diabetes. For each model the Hosmer-Lemeshow statistic was used to check fit, deriving similar levels of statistical significance.

Model 1: The first model examined ethnic differences in diabetes prevalence standardized by age and sex.

Model 2: The second model examined the standardized ethnic differences in diabetes prevalence including age, sex and SES.

Model 3: The third model examined standardized ethnic differences in diabetes prevalence including covariates in models 1 and 2 plus BMI.

Model 4: The final model tests whether the standardized ethnic differences in diabetes prevalence remains when lifestyle factors was included in the model.

All the analysis was performed using the Stata 14 command 'dstdize' with corresponding 95% confidence intervals(266).

Furthermore, because of differences in characteristics within the South Asian population, a subgroup analysis was also performed. Finally, sensitivity analysis was performed excluding individuals with probable Type 1 diabetes by removing those diagnosed with diabetes aged ≤ 30 years(267). All data analyses were undertaken using STATA v14.

3.3 Results

Of the 502 682 UK Biobank participants, 489,079 people of relevant ethnic backgrounds were included in the analysis. Baseline participant characteristics are outlined in Table 3-1. The median age was higher in white participants (58 years) than other ethnicities, suggesting that there were older white participants. The median BMI in Black women was 1.7 kg/m² higher than in Black men (29.7 vs. 28.0 kg/m² respectively). Subgroup analysis revealed that Pakistani and Bangladeshi women had higher BMIs than their male counterparts (Table 3-2). Conversely, median BMI in Chinese men was 1.8 kg/m² higher than in their female counterparts (24.8 vs. 23.0 kg/m² respectively). It must be noted that over 60% of black participants were in the lowest socio-economic quintile.

Table 3-1 Characteristics of study participants by ethnic group and sex

	Women				Men			
	White N= 257,027	South Asian N= 3,660	Black N= 4,614	Chinese N= 965	White N= 214,673	South Asian N= 4,211	Black N= 3,360	Chinese N= 569
	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)
Age (years)	58 (50-63)	53 (46-60)	51 (46-58)	52 (46-58)	58 (51-64)	53 (46-61)	50 (45-58)	51 (45-59)
BMI (kg/m²)	26.1 (23.4-29.6)	26.8 (24.1-30.2)	29.7 (26.1-33.7)	23.0 (20.9-25.4)	27.3 (25.0-30.1)	26.6 (24.4-29.2)	28.0 (25.6-30.6)	24.8 (23.0-27.0)
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Diabetes	8,881 (3.5)	523 (14.3)	479 (10.4)	48 (5.0)	14,049 (6.5)	899 (21.1)	431 (12.8)	44 (7.7)
Townsend deprivation index quintile								
1 (least)	53,241 (20.7)	372 (10.2)	131 (2.8)	148 (15.4)	44,933 (21.0)	382 (9.1)	93 (2.8)	84 (14.8)
2	52,082 (20.7)	358 (9.8)	209 (4.5)	144 (15.0)	44,200 (20.6)	402 (9.6)	152 (4.5)	97 (17.1)
3	53,197 (20.7)	579 (15.8)	391 (8.5)	157 (16.3)	43,292 (20.2)	635 (15.1)	261 (7.8)	80 (14.1)
4	51,385 (20.0)	1,117 (30.6)	974 (21.1)	256 (26.6)	41,631 (19.4)	1,165 (27.8)	690 (20.6)	145 (25.6)
5 (most)	45,818 (17.9)	1,229 (33.6)	2,904 (63.0)	257 (26.7)	40,356 (18.8)	1,619 (38.5)	2,149 (64.3)	161 (28.4)
Household annual income (£)								
<18,000	51,709 (24.4)	1,046 (33.7)	1,267 (36.2)	203 (26.6)	38,471 (20.1)	1,365 (32.8)	881 (33.3)	123 (25.6)
18,000-30,000	55,954 (26.4)	760 (24.5)	1,039 (29.7)	158 (20.7)	46,827 (24.4)	978 (23.5)	724 (27.4)	111 (23.1)
31,000-51,000	54,291 (25.6)	632 (20.4)	775 (22.2)	209 (27.4)	51,730 (27.0)	835 (20.1)	627 (23.7)	124 (25.8)
52,000-100,000	40,033 (18.9)	506 (16.3)	368 (10.5)	135 (17.7)	42,917 (22.4)	714 (17.2)	363 (13.7)	93 (19.3)
>100,000	10,285 (4.8)	155 (5.0)	48 (1.4)	58 (7.6)	11,692 (6.1)	264 (6.4)	50 (1.9)	30 (6.2)
Highest qualification								
Degree	79,001 (37.7)	1,562 (45.3)	1,423 (36.1)	440 (52.9)	74,101 (40.8)	2,258 (53.9)	1,202 (44.3)	319 (66.6)
School	104,871 (50.1)	1,434 (41.5)	1,570 (39.8)	273 (32.8)	74,111 (42.3)	1,454 (34.7)	989 (36.4)	109 (22.8)
HNC/HND	11,176 (5.3)	189 (5.5)	491 (12.4)	35 (4.2)	19,574 (11.2)	290 (6.9)	371 (13.7)	23 (4.8)
Other	14,461 (6.9)	266 (7.7)	460 (11.7)	84 (10.1)	9,635 (5.5)	184 (4.4)	153 (5.6)	28 (5.8)
Lifestyle score								
0-1	116 (0.1)	0	0	1 (0.1)	567 (0.3)	2 (0.1)	17 (0.5)	1 (0.2)
2-3	5,844 (2.3)	32 (0.9)	137 (3.1)	15 (1.6)	13,748 (6.5)	160 (4.0)	265 (8.3)	33 (5.9)
4-5	55,398 (21.8)	628 (17.8)	1,090 (24.9)	229 (24.3)	71,091 (33.4)	1,146 (28.5)	1,186 (37.1)	206 (36.8)
6-7	132,354 (52.1)	2,130 (60.4)	2,163 (49.5)	488 (51.9)	97,903 (46.0)	2,077 (51.6)	1,341 (42.0)	255 (45.5)
8-9	60,363 (23.8)	737 (20.9)	980 (22.4)	208 (22.1)	29,337 (13.8)	643 (16.0)	384 (12.0)	65 (11.6)

a p-value <0.0001 for all variables; med median; IQR interquartile range; Lifestyle score: 0-1 (highest risk), 2-3 (medium -high risk), 4-5 (medium risk), 6-7 (medium-low-risk), 8-9 (lowest risk); N number

Table 3-2 Characteristics of South Asian participants by ethnic group and sex

	Women			Men		
	Indian N= 2,892	Pakistani N= 694	Bangladeshi N= 74	Indian N= 2,961	Pakistani N= 1,090	Bangladeshi N= 160
	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)
Age (years)	53 (47-60)	50 (44-57)	50 (44-59)	55 (47-62)	50 (44-57)	46 (42-54)
BMI (kg/m²)	26.4 (23.9-29.7)	28.5 (25.6-32.1)	29.7 (26.1-33.7)	26.3 (24.2-28.9)	27.3 (25.1-30.1)	25.8 (23.8-27.7)
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Diabetes	373 (12.9)	130 (18.7)	20 (27.0)	577 (19.5)	265 (24.3)	47 (29.4)
Deprivation						
1 (least)	310 (10.7)	59 (8.5)	3 (4.1)	316 (10.7)	62 (5.7)	4 (2.5)
2	307 (10.6)	48 (6.9)	3 (4.1)	314 (10.6)	82 (7.5)	6 (3.8)
3	481 (16.7)	88 (12.7)	10 (13.5)	499 (16.9)	120 (11.0)	16 (10.0)
4	939 (32.5)	156 (22.5)	22 (29.7)	905 (30.6)	238 (21.9)	26 (16.3)
5 (most)	851 (29.5)	342 (49.4)	36 (48.7)	927 (31.3)	587 (53.9)	108 (67.5)
Household annual income (£)						
<18,000	569 (28.2)	234 (49.9)	22 (57.9)	602 (24.8)	414 (49.2)	71 (62.3)
18,000-30,000	517 (25.7)	92 (19.6)	5 (13.2)	599 (24.7)	175 (20.8)	15 (13.2)
31,000-51,000	449 (22.3)	73 (15.6)	4 (10.5)	523 (21.5)	120 (14.3)	20 (17.5)
52,000-100,000	368 (18.3)	52 (11.1)	7 (18.4)	513 (21.1)	95 (11.3)	6 (5.3)
>100,000	111 (5.5)	18 (3.8)	0 (0.0)	191 (7.9)	37 (4.4)	2 (1.7)
Highest Qualification						
Degree	1,030 (45.0)	188 (41.2)	27 (64.3)	1,339 (55.8)	425 (54.0)	62 (62.0)
School	967 (42.3)	207 (45.4)	8 (19.0)	866 (34.8)	283 (36.0)	35 (35.0)
HNC/HND	112 (4.9)	39 (8.5)	6 (14.3)	179 (7.2)	54 (6.9)	1 (1.0)
Other	179 (7.8)	22 (4.8)	1 (2.4)	105 (4.2)	25 (3.2)	2 (2.0)
missing	637	254	30	508	321	61

Table 3-2 Characteristics of South Asian participants by ethnic group and sex (contd)

Lifestyle score						
0-1	0	0	0	2 (0.1)	0	0
2-3	18 (0.6)	13 (1.9)	1 (1.5)	88 (3.1)	62 (6.0)	10 (6.7)
4-5	452 (16.2)	164 (24.5)	12 (18.2)	749 (26.3)	347 (33.8)	50 (33.3)
6-7	1,692 (60.6)	396 (59.2)	42 (63.6)	1,516 (53.2)	493 (48.0)	68 (45.3)
8-9	630 (22.6)	96 (14.4)	11 (16.7)	496 (17.4)	125 (12.2)	22 (14.7)

IQR, interquartile range. Lifestyle score: 0-1 (higher risk), 2-3 (medium high risk), 4-5 (medium risk), 6-7 (medium low risk), 8-9 (lowest risk).

The crude prevalence of diabetes was higher in men than women in all ethnic groups. Overall crude diabetes prevalence was 6.9% in men and 3.7% in women. After standardizing for age, SES, BMI and lifestyle factors, this difference remained with a diabetes prevalence of 6.4% in men and 3.9% in women ($P < 0.0001$) as shown in Figure 3-1. Sensitivity analysis with exclusion of those diagnosed with diabetes aged ≤ 30 years confirmed similar findings (Table 3-3).

After standardizing for age, SES, BMI and lifestyle factors, the standardized diabetes prevalence (with 95% CI) was: 6.0% white men vs. 3.6% white women ($P < 0.0001$); 21.0% South Asian men vs. 13.8% South Asian women ($P < 0.0001$); 13.3% black men vs. 9.7% black women ($P < 0.0001$); and 7.1% Chinese men vs. 5.5% Chinese women ($P = 0.211$) (Figure 3-1 and Table 3-3).

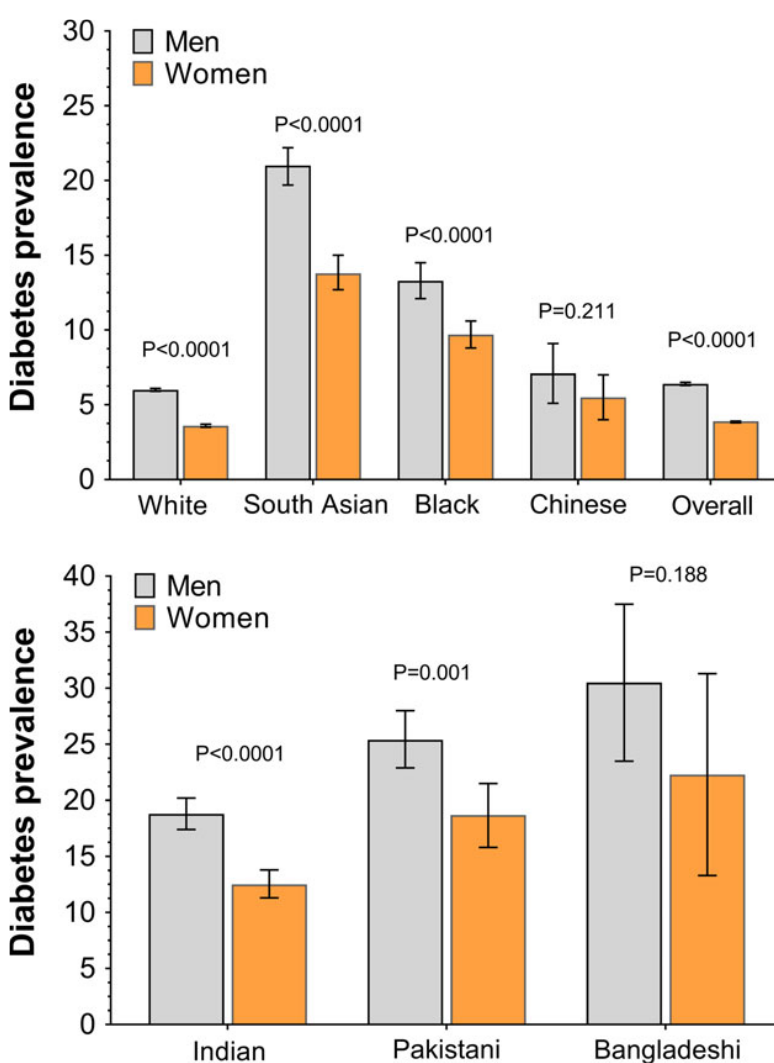


Figure 3-1 Prevalence of diabetes mellitus by ethnicity and sex standardised for age, socioeconomic status, BMI and lifestyle factors.

In Figure 3-1, White, South Asian (including Indian and Pakistani), and Black men have higher diabetes prevalence than their female counterparts with a non-significant difference in Chinese and Bangladeshi individuals. Subgroup analysis in South Asian participants also revealed persistent sex differences in diabetes prevalence after standardization, with the highest prevalence in Bangladeshi, followed by Pakistani, then Indian individuals (Figure 3-1 and Table 3-4). Sex differences persisted after excluding those with likely Type 1 diabetes (Table 3-3).

Table 3-3 Crude and standardized prevalence of diabetes mellitus according to ethnicity and sex

	Women					Men				
	White N= 257,027	South Asian N= 3,660	Black N= 4,614	Chinese N= 965	Overall N=266,266	White N= 214,673	South Asian N= 4,211	Black N= 3,360	Chinese N= 569	Overall N= 223,113
Crude prevalence (%) ^a	3.5 (3.4-3.5)	14.3 (13.2-15.4)	10.4 (9.5-11.3)	5.0(3.6-6.3)	3.7 (3.7-3.8)	6.5 (6.4-6.6)	21.1 (19.9-22.3)	12.8 (11.7-14.0)	7.7 (5.5-9.9)	6.9 (6.8-7.0)
Prevalence standardized by age (%)	3.5 (3.4-3.6)	14.5 (13.3-15.6)	10.4 (9.5-11.2)	5.1 (3.7-6.5)	3.8 (3.7-3.8)	6.5 (6.4-6.6)	20.9 (19.7-22.1)	12.9 (11.8-14.0)	7.6 (5.4-9.7)	6.8 (6.7-6.9)
Prevalence standardized by age and SES (Townsend) (%)	3.5 (3.4-3.6)	14.5 (13.2-15.8)	10.4 (9.5-11.2)	5.0 (3.7-6.4)	3.8 (3.7-3.8)	6.5 (6.3-6.6)	20.9 (19.7-22.0)	12.9 (11.8-14.0)	7.7 (5.5-9.9)	6.8 (6.7-6.9)
Prevalence standardized by age and SES (Household Income) (%)	3.4 (3.3-3.5)	14.2 (13.1-15.3)	10.2 (9.3-11.0)	5.0 (3.6-6.3)	3.7 (3.6-3.7)	6.6 (6.5-6.7)	21.1 (19.8-22.2)	13.0 (11.9-14.1)	7.7 (5.5-9.9)	7.0 (6.9-7.1)
Prevalence standardized by age and SES (Qualification) (%)	3.5 (3.4-3.6)	14.2 (13.1-15.3)	10.4 (9.6-11.3)	5.0(3.6 -6.3)	3.8 (3.7-3.8)	6.5 (6.4-6.6)	21.1 (19.9-22.3)	12.8 (11.7-14.0)	7.8(5.6-10.0)	6.8 (6.7-6.9)
Prevalence standardized by age, SES (Townsend) and BMI (%)	3.6 (3.5-3.7)	13.9 (12.8-15.0)	9.9 (9.1-10.8)	5.5 (4.0-7.0)	3.9 (3.8-3.9)	6.2 (6.1-6.3)	21.2 (20.0-22.5)	13.5 (12.4-14.7)	6.9 (5.0-8.9)	6.5 (6.4-6.6)
Prevalence standardized by age, SES, BMI and lifestyle score (%) ^b	3.6 (3.5-3.7)	13.8 (12.7-15.0)	9.7 (8.8-10.6)	5.5 (4.0-7.0)	3.9 (3.8-3.9)	6.0 (5.9-6.1)	21.0 (19.7-22.2)	13.3 (12.1-14.5)	7.1 (5.1-9.1)	6.4 (6.3-6.5)
Prevalence by age, SES (Townsend), BMI and lifestyle score (excluding type 1 diabetes) % ^c	3.3 (3.2-3.4)	12.8 (11.7-13.9)	8.9 (8.0-9.7)	5.1 (3.6-6.6)	3.6 (3.6-3.7)	6.0 (5.9-6.1)	19.5 (18.3-20.8)	12.3 (11.1-13.5)	6.4 (4.4-8.3)	6.2 (6.1-6.3)

SES, socio-economic status.

^aValues in parentheses are 95% confidence intervals.

^bLifestyle factors include physical activity, TV-viewing, fruit and vegetable intake, processed meat, red meat, oily fish, alcohol intake and smoking.

^cAfter exclusion of those diagnosed with diabetes aged ≤ 30 years, there were: 256 215 White women, 3605 South Asian women, 4570 Black women, 962 Chinese women, 213 483 White men, 4128 South Asian men, 3315 Black men and 564 Chinese men.

Table 3-4 Crude and standardized prevalence of diabetes mellitus in South Asian participants

	Women			Men		
	Indian	Pakistani	Bangladeshi	Indian	Pakistani	Bangladeshi
	N=2,892	N= 694	N= 74	N= 2,961	N= 1090	N= 160
Crude prevalence (%) ^a	18.7 (15.8-21.6)	18.7 (15.8-21.6)	27.0 (16.9-37.1)	24.3 (21.8-26.9)	24.3 (21.8-26.9)	29.3 (22.3-36.4)
Prevalence standardized by age (%)	13.2 (11.9-14.4)	19.3 (16.5-22.2)	24.8 (15.7-33.9)	19.1 (17.8-20.5)	23.9 (21.5-26.3)	30.6 (23.7-37.4)
Prevalence standardized by age and SES (Townsend) (%)	13.2 (11.9-14.4)	19.5 (16.7-22.4)	24.9 (15.8-34.0)	19.1 (17.7-20.5)	23.8 (21.4-26.2)	30.5 (23.7-37.3)
Prevalence standardized by age and SES (Household Income) (%)	13.0 (11.7-14.2)	19.1 (16.3-21.9)	25.6 (16.0-35.2)	19.3 (17.9-20.7)	23.8 (21.3-26.2)	30.1 (23.1-37.2)
Prevalence standardized by age and SES (Qualification) (%)	12.9 (11.7-14.1)	19.0 (16.2-21.8)	24.9 (15.5-34.2)	19.5 (18.1-20.9)	23.9 (21.5-26.3)	31.0(24.0-38.0)
Prevalence standardized by age, SES and BMI (%)	12.6 (11.4-13.8)	18.6 (15.9-21.4)	24.4 (15.3-33.6)	19.3 (17.9-20.7)	24.8 (22.4-27.3)	30.7 (23.9-37.6)
Prevalence standardized by age, SES, BMI and lifestyle score (%) ^b	12.5 (11.3-13.8)	18.7 (15.8-21.5)	22.3 (13.3-31.3)	18.8 (17.4-20.2)	25.4 (22.9-28.0)	30.5 (23.5-37.5)
Prevalence by age, SES, BMI and lifestyle score (excluding type 1 diabetes) % ^c	11.6 (10.4-12.8)	17.2 (14.4-20.0)	19.2 (10.5-28.0)	17.7 (16.2-19.1)	23.4 (20.8-25.9)	28.7 (21.9-35.6)

SES, socio-economic status.

^aValues in parentheses are 95% confidence intervals.

^bLifestyle factors include physical activity, TV-viewing, fruit and vegetable intake, processed meat, red meat, oily fish, alcohol intake and smoking.

^cAfter exclusion of those diagnosed with diabetes aged \leq 30 years, there were: 5403 Indian, 1612 Pakistani and 203 Bangladeshi participants.

3.4 Discussion

3.4.1 Men at Higher Risk

This study confirms men across major ethnic groups including white, South Asian, and black, have a higher prevalence of diabetes compared with women of similar age, BMI, SES and lifestyle in the UK. This difference persisted across South Asian subgroups and after excluding those with probable Type 1 diabetes.

A study of 276,837 people with newly diagnosed diabetes in two Canadian provinces revealed South Asian, White, and Chinese men had higher diabetes incidences women following age-standardisation (272). This is similar to findings in this study. However, Khan's study did not standardise for BMI or socioeconomic status or lifestyle factors which could be considered important steps to determine real sex differences in diabetes prevalence. While their study did not include Black ethnicities, this study shows that the same pattern is found in blacks in the UK. Therefore, the findings my current research has specific strengths beyond existing relevant literature and provides a comprehensive study on sex and ethnic differences in diabetes.

The SABRE study compared diabetes prevalence in European, Indian Asian and African Caribbean participants aged 40-69 years (74). In their study, South Asian men had higher diabetes prevalence than South Asian women (22% vs. 17%) but African Caribbean women had higher diabetes prevalence compared with men (21% vs. 18%). However, the African Caribbeans may not be representative of blacks. This study group together African Caribbeans and Blacks of African origin together and the result shows that black men had higher diabetes prevalence than black women (13.3% vs 9.7%) when standardized by age, SES, BMI and lifestyle score. One other reason where this study defers from the SABRE study is by the sample size for Blacks which was far smaller than the current study (801 in SABRE vs. 7974 in current study). By increasing the sample size, this study improves the precision of diabetes prevalence in Blacks. In addition, the SABRE study did not adjust for BMI which was 3 kg/m² greater in African Caribbean women than men (29.4 vs.26.4 kg/m²) (74).

Interestingly, this study showed a non-significant sex difference in diabetes prevalence among Chinese men and women after standardization (7.1% vs 5.5%) which is likely due to fewer participants in this group (1,534). However, a large study of 46,239 Chinese adults showed that age-standardized prevalence of total diabetes was higher in men (10.6%) than women (8.8%) (85). However, unlike the approach used in this study, these investigators did not account for obvious differences in BMI (which were lower on average in women), socioeconomic status and lifestyle factors (smoking was much more common in men). Therefore, further study is required to address male and female diabetes prevalence in Chinese populations.

3.4.2 Visceral Fat, Hormones and Sex Differences in Diabetes Prevalence

Logue and colleagues have shown that white men develop diabetes at lower BMI levels than women (95). This may relate to men without diabetes being more insulin resistant than women of a comparable BMI, due to men's lower subcutaneous storage capacity and more rapid visceral and ectopic fat accumulation with weight gain (86).

Nordström et al. (273) examined the association of visceral fat with plasma glucose and type 2 diabetes prevalence in 1,393 elderly participants of northern European origin. Type 2 diabetes was more prevalent in men than women (14.6% vs. 9.1%; Odds Ratio 1.72). Interestingly, after they adjusted for visceral fat levels, the prevalence of type 2 diabetes was similar in men and women, suggesting differences in visceral fat may not contribute to sex differences in diabetes prevalence (273). Given that visceral fat levels correlate strongly with liver and pancreatic fat ectopic rather than visceral fat, the differences may explain greater diabetes risk in men (274).

Mechanisms to explain sex differences in diabetes prevalence may also include hormonal influences, including a fall in oestrogen levels and increased androgen predominance seen with the menopause(96,275-277).

3.4.3 Clinical Implications

One of the clinical implications of these findings is that Men are at higher risk of diabetes across a range of ethnicities included in this study, as well as higher mortality risks for any given BMI compared to women (278). However, men are less likely to engage in lifestyle changes, with twice as many women as men enrolling in a weight management trial (279). In men, diabetes is responsible for erectile dysfunction, low testosterone levels and emotional factors -such as depression, anxiety, or stress-that can interfere with sexual feelings. Furthermore, Ahern suggested a sex-bias may exist among GPs who are less likely to offer men referral to commercial weight loss programmes (279).

When these factors are viewed through different cultural and ethnic lenses, it becomes even more difficult to apply a one size fits all solution. For instance, the onset of the above-mentioned problems may not be immediately linked to diabetes as they are less likely to go for medical help.

Black and ethnic minority groups may also face additional barriers to accessing healthcare according to Szczepura (280). These data suggest more should be done to encourage and motivate men to undertake lifestyle changes to mitigate their adiposity-associated risks.

Life can be especially hard for women living with diabetes. Women with diabetes are afflicted by depression, sexual health at risk and eating disorders occur more frequently. This also implies that if non-white ethnic groups are more sexually reproductive in terms of giving birth to more children, then this could also cause higher prevalence among non-white women. Even for those who do not have diabetes, pregnancy comes with the risk of gestational diabetes.

Generally, type 2 diabetes increases cardiovascular disease risk in women more than in men. Type 2 diabetes is the leading cause of death in women with diabetes (91,281-283). Culturally, African women consider their weight to be normal even though they would be classified as overweight by European standards (284,285). These women are less likely to go on a weight loss programme (284,285). Thus, the importance of weight loss and weight maintenance for prevention of diabetes

disease and overall health may need to be emphasized and promoted in this population.

It is important therefore that clinicians and health care professionals are aware of these at-risk groups, particularly men. More is needed to encourage and motivate lifestyle changes. For instance, in the Football Fans for training (FFIT) study, a male-specific weight control intervention delivered with football clubs in Scotland which was aimed at helping obese male football fans to live healthier lifestyle successfully showed that the men who participated in FFIT lost more than 9 times as much weight as men who had not done the programme (286). Another study conducted in other European countries (EUROFIT), showed a significant improvement in diet, weight, wellbeing, and CVD health in men in the intervention group compared to the control group (287).

Couple-based interventions may also prove useful as spousal diabetes history can increase the risk of diabetes by 26%(288).

3.4.4 Study Limitations

The exclusion of people with likelihood of type 1 diabetes diagnosed under the age of 40 may misclassify a small number of individuals (n=7). The researcher acknowledges that diabetes was self-reported. However, it is noted in a study by Eastwood et al. that only 0.001% of people with diabetes could be missed on comparing with primary care reports(289).

Participation rates in UK Biobank was low (5.5% overall response rate), with more women, older and more affluent individuals participating (271). Response rate by ethnicity was not available, but 38,632 participants provided information on the 'year immigrated to United Kingdom'. Of these, 15,271 (39.5%) were from non-white ethnic groups and their median time living in the UK was 34 years, so further work is needed on indigenous population.

This research using the UK biobank participants may not be representative of the general UK population and cannot be used to provide definitive disease prevalence and incidence rate. However, valid assessment of exposure-disease relationships is still generalizable and do not require participants to be representative of the

population at large(271). The standardisation of age, BMI, SES and lifestyle factors provides more confidence that the sex differences are likely robust and not necessarily unique to the population examined.

Finally, although the study by Doherty et al. (290) suggests that women in UK Biobank were more active than men, the 4% higher levels of activity in women are too small to account for sex differences in diabetes prevalence.

In conclusion, this study confirms the sex difference in diabetes prevalence across White, South Asian and Black ethnic groups, but less so in the Chinese participants in the UK Biobank. Men are at higher risk for any given age and BMI than women. These findings suggest more work is needed to increase physician and public awareness of men's greater diabetes risk, to better educate, target and motivate men at elevated risk to take up lifestyle changes to lessen diabetes risk.

**4 Ethnic-Specific Obesity Cutoffs for Diabetes
Risk: Cross-sectional Study of 490,288 UK
Biobank Participants**

4.1 Introduction

According to the World Health Organization (WHO) defines obesity as the excessive accumulation of body fat, which is associated with health risks(291). The rising prevalence of obesity due to sedentary lifestyles (such as being less fit and more sedentary) has become a major public health concern. The prevalence of diabetes is increasing disproportionately amongst people from non-white ethnic groups compared to white populations (112). Non-white ethnic groups later develop diabetes complications (including retinopathy, nephropathy and neuropathy) at more severe rates than white populations(70,72,98,292). Some of these complications can be prevented with early diagnosis and treatment. Therefore, appropriate detection and screening of high-risk individuals in these groups is essential for timely intervention and significance impact on public health.

Obesity is an important driver for the rising type 2 diabetes mellitus levels around the world and about 80% of the cases of type 2 diabetes are attributable to obesity(293). Diabetes and obesity predispose a cardiovascular disease and are typically considered synergetic epidemics with one exacerbating the other, such that the global prevalence distribution of T2Dm reflects similar rates to those of obesity(294,295). This has led to the term 'diabesity' to emphasize the link between these conditions(296,297). Therefore, obesity is one of the most common modifiable risk factors of diabetes.

The body mass index (BMI), is the most commonly used indication of weight adjusted for height as it has high specificity to detect excessive body adiposity and it is a convenient measure used to broadly categorize body weight within populations as underweight (less than 18.0kg/m²), healthy weight (18-24.9kg/m²), overweight (25.0-30.0kg/m²) or obese (over 30.0kg/m²). Recommendations are usually considered for BMI within 18.0-24.9kg/m² range as healthy because they have been associated with desirable health outcomes(298). In population studies, risk for unfavourable health outcomes usually increases for BMI values above the healthy weight level (298).

Overweight and obesity significantly increases the risk of diabetes continuously with increasing BMI such that an individual with a BMI level greater than 30.0kg/m²

have as high as seven-fold risk or more of diabetes compared to those within the normal weight of 18.0-24.9kg/m² BMI levels(101). However, the use of a universal BMI cut off points to assess health risk does not take into account the variation in the body fat pattern on ethnicity. BMI tends to only take into account overall body mass and does not differentiate fat-free mass from fat mass. Consequently, BMI cannot assess body fat distribution which is influenced by visceral (intra-abdominal or android) fat which is a risk factor in the development of diabetes regardless of the total body fat content. For example, Asian population are at higher risk of diabetes at lower levels of BMI and research suggests that abdominal adiposity may independently influence the increased risk of type 2 diabetes in these ethnic population(113,114).

Subsequently, the use of measurements that allow assessment of abdominal adiposity is essential as such measures could help appropriately identify 'at-risk' individuals. Recommended cut-points for a very high waist circumference are 102.0cm for men and 88.0cm for women(299-301). These cut-points may not be appropriate for minority non-white ethnic groups like Asians (consisting of both South Asians, Chinese and Japanese descent) and Black (Caribbean and African descent) ethnic groups in whom the distribution of body fat tends to be different from white ethnic groups(117,161). Epidemiological studies have shown that South Asian, Black and Chinese people experience a higher risk of diabetes at lower levels of obesity than Whites (123-126). Based on these findings there is a growing debate in the validity of conventional clinical cut-points for obesity which were originally derived from data cohorts of white European descent as BMI of ≥ 30.0 kg/m² or greater (World Health Organization & Organization, 2004).

Other obesity indicators include Waist-to-hip ratio (WHR) hip circumference. Experts(302-306) agreed that due to the heterogeneity of obesity levels in different populations there is need for lower anthropometric measures of obesity for non-white ethnic populations that would potentially reflect the true estimate of risk in these populations. Government agencies and health organisations including WHO, IDF, and NICE have subsequently recommended BMI and WC cut-off values for defining obesity in Asian populations (South Asian and Chinese descent) as BMI ≥ 23 kg/m² for adult men and women and waist circumference ≥ 84 cm for women and $90 \geq$ cm for men. However, due to insufficient data to derive

cut-offs for Black populations government organisations have suggested that the European cut-offs should be used until such data are generated (299,300,307,308).

The available data on ethnicity and obesity-specific cut-points for diabetes prediction is limited because most cohorts on obesity/adiposity and ethnic differences often rely on relatively small numbers of non-white participants within limited geographical locations (127). In addition, some studies used body composition methods that have questionable accuracy and precision (144). These factors make it difficult to obtain robust estimates of BMI and waist circumference at which diabetes is prevalence.

Despite diabetes prevalence differing markedly between South Asians and Chinese populations (166), current proposals for ethnicity-specific obesity cut-offs have generally considered Asians as a single group. UK Biobank recruited relatively larger numbers of participants from the Black, Chinese and South Asian populations to make subgroup analysis of South Asians and Chinese possible.

This chapter aims to address the issues with limited sample size and methodology on ethnic differences in obesity-related diabetes, whether the differences still remain after analysis and what is the magnitude the effect. This chapter will also add to the existing approaches for developing ethnic-specific determination of obesity classification for White, Black, Chinese and South Asian populations in the UK. This chapter compares the relationship between these anthropometric measures and the prevalence of diabetes across ethnic groups in the UK Biobank cohort. Furthermore, this chapter determines ethnic specific cut-offs of BMI and waist circumference related-obesity for diabetes risk in Black, Chinese and South Asian ethnic populations that are equivalent to those developed for white populations in terms of diabetes prevalence.

4.2 Methods

4.2.1 Study population

Participants were grouped into four groups: White, South Asian, Black, and Chinese. Volunteers were recruited and screened as detailed in section 2.5.1. A detailed description of the study population and general information on the statistical analysis has been presented in section 2.11-2.12. On the grounds of South Asians exhibiting heterogeneous demographic characteristics (309), Indian and Pakistani participants were considered separately in an additional analysis. The researcher carried out a sub-analysis to determine the obesity cut-offs for Indian and Pakistani groups in comparison to Whites by sex. The interaction between Indian and Pakistani groups was tested in multi-variable model including Indian and Pakistani groups only (men and women separately) and BMI or WC individually.

4.2.2 Anthropometric Assessment

This chapter evaluates various body measures recommended by previous studies as indicators of obesity such as BMI, waist circumference, waist-to-hip ratio (WHR), Body fat percent (BF%) and Waist-to-height ratio (WHtR). The primary exposures were Body Mass Index (BMI), waist circumference, Waist-to-Hip Ratio (WHR) and percentage body fat. Other exposures included in the study were the Townsend deprivation score, alcohol intake, smoking and physical activity.

4.2.3 Data and Statistical analyses

Statistical analyses were performed using Stata version 12.2 (Stata Corporation, College Station, Texas, USA). Participants with missing information on diabetes were excluded, and men and women were analyzed separately. The demographic and anthropometric characteristics of each ethnic group were summarized using the median and interquartile range for continuous variables, and frequencies and percentages for categorical data. The statistical significance of differences between ethnic groups was tested using the Kruskal-Wallis test for continuous variables and Pearson's chi-squared test for categorical variables. Ordinal variables were tested using a chi-squared test for trend. The p-values for all

hypothesis tests were two-sided and $p < 0.05$ was interpreted as statistically significant.

The presence of effect modification by sex ethnicity, obesity (as BMI or WC) and type 2 diabetes was evaluated using multiplicative interaction terms in a logistic regression model. Because interactions between sex and ethnicity were statistically significant ($P < 0.05$), odds ratios and 95%CI stratified by sex and ethnicity were calculated to examine diabetes risk associated with obesity measures.

Univariate binary logistic regression models were used to examine the crude association between level of adiposity and diabetes. Separate models were run for each of the anthropometric measures, and all were treated as continuous variables. All ethnic groups were entered into the same model, and the model was stratified by ethnic group with White used as the referent category. All of the models were re-run adjusting for the potential confounding effects of age and Townsend score. Finally, alcohol consumption, physical activity, and presence/absence of heart disease were also added as covariates. Goodness-of-fit of the logistic regression models were assessed using the area under the receiver operating characteristic curve (ROC AUC).

To determine ethnic specific cut-points for adiposity, BMI and waist circumference were modelled using restricted cubic splines (RCS) with three knots. RCS was preferred over a linear model because the AIC static was lower for all RCS models compared to the linear models, for determining adiposity cut points(310). The age-adjusted interaction with the ethnicity of each of the anthropometric measures were examined separately by sex and plotted the prevalence of diabetes against the level of adiposity by ethnic group. The ethnic-specific cut-off values at which diabetes is prevalent for white men were 30 kg/m² for BMI and 102 cm for waist circumference and for white women, 30 kg/m² and 88 cm respectively(159). The sensitivity analysis was repeated excluding those who had been diagnosed with diabetes for five years or longer, to determine whether this changed the ethnic-specific cut-offs.

4.3 Results

4.3.1 Characteristics of Participants by Ethnic Groups and Sex

Table 4-1 shows the characteristics of the study participants. Of the 502,682 UK Biobank participants, 491,741 (97.8%) belonged to the eligible ethnic groups. Information on diabetes was missing for 1,453 (0.3%) eligible participants. Therefore, the study population comprised 490,288 participants. Of these, 471,174 (96.1%) were white, 9,631 (2.0%) South Asian, 7,949 (1.6%) Black, and 1,574 (0.3%) Chinese. A total of 38,632 participants provided information on the “year immigrated to United Kingdom.” Of these, 15,271 (39.5%) were from non-white ethnic groups, and their median time living in the U.K. was 34 years. Overall, 25,567 (5.2%) had diabetes.

In comparison with white women, most anthropometric measures were higher among South Asian and Black women, and lower among Chinese women. All of the anthropometric measures, other than WHR, suggested that adiposity was highest among Black women. Among men, the results were less consistent across the individual measures. In both sexes, there were significant differences between the ethnic groups in age, socioeconomic status, smoking status, alcohol intake and level of physical activity. The prevalence of diabetes was higher than in all non-white groups and highest among South Asian participants than in whites.

Table 4-1 Logistic regression analysis of the association between adiposity and diabetes by ethnic group and sex

	Women				Men			
	white N= 256,806	South Asian N= 4,479	Black N= 4,596	Chinese N= 965	White N= 214,368	South Asian N= 5,152	Black N= 3,353	Chinese N= 569
	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)
Age (years)	60 (52-65)	54 (48-61)	52 (47-59)	54 (48-60)	60 (53-66)	55 (47-62)	52 (46-59)	53 (47-61)
BMI (kg/m²)	26.1 (23.4-29.6)	26.7 (24.0-30.0)	29.7 (26.1-33.7)	22.9 (21.0-25.4)	27.3 (24.9-30.1)	26.5 (24.4-29.1)	27.9 (25.5-30.6)	24.9 (23.0-27.0)
Weight (kg)	69.1 (61.8-78.6)	65.4 (68.4-74.0)	77.9 (68.4-89.1)	57.2 (52.0-63.4)	84.5 (76.5-94.0)	77.0 (69.7-85.5)	84.2 (76.1-93.9)	70.8 (65.2-77.6)
Bodyfat (%)	36.7 (32.0-41.3)	38.0 (33.8-42.1)	40.4(35.6-44.3)	30.1 (25.9-34.2)	25.4 (21.6-29.1)	26.2 (22.9-29.4)	25.6 (21.7-29.0)	21.1 (17.8-24.7)
WC (cm)	83 (75-92)	86 (78-94)	91(82-100)	75 (70-82)	96 (89-104)	95 (89-102)	94 (87-101)	87 (81-93)
HC (cm)	102 (96-108)	101(95-107)	107 (100-114)	93 (89-98)	103 (99-107)	100 (95-104)	103 (98-108)	96 (93-100)
WHR	0.81 (0.77-0.86)	0.85 (0.80-0.90)	0.84 (0.79-0.90)	0.81 (0.77-0.86)	0.93 (0.89-0.98)	0.95 (0.91-0.99)	0.91 (0.87-0.95)	0.90 (0.87-0.94)
Physical Activity (MET-mins/wk.)	2,533 (1,455-4,547)	2,226 (1,215-4,053)	2,300 (1,299-4,053)	2,314 (1,342-4,485)	2,648 (1,448-5,092)	2,162 (1,158-3,908)	2,415 (1,273-4,938)	2,093 (3,684-1,164)
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Diabetes	8,869 (3.5)	618 (13.8)	475 (10.3)	48 (5.0)	14,014 (6.5)	1,068 (20.7)	431 (12.9)	44 (7.7)
missing	484	86	43	25	629	123	48	15
Heart Diseases	65,603 (25.5)	1,274 (28.4)	1,882 (41.0)	197 (20.1)	74,281(34.6)	1,902 (36.7)	1,242 (36.9)	139 (24.1)
missing	452	84	46	12	357	97	34	7
Deprivation								
1 (least)	52,586 (20.5)	454 (9.9)	125 (2.7)	148 (15.0)	44,358 (20.6)	453 (8.6)	91 (2.7)	83 (14.3)
2	52,766 (20.5)	446 (9.8)	212 (4.6)	145 (14.7)	44,009 (20.5)	476 (9.0)	146 (4.3)	95 (16.3)
3	52,837 (20.5)	699 (15.3)	380 (8.2)	165 (16.7)	42,988 (20.0)	734 (14.0)	264 (7.8)	82 (14.1)
4	51,600 (20.1)	1,337 (29.3)	953 (20.5)	254 (25.7)	41,774 (19.5)	1,445 (27.4)	675 (19.4)	146 (25.1)
5 (most)	47,197 (18.4)	1,625 (35.7)	2,964 (64.0)	275 (27.9)	4,1607 (19.4)	2,158 (41.0)	2,210 (65.3)	176 (30.2)
Alcohol Frequency								
never	20,964 (8.15)	2,472 (54.4)	1,125(24.4)	305 (30.9)	10,989 (5.1)	692 (23.1)	690 (20.4)	123 (21.1)
daily	43,026 (16.7)	131 (2.9)	184 (4.0)	45 (4.6)	56,287(26.2)	404 (13.5)	327 (9.7)	60 (10.3)
3-4 / week	54,723 (21.3)	202 (4.5)	329 (7.1)	42 (4.3)	57,692 (26.9)	464 (15.5)	446 (13.2)	54 (9.3)
1-2 / week	67,868 (26.4)	424 (9.3)	761 (16.5)	108 (10.9)	56,322 (26.2)	667 (22.3)	822 (24.3)	99 (17.0)
1-3 / month	33,734 (13.1)	311(6.8)	648 (14.0)	103 (10.4)	19,019 (8.9)	289 (9.7)	409 (12.1)	69 (11.8)
occasional	36,807 (14.3)	1,004 (22.1)	1,570 (34.0)	384 (38.9)	14,522 (6.8)	480 (16.0)	696 (20.5)	179 (30.7)

a p-value <0.0001 for all variables; med median; IQR interquartile range; BMI body mass index; WC waist circumference; HC hip circumference; WHR waist-to-hip-ratio; N number

4.3.2 Association Between Adiposity and Diabetes

The univariate logistic regression analyses confirmed a stronger association between adiposity and diabetes in non-white groups, among both men and women in Table 4-2. The association was strongest among South Asian participants, irrespective of their sex and the anthropometric measure used. Following adjustment for the potential confounding effects of age and socioeconomic status, the stronger associations in non-White groups increased further. The associations were modestly attenuated following the inclusion of alcohol consumption, physical activity and presence/absence of heart disease in the models, but all associations remained statistically significant, and the association between adiposity and diabetes remained three-to four-fold greater.

Table 4-2 Logistic regression analysis of the association between adiposity and diabetes by ethnic group and sex

		Women						Men							
		white	South Asian		Black		Chinese			White	South Asian		Black		Chinese
		(Ref group)	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	(Ref group)	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
BMI	model 1†	1.0	4.8 (4.3-5.2)	<0.001	2.1 (1.9-2.3)	<0.001	2.7 (2.0-3.7)	<0.001	1.0	4.7 (4.4-5.1)	<0.001	2.0 (1.8-2.3)	<0.001	2.0 (1.5-2.7)	<0.001
	model 2*	1.0	5.4 (4.9-5.9)	<0.001	2.1 (1.9-2.4)	<0.001	3.3 (2.4-4.4)	<0.001	1.0	5.8 (5.4-6.3)	<0.001	2.4 (2.1-2.7)	<0.001	2.6 (1.9-3.6)	<0.001
	model 3#	1.0	3.7 (3.1-4.5)	<0.001	1.5 (1.3-1.8)	<0.001	1.7 (0.9-3.0)	0.052	1.0	4.2 (3.7-4.8)	<0.001	2.2 (1.8-2.6)	<0.001	3.3 (2.1-5.2)	<0.001
WC	model 1†	1.0	4.6 (4.2-5.1)	<0.001	2.1 (1.9-2.4)	<0.001	3.2 (2.4-4.3)	<0.001	1.0	4.6 (4.3-5.0)	<0.001	2.6 (2.3-2.9)	<0.001	2.5 (1.8-3.4)	<0.001
	model 2*	1.0	5.1 (4.6-5.6)	<0.001	2.2 (2.0-2.4)	<0.001	3.7 (2.8-5.0)	<0.001	1.0	5.4 (5.0-5.8)	<0.001	2.8 (2.5-3.2)	<0.001	3.0 (2.2-4.2)	<0.001
	model 3#	1.0	3.6 (3.0-4.2)	<0.001	1.6 (1.3-1.9)	<0.001	2.0 (1.2-3.4)	<0.001	1.0	3.9 (3.4-4.4)	<0.001	2.5 (2.1-3.0)	<0.001	3.6 (2.2-5.6)	<0.001
%BF	model 1†	1.0	5.3 (4.8-5.8)	<0.001	2.2 (2.0-2.5)	<0.001	3.0 (2.2-4.0)	<0.001	1.0	4.6 (4.3-5.0)	<0.001	2.3 (2.0-2.5)	<0.001	2.3 (1.7-3.1)	<0.001
	model 2*	1.0	4.5 (4.1-5.0)	<0.001	2.3 (2.0-2.5)	<0.001	3.4 (2.5-4.6)	<0.001	1.0	4.2 (3.9-4.6)	<0.001	2.3 (2.1-2.6)	<0.001	2.5 (1.8-3.4)	<0.001
	model 3#	1.0	3.1 (2.6-3.7)	<0.001	1.6 (1.3-1.9)	<0.001	1.6 (0.9-2.8)	0.096	1.0	3.2 (2.8-3.6)	<0.001	2.1 (1.8-2.5)	<0.001	3.0 (1.9-4.8)	<0.001
WHR	model 1†	1.0	3.3 (3.1-3.7)	<0.001	2.4 (2.2-2.7)	<0.001	1.6 (1.2-2.2)	<0.001	1.0	3.4 (3.2-3.7)	<0.001	2.9 (2.6-3.2)	<0.001	1.8 (1.3-2.5)	<0.001
	model 2*	1.0	3.6 (3.3-3.9)	<0.001	2.3 (2.1-2.5)	<0.001	1.8 (1.4-2.5)	<0.001	1.0	3.8 (3.6-4.2)	<0.001	2.9 (2.6-3.2)	<0.001	2.1 (1.5-2.9)	<0.001
	model 3#	1.0	2.5 (2.1-3.0)	<0.001	1.6 (1.4-1.9)	<0.001	1.1 (0.7-2.1)	0.453	1.0	3.0 (2.6-3.4)	<0.001	2.6 (2.2-3.1)	<0.001	2.8 (1.7-4.4)	<0.001

OR odds ratio; CI confidence interval; BMI body mass index; WC waist circumference; %BF percentage body fat; WHR waist-to-hip-ratio

Whites are the referent group; p-values are in comparison to the White group. Adiposity included as a continuous variable in models

† Univariate analyses; *adjusted for age and socioeconomic status; #adjusted for age, socioeconomic status, physical activity, heart disease and alcohol consumption

4.3.3 Ethnic-Specific Obesity (BMI) Cut-Offs

In Figure 4-1 and Figure 4-2 below, the prevalence of diabetes is plotted against the level of adiposity by ethnic group. Irrespective of the anthropometric measure used (BMI or waist circumference), the prevalence of diabetes among non-white groups was equivalent to that in the white group at a lower level of adiposity.

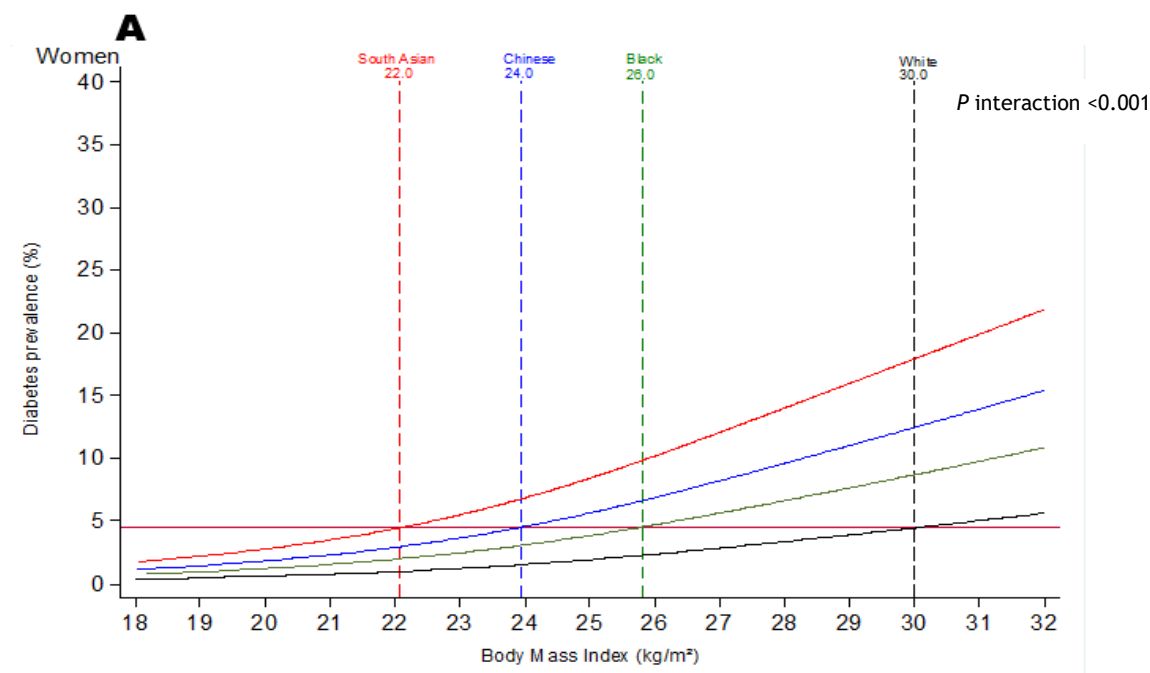


Figure 4-1 Adjusted BMI obesity cut-off for diabetes prevalence (women)

Compared with white women with a BMI of 30kg/m², equivalent diabetes prevalence was 22.0 kg/m² in South Asian women, 26.0 kg/m² in Black women and 24.0 kg/m² Chinese women. In men, the equivalent values were comparable at 21.6 kg/m², 26.0 kg/m² and 26.0 kg/m² for South Asian, Chinese and Black men, respectively (Figure 4-2).

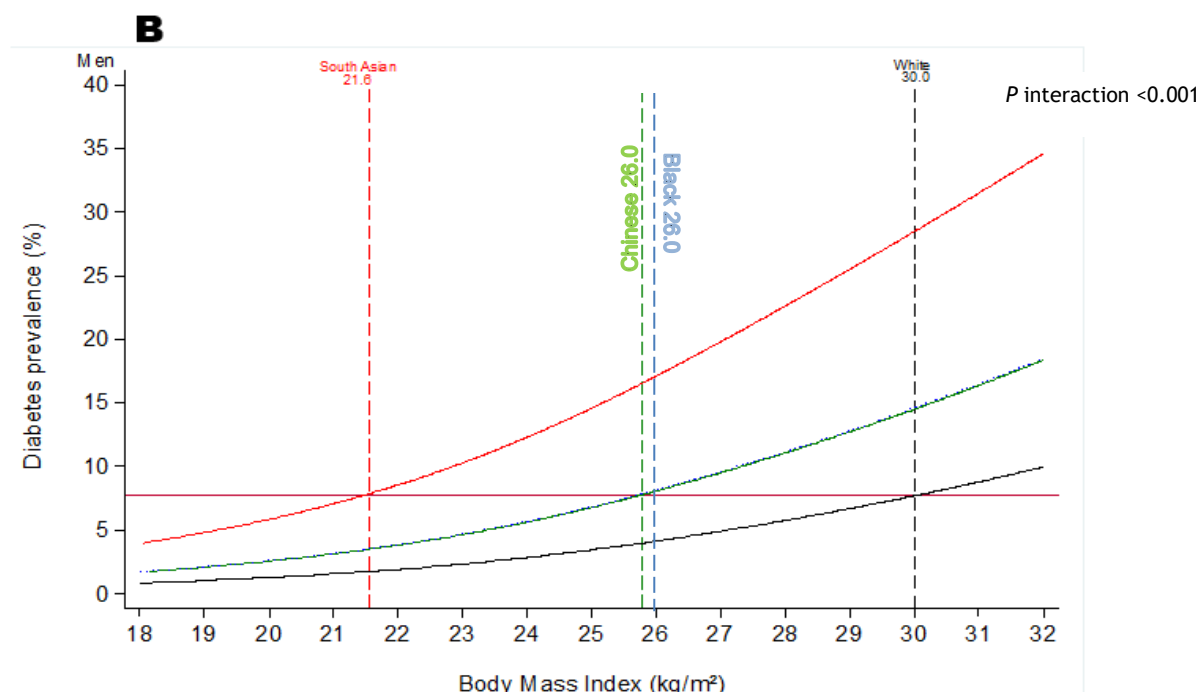


Figure 4-2 Adjusted BMI obesity cut-off for diabetes prevalence (men)

4.3.4 Ethnic-Specific Obesity (WC) Cut-Offs

Table 4-3 and Figure 4-3a shows that for equivalent diabetes prevalence, a waist circumference of length of 88 cm in white women was equivalent to 70 cm in South Asian women, 74 cm in Chinese women, and 79 cm in Black women. Similarly for the equivalent diabetes prevalence for men, a waist circumference of 102 cm in white men was equivalent to 79 cm, 88 cm, and 88 cm in South Asian, Chinese and Black men respectively (Figure 4-3b).

Table 4-3 Adjusted body mass index and waist circumference cut-offs equivalent to conventional obesity thresholds by ethnic group and sex

		White (Reference)	South Asian mean (95% CI)	Black mean (95% CI)	Chinese mean (95% CI)
Women	BMI (kg/m ²)	30.0	22.0 (21.4-23.0)	26.0 (25.3-27.2)	24.0 (22.3-27.1)
	WC (cm)	88.0	70.0 (66.0-72.0)	79.0 (77.3-81.5)	74.0 (69.5-80.0)
Men	BMI (kg/m ²)	30.0	21.6 (21.0-22.6)	26.0 (25.3-27.3)	26.0 (24.0-28.5)
	WC (cm)	102.0	79.0 (77.0-80.4)	88.0 (86.2-90.3)	88.0 (83.4-94.1)

Including all participants with diabetes.

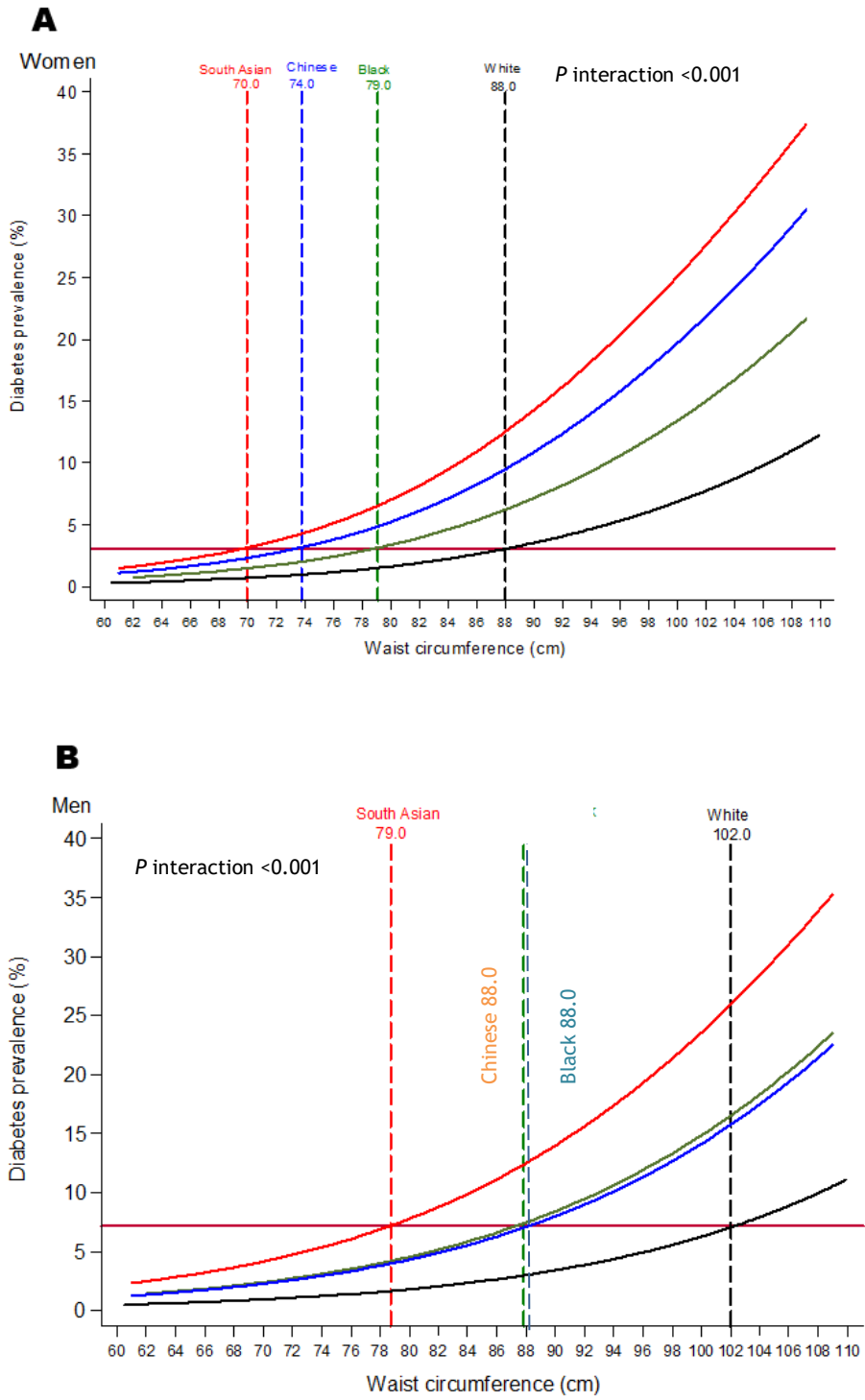


Figure 4-3 Adjusted Waist circumference obesity cut-off for diabetes prevalence

4.3.5 Indian and Pakistani Ethnic Groups (BMI&WC) Cut-Offs

Considering Indians and Pakistanis separately for a diabetes prevalence of 30 kg/m² in Whites, a BMI value of 21.6 kg/m² in Pakistanis women and 22.3 kg/m² in Indian women is equivalent. Similarly for men a BMI value of 21.5 kg/m² and 22.0 kg/m² for Pakistanis and Indians respectively is equivalent to a BMI of 30 kg/m² in Whites (Table 4-4 and Figure 4-4).

Table 4-4 Adjusted body mass index and waist circumference cut-offs equivalent to conventional obesity thresholds in Indian and Pakistani ethnic groups

		White (Reference)	Pakistani mean (95% CI)	Indian mean (95% CI)
Women	BMI (kg/m ²)	30.0	21.6 (20.2-23.5)	22.3 (21.4-23.3)
	WC (cm)	88.0	68.0 (65.5-72.0)	70.0 (69.0-73.0)
Men	BMI (kg/m ²)	30.0	21.5 (20.6-22.8)	22.0 (21.4-22.9)
	WC (cm)	102.0	78.0(75.7-80.7)	80.0 (78.3-82.1)

BMI body mass index, WC waist circumference

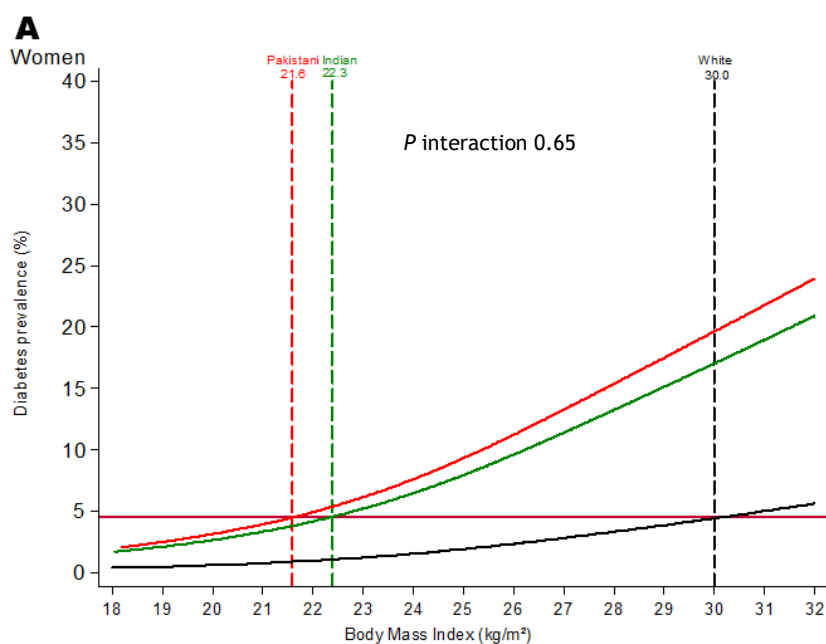


Figure 4-4b Adjusted body mass index cut-off in Indian, Pakistani and White

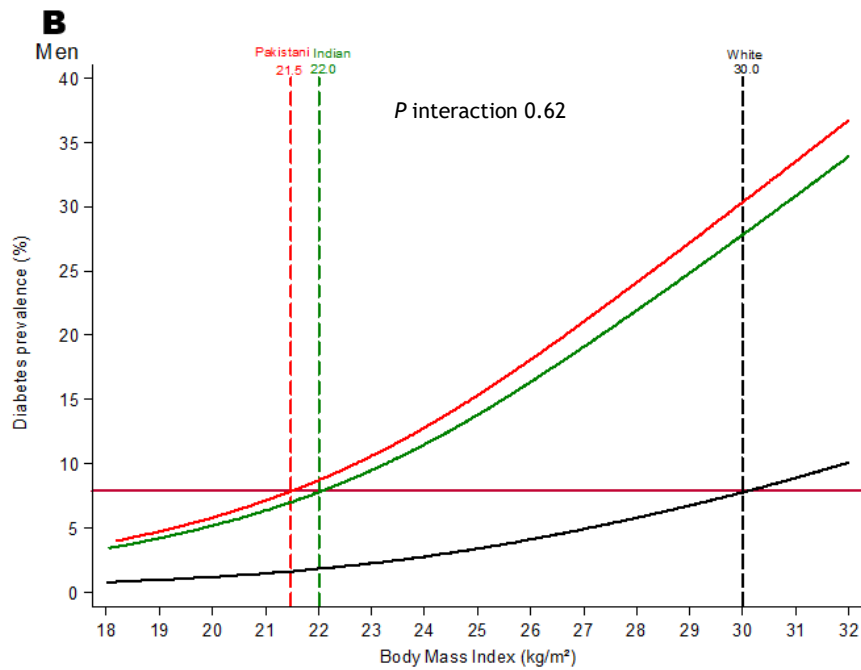


Figure 4-4b Adjusted body mass index cut-off in Indian, Pakistani and White

The waist circumference values for similar diabetes prevalence were lower for Pakistani women than Indian women (68.0 cm vs 70.0 cm). Likewise Pakistani men had lower waist circumference than Indian men (78.0 cm vs 80.0 cm) (Figure 4-5b Adjusted waist circumference cut-points in Indian, Pakistani and White Figure and Table 4-4). None of these differences in cut-offs between Indian and Pakistani groups were statistically significant.

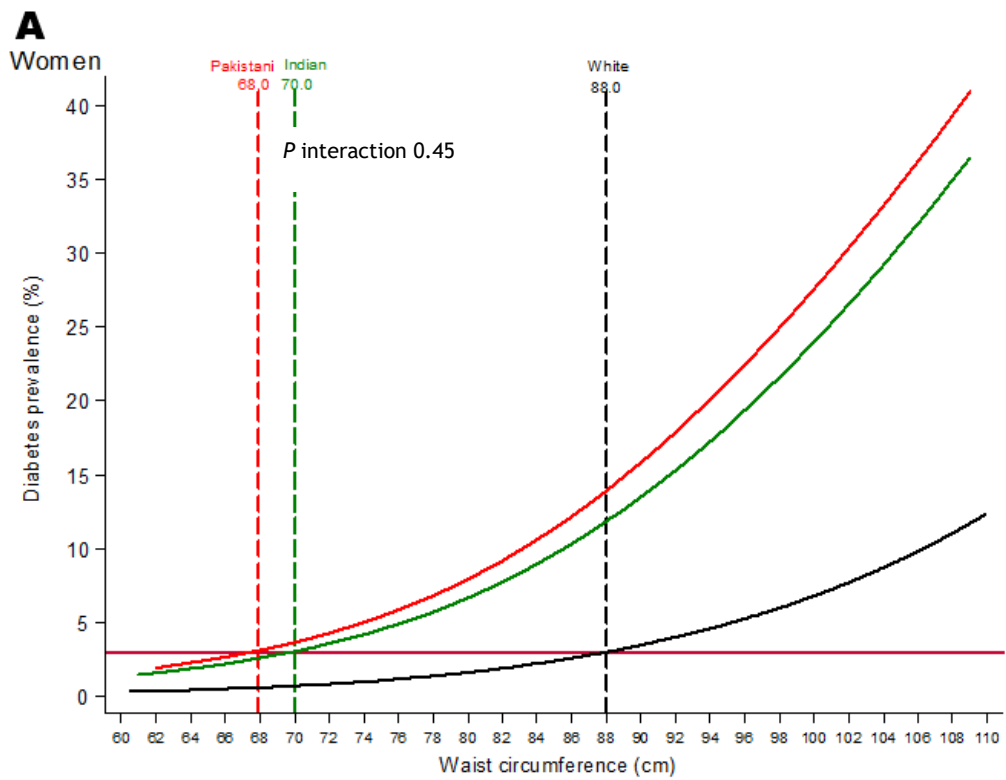


Figure 4-5b Adjusted waist circumference cut-points in Indian, Pakistani and White

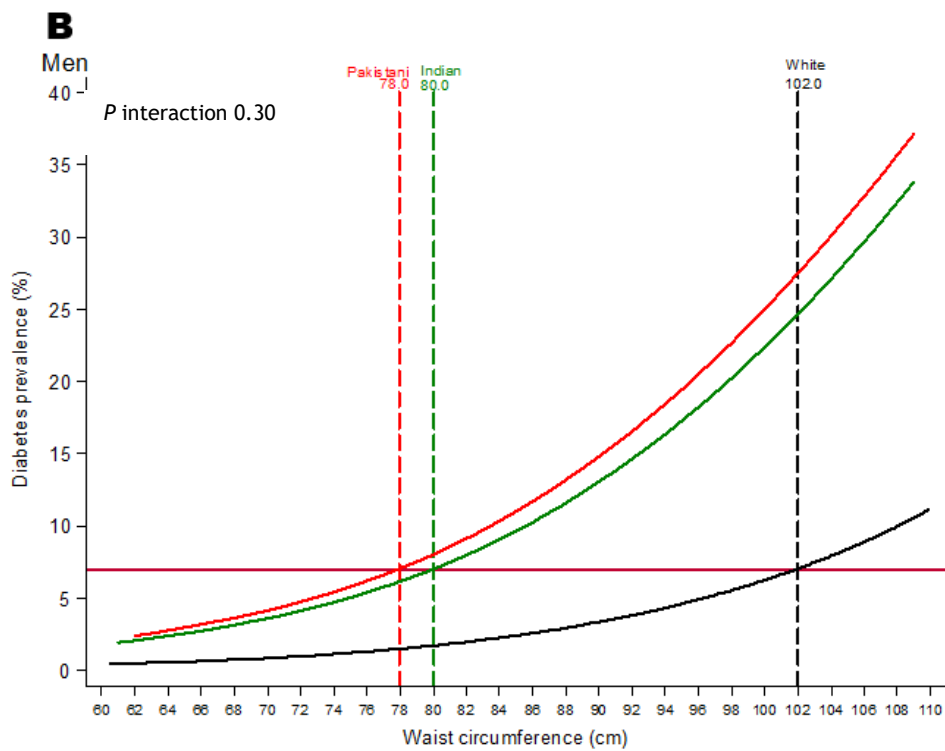


Figure 4-5b Adjusted waist circumference cut-points in Indian, Pakistani and White

4.3.6 Sensitivity Analysis

For sensitivity analysis, I repeated the analyses excluding participants who had been diagnosed with diabetes for five years or longer, the BMI and waist circumference cut-offs were very similar to the previous values for Black and Chinese groups, but the values for South Asian men were slightly higher (Table 4-5).

Table 4-5 Age-adjusted body mass index and waist circumference cut-offs equivalent to conventional obesity thresholds by ethnic group and sex

		White (Reference)	South Asian mean (95% CI)	Black mean (95% CI)	Chinese mean (95% CI)
Women	BMI (kg/m ²)	30.0	22.3 (21.4-23.6)	25.3 (24.2-26.7)	23.4 (20.5-28.1)
	WC (cm)	88.0	72.0 (69.5-75.3)	78.0 (75.3-81.3)	74.0 (68.6-82.7)
Men	BMI (kg/m ²)	30.0	23.4 (22.3-25.0)	26.0 (24.8-27.4)	26.0 (23-30.3)
	WC (cm)	102.0	84.0 (77.0-85.2)	88.0 (85.3-91.5)	88.0 (80.3-101.5)

Including only participants with diabetes diagnosed within last five years.

The areas under the ROC curves showed that the logistic regression models were a good fit, ranging from 74% to 78% (Table 4-6).

Table 4-6 The goodness-of-fit for each model used in analysis by sex

	Female (%)	Male (%)
BMI	77.0	76.0
%BF	74.0	74.0
WC	78.0	76.0
WHR	78.0	75.0

BMI Body mass index; WC waist circumference; %BF percentage body fat; WHR waist-to-hip-ratio.

4.4 Discussion

This study demonstrates ethnic differences in both the prevalence of diabetes and the association between adiposity and prevalent diabetes. Consistent with previous studies, South Asians had the highest prevalence of diabetes, followed by Chinese and Black participants, with whites having the lowest prevalence. Obesity was a risk factor in all ethnic groups but the risk associated with obesity,

as defined by current guidelines, was two-to four-fold higher in non-white participants. In non-white groups, the prevalence of diabetes was equivalent to that in white populations at much lower levels of BMI and waist circumference. Using current guidelines to target interventions at obese individuals would result in a higher risk threshold for diabetes being applied to non-white individuals. The curvilinear relationship between BMI and diabetes contrasts to the U-shaped relationship between BMI and total and cardiovascular mortality, which is not fully understood yet. This simpler relationship, combined with plentiful evidence that diabetes can be prevented by lifestyle changes, justifies the focus on diabetes in deriving ethnic specific cut-offs.

4.4.1 BMI Cut Points for South Asians

The findings are consistent with previous studies in suggesting that the cut-offs currently recommended by the WHO should be reduced when applied to non-white populations (123-125,127,137,160,311). Whilst the current cut-offs apply equally well to diabetes and cardiovascular disease when applied to white populations, studies in non-White populations tend to produce lower ethnic specific equivalents for diabetes than cardiovascular disease (123,126,144).

This study demonstrated that South Asians had an equivalent prevalence of diabetes at a BMI of 22.0 kg/m² in women and 21.6 kg/m² in men, which is at the lower end of the normal BMI range for white populations. This is consistent with previous studies. Based on measuring 2-hour glucose, Bodicoat et al. reported the BMI cut-offs of 21.1 kg/m² for South Asians migrants in the UK(128). A UK study using the Clinical Practice Research Datalink (CPRD) suggested a BMI cut-off of 23.9 kg/m². (137)Another UK study by Gray et al. measuring glycaemic risk score, produced BMI cut-offs of 21.5 kg/m² and 22.6 kg/m² for South Asian men and women, respectively, as being equivalent to a BMI of 30.0 kg/m² in whites (123), and a similar Canadian study by Razak et al. suggested a BMI cut-off of 21.0 kg/m² in South Asian men and women (124).

In contrast, the findings from studies by Tillin et al. and Chiu et al. recommended a higher South Asian cut-off value of 25.2 kg/m² and 24.0 kg/m² respectively based on the adjusted incidence of diabetes (127,144). However, the SABRE study

findings by Tillin and colleagues was based on a 20-year-old small sample sized data, which may not be significant to the current demographics of South Asians (127), while findings presented by Chiu and colleagues did not include any confidence intervals to indicate the precision of their cut-off estimates (144). Nyamdorj et al., pooled data from 30 cross-sectional studies (N=54,467 total participants), conducted in 11 Asian and European countries, reported an equivalent BMI cut-off of 19.0 kg/m² for South Asian groups (150). Using baseline data from native Indians resident in Jaipur and New Delhi (N=985), Bodicoat et al. reported an equivalent BMI cut-off of 18.2kg/m² for indigenous Indians based on fasting glucose(128).

4.4.2 BMI Cut Points for Blacks

Similarly, in this study, the cut-offs for BMI of 26.0 kg/m² suggested for both Black women and men, is comparable to cut-offs of 26.0 kg/m² for Blacks by Chiu et al. (144) and by Stommel et al.(126) based on diabetes incidence and prevalence respectively. Findings from the SABRE study and CRPD data suggests higher cut-points of 27.2 kg/m² and 28.1 kg/m² respectively in Blacks based on diabetes incidence rates (127).

4.4.3 BMI Cut Points for Chinese

In this study cut-offs for BMI of 24.0 kg/m² in Chinese women and 26.0 kg/m² in Chinese men, were comparable to cut-offs range of 23.0 kg/m² in Chinese women and 25.0 kg/m² in Chinese men reported by Nyamdorj et al.(150), 25.0 kg/m² in Chinese population by Chiu et al. (144), 26.0 kg/m² by Stommel et al.(126), and 26.9kg/m² by Caleyachetty et al. In contrast, the cut-off for Chinese 3-5 kg/m² was higher than the value of 21.0 kg/m² recommended by Razak et al. (124) based on the glycaemic risk score.

4.4.4 Waist Circumference Cut Points

In this study, waist circumference for diabetes prevalence was 70 cm in South Asian women and 88 cm in South Asian men, 74 cm in Chinese women and 88 cm in Chinese men, and 79 cm in Black women and 88 cm in Black men. Bodicoat et

al. (128) reported waist circumference of 71.7cm and 78.8cm in migrant South Asian women and men respectively based on 2-hour glucose. In the same study, based on fasting glucose, the researchers reported waist circumference cut-off of 87.1cm in indigenous Indian men but a lower cut-off of 53.5cm for indigenous Indian women (128).

Although based on glycaemic risk score rather than diabetes prevalence, Gray et al. produced an identical waist circumference cut-off value of 69 cm for South Asian women but a lower value of 84 cm for South Asian men (123). Whereas Tillin et al. based-on diabetes incidence suggested 90.6cm and 90.4cm in South Asian and Black men; 84.0cm in South Asian women and 81.2cm in Black women (127). Nyamdorj, et al. study based on diabetes incidence, recommended comparable 70 cm and lower value of 73 cm in South Asian women and men respectively, and lower values of 70 cm and 82 cm in Chinese women and men (150).

4.4.5 Study Contributions

This study builds on the earlier published findings in a few important ways. First, is a comparatively large sample sized study with a total of 490,288 participants, including 9,631 South Asians, 1,534 Chinese, and 7,949 Blacks. It is approximately ten times larger than any other previous investigation on this topic. This allows for a more precise estimate of the equivalent BMI and waist circumference cut points for men and women separately than was previously possible.

This study is novel in presenting associations on three obesity measures i.e., BMI, WC, and Adiposity and diabetes prevalence in four ethnic groups (White, Blacks, Chinese and South Asian). It is also one of the first such studies of Chinese population in the United Kingdom that researcher is aware of that gives a more nuanced picture of adiposity in these groups.

The researcher considered cut points for Indians and Pakistanis separately within the South Asian group and reporting for the first time that equivalent BMI and waist circumference cut points for diabetes prevalence were slightly lower in Pakistanis than Indians. It is of note that 89.4% of South Asian women and 94.8% of South Asian men in the UK Biobank cohort had BMI values $>22.0 \text{ kg/m}^2$ and 21.6

kg/m², respectively. This suggests that, depending on the nature of the intervention, it may sometimes be more feasible and cost-effective to target all South Asians rather than trying to identify the large majority at high risk.

For people with a BMI of approximately 22.0 kg/m², weight loss interventions may not be the most appropriate mechanism for reducing diabetes risk, but other lifestyle interventions such as dietary modification and increased physical activity could be established for them. Studies have shown that physical activity levels are lower in South Asian groups and that South Asians may need to engage in greater levels of physical activity than whites for an equivalent glycaemic risk profile(62,312).

Therefore, future research is required to determine whether interventions aimed at increasing physical activity, rather than weight loss per se, may be more appropriate at this level of BMI. Following on the results shown in this study, the estimated burden of obesity-related diabetes risk among minority ethnic groups may be greatly underestimated using the current WHO, IDF and national guidelines for BMI and waist circumference cut offs. Different BMI and waist circumference cut-offs are necessary for different ethnic groups for appropriate screening and clinical efficacy. Although revised thresholds for South Asians, Chinese and Blacks could greatly increase estimates and establishing a diabetes diagnosis at a lower adiposity threshold potentially will add additional health care costs as a result of more widespread screening, it would be preferable to be more inclusive rather than exclusive to minimize overlooking at-risk cases, which would be beneficial for early identification and management of diabetes in these ethnic groups in the UK population , particularly whereby the screening test is not costly. The costs associated with determining risk from BMI and WC measures are negligible.

Furthermore, this study proposes that prognostic risk assessment tools for early identification of type 2 diabetes include both BMI and WC as risk factors for increased sensitivity and specificity in the prediction of those at risk in minority ethnic groups who develop prediabetes and diabetes at lower adiposity levels. Hsia and colleagues(313) showed in their study of 9756 participants from the NHANES data collected between 2011 and 2012 that using the cut point of lower BMI of 23.0 kg/m² to predict diabetes increased the prevalence of diabetes from

13.1% to 24.3% but also increased the sensitivity of screening for prediabetes and diabetes from 50.2 to 74.1% ($P < 0.0001$) but decreased the specificity from 62.9 to 38.7% ($P < 0.0001$) identifying more people with these conditions. However, the specificity of screening declined, likely due at least in part to the similarity in the prevalence of pre-diabetes in the cohort with BMI $<23.0 \text{ kg/m}^2$ and the cohort with BMI $\geq 23.0 \text{ kg/m}^2$).

The findings reported here on ethnic differences in diabetes risk with respect to BMI are in line with the QDiabetes risk algorithm. For example, a 50 years old man from South Asian descent with BMI of 22.0 kg/m^2 , a Black African man with 26.0 kg/m^2 , a Chinese man with 26.0 kg/m^2 and a White man with 30.0 kg/m^2 of the same age all have the same risk of developing type 2 diabetes (10-11%) within the next 10 years (314,315) This provides further external validity to the findings and suggests that either using the QDiabetes score calculator or the ethnicity-specific BMI thresholds suggested here are valid approaches for assessing ethnicity-specific diabetes risk. While the QDiabetes risk algorithm is more comprehensive, the differential BMI-threshold approach provides a simpler rule-of-thumb approach for assessing risk in circumstances through which using the QRisk calculator may not be appropriate, for example in community-based risk screening. A key observation for such contexts is that the thresholds suggested here are substantially lower than the WHO recommended ethnicity-specific BMI guidelines(155,316).

The findings in this study reveal the associated risk of diabetes with BMI, WC or %BF were more strongly associated with increasing adiposity measures in South Asians and Chinese populations than in Blacks. These disparate observations might be explained by some additional mechanisms. Firstly, mechanisms related to insulin sensitivity and adiposity may differ in Blacks compared to other ethnic groups. For instance, Blacks have less metabolically active adipose tissue including visceral abdominal fat. It also may be possible that there are additional potential confounders, including psychosocial status, physical inactivity, diet, and genetic predisposition may play roles in the marked elevation in diabetes risk (61).

It is possible that people living with diabetes experience weight change following diagnosis which could be associated with elevation of risk factors or lifestyle changes such as food intake and physical activity. In one report using data from

the Danish Diabetes Care in General Practice (DCGP) Study, participants lost on average 2.5 kg in weight after six years of diagnosis (317). In addition, Vierboom et al.(318) showed people diagnosed with diabetes are more likely to experience 10% of unintentional weight loss compared to individuals with no diabetes. The effect of this would be for relationship between prevalence of diabetes for and BMI to be shifted leftwards compared to the relationship between BMI and diabetes incidence. However, the present analysis compared the relative differences between ethnic groups in the relationship between BMI and diabetes prevalence. Thus, unless the difference in weight changes post-diagnosis differed substantially between ethnic groups, the relative ethnic difference in diabetes prevalence at different levels of BMI should not be substantially affected by changes in body weight post-diagnosis. There is no evidence available (to my knowledge) to ascertain whether post-diagnosis changes in BMI differ between ethnic groups. However, in other analyses which have considered ethnic differences in BMI with incident diabetes, the findings have been broadly like those observed in the present analysis(137,144), which suggests that this is unlikely to be a major issue here.

Several hypotheses have been proposed to explain why non-white populations have an equivalent risk of diabetes at lower levels of adiposity. Many researchers attribute this to higher insulin resistance among Asian and Black populations, as a result of which body fat is deposited in the abdomen and liver at a lower BMI, and that the 'thrifty gene' inherited from their ancestors enabled them to store calories more efficiently during long periods of famine, but predisposes to weight gain in our obesogenic environment (319,320). Lower birth weight, shorter limbs relative to the trunk, insufficient physical activity, physiological differences such as low fitness and reduced capacity for fat oxidation between ethnic groups have also been suggested as contributory factors of the observed findings (320,321).

UK Biobank is a very large study and provided sufficient numbers in the four main ethnic subgroups. Therefore, a major strength was the ability to compare several ethnic groups living in the same country within the same study. Previous U.K. cross-sectional studies have been smaller overall, recruited smaller numbers of non-White participants, and compared fewer ethnic groups; for example, the study by Mckeigue et al.(322) was based on 3,754 participants in total.

The researcher had access to several measures of adiposity which were measured by trained staff, using validated methods and standard operating procedures. The researcher was able to adjust for a wide range of confounding factors, but residual confounding can never be fully excluded from an observational study. The results showed that the regression fitted the different models reasonably well, with all producing areas under the curve in excess of 74%. As this is a cross-sectional study of prevalent cases of diabetes, The researcher could not establish a temporal relationship between obesity and diabetes. However reverse causation is unlikely to be a major problem since the subgroup analysis that included only recently diagnosed patients with diabetes (within 5 years) produced very similar cutoff values. Diabetes was ascertained by self-report of a physician diagnosis. Therefore, incomplete ascertainment is possible but unlikely to introduce a systematic error. Indeed, Bays et al.(323) reported that the prevalence of diabetes was similar when based solely on self-report in the SHIELD (Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes) screening survey compared with clinical and laboratory corroboration of self-reports in the National Health and Nutrition Examination Survey. Schneider et al.(324) also showed that self-reported diabetes was >92% reliable and 83% sensitive. I was unable to differentiate between type 1 and type 2 diabetes. However, in the age-group studied, most cases (>90%) will be type 2 and the cutoffs were very similar in the subgroup analysis limited to participants with recently diagnosed diabetes, who are much less likely to be type 1(324). In due course, follow-up of UK Biobank participants will provide data on incident cases of diabetes, which can be used to verify the cut points derived from the baseline data.

This study was conducted in the UK and from migration studies, ethnic groups who emigrate differ from those remaining in their native countries in terms of metabolic risk and that this is due to changes in their lifestyle(325-329). However, I believe that the underlying relationship between adiposity and diabetes in a given ethnic group should be unaffected by country of residence, and therefore the results should be generalizable to people of the same ethnic group who live outside of the UK, including their country of origin. However, further studies should be conducted to corroborate this.

Defining a threshold value for BMI or waist circumference is necessary to target diabetes screening and prevention, including weight reduction interventions. This study adds to the growing evidence that non-White groups face a greater burden of diabetes at lower levels of adiposity. Therefore, applying the same adiposity thresholds in non-White and white populations introduces inequality in terms of disease risk. There is now overwhelming evidence of the need for lower ethnic-specific cutoffs for intervention in non-White populations. Although the precise cutoffs varied slightly between studies, the rankings of ethnic groups have been consistent, with South Asians having the lowest cutoff values and Chinese having values either equal to or below those of Black groups. Lower obesity thresholds should be applied to non-White groups, and should be specific to each ethnic group, to ensure an equitable approach based on equivalent risk. In particular, the present data show that Asians should not be treated as a single group when considering obesity thresholds which was an approach that had been adopted in (161,298,307). This chapter confirm that South Asians require a substantially lower obesity cutoff than Chinese. Moreover, these findings will aid future guidelines in this area, could help promote better public education, and improve recommendations of health measures to attenuate obesity risks in high-risk ethnic populations.

5 Association between grip strength and diabetes prevalence in black, South Asian, and white European ethnic groups: a cross-sectional study of 418,656 UK Biobank participants.

5.1 Introduction

There is evidence that low muscular strength could be an important risk factor for diabetes(217,330). A meta-analysis by Tarp and colleagues(268), included 13 prospective studies with 1,713,468 participants and reported that every SD increment in absolute handgrip strength was associated with a 13% lower risk of diabetes. More recent studies published since this meta-analysis have confirmed this association (217,330,331). There is also evidence that participation in muscle strengthening exercise and moderate-to-vigorous aerobic physical activity (which would be expected to increase cardiorespiratory fitness) independently reduce risk of type 2 diabetes (332,333). Muscular strength may vary by ethnicity (219,334,335). However, it is unclear whether the association between muscular strength and type 2 diabetes also varies according to ethnicity and whether this may contribute to the ethnic differences in diabetes prevalence.

To the researcher's knowledge only one study conducted in the Netherlands by van der Kooi and colleagues (336) studied the association of grip strength and type 2 diabetes in participants from African and South Asian background in comparison with European white ethnic groups living in the Netherlands. Their study had a relatively small sample size of 13,316 participants, and used absolute handgrip strength by summing the maximal handgrip strength of both hands, and did not consider the extent to which strength varying by body mass might have influenced the findings. Relative grip strength (absolute strength corrected for a measure of body size such as body mass calculated by dividing absolute handgrip strength by body mass) has been recommended to address both confounding of strength by body mass and concomitant health risks of increased body weight and low muscular strength (217,337,338) may provide more accurate information as it takes into account the effect of body mass.

The purpose of this study was therefore to determine the associations between muscular strength (measured as grip strength) and diabetes risk in White European, Black and South Asian men and women in UK Biobank to determine:

- a) whether the magnitude of these relationships was similar across ethnic groups
- b) to quantify the extent to which ethnic differences in diabetes prevalence may be associated with ethnic differences in strength.

5.2 Methods

5.2.1 Study Population

This cross-sectional study used baseline data from UK Biobank which recruited 502,682 participants between 2007 and 2010 (5.5% response rate) aged 37-73 years from the general population (270). Participants attended one of 22 assessment centres across England, Wales, and Scotland (270). At the assessment centres, participants completed an electronically signed consent. An extensive baseline information was collected via questionnaires and physical measurements, as previously described in section 2.10.

5.2.2 Definitions and Inclusion Criteria

Out of the 502,682 participants in the UK Biobank, analyses for the current study were conducted on 418,656 participants of White European, Black and South Asian descent, who had data on the exposure (grip strength) and covariates, with no history of heart disease (angina, heart attack and stroke). There were 28,813 cases with heart disease, 38,412 cases with cancer were excluded from the study. These exclusions resulted in the exclusion of 2,268 diabetic participants who also had cancer and 4,997 diabetic participants with heart disease. The status of diabetes (excluding gestational), heart disease and cancer were determined from self-report of a physician diagnosis.

Ethnicity was based on self-classification into the 19 UK Office of National Statistics groups. This study was restricted to participants who identified themselves as: White (British, Irish and other White European), South Asian (Indian, Pakistani and Bangladeshi) and Black (Black-African, Black-Caribbean and other Black).

Participants were excluded from the analyses if they recorded implausible values; defined as the sum of their total physical activity, sleeping time and TV-viewing exceeding 24 hours.

5.2.3 Muscular Strength

Muscular strength was assessed using hand-grip which is a good predictor of type 2 diabetes(339,340). Hand-grip strength was measured using a Jamar J00105 hydraulic hand dynamometer. Isometric grip force was assessed from a single 3-second maximal grip effort of the right and left arms with the participant seated upright with their elbow by their side and flexed at 90° so that their forearm was facing forwards and resting on an armrest. The mean of the right and left values, expressed in absolute units (kg), and relative to bodyweight (kg/kg bodyweight) was used in the analysis (226,341).

5.2.4 Physical Activity

Physical activity was assessed by a self-report questionnaire, based on the International Physical Activity Questionnaire (IPAQ) short form (342), with participants reporting frequency and duration of walking, moderate and vigorous activity undertaken in a typical week. Data were analysed in accordance with the IPAQ scoring protocol(343), due to its validity and reliability of measuring physical activity in middle-aged adults (344) and large populations (345,346). The total physical activity was computed as the sum of walking, moderate and vigorous activity, measured as metabolic equivalents (MET-hours/week).

5.2.5 Adiposity Measurements

Anthropometric measurements were obtained by trained clinic staff using standard operating procedures and regularly calibrated equipment. Weight, percentage body fat and fat-free mass (by bio-impedance) were measured using standard operating procedures, without shoes and with outdoor clothing, using the Tanita BC 418MA body composition analyser. Height was measured, without shoes, using the wall-mounted SECA 240 height measure. BMI was calculated as body mass (kg) divided by the square of height (metres).

5.2.6 Assessment Of Covariates

Potential confounders were identified a priori based on established relationships with either diabetes or muscular strength or both. Area-based socioeconomic status was derived from postcode of residence, using the Townsend score which is derived from Census data on housing, employment, social class and car availability. Age was calculated from dates of birth and baseline assessment. Smoking status was categorised into never, former and current smoking. Dietary information was collected via a self-reported dietary questionnaire, with participants asked how many portions of specified foods they generally ate. Medical history (physician diagnosis of long-standing illness, depression, stroke, angina, myocardial infarction, hypertension, cancer and diabetes) was collected from the self-completed, baseline assessment questionnaire. Further details of these measurements have been discussed in section 2.10.7 of the thesis.

5.3 Statistical Analyses

Descriptive statistics were applied to ethnicity sub-groups. Continuous variables were summarised using the median and inter-quartile range, and categorical using frequencies and percentages. The distribution of grip strength in men and women in each ethnic group was plotted.

Multivariate binary logistic regression models were used to examine associations between grip strength expressed in absolute units (per SD difference and per 5 kg difference), and relative to body weight (per SD difference and per 0.05 kg/kg bodyweight difference) with diabetes within each ethnic group. Models were run initially adjusting for age, education, number of years with diabetes and socioeconomic status (Model 1), then after adding percentage body fat, smoking, dietary intake (fruit and vegetables, alcohol, processed meat, red meat, oily fish), sleep duration and physical activity as additional covariates (Model 2).

Attributable risk (i.e., the number of excess cases that would be avoided if the risk factor was removed) associated with low grip strength (i.e., grip strength below the age and sex specific overall UK Biobank population median). The threshold based on age and sex specific criteria for cut points were used to define

the tertiles expressed in kg was calculated for each ethnicity and sex group (threshold values shown in Table 5-1).

In sensitivity analysis the researcher repeated the attributable risk calculations using the 33rd centile (i.e., lowest tertile), and the 67th centile (i.e., not in the highest tertile) as the thresholds for low grip strength. Those who had been diagnosed with diabetes for five years or longer were also excluded. Analyses were performed using Stata version 14 (Stata Corporation, College Station, Texas, USA). Statistical significance was accepted at $p < 0.05$.

5.4 Results

Main cohort characteristics by ethnic groups are presented in Table 5-1. In both men and women diabetes prevalence was highest in South Asians and lowest in Whites. Reported physical activity was highest in Whites and lowest in South Asians in both sexes.

South Asians reported a higher intake of fruit and vegetable per day, a lower intake of oily fish and a lower total energy intake than White and Black ethnic groups. Reported alcohol intake was higher in Whites than other ethnic groups. South Asian men and women had lower median grip strength, whether expressed in absolute terms or per kg bodyweight, than the other ethnic groups.

As shown in Table 5-3 grip strength median values reduced with increasing age. Grip strength values as substantially lower in women compared with men.

Figures 5-1 through 5-5 shows the visual distribution of the UK Biobank distribution the three ethnic groups. Figure 5-1 below shows the distribution of handgrip strength by age-group in men and women, expressed in absolute terms and per kg bodyweight. The ethnic differences in grip strength were evident across the full age range within the UK Biobank cohort.

Table 5-1 Descriptive characteristics of study population by sex and ethnicity

Men	Men			Women		
	White	Black	South Asian	White	Black	South Asian
N	184,009	3085	4457	224,521	4181	4083
Age (y)	57 (50; 63)	50 (45; 57)	52 (45; 59)	57 (50; 63)	50 (45; 57)	52 (46; 59)
BMI (kg.m ⁻²)	27.2 (24.9; 29.9)	27.9 (25.5; 30.6)	26.5 (24.3; 29.0)	26.0 (23.4; 29.5)	29.5 (26.0; 33.5)	26.5 (23.9; 29.8)
Weight (kg)	84.4 (76.4; 93.7)	84.2 (76.3; 93.9)	77.0 (69.6; 85.3)	68.9 (61.6; 78.3)	68.9 (68.3; 88.8)	65.2 (58.1; 73.7)
Body fat (%)	25.1 (21.3; 28.8)	25.5 (21.7; 28.9)	25.9 (22.6; 29.2)	36.6 (31.8; 41.2)	40.3 (35.4; 44.2)	37.8 (33.7; 42.0)
Fat-free mass (kg)	63.4 (58.7; 68.7)	63.1 (58.2; 68.9)	57.2 (52.7; 62.1)	44.0 (41.2; 47.3)	46.7 (43.3; 50.7)	40.5 (37.9; 43.8)
Hand grip strength (kg)	40.0 (34.0; 46.0)	40.5 (34.0; 47.5)	34.0 (28.0; 40.0)	23.5 (20.0; 28.0)	25.0 (20.5; 30.0)	19.0 (15.0; 23.5)
Hand grip strength (kg/kg)	0.47 (0.40; 0.54)	0.48 (0.39; 0.56)	0.44 (0.36; 0.52)	0.34 (0.27; 0.41)	0.32 (0.25; 0.39)	0.29 (0.23; 0.37)
Physical activity (MET.h.week-1)	27.3 (10.8; 59.1)	22.0 (7.5; 51.3)	18.6 (6.6; 43.6)	23.5 (8.8; 50.4)	20.3 (7.33; 44.2)	16.5 (5.8; 40.0)
Diabetes, n (%)	9,936 (5.4)	362 (11.8)	764 (17.4)	6,739 (3.0)	392 (9.4)	518 (12.8)
Total energy intake (KJ/day)	2237 (1874; 2648)	1989 (1480; 2594)	1961 (1529; 2470)	1917 (1613; 2257)	1845 (1414; 2364)	1709 (1346; 2160)
Fruit & vegetable (g/day)	267 (187; 377)	270 (160; 427)	323 (213; 487)	323 (240; 433)	347 (213; 487)	373 (243; 533)
Oily fish (portion/week)	1.0 (0.5; 1.0)	1.0 (0.5; 3.0)	0.5 (0.5; 1.0)	1.0 (0.5; 1.0)	1.0 (0.5; 3.0)	0.5 (0; 1.0)
Red meat (portion/week)	1.5 (1.5; 2.5)	2.0 (1.5; 4.0)	1.0 (0.5; 2.0)	1.5 (1.5; 2.0)	1.5 (1.0; 2.5)	1.0 (0; 1.5)
Processed meat (portion/week)	2 (1; 3)	2 (1; 3)	1 (1; 2)	2 (1; 2)	1 (1; 2)	1 (0; 2)
Alcohol (g/day)	16 (0; 34)	0 (0; 15)	0 (0; 12)	6 (0; 19)	0 (0; 5)	0 (0; 1)
Sleep duration h/day)	7 (7; 8)	7 (6; 7)	7 (6; 8)	7 (7; 8)	7 (6; 8)	7 (6; 8)

Smoking, n (%)						
Never	92,249 (50.3)	1,852 (60.5)	2,933 (66.6)	133,045 (59.5)	3,235 (77.9)	3,693 (90.8)
Past-smoking	68,744 (37.5)	691 (22.6)	804 (18.3)	71,046 (31.8)	551 (13.3)	232 (5.7)
Current smoking	22,435 (12.2)	519 (17.0)	667 (15.2)	19,707 (8.8)	369 (8.9)	141 (3.5)
Deprivation, n (%)						
1 (least)	39,168 (21.3)	93 (3.0)	389 (8.7)	46,966 (20.9)	124 (3.0)	417 (10.2)
2	38,114 (20.7)	140 (4.6)	436 (9.8)	46,755 (20.9)	194 (4.6)	408 (10.0)
3	37,305 (20.3)	240 (7.8)	624 (14.0)	46,779 (20.9)	366 (8.8)	643 (15.8)
4	35,761 (19.5)	642 (20.9)	1,260 (28.3)	44,777 (20.0)	874 (20.9)	1,232 (30.2)
5 (most)	33,428 (18.2)	1,955 (63.7)	1,741 (39.1)	38,986 (17.4)	2,619 (62.7)	1,377 (33.8)

a p-value <0.0001 for all variables; med: median; IQR: interquartile range; BMI: body mass index; MET: Metabolic equivalent; n: number

Table 5-2 Age- and sex-specific values for median grip strength in the UK Biobank population.

Age range	Women	Men
40-44 years	27.0	43.0
45-49 years	26.0	42.0
50-54 years	25.0	41.0
55-59 years	23.0	40.0
60-64 years	22.0	38.5
65+ years	21.0	36.0

Median grip strength (kg).

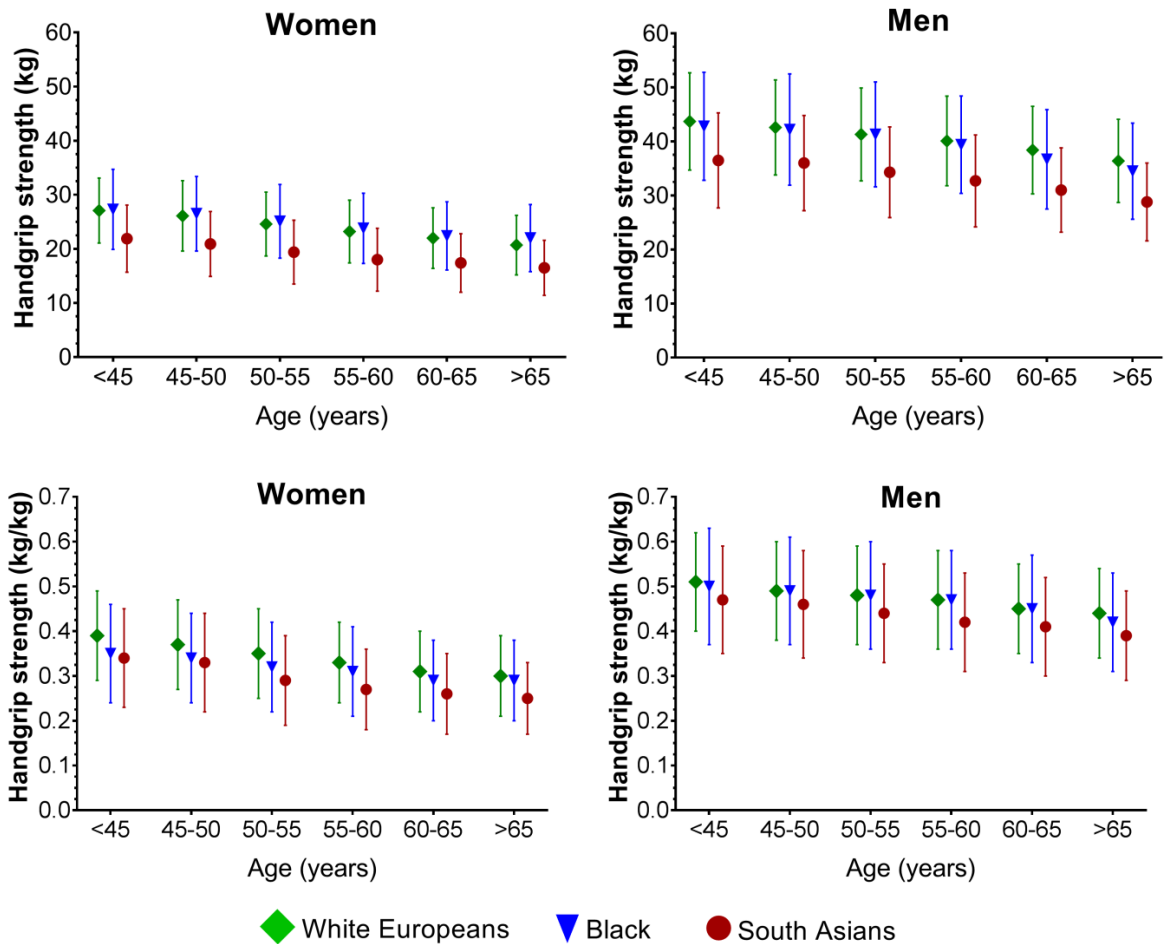


Figure 5-1 Age distribution of handgrip strength by age group and ethnicity (error bars represent standard deviation from the mean)

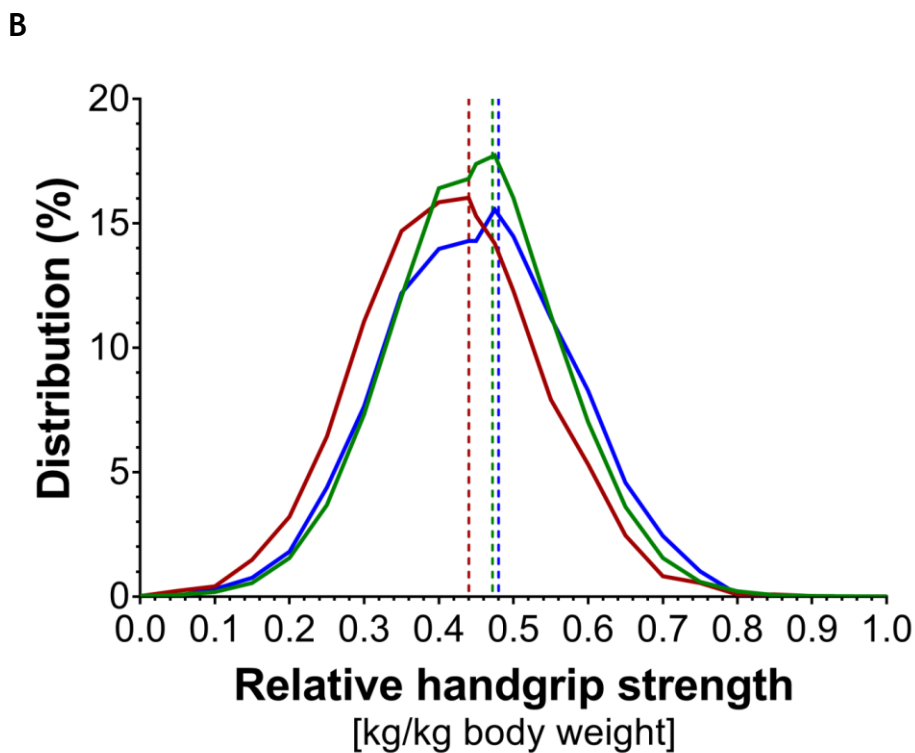
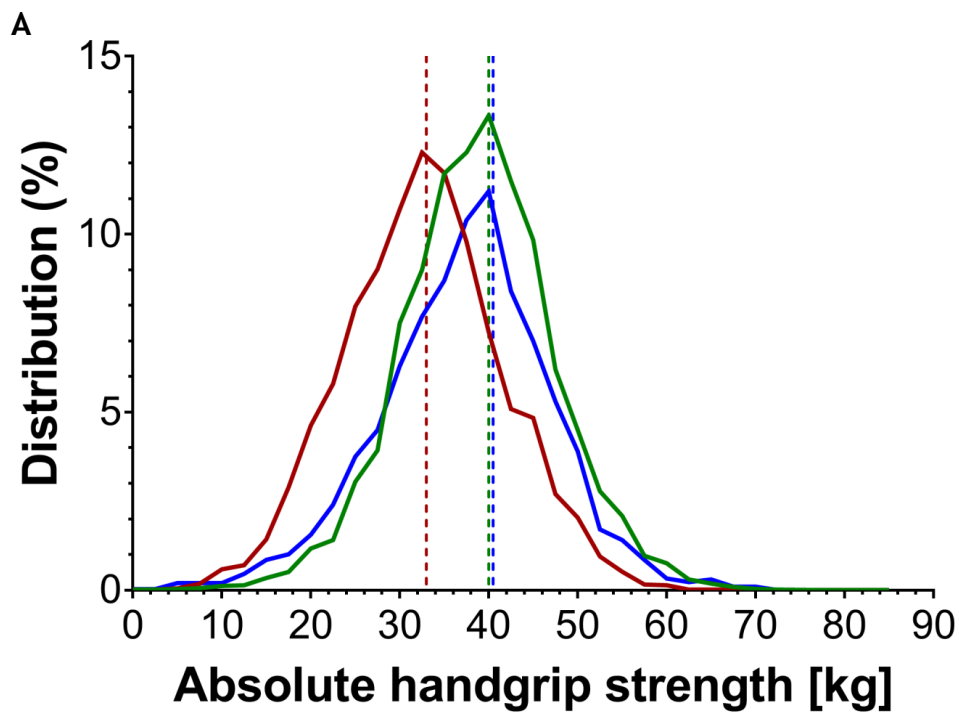


Figure 5-2 Distribution of grip strength in men by ethnic group (A) in absolute terms and (B) relative to bodyweight.

Grip strength in White (green), Black (blue) and South Asian (red). Dotted vertical lines on top panels represent median grip strength values for each ethnic group.

Figures 5-2 shows the population distributions in men for grip strength in the three ethnic groups, showing broadly similar distributions in the Black and White European

groups for men, but in South Asians, the distribution was shifted left in men by ~6 kg in absolute terms and -0.03 kg per kg bodyweight, respectively compared with the other ethnic groups.

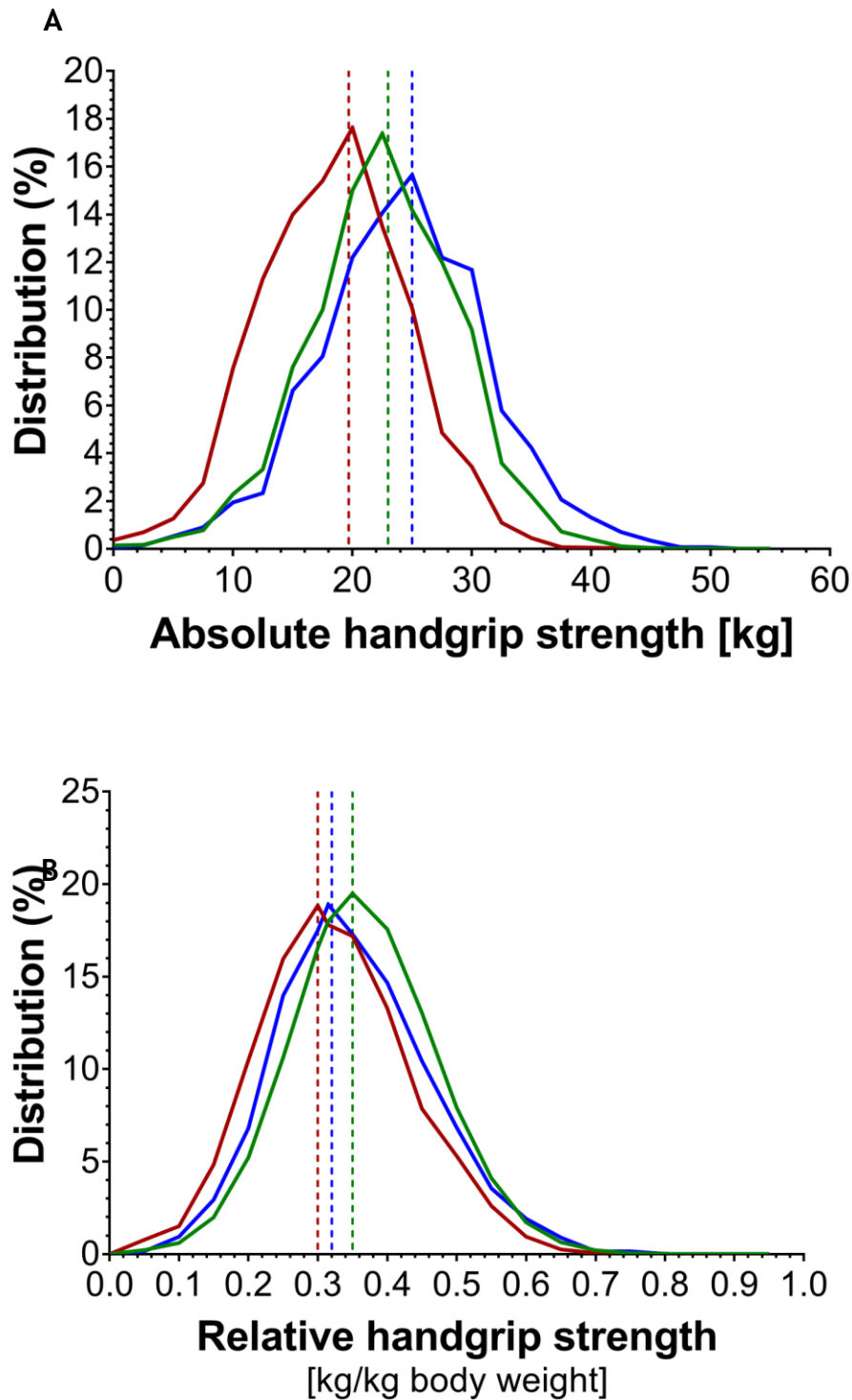


Figure 5-3 Distribution of grip strength in women (A) expressed in absolute terms and (B) relative to bodyweight. Grip strength in White (green), Black (blue) and South Asian (red). Dotted vertical lines on top panels represent median grip strength values for each ethnic group.

Figures 5-3 shows the population distributions for grip strength in the three ethnic groups, in women. This shows the distribution is different across each ethnic group. White European women have higher grip strength followed by Black women. In South Asians, the distribution was shifted left in and women by ~5 kg in absolute terms and ~0.05 kg per kg bodyweight, respectively compared with the White ethnic group.

Figures 5-4 and Figure 5-5 below show diabetes prevalence against hand grip strength in men. The stronger the grip strength the lower the diabetes prevalence. The Diabetes prevalence values were adjusted for age, education, number of years with diabetes, socioeconomic status, percentage body fat, smoking, dietary intake (fruit and vegetables, alcohol, processed meat, red meat, oily fish), sleep duration and physical activity.

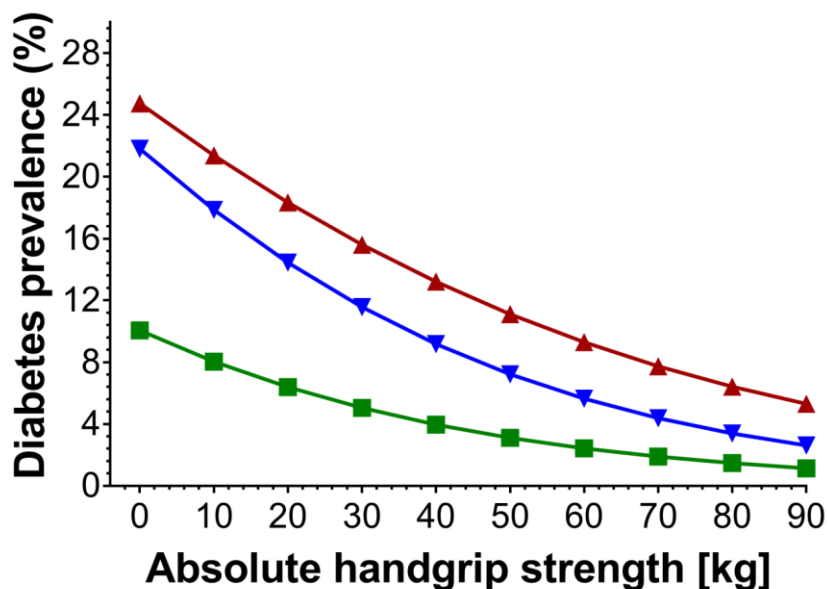


Figure 5-4 Diabetes prevalence of absolute hand grip strength by ethnic groups in men. White (green), Black (blue) and South Asian (red).

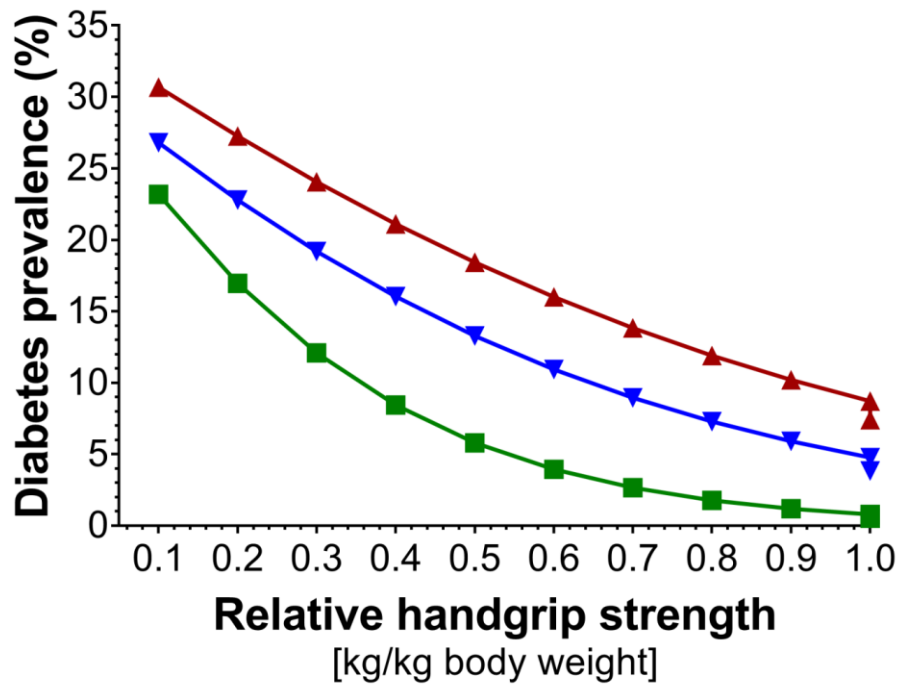


Figure 5-5 Diabetes prevalence of relative hand grip strength by ethnic groups in men.
 White (green), Black (blue) and South Asian (red).

Figure 5-6 and Figure 5-7 below show diabetes prevalence against hand grip strength in women. The stronger the grip strength the lower the diabetes prevalence. The Diabetes prevalence values were adjusted for age, education, number of years with diabetes, socioeconomic status, percentage body fat, smoking, dietary intake (fruit and vegetables, alcohol, processed meat, red meat, oily fish), sleep duration and physical activity.

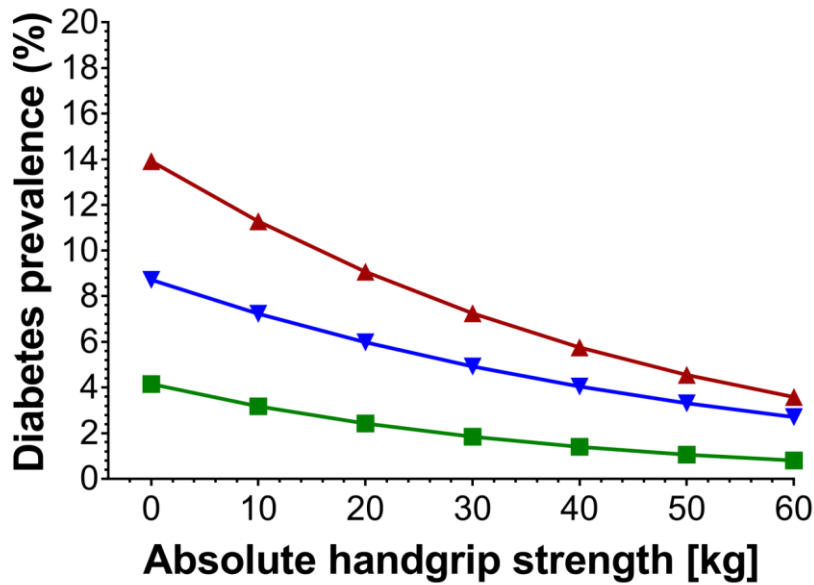


Figure 5-6 Diabetes prevalence of absolute hand grip strength by ethnic groups in women. White (green), Black (blue) and South Asian (red).

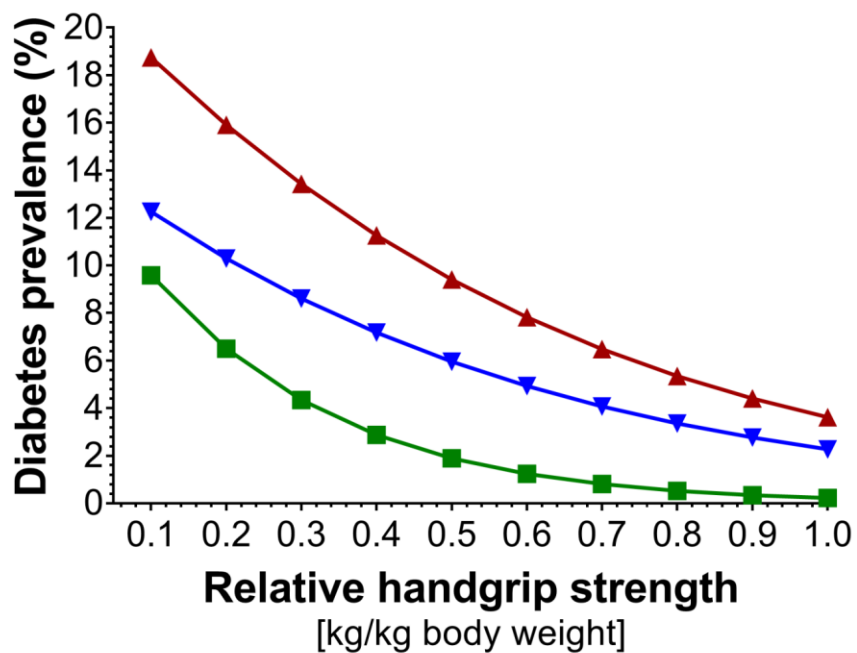


Figure 5-7 Diabetes prevalence of relative hand grip strength by ethnic groups in women. White (green), Black (blue) and South Asian (red).

Table 5-4 shows the association between hand-grip strength and diabetes in models adjusted for major confounding variables in men and women, respectively (Model 2). Diabetes prevalence was highest in South Asians and lowest in Whites for all levels of grip strength, irrespective of whether grip strength was reported in absolute units

or relative to bodyweight ($p < 0.05$ for differences in diabetes prevalence between all ethnic groups).

Table 5-4 also shows odds ratio for diabetes per unit change in grip strength. In all ethnicity and sex groups, lower hand-grip strength was associated with higher diabetes risk, after adjustment for age, education, number of years with diabetes and deprivation, whether grip strength was expressed in absolute terms or relative to body weight. Further adjustment for percentage body fat, smoking, dietary intake (fruit and vegetables, alcohol, processed meat, red meat, oily fish), sleep duration and physical activity attenuated these associations somewhat, but they remained statistically significant. The magnitude of association was similar in men and women, but there was a significant ethnicity interaction, with the association between grip strength and diabetes being strongest in White Europeans and somewhat weaker in Black and South Asian ethnic groups.

Table 5-4 Association between grip strength and risk of diabetes in White, Black and South Asian men and women.

	Men				Women			
	White	Black	South Asian	<i>P</i> _{grip*eth}	White	Black	South Asian	<i>P</i> _{grip*eth}
<i>Absolute handgrip strength [per 5 kg increase]</i>								
Model 1	0.84 (0.83-0.85)	0.86 (0.80- 0.92)	0.90 (0.85-0.94)	0.005	0.84 (0.82-0.86)	0.93 (0.86-1.01)	0.90 (0.83-0.98)	0.040
Model 2	0.85 (0.84-0.86)	0.86 (0.80-0.93)	0.89 (0.85-0.94)	<0.0001	0.88 (0.86-0.90)	0.95 (0.87-1.03)	0.93 (0.85-1.01)	<0.0001
<i>Absolute handgrip strength [per SD increase]</i>								
Model 1	0.76 (0.74-0.77)	0.80 (0.72-0.89)	0.84 (0.77-0.92)	0.012	0.79 (0.77-0.81)	0.91 (0.82-1.00)	0.85 (0.77-0.94)	0.031
Model 2	0.76 (0.75-0.78)	0.81 (0.72-0.91)	0.83 (0.75-0.91)	<0.0001	0.84 (0.82-0.87)	0.94 (0.84-1.04)	0.87 (0.78-0.97)	<0.0001
<i>Relative handgrip strength [per 0.05 kg/kg increase]</i>								
Model 1	0.74 (0.73-0.75)	0.84 (0.80-0.88)	0.87 (0.84-0.90)	<0.0001	0.72 (0.71-0.72)	0.84 (0.79-0.88)	0.84 (0.79-0.88)	<0.0001
Model 2	0.85 (0.84-0.86)	0.88 (0.83-0.93)	0.92 (0.88-0.96)	0.062	0.87 (0.86-0.89)	0.93 (0.86-0.99)	0.91 (0.86-0.97)	0.003
<i>Relative handgrip strength [per SD increase]</i>								
Model 1	0.50 (0.49-0.52)	0.67 (0.60-0.75)	0.73 (0.67-0.79)	<0.0001	0.50 (0.48-0.51)	0.69 (0.61-0.77)	0.70 (0.63-0.77)	<0.0001
Model 2	0.69 (0.67-0.71)	0.74 (0.65-0.85)	0.82 (0.74-0.91)	0.062	0.75 (0.73-0.78)	0.85 (0.74-0.99)	0.82 (0.73-0.93)	0.003

Values are odds ratios (with 95% confidence intervals) for the association of a unit change in grip strength, expressed either in kg or in kg per kg bodyweight, in each sex and ethnicity group. P values refer to the grip strength x ethnicity interaction. Statistical models are as follow:

Model 1: Adjusted for age, education, number of years with diabetes, and socioeconomic status

Model 2: Model 1, plus adjustment for percentage body fat, smoking, dietary intake (fruit and vegetables, alcohol, processed meat, red meat, oily fish), sleep duration and physical activity

Table 5-5 Diabetes prevalence and attributable risk for diabetes of low grip strength in White, Black and South Asian men and women.

	White	Black	South Asian
Men			
Prevalence of diabetes (%)	6.5 (6.3-6.6)	14.6 (12.9-16.4)	18.6 (17.2-19.9)
Prevalence of low grip strength (%)	49.4	52.1	79.1
Odds ratio for diabetes associated with low grip strength	1.5 (1.4-1.6)	1.6 (1.2-2.0)	1.4 (1.1-1.7)
Expected prevalence of diabetes if individuals with low grip strength increased grip strength above the population median (%)	4.4 (4.3-4.6)	10.2 (8.6-12.1)	14.6 (12.3-17.3)
Attributable risk associated with low grip strength (diabetes cases per 100 individuals)	2.0 (1.7-2.2)	4.3 (1.9-6.8)	3.9 (1.1-6.7)
Women			
Prevalence of diabetes (%)	3.4 (3.2-3.5)	10.0 (8.8-11.3)	13.6 (12.4-14.7)
Prevalence of low grip strength (%)	51.5	49.2	81.1
Odds ratio for diabetes associated with low grip strength	1.2 (1.1-1.3)	1.1 (0.8-1.3)	1.6 (1.1-2.0)
Expected prevalence of diabetes if individuals with low grip strength increased grip strength above the population median (%)	2.8 (2.7-2.9)	9.6 (8.3-10.9)	9.4 (7.4-11.8)
Attributable risk associated with low grip strength (diabetes cases per 100 individuals)	0.6 (0.4-0.7)	0.4 (-1.4-2.3)	4.2 (1.6-6.6)

Low grip strength defined as grip strength below the age and sex specific overall UK Biobank population median.

All values adjusted for age, education, number of years with diabetes, socioeconomic status, percentage body fat, smoking, dietary intake (fruit and vegetables, alcohol, processed meat, red meat, oily fish), sleep duration and physical activity.

Values in brackets are 95% CI.

Table 5-5 shows the attributable risk for diabetes associated with low grip strength (i.e., below the age- and sex-specific population median shown in Table 5-3) in each ethnicity and sex group, in analyses adjusted for major confounding variables (Model 2), within the UK Biobank population. The combined effect of high diabetes prevalence and high prevalence of low grip strength in South Asians meant that the attributable risk for diabetes associated with low grip strength was high in both South Asian men and women at 3.9 and 4.2 diabetes cases per 100 individuals, respectively. Attributable risk was also high in Black men at 4.3 cases per 100 individuals, but was lower in Black women (0.4 cases per 100), and in White men (2.0 236 cases per 100) and women (0.6 cases per 100). In sensitivity analyses, changing the threshold for low grip strength from the median to the 33rd centile resulted in attributable risk estimates for low grip strength of 2.2 (95%CI: 1.9-2.5), 4.6 (1.9-7.3) and 2.6 (0.9-5.1) diabetes cases per 100 individuals in White European, Black and South Asian men, respectively, with corresponding values of 0.8 (0.6-1.0), 1.2 (-0.9-3.2) and 3.3 (1.0-5.5) diabetes cases per 100 individuals in White European, Black and South Asian women. Changing the threshold for low grip strength to the 67th centile resulted in attributable risk estimates for low grip strength of 1.8 (1.6-2.0), 4.1 (1.7-6.6) and 3.6 (0.1-7.2) diabetes cases per 100 individuals in White 244 European, Black and South Asian men, respectively, and 0.6 (0.4-0.7), 0.1 (-2.0-1.7) and 2.5 (-0.7-5.7) diabetes cases per 100 individuals in White European, Black and South Asian women.

To minimise the potential effects of reverse causality confounding the results, a sensitivity analysis was performed excluding all participants with diagnosed diabetes of more than five years duration from the data set. This did not alter any of the overall findings.

5.5 Discussion

5.5.1 Ethnic Differences in Hand Grip Strength

Lower grip strength was associated with higher prevalence of diabetes, independent of a range of confounding factors including age, adiposity, years with diabetes, physical activity, sleep duration, smoking, alcohol, dietary factors, and socio-demographic confounders, across all ethnicities in both men and women. Prevalence of diabetes was 3-4-fold higher in South Asians and 2-3-fold higher in Black adults compared to White Europeans across all levels of grip strength, but the population

distribution for grip strength in South Asians was shifted left by 5-6 kg in absolute terms and 0.3-0.5 kg per kg bodyweight, compared to the other ethnic groups. Thus, the attributable risk for diabetes associated with low grip strength, at 4 cases per 100 individuals, was particularly high in South Asian men and women. Attributable risk associated with low grip strength was also high in Black men.

The data revealed a significant interaction with ethnicity in the association between grip strength and diabetes, with the difference in odds for diabetes per unit difference grip strength being higher in White Europeans than the other ethnic groups. However, the higher prevalence of diabetes in South Asians and Blacks compared to Whites, together with the leftward shift in the population distribution of grip strength in South Asians, resulted in a particularly high attributable risk associated with low grip strength in South Asian adults and Black men.

In Black women the association between grip strength and diabetes was less strong than in other groups, at least when grip strength was expressed in absolute terms, resulting in a lower attributable risk associated with low grip strength, despite a relatively high diabetes prevalence.

5.5.2 Clinical Implications

Identifying and addressing modifiable risk factors in high-risk groups is vital in tackling the increasing prevalence of type 2 diabetes. For example, it has been demonstrated that obesity interventions are required at a much lower BMI threshold in Black and South Asian populations if they are to be treated at the equivalent risk of diabetes which has translated into ethnicity-specific public health obesity guidance (300,347): a BMI of 22 kg.m⁻² in South Asians and 26 kg.m⁻² in Blacks confers equivalent diabetes risk to BMI 30 kg.m⁻² in Whites (58). However, reducing BMI below 22 kg.m⁻² in all South Asians may be harder to achieve than improving strength, particularly in South Asian adults, and in Black men. Improving strength could potentially provide a complementary strategy in reducing ethnic inequalities in diabetes.

Resistance training promotes muscle hypertrophy and improves glycaemic control, insulin sensitivity, fat mass and strength in T2D(348). However, intervention studies have shown that muscle strengthening exercise can improve insulin sensitivity and

glycaemic control (105,349,350) . Prospective data from over 130,000 men and women indicated that participation in muscle strengthening exercise was associated with lower risk of incident type 2 diabetes (332,333). The major diabetes prevention trials have focused on weight loss and moderate intensity aerobic physical activity (351). The present results suggest that resistance exercise should be considered as a third important component in future trials. The data also suggest that South Asian adults and Black men should be particularly targeted for interventions to increase strength. This may be particularly important in the context of rapidly increasing rates of diabetes in South Asian populations worldwide (294). Additionally, because handgrip strength testing is non-invasive and easy measure that strongly correlates with type 2 diabetes(268), incorporating routine grip strength measurement as a health screening tool in clinical practice is viable to identify individuals at increased risk of diabetes due to low overall muscle strength and allow the possibility of appropriate early lifestyle interventions.

5.5.3 Study Contributions

This study was both observational and cross-sectional and the direction of the relationship between grip strength and diabetes is not conclusive from the data. Other studies suggest the potential contribution of reverse causality may be relatively small. Two systematic reviews with meta-analysis of cohort studies suggested that low grip strength is predictive of incident type 2 diabetes (228,331). Data from the Health ABC cohort indicated no difference between adults with and without type 2 diabetes and change in grip strength (expressed per kg arm mass) over a 3-year follow-up period (352). Park et al. suggested that diabetes itself may not accelerate age-related declines in grip strength.

The models in this study were adjusted for number of years with diabetes, and excluding individuals with longstanding diabetes in a sensitivity analysis did not alter any of the findings. It is unlikely that grip strength, *per se* is causally related to diabetes, but hand-grip strength is highly correlated with leg strength and provides a valid index of overall limb muscle strength throughout the age range (221,224).

There is evidence that overall muscle strength could be an important, and potentially causal, risk factor for diabetes. It is important to acknowledge that

strength has important genetic component (353-355), and thus it is important to consider the extent to which it is a modifiable diabetes risk factor.

The current study noted lower grip strength in South Asians compared with Whites and Blacks. One explanation may be their lower skeletal muscle mass and anthropomorphic differences(114,356). Studies have shown that South Asians tend to have low skeletal muscle mass for any BMI (357-359) and higher body fat percentages than Black or White ethnic groups, which may explain the greater risk for development of type 2 diabetes(360,361). Second, low grip strength in South Asians maybe augmented by low birth weight(362-364) and childhood undernutrition, compared with Whites(365,366), which leads to vulnerability to insulin resistance, potentially fuelling the progression to type 2 diabetes. Therefore, screening and/or intervention for early years nutrition and further research on the aetiology of muscular strength among South Asians with diabetes is warranted. The risk exacerbates upon exposure to other risk factors including physical inactivity(367,368) and higher sedentary lifestyle(369) amongst South Asians compared to Whites.

Some of the strengths of this study include its large size which provided enough minority ethnic groups to enable ethnic sub-groups comparisons within the same study. Grip strength was objectively assessed using validated methods, trained staff and standard operating procedures. Direct measurement of body fat enabled robust adjustment for adiposity. Diabetes was ascertained by self-report of a physician diagnosis and this has been shown to agree well with laboratory/clinical diagnosis in nationally representative US samples (324) . Diabetes prevalence determined by self-report were only slightly lower (less than 1% difference overall) than when based on self-report and laboratory values (323). Thus, incomplete ascertainment of diabetes cases is likely to be small and unlikely to introduce a systematic error.

The researcher did not distinguish between type 1 and type 2 diabetes and based on UK population data; it is likely that 90% of cases present would have been type 2 diabetes (10,80,370). Assuming no association between grip strength and type 1 diabetes, this would mean that the association between grip strength and type 2 diabetes is likely to be slightly stronger than the present data indicate. This would have no effect on attributable risk estimates as the slight attenuation of the odds

ratio associated with low grip strength, and the slightly higher diabetes prevalence due to inclusion of the type 1 diabetes cases could cancel out.

While UK Biobank was not specifically recruited as a nationally-representative sample of the UK population, diabetes prevalence and mean BMI values in the UK Biobank cohort at baseline were comparable to nationally-representative samples across the ethnic groups (30,371). Therefore, the observations in this study are potentially broadly generalisable to the UK population. While associations between strength and odds of diabetes are likely to be similar for an ethnic group irrespective of location, attributable risk estimates depend on the prevalence of diabetes and population distribution of strength which may differ between the UK and other countries.

In conclusion, this study demonstrated independent associations between muscular strength and diabetes risk in White European, South Asian and Black adults living in the UK. Low strength was associated with a disproportionately large number of diabetes cases in the South Asian adults and Black men in the UK Biobank population, making a clear case for future randomized controlled trials of ethnic-specific interventions to improve strength in these populations. Moreover, muscular strength could be a useful marker to identify people at risk of type 2 diabetes in clinical or public health practice, because as handgrip strength it is an objective, non-invasive and low-cost measure.

6 Association Between Television viewing and Type 2 Diabetes in South Asian, Black and White Ethnic groups

6.1 Introduction

In the previous chapters, risk factors for diabetes including obesity, and muscular grip strength were examined across different ethnic groups to better understand the disparity in diabetes risk amongst ethnic minorities in the United Kingdom. In this chapter sedentary behaviour such as television viewing were examined with respect to ethnicity and the risk of type 2 diabetes. A meta-analysis of 47 studies performed by Biswas et al. in 2015 observed that, compared to those with the lowest amount of sedentary time, those with the highest amount of sedentary time had an 81% increase in their risk of incident type 2 diabetes (211). However, these studies did not explore in sufficient details ethnic disparity.

Sedentary behaviour is defined as sitting or engaging in reclined posture activities which expends approximately up to 1.5 times the metabolic equivalents (METs) of task during waking hours (185,372). A rapidly growing volume of research has emerged, identifying sedentary behaviour as an independent risk factor for type 2 diabetes (200-202). Studies have shown an association between leisure-time sitting, television viewing and total sedentary time with risk of even among individuals who meet recommendations for physical activity levels (201,203,204).

A sedentary behaviour that has seen a dramatic rise over the years is the increased use of screens such as televisions, computers, and mobile phones (373-375). People with high levels of screen time are less likely to engage in physical activities (373-376). A meta-analysis by Grontved et al. (210), reported a dose-response relationship between TV viewing and type 2 diabetes. They reported a 20% increased risk of diabetes for every additional 2 hours of television viewing. This risk was relatively higher than risk associated with 15% increased risk for cardiovascular disease and these associations persisted after adjustment for adiposity (BMI or waist circumferences).

A 3-year follow-up of the US Diabetes Prevention Program demonstrated that there was a greater reduction in Type 2 diabetes incidence in participants with the lowest sedentary time which was independent of their body mass index(205). Paterson et al. (213) reported an increase of 12% in relative risk of type 2 diabetes associated with each additional hour of TV viewing which was attenuated, but still significant, after adjustment for physical activity. Taking TV viewing in the context of overall

total sedentary behaviour, Guo et al. (377) showed that for each 1-h/day increase in total sedentary behaviour, the risk of type 2 diabetes increased by 5% and by 8% for each 1-h/day increase in TV viewing. This means the TV is an important risk factor of type 2 diabetes.

The association between television viewing and diabetes risk have been studied (212,372) but whether this relationship differs across varying ethnicities such as south Asian and Black ethnic groups has been relatively under-studied. This is of concern given the prevalence of type 2 diabetes is substantially higher in non-white populations as reported in chapter four of the thesis. The Black Women's Health Study (BWHS) reported 1.9-fold risk of diabetes amongst black women who spent more than 5 hours watching television in a day relative to those who spent less than 1 hour per day of television viewing (215). Two other studies showed that South Asian women in the UK have higher levels of sedentary behaviours compared to other ethnicities (22,378).

The deleterious effects of sedentary behaviour are not mediated by lower amounts of moderate-to-vigorous intensity physical activity (212). It is more likely that, irrespective of an individual meeting the physical activity recommendation, their health may still be compromised by being sedentary. Understanding how television viewing contributes to type 2 diabetes in non-white ethnic groups is an important area for more research because television viewing is a major contributor to diabetes risk (213,377). Reducing television viewing is a modifiable lifestyle that can be led to reductions in the risks of type 2 diabetes(187).

This chapter investigates ethnic differences in the association between television viewing and type 2 diabetes across South Asian, Black and White adult ethnic groups, using the UK Biobank. The other objectives of the study were:

- to assess the extent to which the ethnic variations in association are independent of physical activity and adiposity.
- investigate the dose-response associations of television viewing time with type 2 diabetes, after adjustment for physical activity and adiposity, both in the overall study population and across different ethnic subgroups.
- to determine the joint association of both television time and physical activity with risk of type 2 diabetes across the different ethnic subgroups.

6.2 Research Design and Methods

6.2.1 Study Design

This chapter is a cross-sectional analysis on baseline data from the UK Biobank (detail in chapter two of this thesis). In summary, the UK Biobank is a large, population-based cohort study examining the inter-relationships between environmental, lifestyle and genetic factors in adults aged between 37-73 years old.

6.2.2 Study Population

The present research used data from UK Biobank participants who identified as White, South Asian or Black ethnicity. Participants who were classified by a physician as having 'diabetes' or 'type 2 diabetes' were selected. In total 486,665 participants, 264,105 women (54.27%) and 222,560 men (45.73%) were included in this analysis because they belonged to the eligible ethnic groups, had data for diabetes status and other independent variables including television viewing and physical activity.

6.2.3 Exclusion Criteria

The following participants were excluded:

- Participants who reported a diagnosis of heart disease (n=28,543) and cancers (n=38,021) were excluded to avoid potential reverse causation. These groups are more likely to be sedentary as a result of their diagnosis (131,379-384).
- Participants with missing information on television viewing and physical activity.
- Participants who reported ethnicity other than white, south Asian or black.
- Participants taking insulin within their first year and were <35 years old at diagnosis were excluded to reduce the likelihood of type 1 and monogenic forms of diabetes.

6.2.4 Measures and Definitions

6.2.4.1 Diabetes

Self-report diabetes status was the primary disease outcome and details of obtaining the data are explained in section 2.9.

6.2.4.2 Television Viewing

TV viewing was determined from respondents' answer to the touchscreen question "In a typical DAY, how many hours do you spend watching TV? (Put 0 if you do not spend any time doing it)". The following checks were performed:

- If answer < 0 then rejected
- If answer > 24 then rejected
- If answer > 8 then participant asked to confirm.

Based on previous work by Hu et al. (208), the cut-points for TV viewing time categories were defined *a priori* into 3 groups:

- < 2 hours,
- 2-4 hours,
- > 4 hours.

The choice of 2 h/day as a threshold for the lowest screen time group is consistent with recommendations on TV viewing (385) and high values > 8 hours were included in the third group(197).

6.2.4.3 Physical Activity

The baseline method for data collection and calculation of physical activity has been described in detail in section 2.10.5 of this thesis. Below, is the description of the categorisation of physical activity for this study.

Physical activity was classified according to the standardised IPAQ-SF scoring guidance (386) as follows:

- Low - not meeting criteria for the 'moderate' or 'high' categories.
- Moderate - five or more days/week spent in any combination of walking, moderate or vigorous-intensity physical activity achieving at least 600 MET minutes/week.
- High - at least three days/week of vigorous-intensity physical activity achieving at least 1,500 MET minutes/week or at least seven days/week spent in any combination of walking, moderate or vigorous-intensity physical activity achieving at least 3,000 MET minutes/week.

6.2.4.4 Assessment of Covariates

Other lifestyle factors which could act as potential confounders were identified *a priori* based on the established relationship of these variables to diabetes and television viewing/physical activity. These included: BMI, Townsend Score for socioeconomic status, smoking, alcohol, and sleep duration.

6.2.5 Statistical Analysis

All data analyses were performed using Stata 14.2 (Stata Corporation, College Station, Texas, USA). The demographic and lifestyle characteristics of each ethnic group were summarized using the median and interquartile range for continuous variables, frequencies and percentages for categorical data. The statistical significance of the differences between ethnic groups was tested using the Kruskal-Wallis test for continuous variables and Pearson's chi-squared test for categorical variables.

The potential interactions between television viewing and physical activity variables and ethnicity, sex, of diabetes were tested by the insertion of an interaction term in the model and calculation of the p value using the likelihood-ratio test. Significant interactions were detected between ethnicity, sex and television time/physical

activity for diabetes ($p < 0.001$), and between television time/physical activity and diabetes ($p < 0.001$). Therefore, all the analyses were reported stratified by ethnicity and sex.

6.2.5.1 Test of Trend

Cuzick test for trend across ordered levels of television time and physical activity categories in progressive models with diabetes outcome as the dependent variable (387).

Multivariate binary logistic regression models were then used to examine the associations between levels of TV viewing and diabetes risk, using TV viewing time < 2 h/day serving as the referent model separately for each ethnic groups by sex.

- Model 1 was the initial model adjusted for age, and socioeconomic status
- Model 2 was adjusted for age, socioeconomic status, smoking, diet and sleep time.
- Model 3 was inclusion of variables in model 2 plus BMI
- Model 4 was a further adjustment for physical activity within each ethnic group, in separate analyses for men and women. Additional analysis using model 4 was performed combining the study population with the least sedentary Whites (separately in men and women) as common reference.

6.2.5.2 Joint Association of Television Viewing and Physical Activity

The joint association risk of type 2 diabetes between television viewing time and physical activity was assessed using model 2 and 3 on nine groups made up of combination of tertiles of TV viewing (low, moderate and high) and physical activity (low, moderate and high). The logistic regression models were used separately on each ethnicity group (South Asian, Black and White) and by sex. The p-values for all hypothesis tests were two-sided and $p < 0.05$ was interpreted as statistically significant.

6.3 Result

6.3.1 Characteristics of the Study Population

Table 6-1 shows the characteristics of the study population by ethnic groups. Out of this subset of participants 469,269 (96.43%) were White; 9,624 (1.98%) were South Asian and 7,772 (1.60%) were Black.

Overall, Pearson correlation showed television time weakly correlated with total physical activity ($r = -0.07$; $P < 0.0001$) and BMI ($r=0.23$; $p<0.001$). Overall, the crude diabetes prevalence was higher in men than in women. Age distribution was similar between men and women. Women had higher values of BMI than men and less physically active compared to men (Table 6-1).

South Asians and Blacks were younger, had lower physical activity levels, consumed less alcohol, were more socioeconomically deprived, and had higher proportion of non-smokers compared to Whites. Moreso, South Asian and Black participants had a lower median sleep duration than Whites. White and South Asians had lower BMI than Black ethnic groups (BMI was highest in Black women). The crude prevalence of diabetes was higher in all ethnic minority groups as compared with Whites. In women diabetes prevalence was 13.7% in South Asians and 10.1 % in Blacks. Among men, the diabetes prevalence was 20.5% in South Asians and 12.8% in Blacks (Table 6-1).

Black women and men spent significantly > 4 hours watching television (20.5% and 19.3% respectively) compared to Whites (12.8% women; 13.6% men) or South Asians (10.8% women; 10.2% men). Time spent in total physical activity was significantly higher ($p < 0.001$) among European women than South Asian or Blacks (Table 6-1).

Table 6-1 Characteristics of study participants by ethnicity and sex

	Women			Men		
	white N= 255,180	South Asian N= 4,444	Black N= 4,481	White N= 214,368	South Asian N= 5,152	Black N= 3,353
	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)	med (IQR)
Age (years)	60 (52-65)	54 (48-61)	52 (47-59)	60 (53-66)	55 (47-62)	52 (46-59)
BMI (kg/m²)	26.1 (23.4-29.6)	26.7 (24.0-30.0)	29.7 (26.1-33.7)	27.3 (24.9-30.1)	26.5 (24.4-29.1)	27.9 (25.5-30.6)
Waist circumference(cm)	83.0 (75.0-92.0)	86.0(78.0-94.0)	91.0(82.0-100.0)	96.0(89.0-104.0)	95.0(89.0-102.0)	94.0(87.0-101.0)
Physical Activity (MET-mins/wk)	2,533 (1,455-4,547)	2,226 (1,215-4,053)	2,300 (1,299-4,053)	2,648 (1,448-5,092)	2,162 (1,158-3,908)	2,415 (1,273-4,938)
Sleep Duration(h/d)	7 (7-8)	7 (6-8)	7(6-8)	7 (7-8)	7 (6-8)	7 (6-7)
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Diabetes	8,710 (3.4)	599 (13.7)	451 (10.1)	13,906 (6.5)	1,042 (20.5)	414 (12.8)
missing	471	75	37	615	108	42
TV Viewing (hr)						
<2hrs	120,612 (47.3)	2,537 (57.1)	1,934 (43.2)	99,403(46.4)	2,960 (57.1)	1,517 (46.1)
2-4 hrs	101,914 (39.9)	1,428 (32.1)	1,630 (36.4)	85,526 (39.9)	1,691 (32.6)	1,139 (34.6)
>4 hrs	32,654 (12.8)	479 (10.8)	917 (20.5)	29,160 (13.6)	529 (10.2)	635 (19.3)
Physical activity (MET/mins-wk)						
Low	36,834 (18.5)	840 (25.0)	762 (21.7)	34,369 (19.0)	1,080 (26.2)	587 (22.5)
Moderate	85,748 (43.0)	1,436 (42.7)	1,420 (40.8)	69,613 (38.4)	1,600 (38.8)	914 (35.1)
High	76,722 (38.5)	1,091 (32.4)	1,303 (37.4)	77,250 (42.6)	1,441 (35.0)	1,104 (42.4)
Smoking status						
None	150,297(58.6)	4,144(91.0)	3,590(77.7)	103,816(48.4)	3,396(65.1)	2,029(60.0)
Previous	83,181(32.4)	260(5.7)	617(13.3)	84,320(39.3)	1,035(19.9)	772(22.8)
Current	23,126(9.0)	151(3.3)	416(9.0)	26,396(12.3)	783(15.0)	579(17.1)

Table 6-1 Characteristics of study participants by ethnicity and sex (contd)

	Women			Men		
	white	South Asian	Black	White	South Asian	Black
	N= 255,180	N= 4,444	N= 4,481	N= 214,368	N= 5,152	N= 3,353
Deprivation						
1 (least)	52,586 (20.5)	454 (9.9)	125 (2.7)	44,358 (20.6)	453 (8.6)	91 (2.7)
2	52,766 (20.5)	446 (9.8)	212 (4.6)	44,009 (20.5)	476 (9.0)	146 (4.3)
3	52,837 (20.5)	699 (15.3)	380 (8.2)	42,988 (20.0)	734 (14.0)	264 (7.8)
4	51,600 (20.1)	1,337 (29.3)	953 (20.5)	41,774 (19.5)	1,445 (27.4)	675 (19.4)
5 (most)	47,197 (18.4)	1,625 (35.7)	2,964 (64.0)	4,1607 (19.4)	2,158 (41.0)	2,210 (65.3)
Alcohol frequency						
1	43,061(16.7)	132 (2.9)	185 (4.0)	56,357 (26.2)	533 (10.1)	327 (9.6)
2	54,761 (21.3)	203 (4.4)	330 (7.1)	57,764 (26.9)	615 (11.7)	446 (13.1)
3	67,910 (26.4)	427 (9.4)	766(16.5)	56,409 (26.2)	917 (14.5)	825 (24.3)
4	33,762 (13.1)	315 (6.9)	650 (14.0)	19,043 (8.9)	409 (7.8)	410 (12.1)
5	36,852 (14.3)	1,005 (22.0)	1,577 (34.0)	14,545 (6.8)	802 (15.3)	697 (20.5)
6	20,998 (8.2)	2,485 (54.4)	1,127 (24.3)	11,026 (5.1)	1,978 (37.7)	692 (20.4)

p-value <0.0001 for all variables; med median; IQR interquartile range; BMI body mass index

6.3.2 Relationship of Television Viewing and Diabetes Risk by Ethnic Groups and Sex

6.3.2.1 Stratification by Ethnic groups and Sex

Table 6-2 and figure 6.1 shows the multivariate adjusted odds of association between diabetes and television viewing time stratified by ethnic groups and sex. The test of interaction between ethnic groups was statistically significant ($p= 0.01$). Therefore, the analysis was done separately for each ethnic group. The results are presented in four models, each progressively adjusting for different sets of variables.

In the age-SES-adjusted model (Model 1), white women who spent 2-4 hours and >4 hours watching television had 54% and 160% higher odds of developing type 2 diabetes, respectively, compared to those who spent <2 hours. These associations remained statistically significant after further adjustments for smoking, alcohol, and sleep time (Model 2), and for BMI (Model 3). In the fully adjusted model (Model 4; figure 6.1a), which included physical activity, the increased risk was 17% and 52% for 2-4 hours and >4 hours of television viewing, respectively.

Similar patterns were observed in white men. In Model 1, the odds of developing type 2 diabetes were 47% and 129% higher for those who spent 2-4 hours and >4 hours watching television, respectively. These associations remained significant in Models 2 and 3. In the fully adjusted model (Model 4; figure 6.1b), the increased risk was 19% and 42% for 2-4 hours and >4 hours of television viewing, respectively.

Among South Asian women, the risk of diabetes increased with increasing TV viewing time. In Model 1, the odds of developing type 2 diabetes were 45% and 121% higher for those who spent 2-4 hours and >4 hours watching television, respectively. These associations remained significant in Model 2. However, adjustment with BMI (Model 3) attenuated these risks. In the fully adjusted model (Model 4, figure 6.1a), the increased risk was 28% and 61% for 2-4 hours and >4 hours of television viewing, respectively. The linear trend remained statistically significant (p -trend =0.002).

In Model 1, South Asian men who spent 2-4 hours and >4 hours watching television had a 30% and 85% higher risk of diabetes, respectively. These risks persisted after controlling for smoking, alcohol, and sleep (Model 2). The additional adjustment with BMI (Model 3) reduced the associated risk of TV viewing and diabetes. In the fully adjusted model (Model 4; figure 6.1b), the increased risk was 22% and 55% for 2-4 hours and >4 hours of television viewing, respectively.

Among Black women, compared to those who spent <2 hours of TV viewing, spending 2-4 hours of TV viewing was associated with a 4% higher risk of diabetes while spending >4 hours of TV viewing was associated with a 44% higher risk of diabetes (Model 1). These risks were slightly higher in Model 2, but were attenuated in Models 3 and 4. In the fully adjusted model (Model 4, figure 6.1a), the risk of diabetes was 1% and 19% for 2-4 hours and >4 hours of television viewing, respectively. However, the association was not statistically significant.

In Black men, compared to those who spent <2 hours of TV viewing, the odds of developing type 2 diabetes for those who spent 2-4 hours and >4 hours watching television were not statistically significant in Models 1, 3, and 4. However, in Model 2, the odds were slightly higher but became weaker and attenuated after adjustment for BMI (Model 3).

On the whole, the results indicate that when fully adjusted for controlling variables, the associated risk between diabetes and TV viewing was overruled in the Black ethnic subgroup. The linear trend remained statistically significant in all groups except for Black men and women. The positive association was more evident in South Asian women.

Table 6-2 Association between Television viewing and risk of diabetes by ethnicity and sex

	Women			Men		
	White	South Asian	Black	White	South Asian	Black
Model 1 Television viewing (hours)						
<2 hours	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
2-4 hours	1.54(1.46-1.62)	1.45(1.20-1.77)	1.04(0.82-1.31)	1.47(1.41-1.53)	1.30(1.14-1.52)	1.00(0.78-1.28)
>4 hours	2.60(2.45-2.76)	2.21(1.71-2.85)	1.44(1.12-1.86)	2.29(2.18-2.40)	1.85(1.49-2.31)	1.42(1.08-1.86)
<i>P-trend</i>	<0.001	<0.001	0.01	<0.001	<0.001	0.02
Model 2 Television viewing (hours)						
<2 hours	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
2-4 hours	1.45 (1.37-1.52)	1.47 (1.20-1.79)	1.08 (0.85-1.38)	1.46(1.38-1.54)	1.32(1.11-1.58)	1.02(0.77-1.36)
>4 hours	2.27 (1.14-2.41)	2.15 (1.65-2.76)	1.46 (1.12-1.90)	2.31(2.17-2.47)	1.96(1.53-2.52)	1.51(1.08-2.10)
<i>P-trend</i>	<0.001	<0.001	0.01	<0.001	<0.001	0.02
Model 3 Television viewing (hours)						
<2 hours	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
2-4 hours	1.17(1.11-1.23)	1.32(1.08-1.63)	1.06(0.83-1.36)	1.20(1.15-1.25)	1.22(1.04-1.44)	0.98(0.76-1.28)
>4 hours	1.54(1.44-1.64)	1.75(1.34-2.30)	1.25(0.95-1.65)	1.46(1.38-1.53)	1.59(1.26-2.01)	1.43(1.07-1.91)
<i>P-trend</i>	<0.001	<0.001	0.13	<0.001	0.001	0.04
Model 4 Television viewing (hours)						
<2 hours	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
2-4 hours	1.17(1.10-1.25)	1.28(1.01-1.63)	1.00(0.75-1.33)	1.19(1.14-1.25)	1.22(1.02-1.47)	0.93(0.69-1.25)
>4 hours	1.52(1.41-1.64)	1.61(1.16-2.24)	1.19(0.87-1.64)	1.42(1.34-1.50)	1.55(1.18-2.03)	1.30(0.93-1.83)
<i>P-trend</i>	<0.001	0.002	0.32	<0.001	0.001	0.22

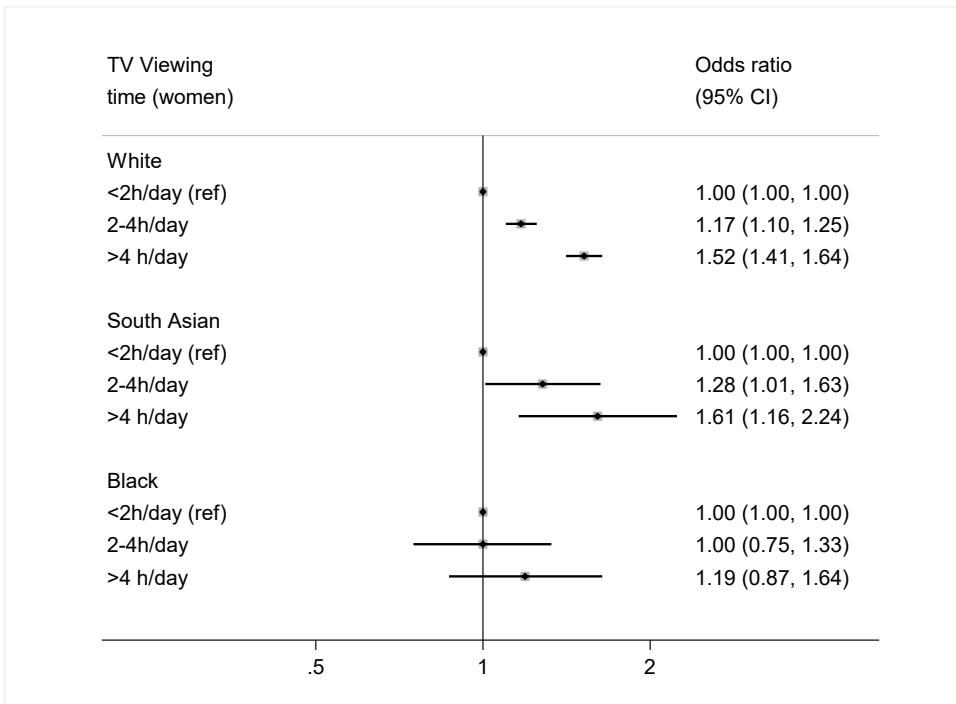
Values are odds ratios (with 95% confidence intervals) for the association of television viewing in each sex and ethnicity group. P trend refer to the dose-response levels of television viewing.

Statistical models are as follow:

Model 1: Adjusted for age, and socioeconomic status; Model 2: Model 1, plus adjustment for smoking, alcohol and sleep duration

Model 3: Model 2, plus adjustment for **BMI**; Model 4: Model 3, plus adjustment for physical activity

A



B

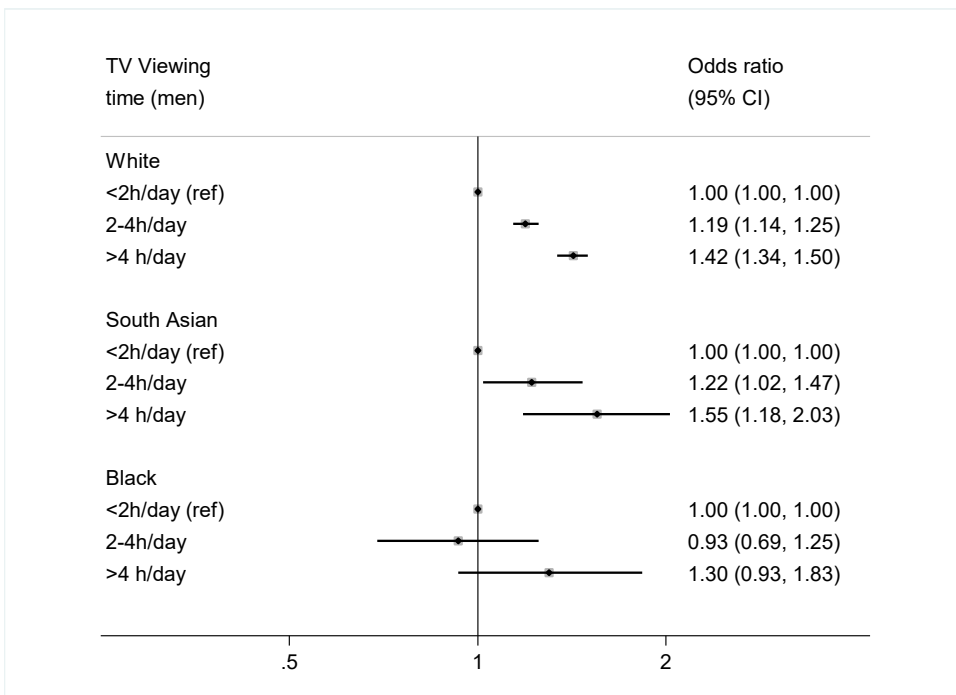


Figure 6-1 Model 4 - Association between television viewing and with risk of diabetes in White, Black and South Asian men (B) and women (A). Error bars represent the 95%CI of the Odds ratio. $p < 0.001$ for comparison between ethnic groups.

6.3.2.2 Stratification by Ethnic groups and Sex with Whites as common reference

The results presented in Table 6-3 and figure 6-2, shows the multivariate adjusted odds of association between diabetes and television viewing time across different ethnic groups taking Whites who spent less than 2 hours of television viewing as the common reference. The analysis was conducted separately for women and men due to the statistically significant interaction between gender and ethnicity ($p < 0.001$).

In Model 1, which adjusted for age and socioeconomic status (SES), the odds of diabetes were found to be 3.58 times higher in Black women and 5.16 times higher in South Asian women compared to White women who watched less than 2 hours of television. This association was observed to strengthen with increased television viewing time. For instance, South Asian women who watched television for 2-4 hours had a 7.66-fold higher risk of diabetes, while Black women had a 3.87-fold higher risk compared to White women.

The trend was similar for television viewing time exceeding 4 hours, with the risk of diabetes being 11.69 times higher in South Asian women and 5.31 times higher in Black women compared to White women. Across all television viewing durations, the risk of diabetes was consistently at least 4-fold higher in South Asian women and at least 2-fold higher in Black women when compared to White women.

Upon further adjustment for lifestyle factors such as alcohol consumption, smoking, sleep time, BMI, and physical activity in Models 2-4, these associations were attenuated but remained statistically significant. As shown in figure 6.2a and model 4, the association between television viewing and diabetes was over 2.5 to 6-fold greater in Black women and South Asian women compared to White women who spent less than 2 hours of TV viewing.

Similar trends were observed among men. In the minimally adjusted Model 1, the risk of diabetes associated with less than 2 hours of television viewing was highest in South Asian men (OR: 4.78), followed by Black men (OR: 2.72), compared to White men. For television viewing time exceeding 4 hours, the risk of diabetes was 9.04

times higher in South Asian men and 3.93 times higher in Black men compared to White men. After adjusting for sociodemographic and lifestyle factors in Model 4 (figure 6.2b), these associations were attenuated but remained significant.

The study findings underscore the importance of television viewing as a lifestyle behaviour that is a particularly significant risk factor for diabetes in non-White ethnic groups. The risk of diabetes was found to be moderately increased in White and Black men and women as TV time increases, with this effect being more pronounced in South Asian women. This highlights the need for targeted interventions to reduce television viewing time in these high-risk populations.

Table 6-3 Association between television viewing and risk of diabetes by ethnicity and sex with White as common reference

	Women				Men			
	White	South Asian	Black	<i>Eth*Sed</i>	White	South Asian	Black	<i>Eth*Sed</i>
Model 1 Television viewing (hours)								
<2 hours	1.00 (ref)	5.16(4.50-5.91)	3.58(3.03-4.22)		1.00 (ref)	4.78(4.31-5.31)	2.72(2.30-3.22)	<0.001
2-4 hours	1.53(1.45-1.61)	7.66(5.60-8.89)	3.87(3.25-4.59)	<0.001	1.46(1.41-1.53)	6.39(5.66-7.21)	2.75(2.28-3.32)	
>4 hours	2.58(2.43-2.73)	11.69(9.39-14.55)	5.31(4.36-6.47)		2.28(2.18-2.39)	9.04(7.44-10.98)	3.93(3.17-4.87)	
<i>P-trend</i>	<0.001				<0.001			
Model 2 Television viewing (hours)								
<2 hours	1.00 (ref)	3.26(2.83-3.76)	2.54(2.13-3.01)		1.00 (ref)	3.84(3.44-4.28)	2.28(1.92-2.71)	
2-4 hours	1.44(1.36-1.51)	4.90(4.20-5.72)	2.98(2.49-3.55)		1.41(1.35-1.46)	5.21(4.61-5.90)	2.45(2.02-2.97)	
>4 hours	2.25(2.11-2.39)	7.23(5.77-9.05)	4.03(3.28-4.95)		2.05(1.95-2.15)	7.14(5.85-8.73)	3.40(2.72-4.24)	
<i>P-trend</i>	<0.001				<0.001			
Model 3 Television viewing (hours)								
<2 hours	1.00 (ref)	3.81(3.29-4.41)	1.99(1.66-2.38)	<0.001	1.00 (ref)	4.77(4.23-5.34)	2.44(2.05-2.91)	<0.001
2-4 hours	1.17(1.11-1.23)	4.98(4.24-5.85)	2.22(1.84-2.67)		1.20(1.15-1.25)	5.97(5.24-6.80)	2.23(1.82-2.73)	
>4 hours	1.54(1.45-1.64)	6.45(5.07-8.21)	2.44(1.95-3.04)		1.46(1.39-1.54)	7.53(6.09-9.32)	3.13(2.47-3.96)	
<i>P-trend</i>	<0.001				<0.001			
Model 4 Television Viewing (hours)								
<2 hours	1.00 (ref)	3.79(3.21-4.49)	2.02(1.64-2.48)	<0.001	1.00 (ref)	4.45(3.93-5.07)	2.41(1.98-2.93)	<0.001
2-4 hours	1.17(1.10-1.24)	4.77(3.95-5.77)	2.16(1.74-2.67)		1.19(1.14-1.25)	5.62(4.85-6.52)	2.10(1.66-2.64)	
>4 hours	1.52(1.41-1.64)	5.81(4.33-7.79)	2.46(1.90-3.17)		1.42(1.34-1.51)	6.92(5.42-8.84)	2.82(2.14-3.71)	
<i>P-trend</i>	<0.001				<0.001			

Values are odds ratios (with 95% confidence intervals) for the association of television viewing in each sex and ethnicity group. P-trend refer to the dose-response levels of television viewing. Statistical models are as follow:

Model 1: Adjusted for age, and socioeconomic status; Model 2: Model 1, plus adjustment for smoking, alcohol and sleep duration

Model 3: Model 2, plus adjustment for smoking, alcohol, sleep duration and BMI; Model 4: Model 3, plus adjustment for physical activity

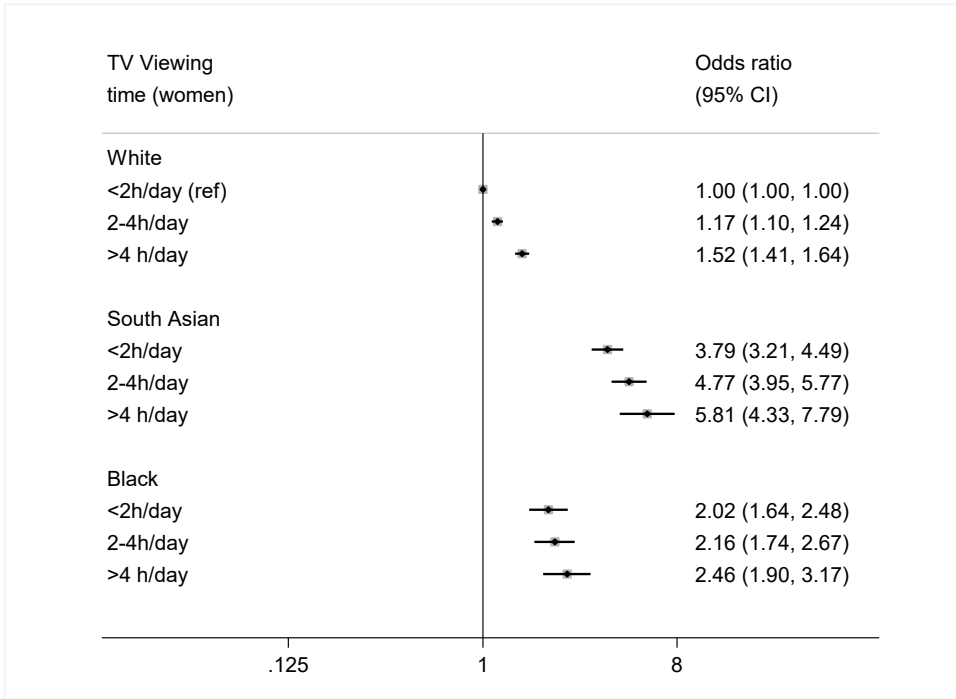
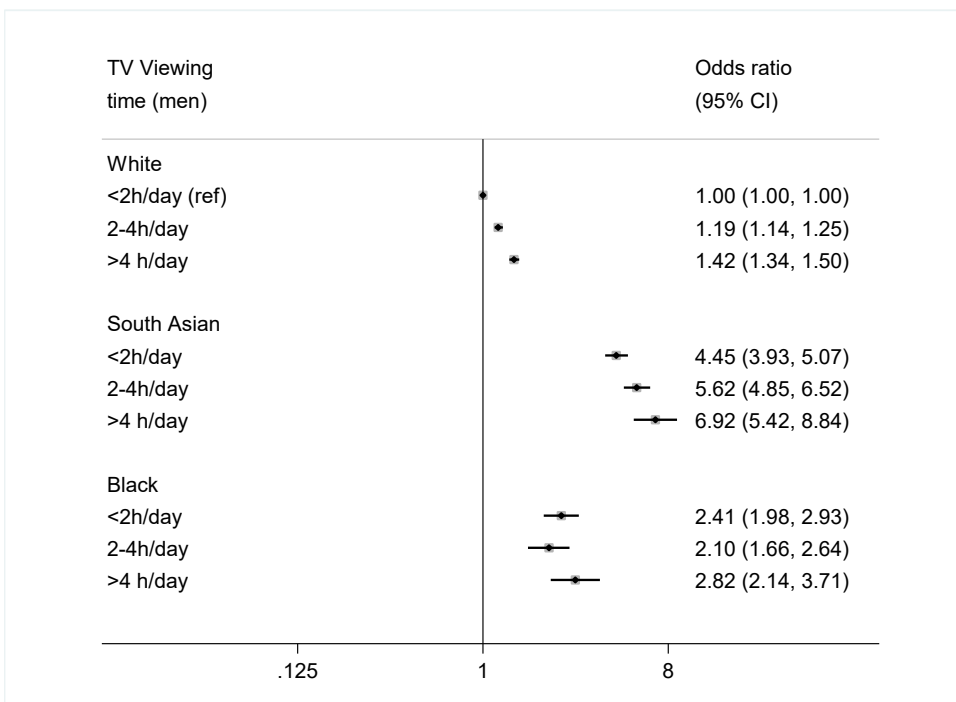
A**B**

Figure 6-2 Model 4 - Association between television viewing and risk of diabetes in White, Black and South Asian men (B) and women (A), with Whites who reported less than 2 hours of television time as common reference. Error bars represent the 95%CI of the Odds ratio. $p < 0.001$ for comparison between ethnic groups.

6.3.3 Ethnic Differences in Joint Association Between Television Viewing and Physical Activity with Diabetes Risk.

6.3.3.1 Stratification by Ethnic groups and Sex

The odds ratio for the joint associations of television viewing time and total physical activity with diabetes are presented in Table 6-4 and Figure 3. Significant interactions were observed between television viewing time (categorized as less than 2 hours, 2-4 hours, and 4 or more hours) and physical activity (categorized as low, moderate, and high) on diabetes risk ($p < 0.001$). These interactions significantly differed among the three ethnic groups ($p < 0.001$).

The combined effect of television viewing time and physical activity categories were stratified by sex and ethnic group. The reference group consisted of individuals within each ethnic group who reported more than 2 hours per day of television viewing and a high level of physical activity. Within all levels of physical activity, increasing amounts of TV viewing time increased the odds of diabetes risk in a dose-response manner. This trend was almost curvilinear, with accelerated odds of diabetes observed with increasing TV viewing time in combination with the lowest levels of physical activity, amongst Whites and South Asians but not in Blacks. In the multivariate-adjusted models, White women who reported the most television viewing time (4 or more hours per day) and the lowest levels of physical activity (3 or fewer days per week) had 89% higher odds of diabetes (OR: 1.89; 95% CI: 1.67-2.15) compared with the reference group. Those who reported the highest level of television viewing time and a moderate level of physical activity had 56% higher odds (OR: 1.56; 95% CI: 1.40-1.77). Even those in the low active group who reported the lowest level of television viewing time (less than 2 hours per day) still had a markedly 25% lower excess odds (OR = 1.25; 95% CI = 1.11-1.42) compared with the reference group than did those reporting the highest level of television viewing (4 or more hours per day) and in the most active group (OR = 1.52; 95% CI = 1.33-1.74).

White men who spent the most television viewing time and had the lowest level of physical activity experienced twofold higher odds of diabetes (OR:2.14; 95CI%:1.94-

2.36). Those who reported the highest level of television viewing time and a moderate level of physical activity had 66% higher odds of diabetes (OR: 1.66; 95%CI: 1.51-1.82). However, those in the low active group who reported the lowest level of television viewing time (less than 2 hours per day) still had an 8% increase in excess odds (OR = 1.41; 95% CI = 1.29-1.55) than did those reporting the highest level of television viewing (4 or more hours per day) and in the most active group (OR = 1.33; 95% CI = 1.21-1.48), when individually compared with the reference group.

In South Asian women, after adjusting for confounders, those reporting the most television viewing time and the lowest levels of physical activity had the highest odds of diabetes within the groups. The results showed that they had twofold higher odds of diabetes (OR:2.06; 95% CI: 1.19-3.57). Those who reported the highest level of television viewing time and a moderate level of physical activity had 76% higher odds (OR: 1.76; 95% CI: 1.03-3.01). Among those in the low active group who reported the lowest level of television viewing time (less than 2 hours per day) had a markedly 58% lower excess odds (OR: 1.13; 95% CI: 0.74-1.73) compared with the reference group than did those reporting the highest level of television viewing and in the most active group (OR: 1.71; 95% CI: 0.86-3.38), although this was not statistically significant.

South Asian men who spent the most television viewing time and had the lowest level of physical activity also experienced twofold higher odds of diabetes (OR:2.34; 95%CI:1.48-3.70). Those in the low active group who reported the lowest level of television viewing time (less than 2 hours per day) still had an 18% increase in excess odds (OR: 1.59; 95% CI: 1.17-2.16) than did those reporting the highest level of television viewing (4 or more hours per day) and in the most active group (OR: 1.41; 95% CI: 0.82-2.42), when individually compared with the reference group.

In Black women, compared with the reference group, those reporting the most television viewing time and the lowest levels of physical activity had 81% higher odds of diabetes (OR:1.81; 95% CI: 1.06-3.09). Those who reported the highest level of television viewing time and a moderate level of physical activity had 90% higher odds (OR: 1.90; 95% CI: 1.20-3.03). The risk was the same for those in the low active group who reported the lowest level of television viewing time (OR = 1.57; 95% CI =

0.96-2.58) and those reporting the highest level of television viewing and in the most active group (OR = 1.56; 95% CI = 0.92-2.64), in comparison with the reference group.

In Black men, compared with the reference group, those who spent the most television viewing time and had the lowest level of physical activity experienced 50% higher odds of diabetes (OR:1.50; 95CI%:0.84-2.67). Those in the low active group who reported the lowest level of television viewing time (less than 2 hours per day) had 18% lower odds of diabetes (OR: 0.82; 95% CI: 0.48-1.40) and those reporting the highest level of television viewing and in the most active group had 43% higher odds (OR: 1.43; 95% CI: 0.84-2.67), when individually compared with the reference group. However, these associations were not statistically significant.

These results show that the risk of diabetes with the associations of TV viewing levels and physical activity disproportionately affect both White and South Asian women more than men. Even a minimal level of physical activity with low exposure to television viewing may be beneficial to women in both groups compared to the men. Conversely, in men, a low level of physical activity with low physical activity was associated with increased risk compared with when they engaged with high physical activity and watched more than 4 hours of television a day. In Blacks, the dose-response gradient of associations between TV viewing and physical activity with diabetes risk in men or women was not seen in this group.

Table 6-4 Joint association between television viewing and physical activity with risk of diabetes by ethnicity and sex.

		White			South Asian			Black		
		TV viewing <2hrs	TV viewing 2-4 hrs	TV Viewing >4 hrs	TV viewing <2hrs	TV Viewing 2-4 hrs	TV Viewing >4 hrs	TV Viewing <2hrs	TV Viewing 2-4 hrs	TV Viewing >4hrs
Women										
Model 1	High PA	1.00 (reference)	1.53 (1.39-1.69)	2.38 (2.10-2.71)	1.00 (reference)	1.80 (1.19-2.71)	2.08 (1.08-4.00)	1.00 (reference)	1.11 (0.71-1.73)	1.56 (0.92-2.64)
	Moderate PA	1.14 (1.03-1.26)	1.77 (1.61-1.94)	2.72 (2.43-3.05)	1.35 (0.94-1.94)	1.60 (1.08-2.37)	2.32 (1.39-3.87)	1.21 (0.79-1.86)	1.26 (0.82-1.94)	1.90 (1.20-3.03)
	Low PA	1.78 (1.59-2.00)	2.64 (2.38-2.93)	4.61 (4.11-5.18)	1.44 (0.95-2.17)	1.89 (1.22-2.95)	3.49 (2.11-5.77)	1.57 (0.96-2.58)	1.25 (0.73-2.13)	1.81 (1.06-3.09)
	P-trend		<0.001			<0.001			<0.001	
Model 2	High PA	1.00 (reference)	1.18 (1.07-1.31)	1.52 (1.33-1.74)	1.00 (reference)	1.63 (1.07-2.49)	1.71 (0.86-3.38)	1.00 (reference)	1.02 (0.64-1.63)	1.19 (0.67-2.09)
	Moderate PA	1.05 (0.95-1.16)	1.23 (1.12-1.36)	1.56 (1.40-1.77)	1.26 (0.87-1.81)	1.37 (0.93-2.07)	1.76 (1.03-3.01)	1.04 (0.66-1.62)	1.15 (0.73-1.80)	1.47 (0.90-2.40)
	Low PA	1.25 (1.11-1.42)	1.44 (1.29-1.61)	1.89 (1.67-2.15)	1.13 (0.74-1.73)	1.37 (0.86-2.20)	2.06 (1.19-3.57)	1.33 (0.79-2.23)	1.05 (0.59-1.86)	1.17 (0.65-2.10)
	P-trend		<0.001			<0.001			<0.001	

Table 6-4 Joint association between television viewing and physical activity with risk of diabetes by ethnicity and sex (contd).

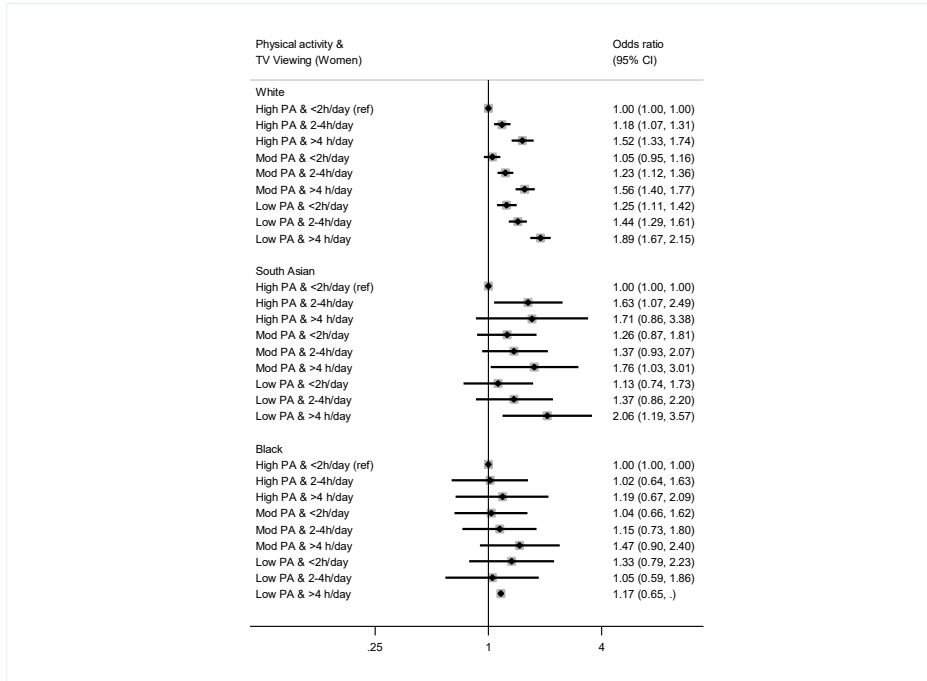
		White			South Asian			Black		
		TV viewing <2hrs	TV viewing 2-4 hrs	TV Viewing >4 hrs	TV viewing <2hrs	TV Viewing 2-4 hrs	TV Viewing >4 hrs	TV Viewing <2hrs	TV Viewing 2-4 hrs	TV Viewing >4hrs
Men										
Model 1	High PA	1.00 (reference)	1.39 (1.29-1.50)	1.94 (1.76-2.14)	1.00 (reference)	1.51 (1.10-2.06)	2.01 (1.23-3.30)	1.00 (reference)	0.84 (0.54-1.31)	1.51 (0.92-2.48)
	Moderate PA	1.22 (1.13-1.32)	1.87 (1.74-2.01)	2.63 (2.41-2.87)	1.41 (1.08-1.86)	1.94 (1.45-2.59)	2.57 (1.71-3.85)	1.15 (0.77-1.74)	1.13 (0.72-1.78)	1.24 (0.74-2.09)
	Low PA	1.80 (1.65-1.97)	2.61 (2.41-2.83)	4.33 (3.97-4.73)	1.72 (1.28-2.31)	1.80 (1.28-2.54)	3.13 (2.03-4.82)	0.87 (0.51-1.46)	1.22 (0.73-2.06)	1.56 (0.91-2.68)
	P-trend		<0.001			<0.001			<0.001	
	High PA	1.00 (reference)	1.17 (1.08-1.26)	1.33 (1.21-1.48)	1.00 (reference)	1.44 (1.05-1.99)	1.41 (0.82-2.42)	1.00 (reference)	0.82 (0.52-1.31)	1.43 (0.84-2.43)
Model 2	Moderate PA	1.19 (1.03-1.29)	1.45 (1.34-1.56)	1.66 (1.51-1.82)	1.37 (1.03-1.81)	1.73 (1.28-2.33)	2.29 (1.49-3.51)	1.16 (0.76-1.76)	1.04 (0.64-1.67)	1.16 (0.67-2.02)
	Low PA	1.41 (1.29-1.55)	1.67 (1.53-1.82)	2.14 (1.94-2.36)	1.59 (1.17-2.16)	1.48 (1.03-2.12)	2.34 (1.48-3.70)	0.82 (0.48-1.40)	1.07 (0.62-1.85)	1.50 (0.84-2.67)
	P-trend		<0.001			<0.001		<0.001		

Values are odds ratio (and 95% CI) for diabetes in different television and physical activity categories by ethnic groups, those with low TV viewing and high physical activity levels as the reference category for each sex.

Model 1: Adjusted for age, and socioeconomic status.

Model: Model 2, plus smoking, alcohol, sleep duration and BMI.

A



B

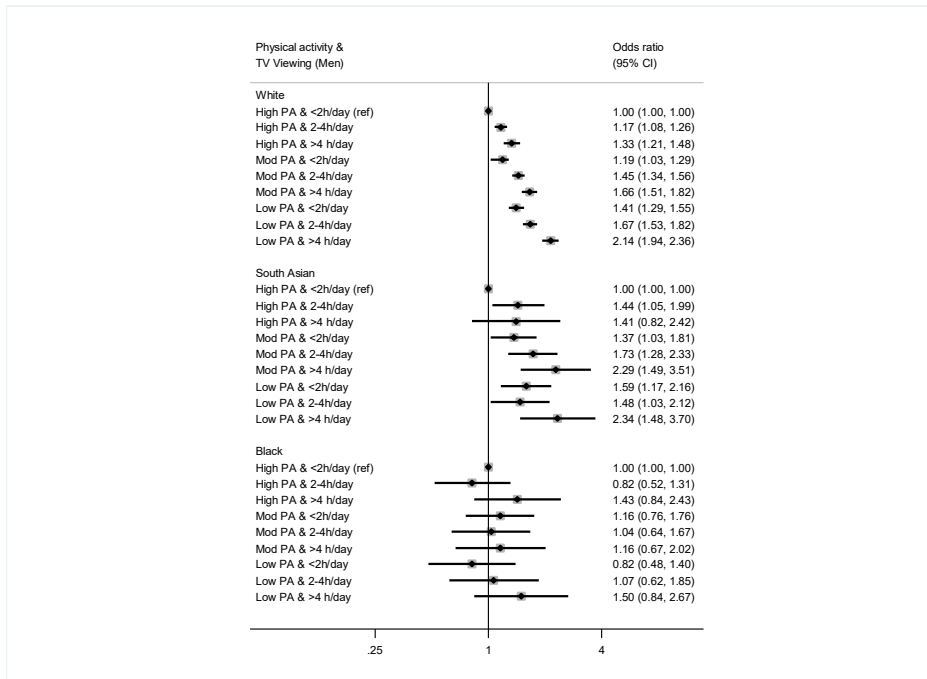


Figure 6-3 Model 4 - Joint association between television viewing and physical activity with risk of diabetes in White, Black and South Asian men (B) and women (A). Error bars represent the 95%CI of the Odds ratio. $p < 0.001$ for comparison between ethnic groups.

6.3.3.2 Stratification by Ethnic groups and Sex with Whites as common reference

Table 6-5 represents the odds of association of diabetes risk in the overall population across ethnic groups when compared with Whites in the high PA and <2 hours/d group.

The study was repeated using Whites who reported less than 2 hours per day of TV viewing time and were in the most active tertile (more than 7 days per week of physical activity) as the common reference group across all ethnic groups (Table 6.5; Figure 6.4). The results were significantly stronger for minority ethnic groups. A significant statistical interaction was observed between sex, ethnicity, TV viewing time and total physical activity ($p < 0.001$), indicating that the association between TV time and diabetes risk varied substantially by level of physical activity, sex, and ethnic groups.

In the multivariate-adjusted model (model 2), amongst the Whites, a dose-response association was observed in the fully adjusted model (model 2) with ORs of diabetes for TV viewing >4 hours in White women were [OR:1.52 (1.33-1.73)], [OR:1.58 (1.40-1.77)] and [OR:1.92 (1.69-2.17)] in high PA, moderate PA and low PA levels, respectively. In White men, compared to those who were in the high PA/low TV group, the OR of diabetes for TV viewing >4 hours were [OR:1.33 (1.21-1.48)], [OR: 1.66(1.52-1.82)], [OR: 2.16(1.96-2.38)] in high PA, moderate PA and low PA levels, respectively.

South Asian women who reported less than 2 hours per day of TV viewing time and were in the most active tertile experienced a threefold increase in odds of diabetes risk (OR:3.64; 95%CI: 2.69-4.92), relative to the reference group. This risk increased by sixfold (OR:6.87; 95%CI:4.28-11.02) in South Asian women who reported the greatest amount of TV time (4 or more hours per day) and were in the lowest tertile of physical activity. South Asian men had a fourfold increase in diabetes risk (OR:4.17; 95%CI:3.35-5.20) if they were in the group that viewed less than 2 hours per day of TV and were most active. This risk increased to about nine times higher (OR: 8.93; 95%CI: 5.91-13.51) for those who watched 4 or more hours per day of TV and were in the lowest tertile of physical activity, relative to the reference group of White men.

Among Black women, the odds of diabetes risk for those who watched the least amount of TV and were more active was twofold (OR: 2.19; 95%CI:1.57-3.05), which was nearly similar to those who reportedly watched 4 or more hours per day of TV and were also the least active (OR: 2.06; 95%CI:1.24-3.40), when compared to the reference group (White women who spent 0-2 hours per day of TV time in the most active tertile). In Black men, the associated diabetes risk was twofold increased (OR: 2.79; 95%CI: 2.07-3.77) for those who reportedly watched less than 2 hours per day of TV and were most active. This risk increased to threefold (OR: 3.58, 95%CI: 2.16-5.93) for those who watched 4 or more hours per day of TV and were also the least active, when compared to the reference group of White men.

These results demonstrate that the risk of diabetes, with the associations of TV viewing levels and physical activity, were disproportionately higher in ethnic minority groups versus the reference group of Whites.

Table 6-5 Joint association between TV viewing and physical activity with risk of diabetes in ethnic groups with Whites as common reference

		White				South Asian			Black		
		TV viewing <2hrs	TV viewing 2-4 hrs	TV Viewing >4 hrs	TV viewing <2hrs	TV Viewing 2-4 hrs	TV Viewing >4 hrs	TV Viewing <2hrs	TV Viewing 2-4 hrs	TV Viewing >4hrs	
<i>Women</i>											
Model 1	High PA	1.00 (reference)	1.52 (1.38-1.68)	2.36 (2.07-6.78)	4.94 (3.68-6.62)	9.08 (6.71-12.29)	10.44 (5.78-18.88)	3.70 (2.69-5.10)	4.36 (3.15-6.04)	5.95 (3.90-9.08)	
	Moderate PA	1.14 (1.04-1.26)	1.75 (1.60-1.93)	2.69 (2.40-3.01)	6.69 (5.29-8.46)	8.01 (6.07-10.57)	11.83 (7.72-18.16)	4.51 (3.35-6.07)	4.79 (3.53-6.49)	7.36 (5.21-10.39)	
	Low PA	1.79 (1.59-2.01)	2.63 (2.37-2.92)	4.58 (4.08-5.14)	7.05 (5.19-9.58)	9.40 (6.63-13.31)	17.35 (11.42-26.37)	5.56 (3.79-8.18)	4.66 (3.00-7.23)	6.57 (4.27-10.12)	
Model 2	High PA	1.00 (reference)	1.18 (1.06-1.31)	1.52 (1.33-1.73)	3.64 (2.69-4.92)	6.05 (4.41-8.31)	6.11 (3.28-11.40)	2.19 (1.57-3.05)	2.28 (1.62-3.22)	2.64 (1.65-4.23)	
	Moderate PA	1.05 (0.95-1.17)	1.23 (1.12-1.36)	1.58 (1.40-1.77)	4.55 (3.55-5.82)	4.98 (3.72-6.67)	6.09 (3.84-9.66)	2.08 (1.50-2.87)	2.50 (1.81-3.46)	3.22 (2.21-4.68)	
	Low PA	1.27 (1.12-1.43)	1.46 (1.30-1.63)	1.92 (1.69-2.17)	4.01 (2.89-5.57)	4.51 (3.08-6.60)	6.87 (4.28-11.02)	2.42 (1.89-3.70)	2.11 (1.30-3.40)	2.06 (1.24-3.40)	
<i>P-trend</i>		<0.001									
<i>Men</i>											
Model 1	High PA	1.00 (reference)	1.39 (1.29-1.50)	1.93 (1.76-2.13)	4.24 (3.43-5.24)	6.55 (5.16-8.32)	8.84 (5.64-13.84)	3.24 (2.43-4.32)	2.76 (1.96-3.90)	5.00 (3.32-7.53)	
	Moderate PA	1.22 (1.13-1.32)	1.87 (1.74-2.01)	2.62 (2.40)	6.00 (4.98-7.23)	8.42 (6.83-10.37)	11.12 (7.83-15.79)	3.73 (2.77-5.03)	3.70 (2.61-5.27)	4.07 (2.64-6.27)	
	Low PA	1.80 (1.65-1.97)	2.61 (2.41-2.83)	4.33 (3.96-4.73)	7.22 (5.81-8.97)	7.61 (5.76-10.05)	13.25 (9.02-19.40)	2.68 (1.73-4.15)	4.09 (2.65-6.33)	5.05 (3.19-8.00)	
Model 2	High PA	1.00 (reference)	1.17 (1.08-1.26)	1.33 (1.21-1.48)	4.17 (3.35-5.20)	6.37 (4.98-8.16)	6.00 (3.61-9.91)	2.79 (2.07-3.77)	2.15 (1.50-3.10)	3.83 (2.41-4.47)	
	Moderate PA	1.19 (1.10-1.29)	1.45 (1.34-1.56)	1.66 (1.52-1.82)	5.75 (4.72-7.00)	7.55 (6.04-9.44)	9.91 (6.81-14.43)	3.28 (2.41-4.47)	2.67 (1.82-3.89)	2.88 (1.80-4.62)	
	Low PA	1.42 (1.30-1.56)	1.68 (1.54-1.83)	2.16 (1.96-2.38)	6.37 (5.04-8.04)	5.79 (4.28-7.82)	8.93 (5.91-13.51)	2.06 (1.30-3.26)	2.73 (1.71-4.35)	3.58 (2.16-5.93)	
<i>P-trend</i>		<0.001									

Values are odds ratios (and 95% CI) for diabetes in different television and physical activity categories and ethnic groups. *Model 1: Adjusted for age, and socioeconomic status. Model 2: Model 1, plus adjustment for smoking, alcohol, sleep duration and BMI

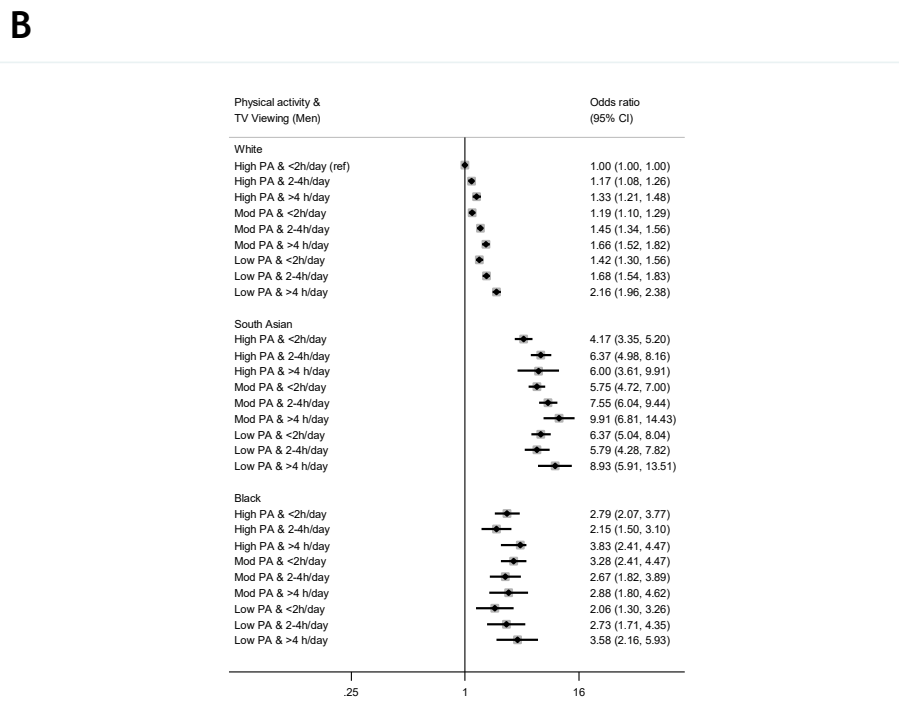
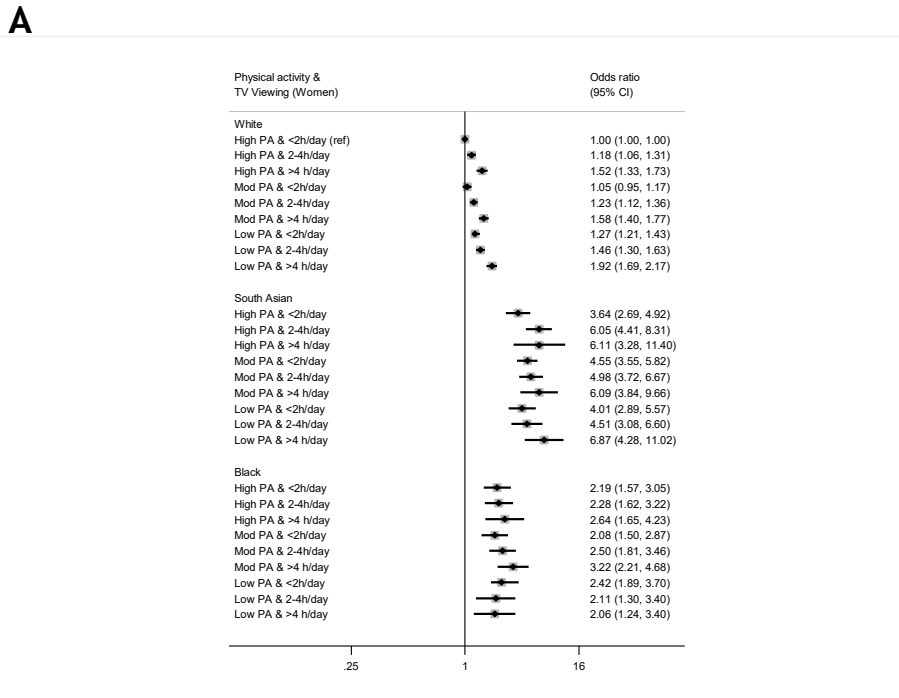


Figure 6-4 Model 4 - Joint association between television viewing and physical activity with risk of diabetes by ethnicity in men (B) and women (A), with Whites reporting high physical activity and less than 2 hours of television viewing as referent group. Error bars represent the 95%CI of the Odds ratio. $p < 0.001$ for comparison between ethnic groups

6.4 Discussion

6.4.1 Study Strengths and Limitations

A major strength of our study was our ability to compare several ethnic groups living in the same geographical location allowing for comparison on shared situations. Previous studies exploring questions on ethnicity and television viewing relationship with type 2 diabetes have relied heavily on small homogenous samples of minority ethnic groups; others have focused association on one minority ethnic group, hence do not allow for ethnic comparison. The data analysis considered adjustment for potentially confounding factors including socioeconomic status, smoking behaviour and age, sleep, adiposity and physical activity to show robustness of the findings.

Despite these strengths, the study has some limitations. The White participants in the UK Biobank data are reported to be more affluent, educated and healthier than the overall UK population(271,388), although whether this is the same for all the ethnic groups has not been determined, given that in this study 65% of Blacks were in the most deprived category. Since self-reported measures of television viewing time, physical activity, dietary intake was used, there is a potential for misclassification and residual confounding effects by these variables due to lack of precision compared to objective measures. The analyses focused on television viewing because it is the most commonly performed form of sedentary lifestyle. However, overall screen time, including computer and mobile device usage, may be more comprehensive for assessing screen-based sedentary time but was not examined. The study population may have been pooled by the sample size of the whites, observed the sample size variation in ethnic groups. Between the minority groups, the South Asians groups alone achieved $p < 0.05$ for the graded associations for television and physical activity, while $p > 0.05$ for Blacks. I did not investigate sub-group differences amongst the South Asian participants to explore heterogeneity within this group. This was due to small sample size within the television time and physical activity categories. Given the greater burden of type 2 diabetes in minority populations (389), this study suggests that other factors that vary by ethnicity may play important roles in the development of type 2 diabetes in non-white populations including social determinants of health, sleep

and stress. The researcher did not look at the independent effect of sleeping patterns and stress in the UK Biobank by ethnicity at this time.

6.4.2 Increased Television Viewing and Low Physical Activity Level Increases Risk of Type 2 Diabetes

The main finding of this study was that the association between television viewing time and odds of diabetes may not be the same across ethnic groups. In minimally adjusted model 1, increasing television viewing was associated with higher diabetes prevalence in both sexes for White, South Asian and Black groups. These associations were attenuated after adjusting for smoking, sleep duration, BMI and physical activity level. In the adjusted model 4, >4 hours of TV viewing time compared to <2 hours of TV per day was associated with 32% and 43% higher odds of diabetes in White women and men, respectively ($P < 0.001$). For South Asian women and men odds of diabetes were both 61% and 55% higher ($P < 0.001$). In Blacks, odds of diabetes were 19% and 30% higher in women and men respectively and was not statistically significant. While the lack of statistical significance of the association in the Black populations may be due to low statistical power. There was also no clear dose-response trend for increasing diabetes risk with greater television viewing in contrast to the White and South Asian groups. This suggests that the weaker association between television viewing and diabetes risk in the Black population may be real.

The higher levels of television viewing time were more strongly associated with diabetes risk in women than in men in both South Asians and Whites. However, the strength of association was more attenuated when adjusted for BMI in Whites than in South Asians, suggesting that the risk of diabetes with television viewing in these groups may be due to a combination of confounding factors e.g., mediation by adiposity. Adjusting for BMI in South Asians partially mediated the association (i.e., was less pronounced compared to Whites), suggesting that the contribution of TV viewing per se, rather than associated effects on BMI may make a larger contribution to diabetes risk in South Asians. This means that irrespective of a South Asian individual reducing their BMI, their susceptibility to diabetes may still be amplified if they spend long periods of time watching television. This may reflect underlying physiological factors or ethnic differences in other behaviours

such as the effect of television food advertisements and programs, and eating energy dense foods while watching television. Therefore, underlying physiological factors or ethnic differences warrant further investigation. Studies postulate that television programs and commercials may influence eating behaviour partly through a stimulus for food and overeating(390). Certain populations may be more susceptible to the adverse effects of television advertising(391). To the researcher's knowledge, this is one of the largest studies to investigate both the independent effect of television viewing alone as a proxy for sedentary behaviour in South Asian population, particularly in the United Kingdom population.

In the joint association of television watching and physical activity level, after adjustment for confounding variable including BMI, the risks of diabetes observed in White and South Asian men and women were dose-dependent, but not in Black men and women. It was observed in model 4, that compared with those in the low TV (< 2 h/d) and high PA group, those in the high TV and low PA group were 89% and 214% at higher odds of diabetes in White women and men respectively, and were 206% and 234% higher odds of diabetes in South Asian women and men respectively. Compared to 17% and 50% higher odds of diabetes in Black women and men respectively. This means that television watching does not increase the risk of diabetes as much as other ethnicities in this study. Therefore, other lifestyle factors may account for Blacks higher risk of type 2 diabetes. Some of the factors include diet(392,393), socioeconomic status (394), sleep insufficiency and chronic stress (395-398).

The findings show that television viewing is associated with a higher risk with type 2 diabetes, while increased physical activity is protective of the disease in Whites. This confirms and extends previous studies examining the relation between television viewing and diabetes in Whites (193). Joseph et al. (24) using data from the Multi-Ethnic Study of Atherosclerosis (MESA) study looked at the association of physical activity, sedentary behaviours and incidence of type 2 diabetes in multiple ethnic groups including Whites and Blacks. The study showed the graded independent associations of physical activity were statistically significant in Whites across all increased levels of physical activity, whilst there was no significant association with television watching for those who spent up to 4 hours of television watching (RR:1.50; 95%CI: 0.91-2.49). The deleterious effect of

television watching was only observed in Whites who spent more than 6 hours of their time watching television RR:4.54 (1.42 to 14.49). Recently, using a two-sample Mendelian randomization analysis method, Deng et al. examined the risk of diabetes in association with time watching television and physical activity in a European white population(193). They found that increased time spent watching television was associated with a 2.35 increased risk of type 2 diabetes (OR: 2.35; 95%CI:1.9-2.9) and self-reported moderate and vigorous PA were associated with 69% (OR: 0.31, 95%CI: 0.18-0.54) and 72% (OR: 0.28; 95% CI: 0.14-0.54) lower risk of type 2 diabetes, respectively. Using Mendelian randomization technique, allowed the researchers to minimize confounding and reversal causation, thereby potentially providing strong evidence of causal inference that TV viewing and physical activity behaviours are associated with the risk of developing type 2 diabetes(193). On the other hand, findings from the UK Whitehall study (399) found that after following a cohort of civil servants for 12 years, there was no link between television sitting and incident diabetes after adjusting for BMI (RR: 1.31; 95CI:0.96 to 1.76), thus depicting the effect obesity has on television viewing behaviour.

Jackson Health study, the authors reported that compared to those who spent >4 hours versus 1 hour of television viewing, the risk of type 2 diabetes in Black participants was 95% which was not statistically significant. In the MESA study (24), television watching was not associated amongst Black ethnic subgroups who spent more up to 4 hours watching television compared to those who spent less than 2 hours of TV viewing (HR:1.47 (95%CI 0.98-2.21). Contrastingly, findings from the Black Women's Health Study (215) reported 1.9-fold risk of diabetes amongst black women who spent more than 5 hours watching television in a day relative to those who spent less than 1 hour per day of television viewing. The authors suggested that reducing sedentary behaviour, particularly television watching, could be an important strategy for preventing the development of type 2 diabetes in this high-risk population. However, the study does not include other ethnic groups to allow for ethnic comparisons. Nevertheless, it is possible that the lack of relationship between sedentary behaviour and type 2 diabetes in Black adults in current study may be influenced by unmeasured confounding lifestyle, and environmental factors that vary by geopolitical location. Notably, majority of studies on television viewing and type 2 diabetes in Black populations have been conducted

in US, whereby the lifestyle behaviour may be different from UK residents. Studies show that US Blacks are more obese, low socioeconomic status and poorer health care compared to UK Blacks (400). Hence, more research on Black ethnic groups in the UK setting is needed to fully understand these potential interactions.

Television watching is related to a lower expenditure of energy, which in turn can lead to weight gain and increased risk of diabetes(187). Adjustment for body mass index attenuated odds of diabetes risk in this study; this is compatible with the association of television watching with type 2 diabetes being at least partially mediated through obesity(401). South Asians and Blacks participants in this study had higher BMI and waist circumference compared to the White participants. Another possible mechanism is that television watching leads to a higher caloric intake and a relatively unhealthy dietary pattern, which is frequently related to more adverse disease outcomes compared with daily sitting time and, therefore, television viewing time could affect diabetes in different mechanisms from other sedentary behaviours.

Conversely, the relationship between physical activity and type 2 diabetes may be mediated through insulin-dependent and insulin-independent actions due to increased levels of glucose transported protein GLUT-4 and muscle glycogen synthase(402). However, the relationship appeared to be mediated by adiposity as the jointed associated risk of physical activity with television watching was modified by adjustment for BMI in this study. Therefore, Physical activity related lifestyle can also lead to weight loss or maintenance of a healthy weight(187,192,403) (27), which in turn can lead to a lower risk of type 2 diabetes. For example, lifestyle interventions such as the Diabetes Prevention Program(205) shows that increase in physical activity also reduce sedentary behaviours including television watching. However, whether this is the same for ethnic minorities is yet to be observed.

An important public health strength of this study is that it has given insight into understanding the ethnic disparities that exist with time spent watching television and risk in the development of type 2 diabetes within a population. This knowledge sets precedence to future interventions aimed at reducing sedentary time among people across ethnic origins. The current findings suggests that prolonged television watching risk was highest in South Asians compared to

Whites; hence they may benefit the most from strategies aimed at altering television viewing habits with other non-screen time activities targeted at increasing their energy expenditure and fitness levels(404). Previous studies (62,172) suggested that South Asians would have to spend up to 225mins/ week of physical activity to combat diabetes risk analogous to Whites in the UK, but the findings in this study is reassuring that a reduced television time combined light-intensity physical activity is also beneficial to ameliorate diabetes risk among this ethnic population. Culturally-tailored interventions that incorporate traditional activities and values may be effective in promoting physical activity in ethnic minority groups. It has been shown that self-efficacy and social support from family, friends, religious community and health care providers play an important role in adoption and maintenance of regular physical activity in these populations(190).

It is possible that the lack of relationship between television watching time and type 2 diabetes in Black adults in this study may be influenced by unmeasured confounding cultural, lifestyle, and environmental factors that vary from other ethnic groups. Nevertheless, more research is needed to fully understand these potential interactions.

6.4.3 Further Research Recommendation

The findings in this research showed prolonged television watching as a detrimental behaviour and risk factor for the development of diabetes, with varying effects between the different ethnic groups examined - significant association in South Asians and not significant in Blacks. Furthermore, the findings emphasis the need to understand the factors behind the low levels of physical activity in South Asians and Blacks. This therefore, suggests that ethnic specific interventions for individuals from South Asian and Black ethnic origin should potentially be explored. Clinical trials on television viewing have successfully led to modified interventions suitable among children, but few interventions have been conducted, mostly in White adults (405). Therefore, supportive to this research will be randomised clinical trials that are ethnic specific and prove efficacious in producing significant and clinical reduction strategies of sedentary behaviour in adults. Potential intervention efforts to reduce television viewing

time could also take account of family units, cultural practices and community environment.

A study conducted in the UK found that South Asian men preferred to socialise while participating in physical activities. Neighbourhoods with greater walkability space was linked with less television viewing and total sedentary time. Further investigation is needed to fully understand potential interactions of other lifestyle factors in Blacks that may explain their high prevalence of type 2 diabetes. Future studies examining reallocating sedentary time with physical activity and sleep should be explored. Reallocating time to sleep from sedentary time may confer some light into diabetes risk in Black ethnic groups. More understanding around how stress/mental health influences the adoption of sedentary and low physical activity behaviours which potentially impacts type 2 diabetes amongst minority ethnic groups. Identified links would help in health intervention strategies in minority ethnic groups.

In summary, this study confirms the association between TV viewing and diabetes affects different ethnic groups in variable magnitude. The study also suggests that even little physical activity with low television-viewing time can significantly reduce the risk of type 2 diabetes. However, TV viewing time is a complex construct that appears to include obesity since the risk of association with diabetes significantly increased after adjusting for BMI. Even after controlling for potential mediators including socioeconomic status and physical activity, part of the association between television viewing and diabetes in South Asians and in whites remained unexplained in our study. This suggests that television viewing per se may have adverse consequences to higher diabetes risk. Given the prominent role that television has in modern society, further research is warranted to better understand why this behaviour is associated with diabetes. As there are few studies in the UK on this type of research it is clear that this field of research needs to expand beyond predominantly white populations and to explore this heterogeneity and avoid potentially inappropriate generalization of findings, whether the ethnic differences are biological, or due to unmeasured confounding factors. This may facilitate the development of public health interventions that more effectively address the ethnic disparities.

In conclusion, sedentary behaviour is a significant risk factor for the development of type 2 diabetes, and ethnic minority groups may be at higher risk due to cultural, social, and environmental factors. Findings from this study provide evidence that television viewing (as sedentary proxy) and physical activity is associated with higher diabetes risk in South Asians and whites but not Blacks and with evidence of mediation by BMI. These findings add to growing evidence that sedentary behaviour, separately from activity, influences health even though uncertainties remain regarding underlying pathways. Therefore, there is a need to develop effective interventions that can promote physical activity and reduce sedentary behaviour in these populations.

7 Discussion and Conclusion

7.1 Introduction

Diabetes is a devastating disease that affects ethnic minorities more adversely compared to European Whites living in westernised countries. In the United Kingdom, ethnic minorities, including, Black African or Black Caribbean (collectively known as Black in the UK), South Asian, and Chinese background, have a higher prevalence and greater burden of diabetes compared to whites, and have higher rates of complications (42,406,407). Despite medical advances and increasing access to medical care within the UK, ethnic disparities in diabetes outcome still persist and the reason for this is not completely understood (406). About 90% of diabetes prevalence is in type 2 diabetes which is described to be ‘rooted in reversible social and lifestyle factors’ (408), and understanding how the lifestyle factors contribute or explain these ethnic differences is important. The research presented in this thesis was aimed at gaining insight into how established and emerging risk factors for type 2 diabetes including age, sex, adiposity, muscular strength, physical activity and television viewing may affect diabetes risk differently in different ethnic groups.

In order to achieve this aim, the UK Biobank study, a large data of middle-aged men and women from different ethnic groups residing in the United Kingdom, was utilized for the analyses to:

1. To investigate the ethnic and sex difference of diabetes prevalence using a robust standardization method.
2. To compare the relationship between adiposity and prevalent diabetes across different ethnic groups and derive robust ethnic-specific obesity cutoffs for Black, Chinese, and South Asian populations that equate to those developed on White populations in terms of diabetes prevalence.
3. To quantify the extent to which ethnic differences in muscular strength might account for the substantially higher prevalence of diabetes in Black and South-Asian compared with White European adults.
4. To examine how the association of television viewing and type 2 diabetes varies by ethnicity in South Asian, Black and White middle-aged adults, using

the UK Biobank data and to assess the extent/pattern to which this association is based on ethnicity is independent of PA and BMI.

The findings, of the presented studies have been discussed in the previous chapters, however, in this chapter, the findings are placed in a broader context. In addition, the strengths and weakness, and the public health implications of these analyses are discussed. Subsequently, some methodological considerations and views on further research regarding ethnic specific issues on diabetes disease are also put forward.

7.2 Key Findings

The ethnic differences in diabetes risk were 3-4 folds higher with South Asians at the highest in risk, Blacks positing the second highest were 2-3 folds higher and subsequently followed by the Chinese were 1.5-fold higher when compared to the white ethnic majority group in this thesis, therefore, verifying existing evidence. This demonstrates that with respect to demographic trend, the prevalence of diabetes among ethnic minority communities in the United Kingdom continues to be a matter of concern for public health. Furthermore, the studies include examining diabetes risk factors among men and women in different ethnic groups which could help improve the understanding of underlying ethnic-sex-specific mechanisms.

7.2.1 Ethnic Differences in Diabetes Prevalence by Sex

Chapter three presents an explorative study of the ethnic differences in diabetes prevalence by sex in those of South Asian, Black, and Chinese descents in comparison with people of White ethnicity, by standardization of prevalence rates to ensure comparability of between ethnic groups (409). This study is the first of its kind in UK to examine ethnic differences in diabetes prevalence after standardizing for a wide range of explanatory factors. The study is the most robust research to estimate the prevalence of type 2 diabetes by sex among different ethnic groups in the United Kingdom, including the Chinese ethnic groups who have not been included in other UK-based studies. After standardizing for age, SES, BMI and lifestyle factors, compared with the White ethnic group (6.0% in men vs 3.6% in women), the

standardized percentage prevalence of type 2 diabetes was higher in the South Asian (21.0% in men vs 13.8% in women) and Black (9.7% in men vs 7.1% in women) groups, while the difference was not statistically significant in Chinese ethnic group (7.1% in men vs 5.5% in women ($p=0.211$)). Further analysis on South Asian subgroups reported highest prevalence in Bangladeshis (30.5% in men vs 22.3% in women), followed by Pakistanis (25.4% in men vs 18.7% women) and lower in Indians (18.8% in men vs 12.5% in women), showed further disparities within ethnic social constructs. The findings suggest that ethnic minority men are more susceptible to diabetes. Hence these differences are vital aspects that could have implications for screening and prevention strategies.

The findings in this research supports existing studies that found diabetes prevalence to be varied across sex and ethnicities (42). In agreement with this thesis, the global diabetes estimate in 2021 (47) was higher in men than women (10.8% vs 10.2%) with largest numbers of diabetes coming from Indian, Pakistani and China. However, the report showed the Pakistani had the highest comparative diabetes prevalence (30.8%). Age-standardised studies conducted by Khan et al. in Canadian Whites, South Asians and Chinese support the evidence of higher prevalence in men compared to women in different ethnic groups.

There is widespread acceptance that the prevalence of type 2 diabetes is higher among ethnic minorities in the UK(142,410). However, there are limited studies that have examined these differences within men and women separately (142). These Studies in the UK(127,411,412), have small sample size, hence, unable to adjust for important risk factors and conducted in a single demographic location. The SABRE study, a London-based study of 2,533 participants Tillin, et al. (66) reported the sex and ethnic differences, whereby the crude diabetes incidence rate per 1000 person years in South Asians (20.8 in men vs 12.0 in women) and African-Caribbeans (16.5 in men vs 17.5 in women) was higher compared to European Whites (7.4 in men vs 7.2 in women). However, the sample size was far smaller than the current study (801 in SABRE vs. 7974 African Caribbean participants in the current study). The SABRE study also did not adjust for BMI which was 3 kg/m² greater in African Caribbean women than men (29.4 vs.26.4 kg/m²). In a cohort of around 13,500 adults, the data suggested that the crude prevalence of type 2 diabetes was

significantly higher in Black Caribbean (9.5% men vs 7.6% women), Black African (4.3% men vs 2.0), Indian (9.2% men vs 5.9% women), Pakistani (7.3% men vs, 8.4% women), Bangladeshi (8.0% men vs 4.5% women) and Chinese (3.4% men vs 3.3% women) than in the general population (3.8% vs 3.1% women). These UK studies were limited by their smaller sample sizes and compared to the current study, did not adjust for differences in prevalence driven by several sociodemographic and lifestyle score as in this study, which are all independent risk factors in their own right for diabetes disease. This study is notable for several reasons. First, it confirms prior research regarding standardized diabetes prevalence higher among men compared to women of similar age. Furthermore, it highlights the major diabetes inequalities amongst ethnic minorities in comparison with White British population using of diabetes prevalence using more advanced standardization considering BMI, SES and lifestyle factors between ethnicities, as a result it methodically demonstrates the variance in diabetes risks over and above these confounders.

The sex differences could be attributed to variability in risk factors for diabetes prevalence between men and women (53,87-93,96,413,414). Nordström et al. (273) examined the association of visceral fat with plasma glucose and type 2 diabetes prevalence in 1,393 elderly participants of northern European origin. Type 2 diabetes was more prevalent in men than women (14.6% vs. 9.1%; Odds Ratio, 1.72). Interestingly, after adjusting for visceral fat levels, the prevalence of type 2 diabetes was similar in men and women, suggesting differences in visceral fat may contribute to sex differences in diabetes prevalence (273). Given that visceral fat levels correlate strongly with liver and pancreatic fat ectopic rather than visceral fat differences may explain greater diabetes risk in men (274). However, men are less likely to engage in lifestyle changes, with twice as many women as men enrolling in a weight management trial (279). Notable, in this study the prevalence of diabetes decreased in women and increased in men across ethnic groups when the models were standardized for BMI and lifestyle scores. These suggest that the disparity in type 2 diabetes could be accounted for in environmental factors including BMI and lifestyle factors, and prompts exploration of underlying mechanisms from these emerging risk factors. It also highlights the need to focus further clinical attention on men and minority ethnic groups with increased risk of

diabetes. Finally, the study demonstrates the importance of systematically considering subgroups of ethnicity and sex in epidemiological research.

7.2.2 Ethnic-Specific Obesity Cut-Off Points of BMI and Waist Circumference

Chapter four, provides the ethnic-specific obesity cut-off points of BMI and waist circumference for standardizing diabetes risk in a multiethnic population. The results from the study data showed that the increase in diabetes risk linked to BMI, waist circumference, percentage body fat and waist-hip ratio was substantially greater in South Asians, Blacks and Chinese people than it is in white ethnic groups. Additionally, the results indicated that obesity thresholds differed by ethnic group and sex for South Asian, Black and Chinese compared with white men and women would need to be lowered to match the equivalent diabetes risk of Whites at the recommended BMI and waist circumference cut-off points. Results indicated that the existing BMI thresholds for obesity need to be lowered to 22.0kg/m² for South Asians, 26.0kg/m² for Blacks, 26.0kg/m² for Chinese men and 24.0kg/m² for Chinese women. Furthermore, the external validity of these threshold was tested using the QDiabetes risk algorithm. For example, a 50-year-old man from South Asian descent with BMI of 22.0 kg/m², a Black African man with 26.0 kg/m², a Chinese man with 26.0 kg/m² and a White man with 30.0 kg/m² of the same age all have the same risk of developing type 2 diabetes (10-11%) within the next 10 years (314,415). Hence, underpins the thesis contribution to existing research. South Asians are heterogenous with regard to diabetes prevalence and risk, therefore the obesity cutoff estimation between South Asian sub-groups found that Pakistani men and women had lower obesity cut offs than Indians. The recommended thresholds were for 21.6kg/m² and 21.5kg/m² for Pakistanis women and men respectively and Indians 22.3kg/m² and 22.0kg/m² in women and men respectively. The findings contribute to the existing literature, supporting the importance of obesity in the ethnic minorities' susceptibility to diabetes. The results notably support the recommendation for lower BMI cutoffs than 30kg/m² for diabetes intervention in South Asian, Black and Chinese ethnic groups.

The thesis findings also suggests that lower waist circumference cutoffs should also be applied for diabetes prevention in ethnic minorities. The recommended cut-off for waist circumference, needs be lowered for women to 70 cm in South Asian women, 79 cm in Black women and 74 cm in Chinese women. This research suggests it should be lowered by 79 cm in South Asian men, and 88 cm in both Black and Chinese men. For the first time the thesis suggests waist circumference cutoffs for diabetes risk in Pakistani and Indian populations separately.

Obesity represents one of the strongest contributors for the development of type 2 diabetes (101), and epidemiological research recognises the distinct patterns in the increasing incidence and prevalence of diabetes and obesity of different ethnic groups at different rates. This study is important when studying ethnicity because BMI and waist circumference measure two distinct types of obesity; BMI measures generalised obesity and waist circumference measures abdominal obesity, both associated with diabetes outcome. Furthermore, it is important as it is suggested in literature that people from different ethnic groups are susceptible to both in different measures/ways.

Studies also show that ethnic minorities particularly South Asians and Chinese have a higher percentage body fat than Whites with the same BMI level(140,416,417). The World Health Organization (WHO) proposed overall body adiposity as defined as a BMI of 30kg/m² be recognised as the cutoff point for adult obesity(418,419), whilst the International Diabetes Federation (IDF) proposed abdominal obesity cutoff level as waist circumference of 102cm in men and 88cm in women(420). However, these recommendations were based on limited evidence conducted in participants from European White ethnic groups. Furthermore, previous studies show that people from non-white ethnic descent have diabetes at lower levels of BMI or waist circumference, which warrants that obesity cut-off-points be ethnic specific, particularly for intervention purposes. In the UK the NICE guidelines recommends that a BMI of 27.5kg/m² should trigger diabetes prevention in South Asians and Chinese groups, albeit, the evidence used for these recommendations are from studies with small ethnic minority sample size or have older participants recruited from one geographical location within the UK or lack adjustment for explanatory variables and the lack of acknowledgement of heterogeneity within ethnic groups

such as South Asians. Hence, these studies are biased by the overestimation of the suggested obesity values. The data used (UK Biobank) in this thesis had a larger ethnic minority sample size and recruited from multiple locations within the UK. The NICE, WHO and IDF guidelines do not have recommendations from those of Black ethnic background due to insufficient evidence hence obesity cut points for Whites are applied to Black ethnic populations. This thesis therefore contributes to the evidence.

The application of these thresholds suggests that diabetes prevention be started at these lower BMI and waist circumference values for individuals from the ethnic minorities, hence may include more people from minority groups for interventions. However, it will ensure that these groups are not excluded from opportunities to prevent diabetes or early diagnosis. These values also have the potential to substantially impact diabetes prevalence with time, and ultimately the public health priorities for obesity prevention strategies, programmes, monitoring and evaluation.

7.2.3 Ethnic Differences in Muscular Strength (Hand-Grip Strength)

Chapter five aimed to address the ethnic differences in muscular strength, analysed as grip strength. The study found that lower grip strength was associated with higher prevalence of diabetes, independent of a range of confounding factors including age, adiposity, years with diabetes, physical activity, sedentary behaviour, sleep duration, smoking, alcohol, dietary factors and socio-demographic confounders, across all ethnicities in both men and women.

In this chapter, the ethnic differences in diabetes risk were evidenced in the difference of prevalence associated with grip and the difference in the magnitude of risk associated with grip strength. Prevalence of diabetes was 3-4-fold higher in South Asians and 2-3-fold higher in Black adults compared to White Europeans across all levels of grip strength. Nevertheless, the data revealed a significant interaction with ethnicity in the association between grip strength and diabetes, with the difference in odds for diabetes per unit difference grip strength being higher in White Europeans than the other ethnic groups. However, the higher prevalence of diabetes in South Asians and Blacks compared to Whites, together with the lower

grip strength of 5-6 kg in absolute terms and 0.3-0.5 kg per kg bodyweight in the population distribution of grip strength in South Asians, compared to the other ethnic groups resulted in a particularly high attributable risk associated with low grip strength, at 4 cases per 100 individuals, in South Asian men and women. Attributable risk associated with low grip strength was also high in Black men, at ~4 cases per 100 individuals, but in Black women the association between grip strength and diabetes was less strong than in other groups, at least when grip strength was expressed in absolute terms, resulting in a lower attributable risk associated with low grip strength, despite a relatively high diabetes prevalence. This underscores that identifying and addressing modifiable risk factors in high-risk groups is vital in tackling the increasing prevalence of type 2 diabetes. Given the low strength levels in South Asians and Blacks, findings from this study recommend that improving muscle strength and quality could potentially provide a complementary strategy in reducing ethnic inequalities in diabetes if considered as a possible additional target for preventive intervention through resistance exercise in addition to weight loss in these high-risk groups.

This thesis is in agreement with a meta-analysis study conducted by Tarp et al performed who reported that in amongst 39,233 cases for each 1 SD higher muscular strength was associated with a 13% (95% CI 6%, 19%) lower RR of type 2 diabetes (268). Conversely, using data from the SABRE study, in elderly South Asians and Black participants, Jones et al. (229) suggested that diabetes does not explain the ethnic differences in skeletal muscle. However, as diabetes was not a primary outcome in their study this gives a paradoxical effect and not a clear understanding of the impact of diabetes risk and muscular strength in ethnic health disparities.

Muscular strength could be a useful marker to identify people at risk of type 2 diabetes in clinical or public health practice, because as handgrip strength it is an objective, non-invasive, low-cost measure, making a clear case for future randomized controlled trials of ethnic-specific interventions to improve strength in these populations.

7.2.4 Ethnic Differences in Association Between Diabetes, Television Viewing and Physical Activity

Chapter six aimed to assess the ethnic differences in association between diabetes with television viewing alone, and joint association with physical activity. Prolonged television watching was positively associated with diabetes. The association of television time with diabetes was higher in higher in South Asian than White ethnic groups independent of confounding risk factors because the excess risk was evident after adjusting for these factors. However, findings for Blacks did not show a significant dose-response effect, between television viewing and diabetes risk. From the findings, BMI could be a large contributor to the associated risk of diabetes and television viewing as adjusting for BMI substantially reduced ethnic differences in diabetes risk in South Asians and Whites. The null effect of television viewing and diabetes in Blacks disappeared when BMI was added in the analyses model. Hence, there could be other behavioural or cultural differences between Blacks and other ethnic groups interacting with the relationship of diabetes with television viewing. For example, cultural behaviours around food intake during television viewing (421). These findings add to growing evidence that sedentary behaviour, separately from activity and influences increased diabetes disease.

The findings show that television viewing is associated with a higher risk with type 2 diabetes, while increased physical activity is protective of the disease in Whites. This confirms and extends to previous studies examining the relation between television viewing and diabetes this ethnic group (193). Recently, using a two-sample Mendelian randomization analysis method, Deng and colleagues examined the risk of diabetes in association with time watching television and physical activity (193). They found that increased time spent watching television was associated with a 2.35 increased risk of type 2 diabetes (OR: 2.35 (1.9-2.9)). Findings from the UK Whitehall study found that after following a cohort of civil servants for 12 years, there was no link between television sitting and incident diabetes after adjusting for BMI (RR: 1.31(0.96 to 1.76)). Joseph et al. (24) using data from the Multi-Ethnic Study of Atherosclerosis (MESA) study looked at the association of physical activity, sedentary behaviours and incidence of type 2 diabetes in multiple ethnic groups including

Whites and Blacks. In this study, the graded independent associations of physical activity were statistically significant in Whites across all increased levels of physical activity, whilst there was no significant association with television watching for those who spent up to 4 hours of television watching RR:1.50 (0.91 to 2.49). The deleterious effect of television watching was only observed in Whites who spent more than 6 hours of their time watching television RR:4.54 (1.42 to 14.49).

To the researcher's knowledge, this the first research to explicitly examine the risk of television viewing time and type 2 diabetes in South Asians. Jackson Health study, the authors reported that compared to those who spent >4 hours versus 1 hour of television viewing, the risk of type 2 diabetes in Black participants was 95% which was not statistically significant. In The MESA study (24), television watching was not associated amongst Black ethnic subgroups who spent more up to 4 hours watching television compared to those who spent less than 2 hours of TV viewing (HR:1.47 (95%CI 0.98-2.21). Contrastingly, findings from the Black Women's Health Study (BWHS) reported 1.9-fold risk of diabetes amongst black women who spent more than 5 hours watching television in a day relative to those who spent less than 1 hour per day of television viewing(215). The authors suggested that reducing sedentary behaviour, particularly television watching, could be an important strategy for preventing the development of type 2 diabetes in this high-risk population. However, the study does not include other ethnic groups to allow for ethnic comparisons. Nevertheless, it is possible that the lack of relationship between sedentary behaviour and type 2 diabetes in Black adults in current study may be influenced by unmeasured confounding lifestyle, and environmental factors that vary by geopolitical location. Notably, majority of studies on television viewing and type 2 diabetes in Black populations have been conducted in US, whereby the lifestyle behaviour may be different from UK residents. Studies show that US Blacks are more obese, low socioeconomic status and poorer health care compared to UK Blacks(422-428). Hence, more research on Black ethnic groups in the UK setting is needed to fully understand these potential interactions.

7.3 Overall Discussion

Holistically, the thesis points to the possibility that diabetes disease in the presence of modifiable lifestyle factors independently affects ethnic groups differently. The data suggests that the magnitude of the risks is particularly higher amongst South Asians and Blacks, but relatively low in Chinese compared to Whites in a UK setting. Furthermore, sex intersects with these variations within ethnic groups and may shape the impact of diabetes within ethnic minority groups. This demonstrates the importance of taking forward an intersectional approach in diabetes interventions to reduce the health disparity between ethnic minorities and Whites (429).

The thesis findings show that obesity cut-off points that are equivalent risk for Type 2 diabetes are lower than the conventional values for South Asians and Blacks compared to the European white population in the UK. These findings have the potential to influence public health actions such that at lower BMI and waist circumference thresholds South Asians, Blacks and Chinese ethnic groups in the UK, should be considered for diabetes screening/intervention to enable early diagnosis and management of type 2 diabetes in these groups. There is ample evidence that diabetes is present among minority ethnic groups at a higher prevalence and lower BMI level than in the European Whites population (42). Studies suggest that by incorporating prevention in health care, individuals can have a better quality of life as well as reduce health care costs (430). The high costs associated with type 2 diabetes are mainly attributable to the management and consequences of complications associated with this disease and these complications have more adverse impact on ethnic minorities, particularly South Asians and Blacks. Thus, it is important to identify individuals who may have or be at increased risk of diabetes in a timely manner. The finding in this thesis suggests that using lower obesity cut points recommendations can be a useful first-step screening test for the identification of undiagnosed diabetes. Given that BMI and Waist circumference, have the advantage of easy availability and are not costly. Currently, the Obesity cut points for diabetes intervention for South Asians and Chinese recommended by NICE in the UK is $27.5\text{kg}/\text{m}^2$ and $30\text{kg}/\text{m}^2$ for Blacks are higher than the findings in the thesis but using the current guidelines are likely to overlook at risk individuals in these ethnic groups. This thesis recommends BMI cut points of $22\text{kg}/\text{m}^2$ in South

Asians and $26\text{kg}/\text{m}^2$ for Blacks and Chinese and waist circumference of 70cm to 79cm in women and 79-88cm in men will include more people to be tested for diabetes, nevertheless will be valuable in capturing individuals that will otherwise not be aware of their high-risk status and reassurance in those with the absence of the disease. However, advocating for BMI below $22\text{ kg}\cdot\text{m}^{-2}$ maybe unrealistic but improving muscular strength and promoting less sedentary television viewing time (more movement) in addition to weight loss programs are required.

The results suggest that improving strength, particularly in South Asian adults, and in Black men, could potentially provide a complementary strategy in reducing ethnic inequalities in diabetes. Clinicians and policies should consider including handgrip strength as a relevant screening tool in primary care. Moreover, it is important to acknowledge that strength has important genetic component (353-355). Therefore, this thesis suggests that ethnic-specific muscular-strengthening activities are important to consider since different ethnic groups may respond differently to exercise regime (either by increased volume or duration of training) to better elucidate potential effects.

These finding challenges the approach of one size fits all towards diabetes prevention intervention suggests that approach to diabetes interventions be both sex and ethnic-specific to make utmost impact in high-risk populations.

7.4 Strengths and Limitations

Throughout this thesis, specific strengths and limitations of the data and analytical approaches within each chapter were considered. Several of these strengths and limitations are common to the thesis as a whole and are discussed below.

7.4.1 Strengths

The main strength of this thesis is the large sample size of the multicentre UK Biobank study. The UK Biobank collected data from 502,682 middle aged adults in the UK, on a broad range of diseases and lifestyle factors, using comparable and standardised methods. The UK Biobank study by design, includes both sexes and

includes a large number of minority ethnic participants, from South Asian, Black and Chinese populations, and providing sufficient statistical power given that inclusion of ethnic minorities in cohort studies is often challenging and results in scanty number of participants, partially due to the relatively low participant rate. By using the UK Biobank, the research was not only able to distinguish the individual ethnic minority groups, but was also able to stratify results by sex and compare several ethnic groups living in the same country within the same study. Previous UK cross-sectional studies have been smaller overall, have recruited smaller numbers of non-white participants, compared fewer ethnic groups and were not robust in analysis.

Throughout this thesis, appropriate statistical methods were used for the data analyses including using multiple logistic regression methodology to control for potential confounders, sensitivity analyses considering diabetes risk factors. This was essential to account for the confounding factors and give robust results which has often been overlooked in previous studies, which can lead to overestimation of the overall variability, potentially leading to spuriously significant results (431). The risk factors were reported both as continuous measures and categorised into clinically relevant pre-defined binary and categorical groups, to align the study findings with public health recommendations and provide a valuable evidence base to inform health policy and public health programmes.

Lastly, the four studies lay the groundwork for future analyses on the ethnic disparity diabetes risk associated with emerging lifestyle factors in United Kingdom. This thesis generated hypotheses based on available measures and cross-sectional data that can be tested in future, longitudinal analyses and clinical trials.

7.4.2 Limitations

As in all epidemiological studies, it is important to consider potential restrictions that could influence the findings and interpretation in this thesis. The studies presented in this thesis are based on cross-sectional data which suggests rather than confirm the inference. Furthermore, as a cross-sectional study it was not possible to assess incidence and may mean a temporal association between exposure and diabetes outcome amongst the UK Biobank participants.

Analyses of associations from cross-sectional data are susceptible to reverse causation. However, sensitivity analyses were conducted in all the studies to exclude the potential influence of long-term diabetes on obesity, grip strength and physical activity and television viewing by including those only recently diagnosed within 5 years with diabetes in the analyses did not alter the findings in this thesis. I recommend a replication with longitudinal data in future study

Most of the risk factors analysed in these ethnic subgroups were relatively common (T2D prevalence of 10-25%) and the prevalence estimates had relatively high precision. However, in the Chinese ethnic groups, the sample size was relatively small, which meant that the prevalence estimates were less precise when analysed with risk factors such as grip strength, physical activity and television viewing. Therefore, participants from Chinese ethnic groups were excluded in some analyses.

Analyses of continuous risk factors as categorical ordinal variables may reduce the number of participants in each stratum or empty cells when categories are created and the analyses are likely to be underpowered with limited ability to detect true associations and reject the null hypothesis (type II error), and therefore lack clinical relevance. However, the large sample size of the UK Biobank for Whites, South Asians and Blacks allowed for comparative number of observations in within the categories, and grouped thresholds were based on extensive review of previous studies and results were interpreted with caution.

Self-reported measures of behavioural risk factors such as physical activity and television viewing, have the potential for recall bias, cultural norms, social and desirability bias, and lead to differential misclassification of the exposure in the relation to diabetes risk. However, in the UK Biobank data this was minimised by using validated questionnaires to collect self-reported measures and trained field team to confirm the information given with participants with outlier values. Self-report questionnaires have higher feasibility for implementation than objective measurement tools in large-scale observational studies such as the UK Biobank study(376,432,433). In addition, self-report questionnaires are cost-effective, easily accessible to a large proportion of the population and participant burden is relatively low.

Confounding occurs when an observed association between a proposed exposure and outcome is influenced by a third independent factor, which is associated with both exposure and outcome but not on the causal pathway. If confounding is not accounted for in analyses, any observed association could be attributable wholly or in part to that confounding factor. In **Chapters 3,4,5 and 6** the research attempted to address potential confounding to the fullest extent possible with the available data through multivariable logistic regression modelling using preselected potential confounders based on findings of previous studies. However, residual confounding may still have been unaccounted for. For example, in **Chapter 6** the ethnic differences in diabetes risk with television viewing was assessed in models adjusted for potential confounders. However, whilst television watching leads to a higher caloric intake and a relatively unhealthy dietary pattern independent of diabetes, differential analyses for dietary pattern was not assessed in the study. This may have caused residual confounding of the associations in the study.

The potential limitation to the generalisability of the study population was in the low overall response rate for UK Biobank at 5.5% (257). While UK Biobank was not specifically recruited as a nationally-representative sample of the UK population, diabetes prevalence and mean BMI values in the UK Biobank cohort at baseline were comparable to nationally-representative samples across all three ethnic groups. UK Biobank is of a sufficient size that it will be possible to obtain reliable estimates of risk factor-disease associations according to a number of subgroups (even though the proportions of people represented in these subgroups may not match those in the general population).

At baseline, the number of diabetic participants was 26,999. Fry et al. have shown that, in comparison to the general population, the prevalence of diabetes was lower in participants of the UK Biobank (257). However, Batty and colleagues conducted a more recent methodological study demonstrated that the estimates of effect sizes obtained from UK Biobank for risk factors and a number of chronic diseases, including diabetes, were comparable to those obtained from 18 nationally representative prospective studies (388) suggesting that, in spite of its low response rate and lack of representativeness, UK Biobank can produce generalisable results.

This study did not analyse for differences between the Black Africans and Black Caribbeans and there may exist differences with the Black subgroup.

7.4.3 Public Health Implications

The studies in this thesis call for action in primary health care and clinical practice. So far, the prevailing approach for Type 2 diabetes prevention has been implementing models that are based on research from predominantly White European populations (434). Treating individuals from minority ethnic groups using these models have underestimated the complexity and scale of the disease in these group. This is clearly reflected in the disproportionate prevalence experiences in these groups. Therefore, more inclusive, multifactorial and strategic approaches are required in order to conform the problem of type 2 diabetes prevention in ethnic minorities (429).

First, opportunistic screening should be made available for individuals from minority ethnic populations for diabetes outcome and intervention at $22\text{kg}/\text{m}^2$ for South Asians and $26\text{kg}/\text{m}^2$ for Blacks and Chinese. Waist measurement should be 79cm for South Asian men, 70cm for South Asian women, 88 cm for Black and Chinese men, 79cm for Black women, and 74cm Chinese for women. The reason this recommendation is important is because screening for blood sugar levels or diabetes is often done based on a person's calculated BMI from their weight by health professionals. However, if those from South Asian, Black or Chinese population are likely to be at risk of diabetes, before the current obesity BMI cut-off of $30\text{kg}/\text{m}^2$ is reached, a large proportion of ethnic minority groups may be overlooked. Subsequently leading to increase in incidences, poor quality of life for patients, more resources in health care management, and high health care expenditure to the patient and government. Furthermore, direct comparisons of different interventions in Blacks, and South Asian subgroups are needed to identify which approach work best for individual groups and whether they respond differently.

It is important therefore that clinicians and health care professionals are aware of these at-risk groups, particularly men, and that more is done to encourage and

motivate lifestyle changes. Couple-based interventions may also prove useful as spousal diabetes history can increase the risk of diabetes by 26%(288).

Engaging in weight loss and physical activity interventions is highly recommended for South Asians and Blacks. A Cochrane systematic review of randomized controlled trials with duration of at least two years showed that combining diet with increased physical activity delays the development and reduces the risk of T2DM in adults with impaired glucose tolerance(435). Intervention studies such as the IDD, Indian diabetes prevention study and NHS diabetes prevention programme have shown that those engaged in physical activity have a reduced risk of diabetes(179). However, how effective this is on ethnic minorities is still debated(436). Weight loss in response to diet and physical activity interventions appears to be smaller in South Asians than other ethnic groups. However, studies also show that South Asians in particular are difficult to recruit for research and have a high loss to follow up in these studies(179). A more culturally-tailored intervention should be adopted for ethnic minorities(437). Hence it is important to consider the cultural and epigenetics factors.

In view of the findings in this research, the risk of diabetes associated with television viewing is an important risk factor for type 2 diabetes and is independent of physical inactivity, which suggests that physical activity interventions alone may not produce meaningful reductions in sedentary time(438,439). This is likely related to the distinct behavioural factors which co-exist with television viewing (e.g. snacking) (212,440). Therefore, it is equally important to directly address reducing television viewing and other sedentary behaviours in order to potentially lower diabetes risk. This can be accomplished through targeted interventions that encourage active transportation, foster environments that support movement and promote taking breaks from sitting. For instance, in the workplace, introducing sit-stand desks and active permissive workstations has been shown to significantly decrease the amount of time spent sitting(192). Furthermore, spending less time affixed to television watching could translate to reduced exposure to unhealthy food advertisements, a known influencer of unhealthy dietary choices(192). Additionally, minimizing snacking during television viewing can contribute to healthier eating habits, ultimately decreasing the risk of diabetes associated with unhealthy dietary patterns

(192). Interventions designed to encourage at-risk individuals to track their television viewing time and set realist goals for reduction could play a crucial role in promoting healthy habits and possibly mitigate the risk of developing type 2 diabetes. Tailoring interventions to address specific sedentary behaviour patterns within diverse ethnic minority population, particularly South Asians holds promise for unique public health implications in preventing and managing type 2 diabetes within these communities. Interventions can be delivered at different levels, including individual, family, community, or environmental, and can involve a range of components, including education, counselling, feedback, incentives, or environmental changes.

Therefore, any strategy to increase the awareness of risk factors and risk factor modification interventions of type 2 diabetes in ethnic minorities in the UK should be inclusive. For example, for South Asian populations, educational materials addressing diabetes and risk factors such as sedentary behaviours, physical activity, muscular fitness and obesity cut-points should be in South Asian languages and using culturally appropriate examples would potentially increase the knowledge and awareness of lifestyle behaviour changes leading to prevention and reduction of these risk factors(441-443).

Furthermore, clinicians and health care providers should be informed and be aware of possible barriers for adhering to positive lifestyle behaviours (such as belief), inadequate health literacy and cultural barriers), and actions should be taken to remove those barriers(441).

7.5 Recommendation for Future Research

Future epidemiological studies should also recognise the heterogeneity within various ethnic groups and examine the subgroups separately to identify diabetes risks specific to that group. Thus, in order to improve public health and epidemiological research in ethnicity and health and to facilitate international comparison, it is recommendable to move beyond the straightforward South Asian/Black/white category and access the considerable ethnic diversity that typify

the population under study. There is need to replicate analyses in Black Africans and Black Caribbeans ethnic groups separately.

This thesis has identified differences in lifestyle-related diabetes risk between ethnic minorities and Whites in the UK. However, to move beyond these associations, mechanistic studies are essential. By understanding the fundamental mechanisms behind these disparities, we can delve into the biological pathways and physiological processes that link lifestyle factors to diabetes development, leading to the creation of more effective interventions to address the disproportionate diabetes burden in these high-risk groups. For example, exploring the mechanisms underlying the observed ethnic differences in fat distribution and accumulation could inform strategies to tackle excess adiposity. Similarly, understanding the reasons behind the earlier decline in beta-cell function and how differences in muscle composition and function in ethnic minorities might affect insulin sensitivity could lead to the development of more targeted interventions. These interventions could extend beyond traditional weight loss strategies and include methods to improve muscle health and address potential differences in insulin sensitivity that are relevant to the ethnic minority population. Key to effectiveness will be appropriate culturally tailoring to different ethnic groups to facilitate long-term adherence to these approaches, which will require co-design with stakeholders the relevant communities and input from social as well as biomedical scientists and healthcare professionals in the intervention development(403,444).

Future research on sedentary lifestyles, particularly prolonged television viewing, should investigate the interplay between behaviour and environment using an ecological model to understand the various settings influencing this behaviour across different ethnic groups. Additionally, studying how reallocating and substitution of sedentary time with physical activity time differentially affects type 2 diabetes risk across ethnic groups can provide valuable insights.

7.6 Conclusion

This thesis has advanced the understanding of ethnic differences in diabetes disease and also demonstrated that the ethnic disparity in diabetes is ubiquitous and remains a major health issue. Specifically, ethnic differences were observed to be independent of obesity, low grip strength and television viewing risk factors and suggests ethnic specific interventions considering the physiological, behavioural and cultural differences will help to ameliorate continuing health disparities experienced by minority ethnic groups particularly the South Asians and Blacks in the United Kingdom.

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