Ethnic Differences in Body Fat Deposition and Liver Fat Content in Two UK-Based Cohorts

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Objective: Differences in the content and distribution of body fat and ectopic lipids may be responsible for ethnic variations in metabolic disease susceptibility. The aim of this study was to examine the ethnic distribution of body fat in two separate UK-based populations.

Methods: Anthropometry and body composition were assessed in two separate UK cohorts: the Hammersmith cohort and the UK Biobank, both comprising individuals of South Asian descent (SA), individuals of Afro-Caribbean descent (AC), and individuals of European descent (EUR). Regional adipose tissue stores and liver fat were measured by magnetic resonance techniques.

Results: The Hammersmith cohort ($n = 747$) had a mean (SD) age of 41.1 (14.5) years (EUR: 374 men, 240 women; SA: 68 men, 22 women; AC: 14 men, 29 women), and the UK Biobank ($n = 9{,}533$) had a mean (SD) age of 55.5 (7.5) years (EUR: 4,483 men, 4,873 women; SA: 80 men, 43 women, AC: 31 men, 25 women). Following adjustment for age and BMI, no significant differences in visceral adipose tissue or liver fat were observed between SA and EUR individuals in the either cohort.

Conclusions: Our data, consistent across two independent UK-based cohorts, present a limited number of ethnic differences in the distribution of body fat depots associated with metabolic disease. These results suggest that the ethnic variation in susceptibility to features of the metabolic syndrome may not arise from differences in body fat.

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Study Importance

What is already known?

- Ethnic differences in susceptibility to metabolic disease are well established.
- Compared with individuals of European descent (EUR), individuals of South Asian descent (SA) have a higher waist circumference and higher total body fat at any given BMI.
- Elevated central adiposity in SA has been linked to greater risk of developing type 2 diabetes, insulin resistance, and cardiovascular disease at a lower BMI compared with EUR.

What does this study add?

- We examined the ethnic distribution of body fat in EUR, SA, and individuals of Afro-Caribbean descent in two separate UK-based populations: the Hammersmith cohort and the UK Biobank.
- Our results, consistent across both cohorts, present a limited number of ethnic differences in the distribution of body fat depots associated with metabolic disease.

How might these results change the direction of research?

- Conventional thinking suggests that differences in body fat distribution are responsible for the ethnic variation in metabolic disease susceptibility.
- Our data indicate that alternative mechanisms should be investigated.

Introduction

Differences in anthropometry and body composition are associated with increased or decreased susceptibility of specific ethnicities to obesity-related metabolic disorders (1-3). Compared with white individuals of European descent (EUR), individuals of South Asian descent (SA) have higher waist circumference (WC), higher waist to hip ratio (4,5), and 5% to 7% higher total body fat at any given BMI (6). Furthermore, elevated central adiposity in SA has been linked to greater risk of developing type 2 diabetes (T2D), insulin resistance, and cardiovascular disease at a lower BMI compared with EUR (7). Accumulation

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of liver fat is also strongly linked to the development of insulin resistance (8), with SA presenting higher levels both postnatally (9) and in adulthood (10).

Individuals of Afro-Caribbean descent (AC) exhibit higher muscle mass and less central adiposity compared with EUR yet have an increased risk of developing hypertension, stroke, and T2D (11,12). The greater susceptibility to develop metabolic diseases in AC therefore appears to be at odds with a favorable profile of reduced body fat and increased muscle mass. Accurate phenotyping including body fat content and distribution is therefore required to determine the potential contribution to ethnic differences in metabolic disease. Previous studies assessing the impact of ethnicity on body fat content have often relied on indirect measurements such as bioelectrical impedance, rather than direct imaging methods for precise mapping and quantification of adiposity (13). As such, there are relatively limited available data regarding specific patterns of body fat distribution and liver fat content in different ethnic groups (14).

In this study, we used magnetic resonance (MR) techniques to assess body fat distribution and anthropometry in two separate UK-based populations, the Hammersmith cohort and the UK Biobank cohort, comprising adult EUR, SA, and AC of both sexes.

Methods

Study population 1: Hammersmith cohort

Subjects. Healthy adult (age ≥ 18 years) volunteers of both sexes were recruited from the UK general population in West London between 1995 and 2014 (15). All volunteers provided written consent, with study ethics obtained from the ethics committee of Hammersmith Hospital and Queen Charlotte's and Chelsea Hospital London Research Ethics Committee (REC: 07Q04011/19). Volunteers were recruited via advertisement in websites, newspapers, and academic newsletters. Participants of all ethnicities were invited to take a part. Individuals suffering from claustrophobia, individuals who were pregnant, and those with metal implants (MR contraindication) were excluded.

Ethnicity classification. Ethnicity was self-reported. SA included participants from Indian, Pakistani, Bangladeshi, and other Asian backgrounds. AC included African, Caribbean, and other black backgrounds. EUR included British, Irish, and other white backgrounds.

Anthropometry measurements. Body mass (kilograms), height (meters), WC (centimeters), and hip circumference (centimeters) were measured in each subject by a single trained researcher (JPM) in the morning following an overnight fast. Height was measured to the nearest 0.01 m using a wall-mounted stadiometer (Seca). Body mass, weight, and fat mass/fat-free mass (FFM) were measured using a calibrated digital platform scale with bioelectrical impedance functionality (Tanita BC-418MA body composition analyzer). WC was measured at the midpoint between the distal border of the lowest rib and the superior border of the iliac crest (16). From these values, BMI (kilograms per meter squared), waist to hip ratio, and waist to height ratio were calculated.

MR imaging and MR spectroscopy. Adipose tissue (AT) content was measured by MR imaging (MRI) using a 1.5-T Philips Achieva scanner as previously described (17). Briefly, subjects lay in a prone position with arms extended above the head and they were scanned from their fingertips to their toes. Whole-body MRI was performed to measure total and regional AT volumes, recorded in liters. Abdominal subcutaneous AT (ASAT) and visceral AT (VAT) were defined as the subcutaneous and internal AT depots within the abdominal region (the region between the femoral heads) and at the top of the liver/bottom of the lungs. Total AT was calculated as the sum of total subcutaneous and internal AT volumes. MR spectroscopy (MRS) was obtained during the same scanning session to measure liver fat content (18).

Study population 2: UK Biobank

Subjects. Participant data from the UK Biobank imaging cohort were collected as previously described (19). Subjects included in this cohort were those scanned first between August 2014 and September 2016. MRI and patient meta-data were acquired through UK Biobank Access Application numbers 9914, 6569, and 23889. The UK Biobank has approval from the North West Multi-Centre Research Ethics Committee and it obtained written consent from all participants prior to involvement. The age range for inclusion was 44 to 73 years, with individuals excluded if they had metal or electric implants or medical conditions that prohibited scanning, if they were pregnant, or if they planned surgery within 6 weeks.

Ethnicity classification. The ethnicity of UK Biobank participants was defined genetically through the projection of UK Biobank individuals into the principal component space of the 1000 Genomes Project samples and subsequent clustering based on a K-means approach, centering on the means of the first four principal components (20).

Anthropometric measurements. Anthropometric measurements were collected at UK Biobank assessment centers; height was measured using the Seca 202 height measure. The average of two blood pressure measurements, taken 2 minutes apart, was obtained using an automated device (Omron).

Blood biochemistry. Blood samples were collected from nonfasted UK Biobank participants and transported by commercial courier to a central laboratory where they were processed by standard biochemical techniques (21).

Imaging protocol. Images were acquired at the UK Biobank Imaging Centre at Cheadle (UK) using a Siemens 1.5-T MAGNETOM Aera scanner. VAT and ASAT were measured using the dual-echo Dixon Vibe protocol, providing a water- and fat-separated volumetric data set covering the neck to the knees, as previously described (22). Thigh volume and adiposity were obtained from image data as previously described (23). VAT and ASAT were defined as subcutaneous AT in the abdomen, measured from the top of the femoral head to the top of the thoracic vertebrae T9. A multi-echo spoiled-gradient-echo acquisition was used to calculate proton density fat fraction maps of the liver (24). Corrected T1 (cT1) values, as markers of liver inflammation and fibrosis, were measured in the UK Biobank as previously described (25).

Physical activity. Specific questions on the frequency and duration of walking (UK Biobank codes 864 and 874), moderate physical activity (884 and 894), and vigorous physical activity (904 and 914) match those used in the short form of the International Physical Activity Questionnaire (IPAQ) (26). This allowed the IPAQ measure

of total physical activity, metabolicequivalent minutes per week, to be calculated for UK Biobank participants. Individuals were excluded from IPAQ analysis if they selected "prefer not to answer" or "do not know" in response to any of the possible six questions on physical activity used to calculate the metabolicequivalent score. For any of the activity categories, a reading <10 minutes was recoded to 0, and values > 1,260 per week (equivalent to an average of 3 h/d) were truncated at 1,260, as recommended (27).

Statistical analysis

Descriptive statistics were obtained for anthropometric and MR measurements. Analyses were carried out in males and females separately, given the well-established sex differences in body fat distribution. The overall effect of ethnicity on study outcomes was assessed using linear regression adjusting for age and BMI for ethnic comparison of VAT, ASAT, percentage of VAT, and liver fat fraction. For UK Biobank analyses, Deprivation Index and IPAQ scores were also included in the linear regression model. Liver fat and liver enzyme values were log-transformed prior to analysis in order to address the nonnormally distributed nature of the data. We performed a sample size–weighted fixed-effects meta-analysis to combine data from both cohorts. Significance was defined as $P < 0.0002$, following Bonferroni correction for multiple tests (250). All data were presented as mean ± SD. Statistical analyses were performed using SPSS Statistics (version 23.0; IBM Corp.). All statistical graphs were plotted using GraphPad Prism (version 7.00 for Windows).

Results

A total of 747 volunteers (456 male and 291 female) from the Hammersmith cohort were included, with an ethnic distribution of 82% EUR, 12% SA, and 5.8% AC and a mean age of 42.6 ± 14.9 years (range, 17-75 years). Baseline characteristics by ethnic group and sex are shown in Table 1. Data from 9,533 UK Biobank individuals (4,592 males and 4,941 females) are presented in Table 2; the ethnic distribution was 98.2% EUR, 1.3% SA, and 0.5% AC, with a mean age of 55.5 ± .5 years (range, 40-70 years).

In both the Hammersmith and UK Biobank cohorts, male SA were shorter and they weighed less compared with counterpart EUR (Tables 1-2). Female SA were shorter compared with female EUR and they presented with a lower body mass than female EUR and AC in both cohorts (Tables 1-2).

Sex- and ethnicity-specific distributions of AT and liver fat fraction are shown in Figure 1 (Hammersmith cohort) and Figure 2 (UK Biobank cohort). Female AC from the Hammersmith cohort had lower liver fat fraction compared with both counterpart EUR and counterpart SA (AC: 1.2% ± 1.5%; EUR: 4.1% ± 11.1%; SA: 6.7% ± 12.3%; $P < 0.0001$ for both; Figure 1H). We did not detect any differences in VAT or liver fat between either male or female SA and EUR in either cohort. No ethnic differences in the liver inflammation marker cT1 were observed in UK Biobank data (Table 4). Male AC presented with lower VAT compared with male EUR in the UK Biobank (EUR: 4.4 ± 1.5 L; AC: 3.6 ± 1.7 L; $P < 0.0001$; Table 4, Figure 2).

Female AC presented with lower VAT compared with both counterpart EUR ($P < 0.0001$) and counterpart SA ($P < 0.0001$) in the Hammersmith cohort (AC: 1.7 ± 0.90 L; EUR: 2.5 ± 1.7 L; SA: 2.4 ± 1.2 L; Figure 1D,

TABLE 1 Baseline characteristics in Hammersmith cohort

	Male						Female					
	EUR ($n = 374$)	SA ($n = 68$)	AC ($n = 14$)	EUR vs. SA	EUR vs. AC	SA vs. AC	EUR ($n = 240$)	SA ($n = 22$)	AC ($n = 29$)	EUR vs. SA	EUR vs. AC	SA vs. AC
Age (y)	45.4 ± 14.5	41.5 ± 18.0	42.0 ± 15.9	0.05	0.39	0.92	39.3 ± 14.5	37.5 ± 13.2	41.1 ± 10.7	0.60	0.52	0.30
Weight (kg)	89.3 ± 16.8	79.2 ± 12.3	89.6 ± 15.6	**<0.0001**	0.78	0.007	75.0 ± 18.2	72.1 ± 17.6	86.0 ± 16.7	0.56	0.002	0.01
Height (m)	1.73 ± 0.07	1.68 ± 0.06	1.68 ± 0.07	**<0.0001**	0.37	0.02	1.66 ± 0.04	1.57 ± 0.02	1.64 ± 0.01	**<0.0001**	0.42	0.002
BMI (kg/m^2)	28.2 ± 4.6	26.9 ± 3.8	28.8 ± 4.0	0.08	0.43	0.10	27.3 ± 6.7	28.2 ± 6.8	31.8 ± 6.3	0.38	0.001	0.12
Waist (cm)	98.2 ± 13.7	95.2 ± 12.7	96.6 ± 12.3	0.42	0.98	0.73	87.4 ± 17.5	90.9 ± 14.1	94.2 ± 15.8	0.19	0.06	0.85
Hip (cm)	104.6 ± 8.4	100. 6 ± 6.2	103.5 ± 11.2	0.001	0.78	0.18	106.1 ± 12.8	104.6 ± 12.4	113.9 ± 12.2	0.99	0.001	0.02
WHR	0.93 ± 0.04	0.95 ± 0.08	0.94 ± 0.02	0.02	0.68	0.57	0.83 ± 0.10	0.90 ± 0.10	0.80 ± 0.10	0.007	0.68	0.007

Baseline characteristics and anthropometry in Hammersmith cohort listed by sex and ethnicity. Data presented as mean ± SD and analyzed by one-way ANCOVA with Bonferroni pairwise correction, *setting a threshold significance at P < 0.0002, highlighted in bold.*
AC, individuals of Afro-Caribbean descent; EUR, individuals of European descent; SA, individuals of South Asian descent; WC, waist circumference; WHR, waist to height ratio.

TABLE 2 Baseline characteristics in UK Biobank cohort

	Male						Female					
	EUR ($n=4,483$)	SA ($n=80$)	AC ($n=31$)	EUR vs. SA	EUR vs. AC	SA vs. AC	EUR ($n=4,873$)	SA ($n=43$)	AC ($n=25$)	EUR vs. SA	EUR vs. AC	SA vs. AC
Age (y)	56.4 ± 7.6	53.6 ± 8.7	48.7 ± 7.1	0.001	**<0.0001**	0.009	54.9 ± 7.4	50.9 ± 8.3	51.0 ± 6.9	**<0.001**	0.009	0.95
Weight (kg)	83.8 ± 13.4	76.6 ± 9.4	87.6 ± 13.0	**<0.0001**	0.43	**<0.0001**	68.7 ± 12.9	66.3 ± 12.1	76.9 ± 12.0	0.12	0.003	0.001
Height (m)	1.76 ± 0.07	1.71 ± 0.06	1.75 ± 0.06	**<0.0001**	0.04	0.009	1.63 ± 0.06	1.57 ± 0.06	1.61 ± 0.07	**<0.0001**	0.02	0.05
BMI (kg/m^2)	27.0 ± 3.9	26.2 ± 3.0	28.6 ± 3.6	0.05	0.06	0.001	25.9 ± 4.7	26.7 ± 4.4	29.8 ± 4.3	0.28	**<0.0001**	0.008
Waist (cm)	93.6 ± 10.1	91.5 ± 8.0	92.0 ± 8.8	0.09	0.60	0.55	81.9 ± 11.3	84.1 ± 12.2	88.3 ± 10.0	0.15	0.003	0.16
Hip (cm)	101.7 ± 7.2	99.2 ± 6.9	102.7 ± 6.2	0.002	0.53	0.02	101.2 ± 9.7	100.3 ± 9.0	106.2 ± 8.5	0.50	0.01	0.01
WHR	1.2 ± 0.1	1.3 ± 0.1	1.2 ± 0.1	**<0.0001**	0.36	**<0.0001**	1.5 ± 0.15	1.5 ± 0.2	1.4 ± 0.1	0.002	0.003	0.001
SBP	138 ± 17	134 ± 18	136 ± 14	0.11	1.00	1.00	131 ± 18	126 ± 21	136 ± 14	0.24	0.35	0.06
DBP	80 ± 10	80 ± 9	81 ± 10	1.00	1.00	1.00	77 ± 10	80 ± 13	84 ± 8	0.31	0.002	0.27

Baseline characteristics and anthropometry in the UK Biobank listed by sex and ethnicity. Data presented as mean ± SD and analyzed by one-way ANCOVA with Bonferroni pairwise correction, setting threshold significance at $P < 0.0002$, highlighted in bold.
AC, individuals of Afro-Caribbean descent; DBP, diastolic blood pressure; EUR, individuals of European descent; SA, individuals of South Asian descent; SBP, systolic blood pressure; WC, waist circumference; WHR, waist to height ratio.

Table 3). In both the Hammersmith and UK Biobank cohorts, bioelectrical impedance data revealed lower FFM in male and female SA men compared with counterpart EUR and AC ($P<0.0001$; Tables 3-4). In the Hammersmith cohort, SA of both sexes presented with a higher body fat percentage compared with respective populations of EUR ($P<0.0001$; Table 3).

VAT as a percentage of body fat was lower in AC compared with EUR and SA in both the UK Biobank cohort (AC vs. EUR: men, $P<0.0001$; women, $P<0.0001$; AC vs. SA: men, $P<0.001$; women, $P<0.0001$) and the Hammersmith cohort (AC vs. EUR: women, $P<0.0001$; AC vs. SA: women, $P<0.0001$). The ratio of VAT to (VAT + ASAT) was higher in male EUR compared with SA in the UK Biobank cohort ($P<0.0001$; Table 4). Female EUR presented with higher VAT/(VAT + ASAT) compared with SA in the UK Biobank cohort ($P<0.0001$; Table 4) and presented with a higher ratio compared with AC in both cohorts ($P<0.0001$ for both; Tables 3-4). Thigh volume was lower in male and female SA compared with counterpart EUR and AC in the UK Biobank cohort ($P<0.0001$ for all; Table 4). No significant ethnic differences in thigh adiposity were observed in either sex. Blood chemistry data from the UK Biobank are shown in Table 5. Male AC presented with lower triglycerides compared with SA (male SA: 2.14 ± 1.26 mmol/L; male AC: 1.15 ± 0.49 mmol/L; $P<0.0001$). No ethnic differences in glycated hemoglobin (HbA_{1c}) or liver enzymes (alkaline phosphatase, alanine aminotransferase, and gamma-glutamyl transferase) were observed in either sex (Table 5).

Statistical assessment of ethnic differences after combining the data from both the Hammersmith and UK Biobank cohorts is shown in Table 6. No significant differences in VAT (men, $P=0.65$; women, $P=0.44$) or liver fat fraction (men, $P=0.11$; women, $P=0.09$) were observed between EUR and SA of either sex.

Discussion

In this cross-sectional study, we investigated ethnic variation in anthropometry and body fat distribution in adult EUR, SA, and AC in two separate UK-based populations. There was a high degree of consensus between both cohorts regarding patterns of sex and ethnic differences, including a notable lack of difference between SA and EUR in VAT and liver fat, two depots previously proposed to underpin ethnic differences in developing features of metabolic syndrome.

Previous studies have shown that adult SA present with a higher body fat percentage, lower lean mass, and greater central visceral fat compared with adult EUR (4-7). This "thin-fat phenotype" reflects a body composition characterized by reduced muscle mass but increased adiposity, a pattern that appears to manifest in the neonatal period. Additional studies have indicated that VAT is associated with insulin resistance, increased inflammatory markers, and metabolic syndrome morbidities in populations of SA (28,29). This predisposition to increased central obesity, reduced FFM, and elevated circulating triglycerides and cholesterol is thought to contribute to the increased susceptibility to developing metabolic syndrome–associated morbidities in SA (30-32). However, after adjustment for age and BMI, we found no differences in VAT between SA and EUR, in either sex, in either the Hammersmith or the UK Biobank cohorts. These data are in agreement with those of previously published studies, which also failed to show consistently higher levels of VAT in SA compared with other ethnicities (33,34).

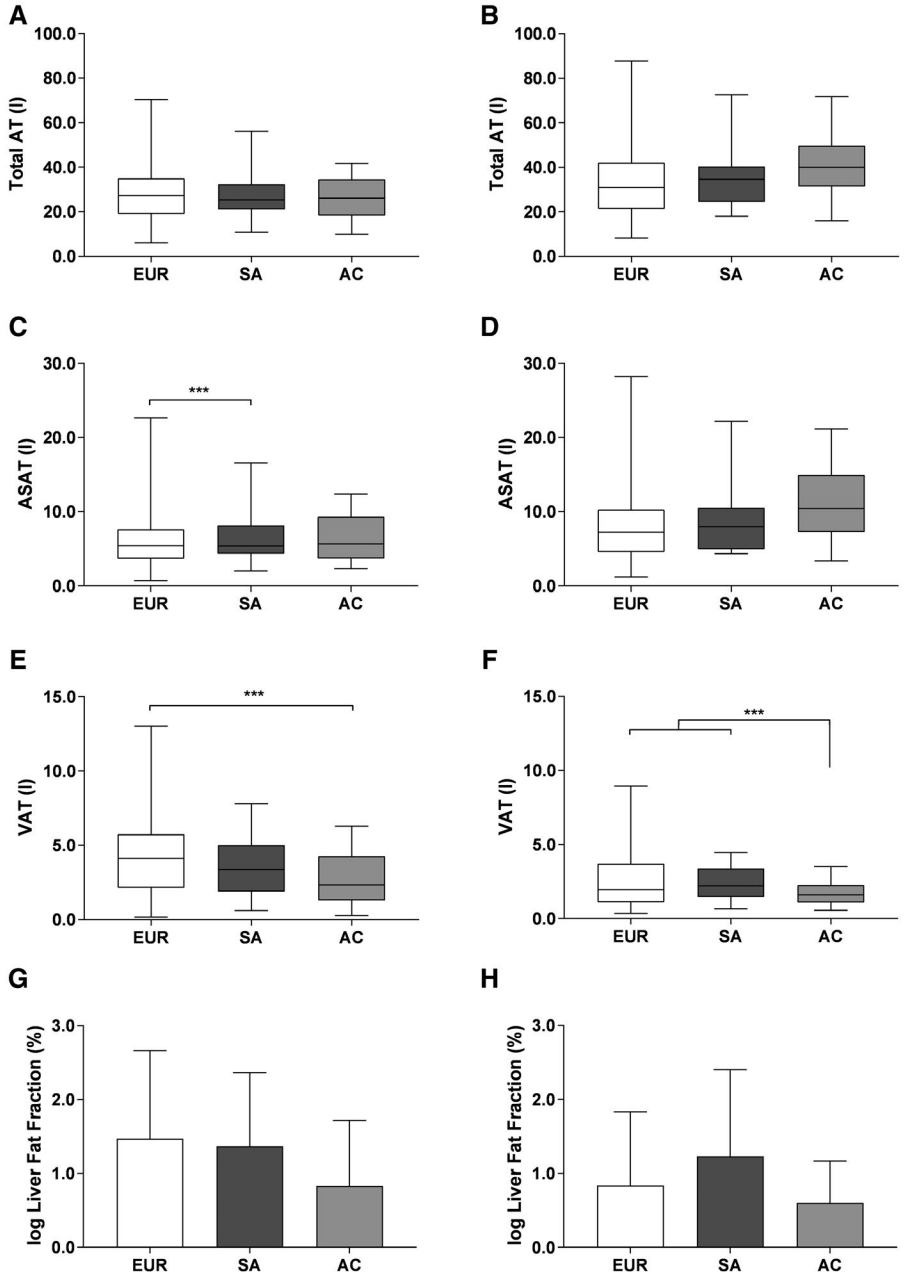

Figure 1 Sex- and ethnicity-specific distribution of adipose tissue (AT) and intrahepatocellular lipid in the Hammersmith cohort. **(A,B)** Total AT, **(C,D)** abdominal subcutaneous adipose tissue (ASAT), **(E,F)** visceral adipose tissue (VAT), and **(G,H)** log liver fat fraction (%) in men and women of white European (EUR), South Asian (SA), and Afro-Caribbean (AC) descent; $n = 747$. Data presented as box and whisker plots and as mean and SD in panels G and H; data analyzed by one-way ANCOVA with Bonferroni correction for pairwise comparisons adjusted for age and BMI; $^{***}P < 0.001$.

Ectopic accumulation of lipids in the liver is also a key marker of cardiovascular risk (8). A limited number of studies have assessed ethnic differences in liver fat; the mediators of atherosclerosis in South Asians living in America and multi-ethnic study of atherosclerosis studies found a greater liver fat content in SA compared with all other ethnic groups (33); the molecular study of health assessment and risk in ethnic groups study found higher liver fat in SA compared with EUR (35). In contrast to these findings, we found no differences in liver fat or cT1 between SA and EUR of either sex, results that were consistent across both study cohorts. It should be noted that although results were in accord using two different liver fat–assessment methods (MRS for the Hammersmith cohort and multi-echo MRI in the UK Biobank cohort), a large level of natural variation in the range of liver fat values was observed using both techniques, which may have contributed to the lack of observed statistical differences.

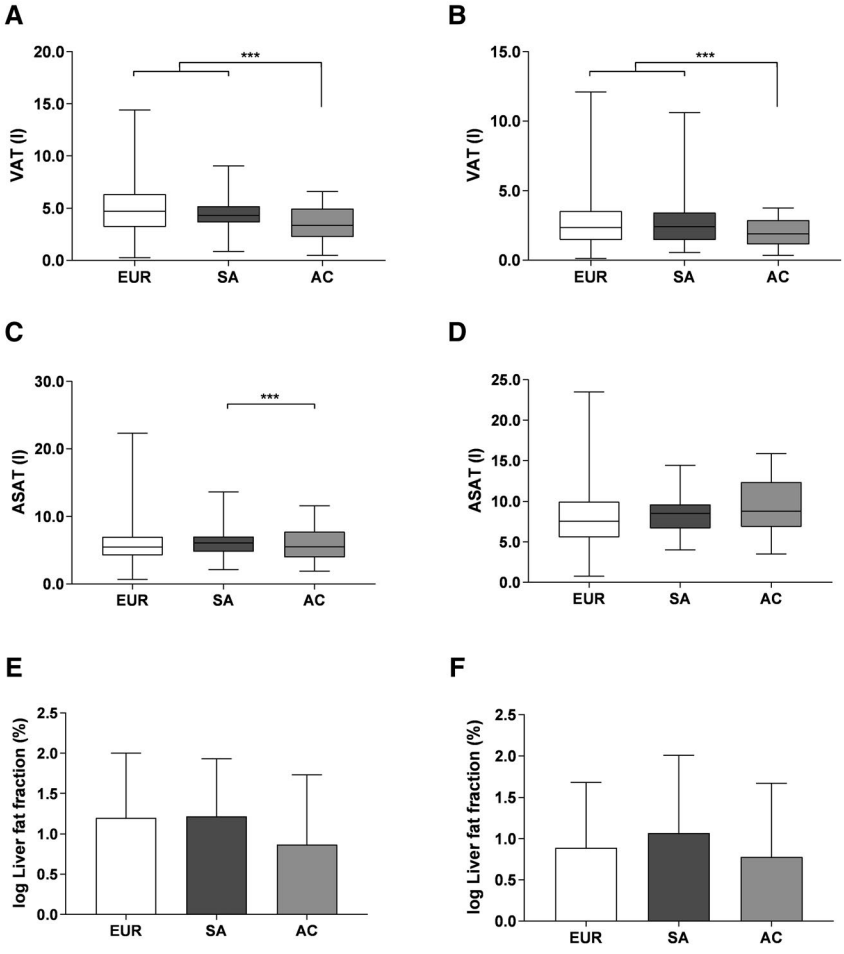

Figure 2 Sex- and ethnicity-specific distribution of adipose tissue and intrahepatocellular lipid in the UK Biobank**. (A,B)** Visceral adipose tissue (VAT), **(C,D)** abdominal subcutaneous adipose tissue (ASAT), and **(E,F)** log liver fat fraction in men and women of white European (EUR), South Asian (SA), and Afro-Caribbean (AC) descent; $n = 9{,}533$. Data presented as box and whisker plots and as mean and standard deviation in panels E and F; data analyzed by one-way ANCOVA with Bonferroni correction for pairwise comparisons adjusted for age and BMI; $^{***}P < 0.001$.

In agreement with published reports (3,36), AC in our study were heavier, were taller, and presented with a significantly reduced percentage of body fat compared with SA and EUR. We also found male and female AC to have significantly less VAT and liver fat compared with other ethnicities, in both cohorts. This favorable adiposity profile has previously been reported in regard to VAT (37) and liver fat (38), and it is paradoxical, given the increased prevalence (almost double) of T2D and hypertension in AC compared with EUR for any given BMI (39). A high ratio of visceral to subcutaneous fat was previously associated with impaired adipogenesis and insulin resistance (40). Here, we found that EUR presented with higher VAT/(ASAT+VAT) values compared with SA and AC in both cohorts, an effect that would seem to be at odds with the increased susceptibility to metabolic disease observed in SA (7).

Increased muscle mass, as seen in AC, was associated with improved insulin sensitivity through increased glucose uptake and oxidization and it may play a role in manifesting a favorable metabolic profile (41). Indeed, the significant 5- to 6-kg reduction we observed in FFM (as a proxy for muscle mass) in SA of both sexes in both cohorts represents a potential mechanism for the adverse metabolic phenotype observed in SA, with lower muscle mass associated with reduced insulin sensitivity and a higher risk of T2D (41). In addition, a reduction in FFM negatively affects various physiological processes and reflects a lowered resting energy expenditure, reductions in neuromuscular capacity, fatigue, and an increased risk of developing injury (42). These data are further reflected in the significant reduction of thigh volume in SA of both sexes compared with counterpart EUR and AC in the UK Biobank cohort, with no accompanying differences in thigh adiposity. However, it should be noted that the relationship between FFM and various measures of glucose metabolism is ambiguous, with more than half of the publications included in a 2016 meta-analysis reporting no relationship or an inverse relationship between FFM and markers of glucose homeostasis (43).

Determining the clinical significance of the ethnic differences in body fat and FFM is complicated by the potentially altered function of these

TABLE 3 Body composition by sex and ethnicity in Hammersmith cohort

				EUR – SA		EUR – AC		SA – AC	
	EUR	SA	AC	Difference (95% CI)	*P* value	Difference (95% CI)	*P* value	Difference (95% CI)	*P* value
Male									
n	374	68	14	—	—	—	—	—	—
Body fat (%)	27.1 ± 7.5	29.9 ± 6.7	25.8 ± 8.1	−4.52 (−6.3 to −2.8)	**<0.0001**	1.42 (−2.2 to 5.0)	1.00	5.94 (9.8 to 2.1)	0.001
Fat-free mass (kg)	64.5 ± 9.8	55.2 ± 7.3	66.3 ± 12.7	7.9 (5.5 to 10.2)	**<0.0001**	−0.57 (−5.4 to 4.25)	1.00	−8.5 (−13.6 to −3.25)	**<0.0001**
TAT (L)	27.6 ± 11.4	26.7 ± 8.9	25.9 ± 9.6	−2.08 (−3.9 to −0.27)	0.02	2.6 (−1.1 to 6.3)	0.27	4.7 (−8.7 to −0.69)	0.02
VAT (L)	4.1 ± 2.4	3.6 ± 1.9	2.6 ± 1.8	−0.03 (−0.50 to 0.44)	1.00	1.49 (0.52 to 2.45)	0.001	1.51 (0.47 to 2.56)	0.002
ASAT (L)	6.0 ± 3.2	6.2 ± 2.8	6.3 ± 3.1	−1.00 (−1.6 to −0.45)	**<0.0001**	0.04 (−1.1 to 1.2)	1.00	1.04 (−2.3 to 0.18)	0.12
VAT/(ASAT + VAT)	0.40 ± 0.11	0.35 ± 0.11	0.29 ± 0.15	0.32 (0.003 to 0.06)	0.03	0.09 (0.03 to 0.16)	0.001	0.06 (−0.004 to 0.13)	0.07
VAT (%)	4.0 ± 0.10	4.0 ± 0.24	2.75 ± 0.53	0.54 (−0.83 to 1.9)	1.00	3.8 (0.95 to 6.6)	0.004	3.2 (0.19 to 6.2)	0.03
Liver fat fraction (%)	8.8 ± 16.0	6.0 ± 9.8	2.9 ± 6.1	−0.15 (−0.44 to 0.14)	0.67	0.65 (0.06 to 1.25)	0.03	−0.80 (−1.44 to 0.16)	0.009
Female									
n	240	22	29	—	—	—	—	—	—
Body fat (%)	37.9 ± 10.2	42.5 ± 7.2	41.6 ± 7.5	−3.98 (−7.1 to −0.86)	0.007	1.16 (−1.65 to 4.0)	0.97	−5.71 (−9.1 to −1.2)	0.006
Fat-free mass (kg)	45.5 ± 7.6	40.4 ± 5.7	49.2 ± 5.7	5.74 (2.3 to 9.1)	**<0.0001**	−1.21 (−4.3 to 1.85)	1.00	−6.95 (2.6 to 11.3)	**<0.0001**
TAT (L)	32.9 ± 15.7	35.2 ± 14.6	41.0 ± 14.5	−0.41 (−3.1 to 2.3)	1.00	1.71 (−0.69 to 4.1)	0.26	2.12 (−5.5 to 1.3)	0.40
VAT (L)	2.5 ± 1.7	2.4 ± 1.2	1.7 ± 0.90	0.17 (−0.29 to 0.63)	1.00	1.59 (1.14 to 1.97)	**<0.0001**	1.39 (0.80 to 1.97)	**<0.0001**
ASAT (L)	8.2 ± 4.9	8.9 ± 4.6	11.1 ± 4.8	−0.067 (−1.0 to 0.89)	1.00	0.14 (−0.72 to 1.0)	1.00	0.21 (−1.0 to 1.4)	1.00
VAT/(ASAT + VAT)	0.23 ± 0.08	0.22 ± 0.06	0.13 ± 0.04	0.01 (−0.03 to 0.05)	1.00	0.09 (0.06 to 0.13)	**<0.0001**	0.08 (0.04 to 0.13)	**<0.0001**
VAT (%)	2.84 ± 0.10	2.94 ± 0.31	1.75 ± 0.27	−0.12 (−0.65 to 0.42)	1.00	1.54 (1.06 to 2.01)	**<0.0001**	1.68 (0.98 to 2.33)	**<0.0001**
Liver fat fraction (%)	4.1 ± 11.1	6.7 ± 12.4	1.2 ± 1.5	−0.34 (−0.71 to 0.04)	0.10	0.64 (0.23 to 0.98)	**<0.0001**	−0.98 (−1.5 to −0.50)	**<0.0001**

Data presented as mean ± SD, analyzed by one-way ANCOVA with Bonferroni correction adjusting for age and BMI, setting threshold significance at $P < 0.0002$, highlighted in bold.
AC, individuals of Afro-Caribbean descent; ASAT, abdominal subcutaneous adipose tissue; EUR, individuals of European descent; SA, individuals of South Asian descent; TAT, total adipose tissue; VAT, visceral adipose tissue.

TABLE 4 Body composition by sex and ethnicity in UK Biobank cohort

				EUR – SA		EUR – AC		SA – AC	
	EUR	SA	AC	Difference (95% CI)	*P* value	Difference (95% CI)	*P* value	Difference (95% CI)	*P* value
Male									
n	4,483	80	31	—	—	—	—	—	—
Body fat (%)	24.7 ± 5.6	26.2 ± 4.4	26.0 ± 5.1	−1.63 (−3.4 to 0.08)	0.07	0.04 (−2.9 to 3.0)	1.00	−1.79 (−5.1 to 1.7)	0.68
Fat-free mass (kg)	63.4 ± 7.3	57.0 ± 6.2	63.8 ± 6.9	5.81 (4.2 to 7.4)	**<0.0001**	1.91 (−0.78 to 4.6)	0.27	−3.89 (−7.0 to −0.78)	0.01
Thigh adipose (%)	8.6 ± 2.2	8.9 ± 2.2	7.9 ± 2.3	−0.52 (−1.03 to −0.01)	0.05	0.60 (−0.25 to 1.46)	0.28	1.12 (0.13 to 2.11)	0.02
Thigh volume (L)	3.1 ± 0.4	2.8 ± 0.4	3.6 ± 0.6	0.37 (−0.26 to 0.47)	**<0.0001**	−0.30 (−0.47 to −0.12)	**<0.0001**	0.66 (0.46 to 0.86)	**<0.0001**
VAT (L)	4.9 ± 2.3	4.4 ± 1.5	3.6 ± 1.7	0.31 (−0.09 to 0.7)	0.18	1.99 (1.3 to 2.7)	**<0.0001**	1.68 (0.9 to 2.45)	**<0.0001**
ASAT (L)	5.9 ± 2.5	6.1 ± 2.0	6.4 ± 2.6	−0.49 (−0.87 to −0.11)	0.05	0.69 (0.07 to 1.3)	0.03	1.18 (0.46 to 1.9)	**<0.0001**
VAT (%)	5.1 ± 0.10	5.4 ± 0.17	3.4 ± 0.28	−0.14 (−0.58 to 0.30)	1.00	1.83 (1.09 to 2.57)	**<0.0001**	1.97 (1.11 to 2.82)	**<0.0001**
VAT/(ASAT + VAT)	0.44 ± 0.08	0.42 ± 0.08	0.36 ± 0.06	0.03 (0.04 to 0.1)	0.02	0.08 (0.04 to 0.05)	**<0.0001**	0.05 (0.01 to 0.1)	0.01
Liver fat fraction (%)	4.7 ± 4.7	4.4 ± 3.5	3.6 ± 4.0	−0.06 (−0.24 to 0.14)	1.00	0.48 (0.16 to 0.79)	0.001	0.53 (0.17 to 0.90)	0.002
cT1	701 ± 55	711 ± 55	692 ± 52	−13.2 (−31.8 to 5.4)	0.37	24.1 (−4.6 to 52.7)	0.16	37.3 (3.3 to 71.3)	0.02
Female									
n	4,873	43	25	—	—	—	—	—	—
Body fat (%)	35.8 ± 6.6	38.1 ± 5.2	40.3 ± 6.5	−1.61 (−3.6 to 0.39)	0.16	−1.59 (−4.2 to 1.0)	0.43	0.02 (−3.2 to 3.3)	1.00
Fat-free mass (kg)	44.1 ± 4.6	40.4 ± 4.5	46.7 ± 4.0	4.5 (3.1 to 5.9)	**<0.0001**	−0.05 (−1.9 to 1.8)	1.00	−4.5 (−6.9 to −2.2)	**<0.0001**
Thigh adipose (%)	9.7 ± 2.2	10.6 ± 2.0	9.3 ± 1.4	−1.05 (−1.7 to −0.34)	**<0.0001**	0.98 (0.05 to 1.9)	0.03	2.02 (0.87 to 3.2)	**<0.0001**
Thigh volume (L)	2.1 ± 0.3	1.9 ± 0.3	2.4 ± 0.3	0.27 (0.17 to 0.37)	**<0.0001**	−0.21 (−0.34 to −0.08)	**<0.0001**	−0.48 (−0.64 to −0.32)	**<0.0001**
VAT (L)	2.6 ± 1.5	2.7 ± 1.7	2.0 ± 1.0	0.24 (−0.13 to 0.60)	0.36	1.56 (1.1 to 2.0)	**<0.0001**	1.31 (0.72 to 1.9)	**<0.0001**
ASAT (L)	8.0 ± 3.4	8.6 ± 2.6	9.4 ± 3.5	0.04 (−0.6 to 0.6)	1.00	1.16 (0.4 to 1.9)	0.001	1.13 (0.2 to 2.1)	0.015
VAT (%)	3.3 ± 0.12	3.5 ± 0.18	1.7 ± 0.24	−0.02 (−0.49 to 0.44)	1.00	1.63 (1.03 to 2.23)	**<0.0001**	1.65 (0.89 to 2.41)	**<0.0001**
VAT/(ASAT + VAT)	0.24 ± 0.06	0.22 ± 0.06	0.17 ± 0.06	0.01 (−0.01 to 0.04)	0.44	0.08 (0.05 to 0.11)	**<0.0001**	0.61 (0.02 to 0.10)	**<0.0001**
Liver fat fraction (%)	3.6 ± 4.5	4.8 ± 5.7	3.3 ± 3.2	−0.12 (−0.38 to 0.15)	0.88	0.49 (0.16 to 0.83)	0.001	0.61 (0.18 to 1.03)	0.002
cT1	683 ± 51	702 ± 63	702 ± 54	−15.3 (−37.6 to 7.0)	0.42	−19.4 (−46.8 to 8.0)	0.39	−4.1 (−39.2 to 31.1)	1.00

Data presented as mean ± SD and analyzed by one-way ANCOVA with Bonferroni correction adjusting for age, BMI, International Physical Activity Questionnaire score, and Deprivation Index, setting threshold for significance at $P < 0.0002$, highlighted in bold.

AC, individuals of Afro-Caribbean descent; ASAT, abdominal subcutaneous adipose tissue; cT1, corrected T1; EUR, individuals of European descent; SA, individuals of South Asian descent; VAT, visceral adipose tissue.

TABLE 5 Blood biochemistry by sex and ethnicity in UK Biobank cohort

				EUR – SA		EUR – AC		SA – AC	
	EUR	SA	AC	Difference (95% CI)	*P* value	Difference (95% CI)	*P* value	Difference (95% CI)	*P* value
Male									
n	4,483	80	31	—	—	—	—	—	—
Glucose (mmol/L)	5.1 ± 1.2	4.7 ± 0.58	4.7 ± 0.70	0.33 (0.01 to 0.66)	0.04	0.46 (–0.09 to 1.0)	0.13	0.12 (–0.50 to 0.75)	1.00
Cholesterol (mmol/L)	5.6 ± 1.1	5.25 ± 1.1	5.1 ± 1.2	0.27 (–0.05 to 0.60)	0.13	0.57 (0.03 to 1.11)	0.04	0.30 (–0.33 to 0.93)	0.76
Triglycerides (mmol/L)	1.9 ± 1.1	1.15 ± 0.49	2.1 ± 1.3	–0.21 (–0.52 to 0.10)	0.32	0.98 (0.46 to 1.5)	0.001	1.19 (0.58 to 1.8)	**<0.0001**
C-reactive protein (mg/L)	2.1 ± 3.5	1.7 ± 2.1	1.5 ± 1.5	0.38 (–0.63 to 1.4)	1.00	0.94 (–0.76 to 2.6)	0.56	0.55 (–1.4 to 2.5)	1.00
HbA_{1c} (mmol/mol)	35.3 ± 5.4	36.6 ± 4.3	37.5 ± 5.2	–2.5 (–3.9 to –0.95)	0.0003	–1.7 (–4.4 to 1.0)	0.40	0.75 (–2.3 to 3.9)	1.00
HDL cholesterol (mmol/L)	1.31 ± 0.30	1.16 ± 0.24	1.32 ± 0.26	0.13 (0.05 to 0.22)	0.001	–0.09 (–0.24 to 0.06)	0.44	–0.22 (–0.39 to –0.05)	0.005
ALT (U/L)	26.6 ± 13.6	25.8 ± 11.8	27.8 ± 17.4	1.3 (–2.5 to 5.1)	1.00	0.8 (–5.6 to 7.2)	1.00	–0.4 (–7.8 to 7.0)	1.00
ALP (U/L)	79.5 ± 23.8	84.4 ± 16.6	80.9 ± 21.3	–4.9 (–11.9 to 2.2)	0.29	3.8 (–8.0 to 15.6)	1.00	8.6 (–5.0 to 22.3)	0.39
GGT (U/L)	41.6 ± 37.9	36.4 ± 24.2	36.4 ± 24.2	4.7 (–6.3 to 15.6)	0.92	–10.4 (–28.7 to 8.0)	0.53	–15.0 (–36.2 to 6.2)	0.27
Female									
n	4,873	43	25	—	—	—	—	—	—
Glucose (mmol/L)	4.96 ± 0.83	4.68 ± 0.49	4.82 ± 1.18	0.27 (–0.05 to 0.57)	0.13	–0.001 (–0.48 to 0.60)	0.46	–0.28 (–0.85 to 0.29)	0.71
Cholesterol (mmol/L)	5.88 ± 1.06	5.53 ± 1.02	5.56 ± 1.08	0.21 (–0.20 to 0.63)	0.67	0.23 (–0.34 to 0.79)	1.00	0.02 (–0.69 to 0.71)	1.00
Triglycerides (mmol/L)	1.46 ± 0.79	1.38 ± 0.71	1.11 ± 0.72	0.05 (–0.25 to 0.35)	1.00	0.48 (0.06 to 0.89)	0.02	0.42 (–0.08 to 0.93)	0.14
C-reactive protein (mg/L)	2.2 ± 3.7	3.1 ± 3.4	4.5 ± 6.4	–0.7 (–2.1 to 0.69)	0.67	–2.1 (–4.1 to –0.22)	0.02	–1.4 (–4.0 to 0.95)	0.45
HbA_{1c} (mmol/mol)	34.9 ± 4.7	37.5 ± 3.0	35.8 ± 3.3	–1.5 (–3.2 to 0.23)	0.11	–2.5 (–4.9 to –0.18)	0.03	–1.0 (–4.0 to 1.9)	1.00
HDL cholesterol (mmol/L)	1.62 ± 0.37	1.41 ± 0.32	1.61 ± 0.45	0.18 (0.04 to 0.32)	0.008	–0.01 (–0.31 to 0.11)	0.78	–0.28 (–0.53 to –0.03)	0.03
ALT (U/L)	19.5 ± 13.5	20.2 ± 10.5	18.9 ± 6.5	–0.91 (–6.4 to 4.6)	1.00	2.2 (–5.5 to 9.8)	1.00	3.1 (–6.3 to 12.5)	1.00
ALP (U/L)	81.3 ± 24.8	83.1 ± 16.9	76.9 ± 21.3	–3.0 (–12.4 to 6.4)	1.00	3.9 (–8.9 to 16.7)	1.00	6.9 (–8.9 to 22.7)	0.89
GGT (U/L)	27.2 ± 27.6	27.7 ± 26.1	31.5 ± 13.9	1.8 (–8.5 to 12.2)	1.00	–2.6 (16.6 to 11.6)	1.00	–4.3 (–21.8 to 13.1)	1.00

Data presented as mean ± SD and analyzed by one-way ANCOVA with Bonferroni correction adjusting for age, BMI, International Physical Activity Questionnaire score, and Deprivation Index, setting threshold for significance at $P < 0.0002$, highlighted in bold.
AC, individuals of Afro-Caribbean descent; ALP, alkaline phosphatase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; HbA_{1c}, glycated hemoglobin; HDL, high-density lipoprotein; EUR, individuals of European descent; SA, individuals of South Asian descent.

TABLE 6 Ethnic comparison by sex

	EUR – SA		EUR – AC		SA – AC	
	Difference (95% CI)	*P* value	Difference (95% CI)	*P* value	Difference (95% CI)	*P* value
Male						
Body fat (%)	−3.1 (−4.3 to 2.9)	**<0.0001**	0.60 (−1.7 to 2.9)	0.61	1.95 (−0.49 to 4.4)	0.12
Fat-free mass (kg)	6.47 (5.2 to 7.8)	**<0.0001**	1.31 (−1.0 to 3.7)	0.27	−5.11 (−7.8 to −2.45)	0.0001
Liver-fat fraction (%)	−0.09 (−0.24 to 0.07)	0.28	0.52 (0.23 to 0.80)	0.002	0.30 (−0.03 to 0.63)	0.08
VAT (L)	0.17 (−0.14 to 0.47)	0.29	1.80 (1.27 to 2.38)	**<0.0001**	1.61 (0.99 to 2.24)	**<0.0001**
ASAT (L)	−0.65 (−0.96 to −0.34)	**<0.0001**	0.54 (−0.01 to 1.09)	0.05	0.62 (−0.002 to 1.24)	0.05
VAT (%)	−0.08 (−0.49 to 0.34)	0.72	2.0 (1.24 to 2.67)	**<0.0001**	2.1 (1.23 to 2.88)	**<0.0001**
VAT/(ASAT + VAT)	0.03 (0.003 to 0.05)	0.03	0.07 (0.04 to 0.09)	**<0.0001**	0.05 (0.02 to 0.09)	0.01
Female						
Body fat (%)	−2.3 (−4.0 to −0.62)	0.01	−0.32 (2.2 to 1.6)	0.74	−2.3 (−4.8 to 0.23)	0.08
Fat-free mass (kg)	4.7 (3.4 to 6.0)	**<0.0001**	−0.36 (−1.9 to 1.2)	0.66	−5.5 (−7.1 to −3.0)	**<0.0001**
Liver-fat fraction (%)	−0.19 (−0.41 to 0.02)	0.08	0.56 (0.30 to 0.80)	**<0.0001**	−0.06 (−0.38 to 0.27)	0.73
VAT (L)	0.21 (−0.07 to 0.49)	−0.14	1.58 (1.27 to 1.88)	**<0.0001**	1.35 (0.93 to 1.78)	**<0.0001**
ASAT (L)	0.01 (−0.49 to 0.51)	0.97	0.71 (0.14 to 1.28)	0.01	0.78 (0.02 to 1.53)	0.04
VAT (%)	−0.06 (−0.41 to 0.28)	0.72	1.57 (1.20 to 1.95)	**<0.0001**	1.67 (1.16 to 2.17)	**<0.0001**
VAT/(ASAT + VAT)	0.01 (−0.01 to 0.03)	0.36	0.08 (0.06 to 0.11)	**<0.0001**	0.07 (0.04 to 0.10)	**<0.0001**

Sample size–weighted fixed-effects meta-analysis performed to combine data from both Hammersmith and UK Biobank cohorts to increase power. Data presented as mean difference (95% CI) meta-analyzed across two studies per trait and analyzed by one-way ANCOVA with Bonferroni pairwise correction, *setting a threshold significance at P < 0.0002, highlighted in bold*.
AC, individuals of Afro-Caribbean descent; ASAT, abdominal subcutaneous adipose tissue; EUR, individuals of European descent; SA, individuals of South Asian descent; VAT, visceral adipose tissue.

tissues across different ethnicities (44). Furthermore, as the lack of differences we observed in VAT and ASAT between SA and EUR attests, it is, in effect, the reduction in FFM that is responsible for the increased body fat percentage in SA, as opposed to an actual increase in fat. The only way to definitively answer these questions will be to link anthropometry and body composition to clinical outcomes and diagnoses in longitudinal analyses. Unfortunately, we are currently restricted by the limited amount of disease status and classification data available from the UK Biobank for the individuals included in this study. However, it is hoped that as more participants are scanned, including the collection of imaging data for the same individual at multiple time points, longitudinal and outcome studies will become feasible.

The statistical approach we employed to assess ethnic differences in anthropometry and body composition is worth consideration. By adjusting for BMI in our analysis, we attempted to remove its potential confounding influence on ethnic differences in body fat. However, within this statistical adjustment is the tacit acceptance that BMI behaves similarly in different ethnicities. Accumulated evidence suggests that male and female SA have a greater risk for developing cardiovascular disease at lower BMI levels than other ethnicities (45). Ethnic differences may therefore exist in the strength of the relationships between body size and metabolic and cardiovascular risk factors, and this has prompted calls for lower BMI cutoffs for SA (46). However, directly excluding this confounder for our analyses by matching individuals on BMI is hindered by the lack of consensus regarding appropriate BMI cutoffs for SA, mostly due to variation within SA themselves (47). It should be noted that even without adjustment for BMI, we found no statistical differences between SA and EUR regarding VAT or liver fat. Furthermore, combining the two data sets also revealed no significant differences between EUR and SA in VAT or liver fat fraction, in either sex.

The strengths of this study lie in the relatively large number of participants and the experimental techniques used to measure body fat and liver fat deposition, which are considered the gold standard (17,24). The weaknesses lie in the lack of blood biochemistry data for the Hammersmith cohort and the lack of insulin levels for the UK Biobank cohort. In addition, UK Biobank participants were not fasted prior to sample collection, and data are therefore unsuitable to accurately characterize ethnic differences in glucose metabolism and insulin sensitivity. The long-term evaluation of glucose control afforded by HbA_{1c} analysis somewhat overcomes this lack of continuity we see in blood sample collection. However, we observed no significant ethnic differences in HbA_{1c}, suggesting no ethnic differences in metabolic disease in the UK Biobank. Furthermore, the lack of metabolic data (e.g., fasted blood biochemistry samples) and insufficient information on disease classification in the data sets restrict our ability to currently link fat depots to pathophysiology. In order to substantiate the role of VAT and liver fat, or lack thereof, we are therefore limited to indirectly characterizing our study groups as "normal" on the basis of our comprehensive replication of previously published ethnic differences in anthropometry (4-6).

With regard to additional outcomes, assessment of ectopic pancreatic fat was not available in either cohort and would have provided an opportunity to investigate a depot linked to the pathophysiology of metabolic disease (48). Last, both cohorts may be subject to "healthy volunteer" selection bias (37). Neither the Hammersmith cohort nor the UK Biobank cohort is fully representative of the general population. Furthermore, the ethnic differences in body composition, or lack thereof, we present here are limited to UK-based populations. There are striking differences in body fat and metabolic profiles between UK-based ethnic minorities and individuals living in their ancestral country of origin (49,50). This is an effect further

confounded by differences in body composition between SA living in rural and urban areas (51).

Overall, we demonstrate a high degree of continuity in ethnic and sex differences in anthropometry and body composition in two separate UK-based populations. The lack of difference in VAT and liver fat we observed between SA and EUR suggests that these adverse metabolic depots may not be responsible for the disproportionate increase in metabolic syndrome–associated morbidities in SA.O

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Author contributions: ELT, JDB, JPM, and APG conceived and carried out the experiments. WA, HY, RB, HRW, and JRCP analyzed the data. All authors were involved in writing the paper and had final approval of the manuscript.

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