



Differences in Body Composition Convey a Similar Risk of Type 2 Diabetes Among Different Ethnic Groups With Disparate Cardiometabolic Risk—The HELIUS Study

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Marleen Zethof,^{1,2}
Charlotte M. Mosterd,^{1,3} Didier Collard,²
Henrike Galenkamp,¹ Charles Agyemang,¹
Max Nieuwdorp,²
Daniël H. van Raalte,³ and
Bert-Jan H. van den Born^{1,2}

OBJECTIVE

Studies have shown a disparate association between body composition and the risk of type 2 diabetes. We assessed whether associations between differences in body composition and type 2 diabetes vary among ethnic groups with disparate cardiometabolic risk.

RESEARCH DESIGN AND METHODS

We used data from the Healthy Life in an Urban Setting (HELIUS) study, including individuals aged 18–70 years of African Surinamese ($n = 3,997$), South Asian Surinamese ($n = 2,956$), Turkish ($n = 3,546$), Moroccan ($n = 3,850$), Ghanaian ($n = 2,271$), and Dutch ($n = 4,452$) origin living in Amsterdam. Type 2 diabetes was defined using the World Health Organization criteria. Logistic regression was used to assess the relation between body composition and type 2 diabetes. Waist-to-hip ratio (WHR), waist circumference, BMI, and body fat percentage by bioelectrical impedance were used to estimate body composition.

RESULTS

Per unit change in BMI, only Ghanaian (odds ratio [OR] 0.94 [95% CI 0.89–0.99]) and Moroccan (0.94 [0.89–0.99]) women had a smaller increase in type 2 diabetes compared with the Dutch population, whereas the ORs for body fat percentage were 0.94 (0.89–1.00) for Ghanaian, 0.93 (0.88–0.99) for Moroccan, and 0.95 (0.90–1.00) for South Asian Surinamese women. There was no interaction between WHR and ethnicity on the risk of type 2 diabetes, and there were no differences in men. WHR had the highest precision in predicting type 2 diabetes in both men (C statistic = 0.78) and women (C statistic = 0.81).

CONCLUSIONS

The association between differences in body composition and type 2 diabetes is roughly the same in all ethnic groups. WHR seems the most reliable and consistent predictor of type 2 diabetes regardless of ethnic background.

It has been well established that large differences exist in body composition among ethnic minority groups and that these differences have an important impact on the

¹Department of Public and Occupational Health, Amsterdam University Medical Centers, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands

²Department of Vascular Medicine, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, the Netherlands

³Diabetes Center, Department of Internal Medicine, Amsterdam University Medical Centers, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands

Corresponding author: Bert-Jan H. van den Born, b.j.vandenborn@amsterdamumc.nl

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risk of type 2 diabetes (1–3). The Northern Manhattan study showed that Hispanic and non-Hispanic Black individuals had a higher risk of diabetes than White individuals (4). In the U.K., the prevalence of type 2 diabetes is approximately three to five times higher in ethnic minorities compared with the White British population, and the onset of type 2 diabetes also occurs 10–12 years earlier (5).

We previously reported that the odds of type 2 diabetes are three to five times higher in individuals of South Asian descent living in the Amsterdam area compared with native Dutch, two to four times higher in migrants of Turkish and Moroccan descent, and two to three times higher in sub-Saharan Africans (1). Additionally, migration history seems to contribute to the unequal burden of type 2 diabetes among ethnic groups: Ghanaians who migrated directly to the Netherlands from sub-Saharan Africa had a higher prevalence and higher odds of type 2 diabetes compared with men of African Surinamese origin, who are also of West African descent but have migrated via Suriname (2). The underlying mechanisms of the increased risk of type 2 diabetes in migrants are complex and not fully understood.

Adiposity, in particular central adiposity, is known to be the most important risk factor for developing type 2 diabetes by dysregulating adipokine secretion, subclinical inflammation, and an increased release of fatty acids into the circulation (6–9). Population studies have shown that waist circumference and the waist-to-hip ratio (WHR) are the best discriminators for type 2 diabetes among different ethnic groups (10,11), whereas relationships with body fat percentage and BMI vary. This may be due to differences in body composition, such as central versus peripheral fat depots, differences in appendicular skeletal muscle, and body build. Asian individuals, for example, have a higher tendency toward abdominal obesity compared with non-Asian populations, and health risks associated with obesity occur at a lower BMI compared with Europeans (12–15). In contrast, Mexican Americans have a higher risk of developing type 2 diabetes for a given WHR compared with American Indians. These differences have led to ethnicity-specific cutoffs for overweight, as recommended by the World Health Organization (WHO) and International Diabetes Federation (16–18). However, to what extent, for a given difference in body

anthropometric characteristics, the risk of type 2 diabetes differs among ethnic groups is still unclear.

The aim of the current study was to examine the extent to which the association between the different parameters of body composition and type 2 diabetes is different among ethnic minority groups participating in a large multiethnic population based study living in Amsterdam.

RESEARCH DESIGN AND METHODS

We used the Healthy Life in an Urban Setting (HELIUS) study to investigate the association between anthropometric measurements (BMI, WHR, waist circumference, and body fat percentage) and type 2 diabetes among different ethnic groups. The rationale, conceptual framework, design, and methodology of the HELIUS study have been described elsewhere (19). In brief, the HELIUS study is a large-scale prospective multiethnic cohort study on health and health care use conducted in Amsterdam, the Netherlands.

Baseline data collection took place between January 2011 and June 2015 and included people aged between 18 and 70 years of African Surinamese, South Asian Surinamese, Turkish, Moroccan, Ghanaian, and Dutch origin. These ethnic groups were chosen because they comprise the largest ethnic minority groups in Amsterdam, where 35% of inhabitants have a non-Western origin. On the basis of their migration background, which traces back to West Africa (Ghanaians and African Surinamese), Northern India (South Asian Surinamese), Morocco, and Turkey, they are among the main ethnic minority groups in Europe outside of the European Union (20). Details on sociopolitical background and migration history are described by Snijder et al. (21). All participants were randomly selected through the municipality registry of Amsterdam and stratified for ethnic background to generate comparable group sizes.

All data were collected through questionnaires, a physical examination, and fasting venous blood sampling. Study protocols were approved by the Amsterdam University Medical Centers Institutional Review Board, location Academic Medical Center. All participants provided written informed consent.

For this study, we excluded all individuals with unknown or different ethnic background and missing information on anthropometric measurements and data on the presence of type 2 diabetes. The analysis included 21,072 participants, including African Surinamese ($n = 3,997$), South Asian Surinamese ($n = 2,956$), Turkish ($n = 3,546$), Moroccan ($n = 3,850$), Ghanaian ($n = 2,271$), and Dutch ($n = 4,452$) origin (Supplementary Fig. 1).

Information on ethnic origin was obtained by questionnaire. The definition of non-Dutch ethnic origin was being born outside of the Netherlands and having at least one parent born abroad (first generation) or being born in the Netherlands with both parents born outside the Netherlands (second generation). People were considered Dutch when they were born in the Netherlands, and their parents were born in the Netherlands. Participants of Surinamese ethnic origin were further classified according to self-reported ethnic origin (obtained by questionnaire) into “African,” “South Asian” or “other.”

Following WHO criteria, individuals were classified as having type 2 diabetes if they had a fasting plasma glucose level ≥ 7.0 mmol/L, had self-reported diabetes, or were treated with glucose-lowering medication (22). Participants were asked to bring their medication for verification. Self-reported diabetes was present if participants responded positively to the question of whether they were diagnosed with diabetes by a health care professional. Glucose was measured by enzymatic colorimetric spectrophotometry in fasting blood samples. The concentration of HbA_{1c} was determined on whole blood using high-performance liquid chromatography technology (Tosoh, Tokyo, Japan).

Fat mass was measured by arm-leg bioimpedance taken with a Bodystat 1500 analyzer (Bodystat Ltd, Isle of Man, U.K.). The body fat percentage was calculated by applying the formula of Kyle et al. (23) on the Bodystat output. Weight and height were measured in duplicate while the individual was barefoot and wearing light clothes on a Seca 877 scale and a Seca 217 stadiometer, respectively. BMI was calculated as weight (kg) divided by height squared (m^2).

Waist circumference was measured at the level midway between the lower rib margin and the iliac crest. Hip

circumference was measured at the widest point measured over the trochanter major. WHR was calculated as waist circumference divided by hip circumference. Measurements of waist and hip circumference were performed twice, and the average was used for further analysis.

Statistical analysis was performed by using R 3.65.1 software (The R Foundation for Statistical Computing, 2018). Given the well-known sex differences in body composition, baseline characteristics were stratified by both sex and ethnicity and are presented as means with SDs for normally distributed continuous data or as median and interquartile range (IQR) if data were skewed. Age-adjusted logistic regression analysis was performed to study the relation between body composition, defined by BMI, WHR, waist circumference, or body fat percentage, and diabetes. Standardizing of the measurements was obtained by dividing the anthropometric measurements by the SD. Analyses were performed separately for men and women. We assessed the influence of ethnicity on

the relation between type 2 diabetes and the anthropometric measurements by adding an interaction term to the logistic regression model, and subsequently estimated ethnicity-specific odds ratios (ORs) using the same models. In addition we depicted the interaction term taking the people with Dutch origin as the reference population.

The primary objective was to assess the association between body composition and the prevalence of diabetes. The receiver operating characteristic (ROC) curve and the corresponding area under the ROC curve (AUC) were calculated using WHR, waist circumference, BMI, or fat percentage as a predictor for type 2 diabetes. Secondly, we assessed the diagnostic accuracy of the different anthropometric measurement in clinical practice by using the WHO-recommended cutoffs taking ethnicity into account, including separate values for BMI, waist circumference, and WHR for South Asian Surinamese men and women (16,17). WHR was depicted as percentage and therefore multiplied by

100. Ethnicity- and sex-specific criteria were not used to assess the relation between body fat percentage and type 2 diabetes because a previous study from our group showed that in a subset of the current study, specific cutoff values did not improve the relation between fat distribution and type 2 diabetes (2).

RESULTS

Baseline characteristics of the study subjects stratified by ethnicity and sex are reported in Table 1. Turkish and Moroccan men and women were, on average, younger than the other ethnic groups. Turkish men and Ghanaian women had the highest BMI and waist circumference, whereas South Asian Surinamese men and women had the highest WHR. Of all measures of body composition, Dutch men and women had the most favorable measures. Type 2 diabetes was highest in South Asian Surinamese men and women, with an overall prevalence of 22.1%, whereas

Table 1—Characteristics of the study population by sex and ethnicity

	Dutch	South Asian Surinamese	African Surinamese	Ghanaian	Turkish	Moroccan
Men						
<i>n</i>	2,034	1,323	1,554	873	1,602	1,498
Age (years)	46.85 (13.81)	44.73 (13.64)	48.01 (12.89)	46.90 (11.46)	40.80 (12.12)	42.06 (12.72)
Diabetes	112 (5.5)	312 (23.6)	217 (14.0)	155 (17.8)	197 (12.3)	198 (13.2)
Age at diabetes onset (years)	44.26 (19.27)	43.76 (13.54)	44.77 (15.30)	45.05 (10.85)	41.96 (12.61)	41.87 (16.08)
Use of diabetes medication	44 (2.2)	205 (15.5)	111 (7.1)	66 (7.6)	95 (5.9)	109 (7.3)
Height (cm)	182.58 (7.18)	172.11 (6.42)	176.16 (6.81)	171.68 (6.47)	172.94 (6.83)	174.76 (6.46)
Body weight (kg)	84.06 (13.35)	76.71 (13.82)	81.80 (15.28)	79.03 (12.62)	83.16 (13.51)	81.63 (13.70)
BMI (kg/m ²)	25.22 (3.78)	25.85 (4.18)	26.31 (4.43)	26.78 (3.75)	27.82 (4.34)	26.69 (3.99)
Waist circumference (cm)	93.90 (11.73)	93.96 (12.15)	92.23 (12.50)	92.07 (11.16)	97.19 (11.87)	95.01 (11.19)
WHR	0.93 (0.07)	0.97 (0.08)	0.93 (0.07)	0.94 (0.07)	0.96 (0.07)	0.94 (0.07)
Body fat percentage (%)	24.06 (5.72)	25.70 (6.23)	24.23 (6.35)	24.20 (5.96)	25.94 (5.86)	25.46 (5.82)
Fasting glucose (mmol/L)	5.50 (0.79)	6.00 (1.54)	5.60 (1.29)	5.59 (1.44)	5.64 (1.12)	5.76 (1.40)
HbA _{1c} (%)	5.46 (0.47)	6.06 (0.97)	5.80 (0.85)	5.81 (0.94)	5.70 (0.76)	5.74 (0.81)
HbA _{1c} (mmol/mol)	36.22 (5.13)	42.70 (10.57)	39.86 (9.26)	40.02 (10.29)	38.84 (8.28)	39.18 (8.83)
Women						
<i>n</i>	2,418	1,633	2,443	1,398	1,944	2,352
Age (years)	45.60 (14.19)	46.10 (13.17)	47.85 (12.25)	43.50 (10.67)	39.94 (12.13)	39.50 (12.92)
Diabetes	63 (2.6)	342 (20.9)	352 (14.4)	174 (12.4)	204 (10.5)	278 (11.8)
Age at diabetes onset (years)	49.39 (14.48)	43.20 (14.30)	45.03 (13.64)	44.34 (12.30)	42.47 (10.86)	41.17 (13.31)
Use of diabetes medication	35 (1.4)	212 (13.0)	232 (9.5)	93 (6.7)	116 (6.0)	172 (7.3)
Height (cm)	169.53 (6.68)	158.21 (6.09)	163.78 (6.32)	161.57 (5.76)	159.01 (5.97)	161.02 (6.06)
Body weight (kg)	69.98 (12.79)	66.94 (13.94)	77.34 (16.56)	77.39 (14.70)	73.43 (15.75)	72.89 (14.78)
BMI (kg/m ²)	24.38 (4.48)	26.74 (5.28)	28.83 (5.91)	29.63 (5.34)	29.14 (6.51)	28.16 (5.75)
Waist circumference (cm)	85.46 (12.57)	90.09 (13.43)	93.54 (14.78)	94.10 (13.07)	92.25 (15.26)	92.05 (14.61)
WHR	0.84 (0.08)	0.90 (0.08)	0.88 (0.08)	0.88 (0.08)	0.87 (0.09)	0.86 (0.09)
Body fat percentage (%)	32.98 (6.07)	37.03 (6.15)	37.14 (6.24)	37.84 (6.09)	37.23 (6.37)	37.50 (6.15)
Fasting glucose (mmol/L)	5.13 (0.68)	5.63 (1.49)	5.41 (1.35)	5.25 (1.05)	5.32 (1.19)	5.36 (1.25)
HbA _{1c} (%)	5.44 (0.42)	5.98 (0.90)	5.84 (0.88)	5.74 (0.82)	5.66 (0.78)	5.66 (0.77)
HbA _{1c} (mmol/mol)	35.98 (4.59)	41.86 (9.85)	40.28 (9.64)	39.25 (9.01)	38.39 (8.47)	38.34 (8.39)

Data are presented as mean (SD) for continuous variables and as *n* (%) for categorical variables. All differences, except age, onset of diabetes, and use of diabetes medication were significant at $P < 0.01$.

Dutch men and women had the lowest prevalence of type 2 diabetes (3.9%).

ROC curves of BMI, WHR, fat percentage, and waist circumference as predictors of type 2 diabetes in men and women are shown in Fig. 1. The overall accuracy of measures of body composition to predict type 2 diabetes was better in women than in men, with ROC curves ranging between 0.71 and 0.82 in women and between 0.64 and 0.80 in men. In both men and women, WHR had the highest accuracy to predict type 2 diabetes. This was also true for all the individual ethnic groups, although the AUC was generally lower in Ghanaian men (AUC, 0.71; sensitivity, 0.88; specificity, 0.31) and women (AUC, 0.80; sensitivity, 0.91; specificity, 0.37) (Supplementary Table 1).

Figure 2 shows the age-adjusted change in OR per unit increase in BMI, WHR, fat percentage, and waist circumference stratified by sex and ethnic group. There were significant differences in the risk of type 2 diabetes and the association with BMI and body fat percentage in women, with Dutch women having the highest OR of type 2 diabetes per unit change in BMI and body fat percentage, whereas Ghanaian and Moroccan women had the lowest OR per change in BMI or body fat percentage. For waist circumference and WHR, the association with type 2 diabetes was the same among women of different ethnic groups. For men, there was no significant difference in measures of body composition and type 2 diabetes. Results were the same when

standardized coefficients were used to explore the association between changes in measures of body composition and type 2 diabetes (Supplementary Fig. 2). After standardization for the differences in distribution of the anthropometric measures, we found the strongest association for WHR and waist circumference, with ORs ranging between 1.29 and 3.53, while we found weaker associations with BMI and fat percentage, ranging between 1.06 and 2.92.

In men, we did not find a significant interaction between measures of body composition and the risk of type 2 diabetes. In women, however, we found a significant interaction in the association between both BMI ($P = 0.01$) and body fat percentage ($P = 0.03$) and the risk of type 2 diabetes. The odds of type 2 diabetes for a given increase in WHR and waist circumference did not differ between ethnic groups (Table 2).

CONCLUSIONS

We show that the association between body composition and type 2 diabetes is comparable across ethnic groups, despite large differences in the prevalence of type 2 diabetes and despite the use of ethnicity-specific cutoffs for body composition. Only in women statistically significant variations in the association between BMI, body fat percentage, and the risk of type 2 diabetes were present across ethnic groups, but not in waist circumference or WHR. In both men and women, WHR and waist circumference were superior in predicting type 2 diabetes compared with BMI or body

fat percentage. The ROC curves and reported SDs show that WHR was more accurate and precise in predicting type 2 diabetes compared with waist circumference. In line, after standardization, we observed the highest ORs for WHR and waist circumference for the presence of type 2 diabetes.

Many studies have demonstrated that the relation between BMI and the percentage of body fat not only depends on age and sex but also differs across ethnic groups, in particular in Asian populations (17,24). For example, populations of South Asian descent in the U.K. and U.S. tend to have a higher percentage of body fat at a given BMI and have more features of the metabolic syndrome at a given waist circumference (3,25,26). In addition, rates of coronary artery disease and cardiovascular mortality are higher among South Asians (27,28), while the prevalence of impaired glucose tolerance and diabetes is up to six times higher (3,21,29). Because BMI systematically underestimates the percentage of body fat and cardiovascular disease risk among Asian populations, the WHO has recommended separate classification criteria for overweight, obesity, and abdominal obesity in Asian populations to improve early identification of individuals at increased cardiometabolic risk (17). Using the ethnicity-specific WHO cutoffs, we show that the diagnostic accuracy for the different measures of body composition was roughly the same in the different ethnic groups, except for Ghanaian men and women. This confirms previous findings that different criteria need to be applied for individuals of South Asian descent, but also points towards possibilities for improvement in creating cutoffs in other populations, in particular those with African ethnicities.

There are different theories to explain the increased risk of type 2 diabetes between ethnic groups. It has been suggested that exposure to several ecological stressors is creating a variability within metabolism and body size and composition (30). Moreover, the long-term exposure of specific diseases might have altered the metabolic profile of adipose tissue within each ethnic group. Despite large differences in the overall risk of type 2 diabetes and different cutoffs for BMI and waist circumference, our study shows that there are

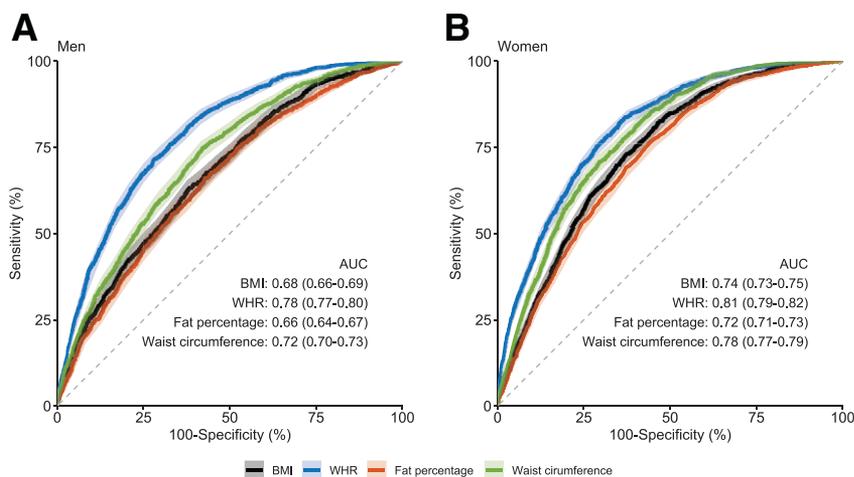


Figure 1—ROC curve of BMI, WHR, fat percentage, and waist circumference as a predictor of type 2 diabetes with corresponding AUC.

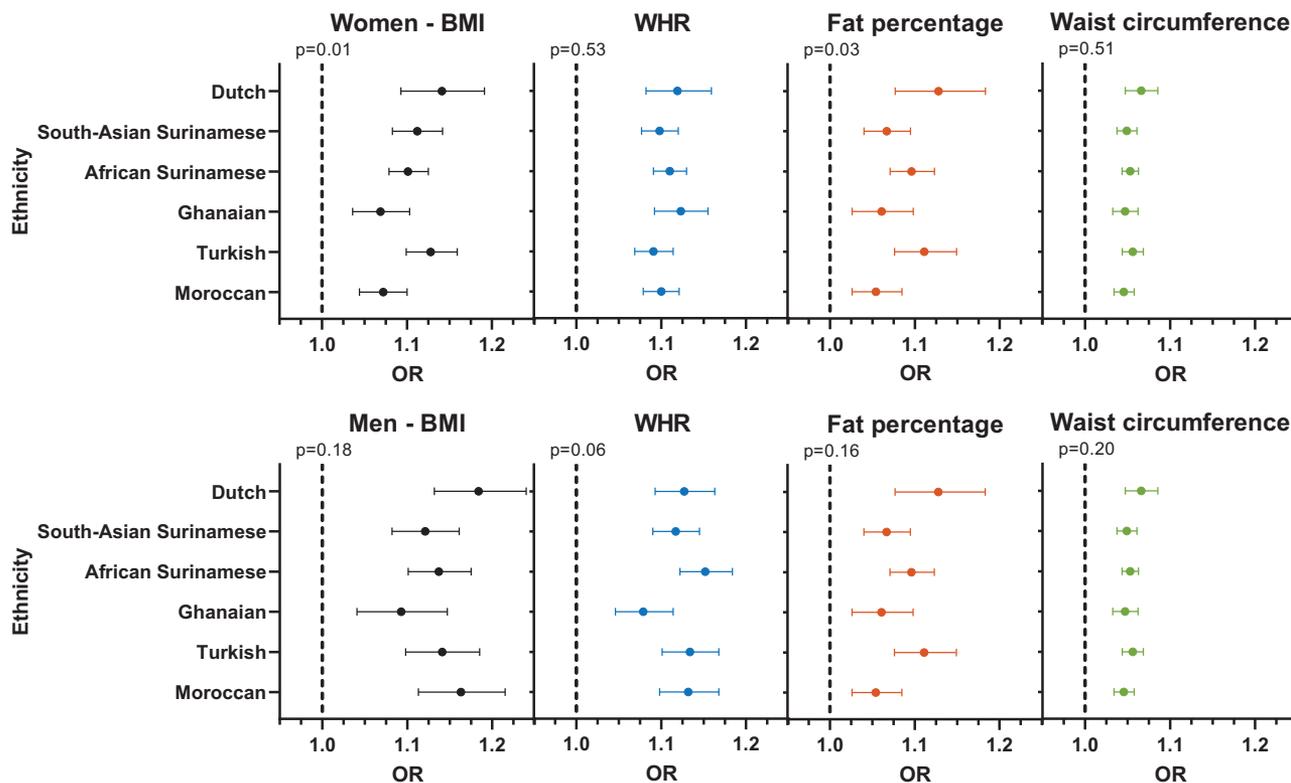


Figure 2—Age-adjusted ORs for the relation between the presence of type 2 diabetes and changes in BMI, WHR, fat percentage, and waist circumference taking the interaction between ethnicity and anthropometric measures into account; WHR was multiplied by 100.

no important ethnic differences in the relation between type 2 diabetes and changes in body composition.

Because there are no important ethnic differences in the associations between changes in body composition and the risk of type 2 diabetes, our

results suggest that regardless of ethnic origin, the risk of the development of type 2 diabetes for a given increase in body fat is the same. These findings are supported by a recent publication that used aggregated data from the Multi Ethnic Study in Atherosclerosis

(MESA) and the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study showing that the point estimates of the association between different fat deposits are comparable among different ethnic groups (3).

Table 2—OR for the interaction between body composition measures and ethnicity on type 2 diabetes, adjusted for age, the Dutch as reference group, stratified by ethnicity and sex

Ethnicity	BMI		WHR		Fat percentage		Waist circumference	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Men								
Overall significance		0.18		0.06		0.16		0.20
Dutch	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
South Asian Surinamese	0.94 (0.89–1.00)	0.05	0.99 (0.95–1.03)	0.65	0.97 (0.93–1.02)	0.24	1.02 (0.96–1.08)	0.52
African Surinamese	0.96 (0.91–1.01)	0.14	1.02 (0.98–1.07)	0.29	0.99 (0.95–1.04)	0.69	0.95 (0.89–1.00)	0.07
Ghanaian	0.92 (0.86–0.98)	0.02	0.96 (0.92–1.00)	0.05	0.94 (0.89–0.99)	0.01	0.96 (0.91–1.02)	0.20
Turkish	0.96 (0.91–1.02)	0.19	1.01 (0.96–1.05)	0.79	0.97 (0.93–1.02)	0.29	0.92 (0.86–0.99)	0.02
Moroccan	0.98 (0.92–1.04)	0.53	1.00 (0.96–1.05)	0.84	0.98 (0.93–1.03)	0.49	0.98 (0.92–1.04)	0.43
Women								
Overall significance		0.01		0.53		0.03		0.51
Dutch	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
South Asian Surinamese	0.98 (0.93–1.03)	0.32	0.98 (0.94–1.02)	0.33	0.95 (0.90–1.00)	0.04	0.98 (0.96–1.01)	0.14
African Surinamese	0.97 (0.92–1.01)	0.15	0.99 (0.95–1.03)	0.67	0.97 (0.92–1.02)	0.29	0.99 (0.97–1.01)	0.23
Ghanaian	0.94 (0.89–0.99)	0.02	1.00 (0.96–1.05)	0.90	0.94 (0.89–1.00)	0.04	0.98 (0.96–1.00)	0.12
Turkish	0.99 (0.94–1.04)	0.66	0.97 (0.94–1.01)	0.21	0.99 (0.93–1.04)	0.61	0.99 (0.97–1.01)	0.38
Moroccan	0.94 (0.89–0.99)	0.01	0.98 (0.94–1.02)	0.37	0.93 (0.88–0.99)	0.02	0.98 (0.96–1.00)	0.07

WHR was multiplied by 100. Ref, reference group.

Although we found similar ORs for the association between the different anthropometric measurements and type 2 diabetes, there was a significant interaction between type 2 diabetes and either BMI or body fat percentage in women of Ghanaian and Moroccan descent. This could point toward ethnic disparities in the relation between type 2 diabetes and BMI and body fat percentage and type 2 diabetes in these women, but may also suggest differences in the distribution of fat and muscle mass. BMI is a reflection of both muscle and fat mass, whereas body fat percentage is susceptible to differences in the amount of visceral and subcutaneous fat. In contrast, the interaction with waist circumference and WHR was consistent among men and women of all ethnic groups in our study, and both measures also had a much smaller individual and ethnic variation compared with BMI and body fat percentage. In line with previous recommendations, our study thereby confirms that waist circumference and WHR may be preferred to estimate cardiometabolic risk, especially in multiethnic populations with large differences in body composition (31).

An important strength of the present population-based study is that different ethnic groups were studied with large disparities in cardiometabolic risk. Additional strengths include the relatively large number of well-characterized participants from six different ethnic groups living in the same geographic environment. Furthermore, we investigated the strength of the interaction between BMI, fat percentage, and WHR in relation to the development of type 2 diabetes between ethnicities instead of comparing the prevalence of type 2 diabetes at a certain value of anthropometric measure. This enabled us to compare the risk of type 2 diabetes that can be attributed to body composition among the ethnic groups.

Limitations of this study included the cross-sectional design, which renders it impossible to make causal inferences on the role of ethnic differences in body composition in the development of diabetes. Anthropometric measurements were performed by trained nurses according to standardized procedures. However, measurements of waist circumference and WHR can be affected by interobserver variations.

Finally, body fat percentage was measured using bioelectrical impedance, which is less accurate compared with the gold standard of DEXA. Also, sex- and ethnicity-specific algorithms to convert bioelectrical impedance analysis measurements into estimates of body fat might have improved the performance of body fat as a predictor of type 2 diabetes (32).

Conclusion

Despite large differences in the prevalence of type 2 diabetes between ethnic groups, the association between the different measures of body composition and type 2 diabetes is roughly the same. These results imply that despite the variations in body build that exist among ethnic groups, the risk of type 2 diabetes is similar. Compared with the other measures of body composition, WHR had the highest accuracy and precision in predicting type 2 diabetes across the different ethnic groups. The results of this study further support previous findings that have demonstrated that overweight is an important problem among ethnic minority populations and is likely responsible for most of the discrepancies in type 2 diabetes. The reasons behind the high prevalence of obesity among ethnic minority populations need further exploration to improve programs that are aimed at reducing ethnic disparities in obesity and type 2 diabetes.

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B.-J.H.v.d.B. critically revised the manuscript. D.C. and H.G. contributed to the statistical analysis. All authors contributed to the design of the work. B.-J.H.v.d.B. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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