

What are the cut-off points for body mass index (BMI) and waist circumference among adults from black, Asian and other minority ethnic groups living in the UK that are 'risk equivalent' to the current thresholds set for white European populations? Analyses from the ADDITION-Leicester Study

Danielle Morris^a, Kamlesh Khunti^a, Laura Gray^b, Naveed Sattar^c, Melanie Davies^a

^a Diabetes Research Unit , University of Leicester

^b Department of Health Sciences, University of Leicester

^c Institute of Cardiovascular and Medical Sciences, University of Glasgow

EXECUTIVE SUMMARY

Body mass index (BMI) and waist circumference are commonly used measures of adiposity; high levels of which indicate increased risk of diabetes, cardiovascular disease and early mortality. Guidelines from leading health organisations recommend intervening to prevent adverse outcomes when BMI and/or waist circumference reach high levels. These levels are currently defined as overweight (BMI of 25.0-29.9kg/m²), obese (BMI ≥30kg/m²) and very high waist circumference (≥102cm for men and ≥88cm for women). However, these existing cut-offs are based on data predominantly from white European populations and evidence suggests that they may not be applicable to other populations. In particular, the distribution of body fat appears to differ between ethnic groups implying that these cut-points might need updating for use in non-white populations. This report addresses this issue by identifying BMI and waist circumference cut-points in South Asian and black populations that are risk equivalent in terms of dysglycaemia to those used in white populations. We used data from a population-based, cross-sectional screening study conducted in Leicestershire, UK (ADDITION-Leicester). Participants were aged 40-75 years and of white (n=4599), South Asian (n=1310) or black (n=109) ethnicity. Weight, height and waist circumference were objectively measured, ethnicity was self-reported based on census categories, and principal components analysis was used to define a glycaemic factor that was a combination of fasting glucose, 2-hour glucose and HbA1c. Equivalent cut-points were found using fractional polynomial models with the glycaemic factor as the outcome and ethnicity, adiposity (BMI or waist circumference) and their interaction as covariates. Models were fitted with and without adjustment for age, sex, smoking status, socio-economic status and physical activity. In the adjusted models, derived obesity cut-points were **confidential information removed** for South Asian and **confidential information removed** for black populations. Derived overweight cut-points were **confidential information removed** for South Asian and **confidential information removed** for black populations. For men, derived high waist circumference cut-points were **confidential information removed** for South Asian and **confidential information removed** for black populations. For women, derived high waist circumference cut-points were **confidential information removed** for South Asian and **confidential information removed** for black populations. Important limitations of this work include its cross-sectional nature, the small sample size for the black population, and that some of the confidence intervals are fairly wide. Moreover, some of the estimated cut-points are very low and should be interpreted as a suggestion that the cut-point needs lowering, rather than a precise estimate of what that cut-point should be, and that perhaps non-white ethnicity in itself is a risk factor for high glucose levels that at least equals the risk associated with adiposity in white Europeans. These findings add to existing evidence that health interventions are required at a lower BMI and waist circumference for people of South Asian ethnicity. They are also indicative that the cut-points require lowering for people of black ethnicity, but are not conclusive due to the very small sample size in that group.

1 BACKGROUND

There is an extensive literature showing that high levels of adiposity are related to morbidity and mortality, which has resulted in leading health organisations recommending weight loss interventions for overweight and obese individuals (1,2). These individuals are typically identified using body mass index (BMI) and/or waist circumference as both measures are strongly correlated with body fat and are simple to measure.

BMI is calculated as weight in kilograms divided by height in metres squared, and is often categorised for ease of interpretation. The World Health Organisation (WHO) and the National Institute for Health and Clinical Excellence (NICE) define the following cut-points for BMI: $<18.5\text{kg/m}^2$ underweight, $18.5\text{-}24.9\text{kg/m}^2$ healthy weight, $25.0\text{-}29.9\text{kg/m}^2$ overweight, and $\geq 30\text{kg/m}^2$ obese (1,2). These cut-points were based on visual inspection of the relationship between BMI and mortality, which tends to be J or U shaped, and guidelines suggest intervening when BMI reaches at least 25kg/m^2 , with a greater focus on 30kg/m^2 or higher (1,2). Despite its wide spread use, it is acknowledged that BMI has limited use in some populations, such as very muscular individuals (2). Moreover, BMI tends to reflect overall adiposity whereas research suggests that abdominal adiposity may independently influence health outcomes (3,4). Consequently, the use of measurements that reflect abdominal adiposity, such as waist circumference, is increasing. Recommended cut-points to define a very high waist circumference are 102cm for men and 88cm for women (2,5). However, these cut-points were derived based on their ability to detect an obese BMI, rather than on their relationship with health outcomes (6).

The derivation of the BMI and waist circumference cut-points mostly used data from Western European or American populations (1). There is growing interest in the validity of these cut-points in other populations. In particular, it has been debated whether these cut-points can be applied to Black and Minority Ethnicity (BME) groups in whom the distribution of body fat tends to be different to white populations (7,8). Indeed, studies have shown that BME populations have a similar level of health risks at lower adiposity thresholds than white populations (9).

This report aims to add to the evidence on this topic by presenting results from the ADDITION-Leicester study, a large population-based cross-sectional study conducted in Leicestershire, UK, which is an area with a large BME population (10), predominantly comprising those of South Asian ethnicity. This report uses objectively measured weight, height and waist circumference data to identify BMI and waist circumference cut-points in South Asian and black populations that are risk equivalent in terms of dysglycaemia to those used in white populations. The findings presented are an update of a previous analysis based on this study population (11).

2 METHODS

2.1 THE ADDITION-LEICESTER STUDY

The ADDITION-Leicester study is a UK-based two phase study (NCT00318032). The first phase was a population level study where people were screened for type 2 diabetes mellitus. In the second phase, screened individuals who were found to have type 2 diabetes were enrolled into a randomised controlled trial (12-15). Only data from the screening stage were used in these analyses. All general practices in the Leicestershire and Rutland Strategic Health Authority were invited to participate and those that agreed were asked to identify patients that met the inclusion and exclusion criteria for the study. The inclusion criteria for the screening stage were that participants must be aged 40-75 years inclusive if they were of white European ethnicity and 25-75 years inclusive if they were of Asian, black or Chinese ethnicity. The different age criteria were used for the screening study because the prevalence of type 2 diabetes is low among white Europeans younger than 40 years of age but is more common among younger adults of non-white ethnicity. Exclusion criteria included previous diagnosis of diabetes, being housebound, presence of a terminal illness, active psychotic illness, pregnancy or lactation. A random sample of eligible individuals (18,113 white Europeans; 12,837 BME individuals) was then sent an invitation pack and a pre-screening questionnaire (15). Invitation packs were available in English, Hindi, Gujarati, Urdu and Punjabi. Those responding to this letter were invited to a screening appointment, which 4687 (25.9%) of white Europeans and 2062 (16.1%) of BME individuals attended (15). Ethical approval was obtained from the local research ethics committees (64/2004), and all participants gave written informed consent.

2.2 ANALYSIS POPULATION

Of the participants screened in the ADDITION-Leicester study (n=6749), we excluded from these analyses those who were younger than 40 years of age (n=359) to account for the ethnic differences in age inclusion criteria for the ADDITION-Leicester study (40-75 years for white Europeans, 25-75 years for all other ethnic groups). Furthermore, we excluded those whose ethnic group was unknown (n=203) or was not white, South Asian (i.e. of Indian, Pakistani, Bangladeshi, or Sri Lankan ethnicity) or black (n=35), those whose waist circumference and BMI were both missing (n=8) and those who had missing fasting glucose, 2-hour glucose or HbA1c (n=126) because this information was required for the analysis. Thus, 6018 ADDITION-Leicester participants were included in these analyses (4599 white, 1310 South Asians, 109 black). Baseline characteristics of these participants are shown in Table 1.

TABLE 1. SUMMARY CHARACTERISTICS OF THE OVERALL STUDY POPULATION AND BY ETHNIC GROUP.

Confidential information removed (Table 1 data)

Abbreviations: METS, Metabolic equivalents; SA, South Asian.

Data are presented as mean (standard deviation) for continuous variables or N [%] for categorical variables.

^a P-values were calculated using t-tests for continuous variables and χ^2 tests for categorical variables. They show whether the baseline variable of interest is significantly different between the ethnic groups.

^b Number of missing values: Height, Weight, Body Mass Index, Waist circumference, Hip circumference, Waist-to-hip ratio, LDL cholesterol, HDL cholesterol, Total cholesterol, Triglycerides, Systolic blood pressure, Diastolic blood pressure, Index of Multiple Deprivation, Smoking Status, Total METS **Confidential information removed (missing values n=)**. No missing values for fasting glucose, 2-hour glucose, HbA1c, age, or sex.

2.3 VARIABLES

GLYCAEMIC VARIABLES

Standardised operating procedures were used for the screening. Individuals were asked to fast for eight hours prior to attending the screening appointment. Before beginning the overnight fast, participants were asked to consume their regular evening meal and snacks, but refrain from alcohol consumption. At the screening visit, a standard 75g oral glucose tolerance test (OGTT) was undertaken. This test was postponed if in the preceding three days instructions to follow a normal unrestricted diet were not followed or the participant reported fever or unusual physical activity. On the day of testing, prescribed morning medications were permitted but participants are asked not to run to their appointment or smoke until after the test. Plasma samples were obtained immediately before (fasting blood glucose) and 120 minutes after (2-hour blood glucose) the glucose challenge along with fasting samples for glycosylated haemoglobin (HbA1c). All biochemical measurements were performed in house at the University Hospitals of Leicester NHS trust. Glucose samples were taken in fluoride oxalate test tubes and placed immediately in a portable 4 litre 4°C refrigerator. HbA1c was analysed by a DCCT aligned Biorad Variant HPLC II system (Bio-Rad laboratories, Hemel Hempstead, UK). The imprecision coefficient of variation of this machinery is <0.1%, the reference intervals fit with national recommendations valid for carriers of variant Hb S, C and Q. Samples are processed within a maximum of two hours, using an Abbott Aeroset clinical chemistry analyser (Abbott laboratories, Maidenhead, UK), which employs the hexokinase enzymatic method. This machinery has an imprecision coefficient of variation of 1.61%.

ANTHROPOMETRIC VARIABLES

Anthropometric measurements were performed by trained staff following standard operating procedures, with height measured to the nearest 0.1 cm using a rigid stadiometer and weight in light indoor clothing measured to the nearest 0.1 kg with a Tanita scale (Tanita, Europe). BMI (kg/m^2) was calculated as weight in kilograms divided by height in metres squared. Waist circumference was measured at the mid-point between the lower costal margin and the level of the anterior superior iliac crest to the nearest 0.1 cm.

DEMOGRAPHIC AND LIFESTYLE VARIABLES

Participants were asked to classify their ethnicity into one of the 16 categories used in the 2001 national census. We then used the same groupings as in the census: white (white British, white Irish, or any other

white background), mixed ethnicity (white and black Caribbean, white and black African, white and Asian, or any other mixed background), Asian or Asian British (Indian, Pakistani, Bangladeshi, or Any other Asian Background), black or black British (Caribbean, African, or any other black background), and other ethnic group (Chinese or any other ethnic group). People who identified themselves as being of mixed ethnicity, Chinese or in any other ethnic group were not included in these analyses due to the very small number of study participants in these groups (35 in total). Furthermore, participants who did not report an ethnic group were also excluded from these analyses since ethnicity was a key variable in these analyses (n = 203).

Sex and smoking status were self-reported. Age was calculated using the participant's reported date of birth and the date that they attended their ADDITION-Leicester screening visit. Socio-economic status was measured using the Index of Multiple Deprivation (IMD) 2007 scores, which are a publicly available measure that assign a score based on the participant's residential area (http://data.gov.uk/dataset/index_of_multiple_deprivation_imd_2007). IMD scores are a continuous measure calculated using a variety of indicators including income, employment, education and living environment and a higher score indicates higher deprivation. Note that these scores are sometimes used to rank localities in terms of their deprivation, but these analyses used the raw scores (which are continuous) rather than the ranks (which are ordinal).

Physical activity was self-reported using a validated questionnaire (International physical activity questionnaire; IPAQ). The short last seven days self-administered format of IPAQ was used (16). IPAQ measures walking, moderate and vigorous physical activity over a seven-day period. Total METS (metabolic equivalents) per week are estimated by summing the time spent in walking, moderate and vigorous physical activity.

2.4 STATISTICAL ANALYSIS

The aim of these analyses was to ascertain BMI and waist circumference cut-points for BME groups that are risk equivalent in terms of dysglycaemia to the currently used standards that were derived in white populations. For BMI, these cut-points are 25kg/m² for overweight and 30kg/m² for obese (1,2). A raised waist circumference is defined as 102cm or higher for men and 88cm or higher in women (2,5). Since BMI cut-points are not currently gender-specific, analyses regarding BMI were performed on the population as a whole. Conversely, waist circumference cut-points as currently defined are gender-specific and so waist circumference analyses were conducted separately for men and women.

Dysglycaemia was used as the outcome and was derived by combining fasting glucose, 2-hour glucose and HbA1c into a single measure, which will be referred to as the glycaemic factor, using principal components analysis. This outcome was chosen for several reasons. An ideal outcome would have been incident health outcomes, such as diabetes, cardiovascular disease or mortality; however, this information was unavailable due to the cross-sectional nature of this study. It also does not make sense to use prevalent diabetes as an

outcome in our study as people with known diabetes were excluded prior to the screening stage, and so our diabetes outcome is prevalent undiagnosed diabetes, rather than diabetes *per se*. Instead we used dysglycaemia as a marker of future health outcomes because people with high glucose levels are known to have a high risk of progressing to overt diabetes (17), as well as a high risk of developing the micro- and macro-vascular complications associated with diabetes (18). Moreover, fasting glucose, 2-hour glucose and HbA1c appear to reflect different underlying biomedical mechanisms and detect hyperglycaemia in different groups of individuals to some extent (19). Thus, it is important to use an outcome measure that captures an overall indication of glycaemia levels, rather than a single measure. This approach of using diabetes and cardiovascular risk factors, such as high glucose, to derive cut-points is a common one that has been used in several studies previously (20).

To find a BMI cut-point equivalent to 30kg/m^2 , a fractional polynomial model was fitted with the glycaemic factor (continuous) as the outcome variable and ethnicity (categorical: white, South Asian, black), BMI (continuous) and an interaction between the two (continuous, BMI*ethnicity) as the explanatory variables. The fractional polynomial model tests linear and non-linear terms for the continuous variables and selects the best fitting, most parsimonious terms for the final model. The interaction term was included as it allows the relationship between BMI and the glycaemic factor to differ by ethnic group. The fitted values were then used to find the average glycaemic factor for a white individual with a BMI of 30kg/m^2 (G). The equivalent BMI cut-points in the South Asian and black groups were then found by identifying the BMI in those groups for which the average glycaemic factor was equal to G. During model testing, it was found that the glycaemic factor was non-Normally distributed and so it was transformed by adding 10 and then taking the natural logarithm; this transformed glycaemic factor was used as the outcome in all models to improve their fit.

As in other studies on this topic (21), a 95% confidence interval (CI) was estimated using a method similar to the fiducial approach. This involved finding the point on the lower and upper confidence bands where the average glycaemic factor was G and using the corresponding BMIs as the upper and lower estimates of the CI, respectively. A demonstration of this approach is outlined in Section 3.1. The resulting CIs are not symmetrical. This is because the way in which they are derived is more similar to a Bayesian approach, i.e. they are derived internally from the observed data, as opposed to a standard Frequentist approach which uses equations that impose symmetry to estimate CIs.

In addition to the unadjusted analyses, the analyses were repeated with adjustment for age (continuous), sex (categorical: male, female), smoking status (categorical: non-smoker, ex-smoker, current smoker), IMD score (continuous) and physical activity (continuous). The same process was then performed for a BMI cut-point of 25kg/m^2 , waist circumference of 102cm for men, and waist circumference of 88cm for women, except that the waist circumference analyses were not adjusted for sex since they were conducted separately for men and women. All analyses were performed in Stata v12.1 and p-values less than 0.05 were considered to be statistically significant.

As outlined in the Background section, the original waist circumference cut-points were derived based on their ability to detect obesity defined as a BMI of $\geq 30 \text{ kg/m}^2$ (6). Therefore, as a secondary analysis, we derived a further set of waist circumference cut-points by using the approach taken in the original study. For each ethnicity and gender group, the sensitivity and specificity of each waist circumference cut-point to detect BMI $\geq 30 \text{ kg/m}^2$ was estimated. The optimal cut-point was then taken to be the cut-point that had the highest Youden index (calculated as sensitivity + specificity – 1). These analyses were then repeated instead defining obesity based on the ethnic-specific cut-points derived in the primary analyses.

3 FINDINGS

3.1 OBESE BODY MASS INDEX

Appendix 1 shows the unadjusted model for the relationship between BMI and the glycaemic factor by ethnic group, and the BMI cut-points can be found by solving this equation. For illustrative purposes, the model is also shown in Figure 1, Panel A and the method for finding the BMI cut-points from the graph is as follows. The transformed glycaemic factor for a BMI of 30 kg/m^2 in the white group can be read off the graph as 2.27 (Line C). The equivalent BMI cut-point for the South Asian group can be read from where Line C crosses the fitted line for the South Asian group as **Confidential information removed**. Likewise, Line B shows the cut-point for the black group to be **Confidential information removed**.

Table 2 shows these estimates along with their associated CIs. As with the cut-point estimates, the CIs were found using the equations in Appendix 1 but, for illustration purposes, the process is also shown in Appendix 2. As before, line C shows the average glycaemic factor for a BMI of 30 kg/m^2 in the white group, the dashed line shows the relationship between BMI and the glycaemic factor in the South Asian group, and line A shows the cut-point estimate for BMI in the South Asian group. Additionally, this graph also shows the confidence bands for the association in the South Asian group (for simplicity the confidence bands for the white group are not shown). As in Figure 1, line A indicates the intersection between line C and the fitted line for South Asians. The upper confidence limit is found similarly by identifying the point where line C intersects with the lower confidence band for the South Asians. Likewise, the lower confidence limit is found by identifying the point where line C intersects with the upper confidence band for the South Asians. As explained in Section 2.4, using a fiducial approach and deriving the CIs from the data means that the CIs are not symmetrical.

Figure 1, Panel B also shows the association between BMI and the glycaemic factor by ethnicity, but this time adjusted for smoking status, deprivation score, age, sex and physical activity. Again, the cut-points can either be read off the graph or found by solving the equation in Appendix 1. The cut-points equivalent to 30 kg/m^2 in the white group are **Confidential information removed** for South Asians and **Confidential information removed** for black participants (Table 2).

FIGURE 1. OBESE BODY MASS INDEX

PANEL A. UNADJUSTED

Confidential information removed

PANEL B. ADJUSTED FOR AGE, SEX, SMOKING STATUS, DEPRIVATION SCORE AND PHYSICAL ACTIVITY

Confidential information removed

Abbreviations: BMI, Body mass index.

TABLE 2. BODY MASS INDEX AND WAIST CIRCUMFERENCE CUT-POINTS FOR PEOPLE OF SOUTH ASIAN OR BLACK ETHNICITY EQUIVALENT IN TERMS OF DYSGLYCAEMIA TO THOSE IN PEOPLE OF WHITE ETHNICITY.

Confidential information removed

Abbreviations: BMI, Body mass index.

^a All estimates were adjusted for smoking status, deprivation score, age and physical activity. Additionally, the BMI estimates were adjusted for sex.

^b These estimates extrapolate beyond the range of the data (BMI range in South Asians = **Confidential information removed**; waist circumference range in black men = **Confidential information removed**). See *Discussion and Conclusions* for more detail.

3.2 OVERWEIGHT BODY MASS INDEX

Figure 2 and Table 2 show the unadjusted and adjusted BMI cut-points for South Asian and black participants that were equivalent to a BMI of 25kg/m² in white participants. For South Asians, this cut-point was **Confidential information removed** in unadjusted analyses and **Confidential information removed** in adjusted analyses. For black participants, this cut-point was **Confidential information removed** in unadjusted analyses and **Confidential information removed** in adjusted analyses.

3.3 WAIST CIRCUMFERENCE IN MEN

Figure 3 and Table 2 show the unadjusted and adjusted waist circumference cut-points for South Asian and black male participants that were equivalent to a waist circumference of 102cm in white men in terms of dysglycaemia. For South Asian men, this cut-point was **Confidential information removed** in unadjusted analyses and **Confidential information removed** in adjusted analyses. For black men, this cut-point was **Confidential information removed** in unadjusted analyses and **Confidential information removed** in adjusted analyses.

Table 3 shows the cut-points derived for waist circumference in terms of detecting obesity and their associated sensitivity and specificity. Among white men, the optimal cut-point for detecting a BMI of $\geq 30\text{kg/m}^2$ was **Confidential information removed**; very similar to the currently used cut-point of 102cm. Among South Asian men, the optimal cut-point for detecting a BMI of $\geq 30\text{kg/m}^2$ was **Confidential information removed** and for detecting a BMI of $\geq 22\text{kg/m}^2$ was **Confidential information removed**. Among black men, the optimal cut-point for detecting a BMI of $\geq 30\text{kg/m}^2$ was **Confidential information removed** and for detecting a BMI of 27kg/m^2 was **Confidential information removed**.

3.4 WAIST CIRCUMFERENCE IN WOMEN

Figure 4 and Table 2 show the waist circumference cut-points for South Asian and black female participants that were equivalent to a waist circumference of 88cm in white women. For South Asian women, this cut-point was **Confidential information removed** in unadjusted analyses and **Confidential information removed** in adjusted analyses. For black women, this cut-point was **Confidential information removed** in unadjusted analyses and **Confidential information removed** in adjusted analyses.

Table 3 shows the cut-points derived for waist circumference in terms of detecting obesity. Among white women, the optimal cut-point for detecting a BMI of $\geq 30\text{kg/m}^2$ was **Confidential information removed**; this is much higher than the currently used cut-point of 88cm. Among South Asian women, the optimal cut-point for detecting a BMI of $\geq 30\text{kg/m}^2$ was **Confidential information removed** and for detecting a BMI of

$\geq 22\text{kg/m}^2$ was **Confidential information removed**. Among black women, the optimal cut-point for detecting a BMI of $\geq 30\text{kg/m}^2$ was **Confidential information removed** and for detecting a BMI of 27kg/m^2 was **Confidential information removed**.

FIGURE 2. OVERWEIGHT BODY MASS INDEX

PANEL A. UNADJUSTED

CONFIDENTIAL INFORMATION REMOVED

PANEL B. ADJUSTED FOR AGE, SEX, SMOKING STATUS, DEPRIVATION SCORE AND PHYSICAL ACTIVITY

Confidential information removed

Abbreviations: BMI, Body mass index.

FIGURE 3. WAIST CIRCUMFERENCE IN MEN

PANEL A. UNADJUSTED

CONFIDENTIAL INFORMATION REMOVED

PANEL B. ADJUSTED FOR AGE, SMOKING STATUS, DEPRIVATION SCORE AND PHYSICAL ACTIVITY

Confidential information removed

FIGURE 4. WAIST CIRCUMFERENCE IN WOMEN

PANEL A. UNADJUSTED

CONFIDENTIAL INFORMATION REMOVED

PANEL B. ADJUSTED FOR AGE, SMOKING STATUS, DEPRIVATION SCORE AND PHYSICAL ACTIVITY

CONFIDENTIAL INFORMATION REMOVED

TABLE 3. WAIST CIRCUMFERENCE CUT-POINTS DERIVED BASED ON THEIR ABILITY TO DETECT OBESITY.

Confidential information removed

^a Obesity cut-point as originally defined.

^b New ethnic-specific obesity cut-point from Table 2.

4 DISCUSSION AND CONCLUSIONS

This study found that South Asian and black individuals have dysglycaemia at lower levels of BMI and waist circumference than white individuals, adding further support that health interventions should occur at lower adiposity levels in BME groups.

This report presents both unadjusted findings and those adjusted for sex (where appropriate), age, social deprivation, smoking status and physical activity. These factors were chosen as likely confounders of the association between BMI, waist circumference and health outcomes. BMI was derived by Adolphe Quetelet as a measure of excess fat and was originally intended for use at a population level, rather than an individual level (22). As well as fat, BMI is likely to also capture other factors to some extent. For example, it is a well-known weakness of BMI that it cannot distinguish between fat and muscle. Thus, any association between BMI and dysglycaemia may reflect the effect of muscle, rather than or as well as fat, on dysglycaemia. However, BMI may reflect other factors that could affect health outcomes, such as smoking. Indeed, much criticism was levelled at the original analyses of BMI cut-points in white populations because adjustment was not made for smoking status, potentially resulting in low BMI groups having an artificially increased mortality risk due to the high prevalence of smokers in low BMI groups (23), though a recent systematic review does not support this argument (24). Similarly, age, sex, physical activity and socio-economic status might be confounders. By including these terms in the adjusted model, their effects are removed from the BMI term and so the adjusted models should show the relationship between body fat and dysglycaemia to a greater extent. For that reason, the remainder of this discussion only pertains to the adjusted analyses.

In South Asians, our results suggest that obesity should be defined as a BMI of **Confidential information removed** or higher, overweight as a BMI of **Confidential information removed** or higher, and a very high waist circumference as **Confidential information removed** or higher in men and **Confidential information removed** or higher in women. There were 1310 people of South Asian origin in our study and 755 (376 men, 379 women) of these had complete covariate data and thus were included in the adjusted models. Importantly, while some of the CIs were fairly wide, none of them included the cut-point for the white population further suggesting that the BMI and waist circumference cut-points for South Asians should be lowered. Our cut-point of **Confidential information removed** for obesity is consistent with other estimates which tend to range between 21 and 29kg/m², with most estimates between 23 and 27kg/m² (20,21,25). However, it is lower than the cut-points of 25kg/m² and 27.5kg/m² that have been recommended by expert groups (26-28). Our cut-point of **Confidential information removed** for overweight is extremely low and is very close to the lower range of the observed data (15.3-52.7kg/m²). Therefore, this finding should be interpreted as adding to the evidence that the overweight cut-point for South Asians should be lower than 25kg/m², rather than as an accurate estimate of what that cut-point should be, and perhaps that South Asian ethnicity confers a risk of dysglycaemia that is at least equal to the risk of being overweight in the white population. Furthermore, weight loss at such low BMIs would not be recommended and so activities, such as walking, that

appear to lower glycaemia without inducing weight loss might be a preferable strategy for reducing risk among overweight South Asians (29).

In black populations, our results suggest that obesity should be defined as a BMI of **Confidential information removed** or higher, overweight as a BMI of **Confidential information removed** or higher, and a very high waist circumference as **Confidential information removed** or higher in men and **Confidential information removed** or higher in women. In contrast with South Asians, evidence suggests that individuals of black origin have a lower body fat percentage than individuals of white origin at the same BMI (8). Despite this, we found BMI and waist circumference cut-points in the black group that were lower than the established cut-points, with the exception of waist circumference in women. However, the sample size for the adjusted analyses in the black group was only 76 (28 men, 48 women), which suggests that our findings in this population are not robust, and resulted in wide CIs that included the cut-points for the white population. Therefore, our findings should be interpreted as being suggestive that it might be desirable to lower cut-points for people of black ethnicity, but that more research is required before doing so. This interpretation is supported by the fact that few other studies recommend lowering the cut-points for this population and some actually argue that they should be higher than in white populations (25,30).

The waist circumference cut-points discussed so far were derived based on their ability to detect dysglycaemia, a marker for current and future health outcomes. As a secondary analysis, we also derived waist circumference cut-points based on its ability to detect obese BMI (either as currently defined or based on ethnic-specific cut-points) as this was the method that was originally used to define waist circumference cut-points (6). When obesity was defined as a BMI of $\geq 30\text{kg/m}^2$, we derived cut-points of **Confidential information removed** for white and South Asian men and **Confidential information removed** for black men. In contrast with our previous conclusions, this suggests that the current cut-point of 102cm should only be lowered for black, and not South Asian, men. Among women, we derived cut-points of **Confidential information removed** for white women, **Confidential information removed** for South Asian women and **Confidential information removed** for black women. Importantly, our cut-point for white women is much higher than that currently used (88cm) and while the South Asian cut-point is also higher than the current definition it is 4cm lower than the white cut-point in our study. We would argue that deriving waist circumference cut-points based on their ability to detect obese BMI is not the best approach. Instead, it is better to derive waist circumference cut-points based on their ability to derive health risk as waist circumference reflects abdominal, rather than overall, adiposity and has been shown to have associations with health outcomes that are independent of BMI (3,4). Therefore, our waist circumference cut-points based on dysglycaemia, rather than BMI, have a more useful interpretation.

The limitations of our study should be considered when interpreting the results. The primary limitation is that these analyses are based on a cross-sectional study and so we were unable to estimate cut-points based on future health outcomes, such as cardiovascular disease or mortality. Instead, we based the cut-points on dysglycaemia as a combination of fasting glucose, 2-hour glucose and HbA1c. Similarly, many

other studies on this topic have used cardiovascular risk factors as a proxy for future health outcomes (20) and this approach is justified since high glucose levels are associated with future risk of cardiovascular disease and early mortality (31,32). A more detailed rationale for choosing this outcome and its associations with current and future health risks are detailed in Section 2.4.

A further limitation of our work was the small number of participants who identified themselves as being of black ethnicity. As already discussed, this resulted in fairly wide confidence limits and means that our findings regarding altering BMI and waist circumference cut-points for people of black ethnicity are suggestive, rather than conclusive. Further work could focus on validating these cut-points in an external black population. The strengths of our study include the large overall sample size, the investigation of non-linear associations, comprehensive adjustment for potential confounders, and the accurate, objective measurement of anthropometric and glycaemic variables.

In conclusion, this study used cross-sectional data with objectively measured anthropometric variables to identify cut-points for BMI and waist circumference in South Asian and black populations living in the UK that are risk equivalent in terms of dysglycaemia to those in white populations. This study adds to existing evidence that cut-points should be lower for South Asian than white populations. They are also suggestive that the cut-points may need lowering for people of black ethnicity, but are inconclusive due to a very small sample size.

APPENDIX 1. UNADJUSTED AND ADJUSTED MODELS USED TO FIND CUT-POINTS.

Confidential information removed

Abbreviations: BMI, Body mass index; IMD, Index of Multiple Deprivation.

Note: Outcome is glycaemic factor transformed by adding 10 and then taking the natural logarithm.

^a BMI in the models to find BMI cut-points. Waist circumference in the models used to find waist circumference cut-points.

APPENDIX 2. FIGURE SHOWING PROCESS USED TO DERIVE CONFIDENCE INTERVALS.

Confidential information removed

REFERENCE LIST

- (1) World Health Organization. Physical status: The use and interpretation of anthropometry: report of a WHO Expert Committee. 1995.
- (2) National Institute for Health and Clinical Excellence. Obesity: guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children. NICE clinical guidance 43. 2006.
- (3) Pischon T, Boeing H, Hoffmann K, et al. General and Abdominal Adiposity and Risk of Death in Europe. *N Engl J Med* 2008 11/13; 2013/01;359(20):2105-2120.
- (4) Wang Y, Rimm EB, Stampfer MJ, et al. Comparison of abdominal adiposity and overall obesity in predicting risk of type 2 diabetes among men. *The American Journal of Clinical Nutrition* 2005 March 01;81(3):555-563.
- (5) World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organization Technical Report Series 2000;894:1-253.
- (6) Lean MEJ, Han TS, Morrison CE. Waist circumference as a measure for indicating need for weight management. *BMJ* 1995;311(6998):158-161.
- (7) Wang J, Thornton JC, Russell M, et al. Asians have lower body mass index (BMI) but higher percent body fat than do whites: comparisons of anthropometric measurements. *American Journal of Clinical Nutrition* 1994;60(1):23-28.
- (8) Rahman M, Berenson AB. Accuracy of current body mass index obesity classification for white, black, and Hispanic reproductive-age women. *Obstetrics and gynecology* 2010;115(5):982-988.
- (9) Wen CP, David Cheng TY, Tsai SP, et al. Are Asians at greater mortality risks for being overweight than Caucasians? Redefining obesity for Asians. *Public Health Nutr* 2009;12(04):497.
- (10) Office for National Statistics. 2011 Census, Key Statistics for Local Authorities in England and Wales. 2012; Available at: <http://www.ons.gov.uk/ons/rel/census/2011-census/key-statistics-for-local-authorities-in-england-and-wales/index.html>, 2012.
- (11) Gray LJ, Yates T, Davies MJ, et al. Defining obesity cut-off points for migrant south asians. *PLoS ONE* 2011 Article Number: e2;6(10).
- (12) Sandbaek A, Griffin SJ, Rutten G, et al. Stepwise screening for diabetes identifies people with high but modifiable coronary heart disease risk. The ADDITION study. *Diabetologia* 2008;51(7):1127-1134.
- (13) Webb DR, Khunti K, Srinivasan B, et al. Rationale and design of the ADDITION-Leicester study, a systematic screening programme and randomised controlled trial of multi-factorial cardiovascular risk intervention in people with type 2 diabetes mellitus detected by screening. *Trials* 2010;11:16.

- (14) Griffin SJ, Borch-Johnsen K, Davies MJ, et al. Effect of early intensive multifactorial therapy on 5-year cardiovascular outcomes in individuals with type 2 diabetes detected by screening (ADDITION-Europe): a cluster-randomised trial. *Lancet* 2011;378(9786):156-167.
- (15) Webb DR, Gray LJ, Khunti K, et al. Screening for diabetes using an oral glucose tolerance test within a western multi-ethnic population identifies modifiable cardiovascular risk: The ADDITION-Leicester study. *Diabetologia* 2011;54(9):2237-2246.
- (16) Craig CL, Marshall AL, Sjostrom M, et al. International Physical Activity Questionnaire: 12-Country Reliability and Validity. *Medicine and science in sports and exercise* 2003;35(8):1381-1395.
- (17) Gerstein HC, Santaguida P, Raina P, et al. Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: A systematic overview and meta-analysis of prospective studies. *Diabetes research and clinical practice* 2007;78(3):305-312.
- (18) Ford ES, Zhao G, Li C. Pre-Diabetes and the Risk for Cardiovascular Disease: A Systematic Review of the Evidence. *Journal of the American College of Cardiology* 2010;55(13):1310-1317.
- (19) Mostafa SA, Davies MJ, Srinivasan BT, et al. Should glycated haemoglobin (HbA1c) be used to detect people with type 2 diabetes mellitus and impaired glucose regulation? *Postgraduate Medical Journal* 2010.
- (20) Low S, Chin MC, Ma S, et al. Rationale for redefining obesity in Asians. *Annals Academy of Medicine Singapore* 2009;38(1):66-74.
- (21) Razak F, Anand SS, Shannon H, et al. Defining obesity cut points in a multiethnic population. *Circulation* 2007 Apr 24;115(16):2111-2118.
- (22) Eknoyan G. Adolphe Quetelet (1796–1874)—the average man and indices of obesity. *Nephrology Dialysis Transplantation* 2008 January 01;23(1):47-51.
- (23) Manson JE, Stampfer MJ, Hennekens CH, et al. Body weight and longevity: A reassessment. *JAMA* 1987;257(3):353-358.
- (24) Flegal KM, Kit BK, Orpana H, et al. Association of all-cause mortality with overweight and obesity using standard body mass index categories: A systematic review and meta-analysis. *JAMA* 2013;309(1):71-82.
- (25) Chiu M, Austin PC, Manuel DG, et al. Deriving Ethnic-Specific BMI Cutoff Points for Assessing Diabetes Risk. *Diabetes Care* 2011 August 01;34(8):1741-1748.
- (26) Kumar S, Hanif W, Zaman MJ, et al. Lower thresholds for diagnosis and management of obesity in British South Asians. *Int J Clin Pract* 2011;65(4):378-379.
- (27) WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363(9403):157-163.

(28) Misra A, Chowbey P, Makkar BM, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. *Journal of the Association of Physicians of India* 2009;57:163-170.

(29) Yates T, Davies MJ, Sehmi S, et al. The Pre-diabetes Risk Education and Physical Activity Recommendation and Encouragement (PREPARE) programme study: are improvements in glucose regulation sustained at 2 years? *Diabetic Med* 2011;28(10):1268-1271.

(30) Evans EM, Rowe DA, Racette SB, et al. Is the current BMI obesity classification appropriate for black and white postmenopausal women? *International journal of obesity* 2006;30:837-843.

(31) Gerstein HC. Glucose: a continuous risk factor for cardiovascular disease. *Diabetic Medicine* 1997;14(S3):S25-S31.

(32) Balkau B, Shipley M, Jarrett RJ, et al. High Blood Glucose Concentration Is a Risk Factor for Mortality in Middle-Aged Nondiabetic Men: 20-year follow-up in the Whitehall Study, the Paris Prospective Study, and the Helsinki Policemen Study. *Diabetes Care* 1998 March 01;21(3):360-367.