



## ORIGINAL ARTICLE

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# MRI assessment of adipose tissue fatty acid composition in the UK Biobank and its association with diet and disease

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## Abstract

**Objective:** This study aimed to assess the fatty acid (FA) composition of abdominal subcutaneous and visceral adipose tissue (ASAT and VAT, respectively) in the UK Biobank imaging cohort ( $N = 33,823$ ) using magnetic resonance imaging (MRI).

**Methods:** We measured the fractions of saturated, monounsaturated, and polyunsaturated FA (fSFA, fMUFA, and fPUFA, respectively) in ASAT and VAT from multiecho MRI scans. We selected a subcohort of participants who followed a vegan and an omnivore diet ( $N = 36$ ) to validate the effect of diet on adipose tissue. In the wider imaging cohort, we examined the relationships between adipose tissue FA composition and various traits related to disease and body size.

**Results:** We measured adipose tissue FA composition for over 33,000 participants, revealing higher fSFA and fPUFA and lower fMUFA in VAT ( $p < 0.00016$ ). fMUFA and fPUFA were higher in ASAT and lower in VAT for women ( $p < 0.00016$ ). Vegan participants exhibited lower fSFA in both ASAT and VAT ( $p < 0.00016$ ). VAT fSFA and fMUFA showed significant associations with disease, as well as anthropometric variables.

**Conclusions:** This extensive analysis revealed the relationships between adipose tissue FA composition and a range of factors in a diverse population, highlighting the importance of studying body adipose tissue beyond its quantity.

## INTRODUCTION

Although adipose tissue content and distribution are strongly associated with the development of metabolic disease, adipose tissue composition, a reflection of long-term dietary fatty acid (FA) intake, is also thought to play a significant role [1]. Indeed, the relative proportions of dietary saturated, unsaturated, mono-unsaturated, and polyunsaturated FA (SFA, UFA, MUFA, and PUFA, respectively) are associated with the development of type 2 diabetes (T2D) [2], hypertension [3], and cardiovascular disease (CVD) [4].

Adipose tissue FA composition reflects long-term dietary and habitual FA intake, with gas-liquid chromatography (GLC) of adipose tissue biopsies being the gold standard for its measurement [5]. However, the invasiveness of this method limits the sample size and the anatomical location that can be studied. Noninvasive methods such as in vivo carbon-13 ( $^{13}\text{C}$ ) and proton ( $^1\text{H}$ ) magnetic resonance spectroscopy (MRS) have been used to measure human adipose tissue FA composition [6]. Although these methods cannot measure individual FA like GLC, they estimate the relative proportions of SFA, UFA, MUFA, and PUFA. Therefore, they have been applied to the study of adipose tissue FA composition in relationship to diet [7],

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development [8], and disease [9]. However, these noninvasive methods have not been widely adopted despite their potential, mainly due to the considerable technical demands, significantly limiting their applicability. Hamilton et al. [10] developed a  $^1\text{H}$  MRS method to characterize the liver fat FA composition, later applied by Bydder et al. [11] to estimate adipose tissue composition from magnetic resonance imaging (MRI). This approach of measuring adipose tissue FA composition is increasingly being used [11–13], partly due to its applicability on most MRI scanners, providing estimates for the number of double bonds (NDB), the number of methylene-interrupted double bonds (NMIDB), and the FA chain length [10]. These parameters enable the derivation of fractions of saturated, unsaturated, monounsaturated, and polyunsaturated FA (fSFA, fUFA, fMUFA, and fPUFA, respectively), which have been validated against GLC and MRS [14].

In addition to being widely available, MRI assessment of adipose tissue composition provides enhanced spatial information, allowing simultaneous estimation across multiple adipose tissue depots and sites such as the liver, muscle, and bone marrow [15]. This enables the detection of differences in FA composition between visceral adipose tissue (VAT) and abdominal subcutaneous adipose tissue (ASAT) depots and between superficial and deep layers of ASAT [16].

Previous studies have demonstrated that FA composition of adipose tissue influences the risk of various diseases such as insulin resistance [17] and osteoporosis [18] and all-cause mortality [19]. However, MRI assessment of adipose tissue composition in large cohorts has been scarce, with most studies involving only a few tens or hundreds of participants, reflecting challenges in scaling up these methods [12].

Our study aimed to test the feasibility of using MRI to measure adipose tissue composition in a large cohort of participants and determine the FA composition of VAT and ASAT. We also sought to confirm previous observations regarding the relationship between ASAT and VAT FA composition and habitual diet. Finally, we explored the effect of adipose tissue FA composition on factors such as lifestyle and disease, including hypertension, T2D, and CVD.

## METHODS

### Data

Images were obtained using a Siemens Aera 1.5-T scanner (Syngo MR D13; Siemens, Erlangen, Germany), with full details of the UK Biobank abdominal MRI protocol previously reported [20]. Our analysis used the neck-to-the-knee, chemical-shift-based images and the pancreas single-slice multiecho sequence in 33,823 participants. Specifically, the single-slice multiecho sequence for the pancreas was acquired using the following set of parameters: repetition time (TR) = 27 ms; echo time (TE) = 2.38/4.76/7.15/9.53/11.91/14.29/16.67/19.06/21.44/23.82 ms; flip angle = 20°; bandwidth = 710 Hz; voxel size 2.5 × 2.5 × 6.0 mm and 160 × 160 matrix. SAT and VAT segmentations were obtained from the three-dimensional chemical-shift-encoded MRI sequences using a deep learning algorithm [21] and projected into the single-slice multi-echo data.

### Study Importance

#### What is already known?

- The fatty acid (FA) composition of adipose tissue is an independent risk factor for hypertension, type 2 diabetes, and cardiovascular disease.
- There has yet to be a large-scale population study of adipose tissue FA composition, principally due to the invasive nature of available methods.

#### What does this study add?

- We show that magnetic resonance imaging-based methods can be readily applied across a large population ( $n = 33,823$ ) while confirming and expanding on the associations between dietary patterns and FA composition in both abdominal subcutaneous and visceral adipose tissue (VAT).
- Models involving saturated and monounsaturated FA composition in VAT demonstrate significant associations with disease outcomes, anthropometric variables, dietary macronutrient intake, and physical activity.

#### How might these results change the direction of research or the focus of clinical practice?

- Our findings highlight the importance of evaluating adipose tissue composition and its relationship with dietary and disease traits.
- These insights underscore the significance of evaluating adipose tissue's quality (composition). Identifying an “adverse phenotype” may contribute to informed lifestyle recommendations designed to alleviate the consequences of metabolic dysfunction.

Fully anonymized images and participant metadata from the UK Biobank cohort were obtained through UK Biobank Access Application number 44584. The UK Biobank has approval from the North West Multi-Centre Research Ethics Committee (Research Ethics Committee reference: 11/NW/0382), with informed consent obtained from all participants. All methods were performed in accordance with the relevant guidelines and regulations as presented by the appropriate authorities, including the Declaration of Helsinki. Additional information may be found on the UK Biobank researchers and resource catalog pages (<http://www.ukbiobank.ac.uk>).

### Phenotype definitions

We used anthropometric measurements, including age, body mass index (BMI), and waist and hip circumference, obtained at the UK

Biobank imaging assessment. We also used self-reported race and ethnicity and sex, as well as Townsend deprivation index from the initial UK Biobank assessment visit. We calculated participants' excess metabolic equivalents of task (MET) in hours per week by multiplying the time in minutes spent in each physical activity, including walking and moderate and vigorous activity, by the number of reported days doing the exercise and the respective MET scores using previously described methods [22]. We used the vigorous MET as a more reliable measure of intensive physical activity. All physical activity measures and alcohol intake frequency and smoking were self-reported at the UK Biobank imaging visit. Inflammatory biomarkers, including C-reactive protein and white blood cell count (WBCC), were obtained at the initial assessment visit.

UK Biobank dietary information was collected using the Oxford WebQ ([www.ceu.ox.ac.uk/research/oxford-webq](http://www.ceu.ox.ac.uk/research/oxford-webq)), a web-based recall questionnaire for large population studies. We calculated mean values from the data of the five dietary assessments for which UK Biobank participants completed the questionnaires. We estimated the dietary intake of PUFA by subtracting SFA and MUFA intake from total fat intake. The primary exposure variables were the dietary intake derived from the macronutrients, including carbohydrate, fat, and protein, and components, including MUFA, PUFA, and SFA, in grams, as well as the energy intake (in kilojoules). In our following analysis, all dietary intake from the FA components will be referred to as dietary MUFA, PUFA, and SFA.

Given that previous studies have shown, using in vivo  $^{13}\text{C}$  MRS, that vegan individuals show significant differences in adipose tissue composition compared with omnivore individuals [23], we studied a subcohort of vegan participants as proof of principle for our methods. Vegan participants were defined by self-reporting, at the first imaging visit, habitual "vegan diet" or "never" consuming meat, fish, dairy, and

eggs, whereas omnivore participants were selected by self-reporting "once a week" consumption of meat, fish, dairy, and eggs [24]. Relevant conditions of interest, including hypertension, T2D, and CVD, were defined at the time and before the imaging visit. A summary of the codes corresponding to the diet and disease conditions considered is shown in Table S1.

## Data analysis

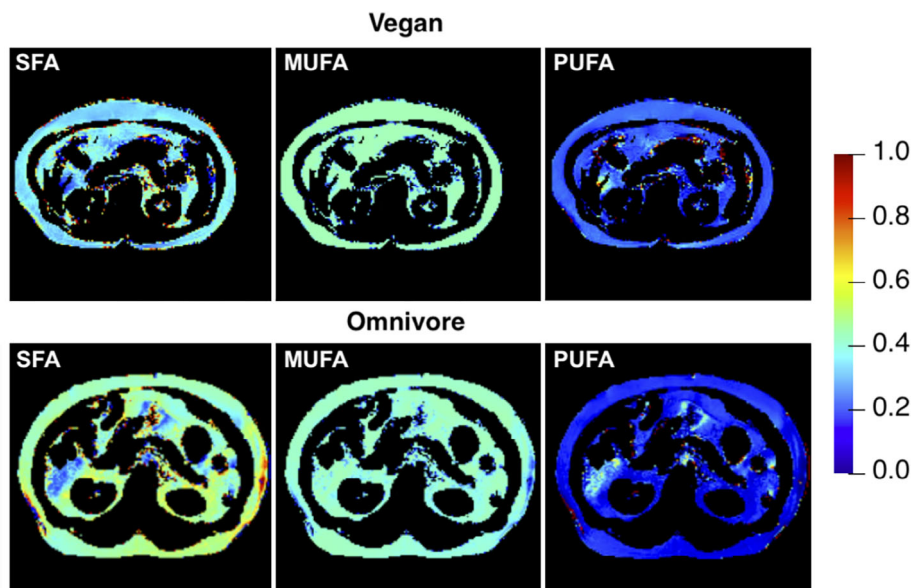
The MRI-based method used to quantify adipose tissue FA composition in this study is based on Bydder et al. [11], in which the NDB, NMIDB, and chain length describe triglyceride molecules. In brief, NDB were determined iteratively by fitting the MR signal in a non-linear least-square approach as a function of the echo times. An example of the maps of magnitude, field inhomogeneity (B0), and phase ( $\varphi$ ) of the vegan and omnivore participants, as well as the fitted complex-valued data for four representative voxels in the omnivore participant in Figure 1, is shown in Figure S1. The graph plots show that the curve fitting estimates the signal well, indicating a good match between the fitted curves and the data.

The NMIDB were subsequently calculated from the NDB using a previously described heuristic technique ( $\text{NMIDB} = 0.093 \times \text{NDB}^2$ ) [11]. Bound constraints for NDB were  $1 \leq \text{NDB} \leq 6$ .

FA composition was derived from NDB and NMIDB using the following relationships [25]:

$$\text{fMUFA} = (\text{NDB} - 2 \times \text{NMIDB})/3$$

$$\text{fPUFA} = \text{NMIDB}/3$$



**FIGURE 1** Examples of estimated fSFA, fMUFA, and fPUFA maps on the ASAT and VAT of a vegan and an omnivore participant. The fSFA and fPUFA are visibly different between the two participants. ASAT, abdominal subcutaneous adipose tissue; fMUFA, monounsaturated fatty acid fraction; fPUFA, polyunsaturated fatty acid fraction; fSFA, saturated fatty acid fraction; VAT, visceral adipose tissue.

$$fUFA = (NDB - NMIDB) / 3$$

$$fSFA = 1 - fUFA = 1 - (fPUFA + fMUFA)$$

where fUFA is the UFA fraction, fSFA is the SFA fraction, fMUFA is the MUFA fraction, and fPUFA is the PUFA fraction. All of the estimated adipose tissue FA composition values fell within the range of 0 to 1. Estimates of NDB, NMIDB, fUFA, fMUFA, fPUFA, and fSFA were calculated voxel-by-voxel, creating FA composition maps.

Segmentations of SAT and VAT were used to isolate these two adipose tissue compartments on the FA composition maps. Postprocessing included one iteration of binary erosion to the ASAT and VAT masks to remove voxels that suffer from partial-volume effects where non-adipose tissue may be present. Voxels within these masks with an estimated fat fraction below 20% were also removed, as suggested by Bydder et al. [11]. Our analysis will mainly focus on fMUFA, fPUFA, and fSFA values to describe FA composition in adipose tissue.

## Quality control

After postprocessing of ASAT and VAT segmentations, 197 participants were excluded because no voxels remained in the fat depot masks, which was confirmed by visual inspection. We further conducted quality control measures to determine potential outliers in the estimated NDB values by visually examining the lowest and highest values of their respective ranges (i.e.,  $NDB > 1$  and  $NDB < 6$ ), resulting in the exclusion of an additional 43 participants. For consistency in the sample size, participants with missing data for one fat depot (e.g., ASAT) were excluded from the study, even if the other fat depot (e.g., VAT) had full coverage. From the initial 33,823 participants, a total of 33,583 were included in our analysis (0.7% of the data excluded). A flow diagram of the inclusions/exclusions in the study population is shown in Figure S2.

## Statistical analysis

Descriptive characteristics are presented as means and standard deviations (SD) for quantitative variables and as counts for categorical variables using the R software environment (<https://www.Rproject.org/>). All results measured from the FA composition maps are expressed as means (SD). The Wilcoxon rank sum test was used to compare means between groups, and the Wilcoxon signed rank test was used for groups with paired observations. We assessed the effect of adipose tissue FA composition on vegan and omnivore participants after adjusting for age, sex, alcohol, smoking, MET, and the Townsend deprivation index using linear regression models and using the adipose tissue FA composition measurements as dependent variables in each analysis. BMI was excluded from the linear regression analysis owing to its high correlation with FA composition in both ASAT and VAT. In the full imaging cohort, we evaluated the impact of adipose tissue FA composition on anthropometric, lifestyle, and disease factors using

linear regression models, adjusting for age; sex; race and ethnicity; BMI; alcohol intake frequency; smoking; vigorous MET; the Townsend deprivation index; intake from macronutrients, including fat, carbohydrate, and protein and their components, including dietary MUFA, PUFA, and SFA; hypertension; T2D; and CVD. To avoid issues related to collinearity among dietary variables, we excluded the intake of dietary PUFA and dietary fat from our model. In our linear regression analyses, we excluded all participants who, at any of the five dietary assessments, reported that what they ate or drank yesterday was not typical [26]. All continuous variables were standardized, with units in 1 SD, before being included in the linear regression models. Summaries of the linear regression analysis are reported as standardized regression coefficients ( $\beta$ ) with standard errors in the tables and as standardized regression coefficients with 95% confidence intervals (CI) in the figures. After counting the hypothesis tests, the Bonferroni-corrected threshold for statistical significance was  $0.05/309 = 0.00016$ .

## RESULTS

### Baseline and adipose tissue composition characteristics

Baseline characteristics and summary statistics of the whole cohort, including adipose tissue FA composition, are provided in Tables 1 and 2 and in Tables S2 and S3. Of the 33,583 participants, 96.8% were of White race and ethnicity, and 51.4% were women, with an average (SD) age of 63.80 (7.50) years for women and 65.17 (7.80) years for men.

fSFA and fPUFA were higher in VAT, whereas fMUFA was lower in VAT than in ASAT ( $p < 0.00016$ ) for both men and women. ASAT fMUFA and fPUFA were significantly higher and fSFA was significantly lower in women than in men. Conversely, VAT fMUFA and fPUFA were significantly lower and fSFA was significantly higher in women than in men (Table 2).

In order to validate our adipose tissue FA composition measurements, we examined a subset of vegan and omnivore participants. This subgroup was selected because vegan participants are known to have marked differences in dietary fat intake (elevated unsaturated fat consumption), which is reflected in their adipose tissue composition. We identified 51 vegan participants in the UK Biobank, from which only 18 had complete pancreas multiecho scans, leading us to match 18 vegan participants with 18 omnivore participants based on sex. Figure 1 illustrates an example of FA composition in ASAT and VAT for representative vegan and omnivore participants, whereas baseline characteristics and summary statistics of adipose tissue FA composition are provided in Table 3 and in Tables S4 through S6.

Vegan participants exhibited higher fMUFA in ASAT than VAT ( $p < 0.00016$ ), with no other significant adipose tissue-specific differences in FA composition observed in vegan and omnivore participants. Significantly lower fSFA was observed in the ASAT of vegan compared with omnivore participants (0.34 [0.03] vs. 0.42 [0.05],  $p < 0.00016$ ; Table 3). Similarly, in VAT, fSFA was significantly lower,

**TABLE 1** Demographics of the full cohort, separated by sex.

	All	Women	Men
N	33,583	17,264	16,319
White	32,494	16,721	15,773
Asian	363	137	226
Black	212	118	94
Chinese	102	59	43
Others	323	190	133
Age (y)	64.47 ± 7.68	63.80 ± 7.50	65.17 ± 7.80**
Weight (kg)	75.98 ± 14.73	68.97 ± 12.81	83.40 ± 12.86**
Height (m)	1.69 ± 0.09	1.63 ± 0.06	1.76 ± 0.06**
BMI (kg/m <sup>2</sup> )	26.46 ± 4.25	26.04 ± 4.64	26.89 ± 3.74**
Townsend deprivation index	-1.90 ± 2.72	-1.84 ± 2.73	-1.96 ± 2.71**
Energy (kJ)	8764.34 ± 2372.48	8099.30 ± 2052.21	9475.21 ± 2483.10**
Dietary MUFA (g)	26.96 ± 10.73	25.08 ± 9.65	28.96 ± 11.44**
Dietary PUFA (g)	19.90 ± 7.51	18.77 ± 6.92	21.11 ± 7.92**
Dietary SFA (g)	27.54 ± 11.78	25.57 ± 10.67	29.64 ± 12.52**
Fat (g)	74.40 ± 27.93	69.43 ± 25.18	79.71 ± 29.69**
Carbohydrate (g)	256.47 ± 75.01	238.90 ± 67.33	275.25 ± 78.18**
Protein (g)	81.74 ± 23.23	77.24 ± 20.46	86.55 ± 24.99**
CRP (mg/L)	2.03 ± 3.44	2.10 ± 3.55	1.94 ± 3.33*
WBCC (10 <sup>9</sup> cells/L)	6.59 ± 1.83	6.59 ± 1.69	6.58 ± 1.97
Hypertension	12,093	4946	7147
T2D	1765	586	1179
CVD	3306	977	2329

Note: Values are reported as mean ± SD for continuous variables and counts (n) for categorical variables. Significance refers to the *p* value for a Wilcoxon rank sum test, in which the null hypothesis is the medians between the two groups (women and men) are equal.

Abbreviations: CRP, C-reactive protein; CVD, cardiovascular disease; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; T2D, type 2 diabetes; WBCC, white blood cell count.

\*Statistical significance for *p* < 0.05.

\*\*Statistical significance after Bonferroni correction (*p* = 0.00016).

**TABLE 2** Summary statistics for the full cohort's FA composition in ASAT and VAT, separated by sex.

	All (N = 33,583)	Women (n = 17,264)	Men (n = 16,319)
<b>ASAT</b>			
fSFA	0.44 ± 0.04	0.43 ± 0.03	0.45 ± 0.04**
fMUFA	0.40 ± 0.03	0.41 ± 0.02	0.40 ± 0.03**
fPUFA	0.15 ± 0.05	0.16 ± 0.04	0.15 ± 0.05**
fUFA	0.56 ± 0.04	0.57 ± 0.03	0.55 ± 0.04**
<b>VAT</b>			
fSFA	0.47 ± 0.04	0.48 ± 0.04	0.46 ± 0.03**
fMUFA	0.36 ± 0.03	0.35 ± 0.03	0.37 ± 0.03**
fPUFA	0.18 ± 0.04	0.17 ± 0.04	0.18 ± 0.03**
fUFA	0.53 ± 0.04	0.52 ± 0.04	0.54 ± 0.03**

Note: Values are reported as mean ± SD. Significance refers to the *p* value for a Wilcoxon rank sum test, where the null hypothesis is the medians between the two groups are equal. After Bonferroni correction (*p* = 0.00016), all comparisons between FA composition in ASAT and VAT, for the full cohort and separated by sex, were statistically significant.

Abbreviations: ASAT, abdominal subcutaneous adipose tissue; fMUFA, monounsaturated fatty acid fraction; fPUFA, polyunsaturated fatty acid fraction; fSFA, saturated fatty acid fraction; fUFA, unsaturated fatty acid fraction; VAT, visceral adipose tissue.

\*\*Statistical significance between the vegan and omnivore participants after Bonferroni correction (*p* = 0.00016).

**TABLE 3** Summary statistics for FA composition in ASAT and VAT of the vegan and omnivore participants.

	Vegan (n = 18)	Omnivore (n = 18)
<b>ASAT</b>		
fSFA	0.34 ± 0.03	0.42 ± 0.05**
fMUFA	0.43 ± 0.02	0.39 ± 0.07*
fPUFA	0.23 ± 0.03	0.20 ± 0.13*
fUFA	0.66 ± 0.03	0.58 ± 0.05**
<b>VAT</b>		
fSFA	0.36 ± 0.04	0.43 ± 0.03**
fMUFA	0.38 ± 0.04 <sup>a</sup>	0.39 ± 0.02
fPUFA	0.27 ± 0.07 <sup>b</sup>	0.18 ± 0.03**
fUFA	0.64 ± 0.04	0.57 ± 0.03**

Note: Values are reported as mean ± SD. Significance refers to the *p* value for a Wilcoxon rank sum test, in which the null hypothesis is the medians between the two groups are equal.

Abbreviations: ASAT, abdominal subcutaneous adipose tissue; fMUFA, monounsaturated fatty acid fraction; fPUFA, polyunsaturated fatty acid fraction; fSFA, saturated fatty acid fraction; fUFA, unsaturated fatty acid fraction; VAT, visceral adipose tissue.

<sup>a</sup>Statistical significance between FA composition in ASAT and VAT after Bonferroni correction (*p* = 0.00016).

<sup>b</sup>Statistical significance between FA composition in ASAT and VAT for *p* < 0.05.

\*Statistically significant for *p* < 0.05.

\*\*Statistical significance between the vegan and omnivore participants after Bonferroni correction (*p* = 0.00016).

whereas fPUFA was significantly higher in vegan compared with omnivore participants (*p* < 0.00016).

### FA composition of adipose tissue, anthropometric characteristics, and diet and disease

A summary of the linear regression models for vegan and omnivore participants is provided in Table S7. fSFA in VAT was positively associated with an omnivore diet, with a standardized regression coefficient of 1.556 (*p* < 0.00016) and *R*<sup>2</sup> of 0.52. The estimated SD value for fSFA in VAT was 0.05, meaning, on average, consuming an omnivore diet results in a 0.078 increase in fSFA in VAT compared with a vegan diet. None of the models detected any further statistically significant associations. This could be attributed to the small number of participants available for this substudy (*N* = 36).

Statistical linear regression models were used to investigate the effect of fSFA, fMUFA, and fPUFA in ASAT and VAT on diet, lifestyle factors, and disease within the larger cohort (Table S8 and Figure 2). Of the initial 33,583 UK Biobank participants, a total of 21,463 completed at least one dietary questionnaire. The exclusion of 8132 participants whose dietary assessments indicated atypical diets and 1203 participants with missing anthropometric, inflammatory, and lifestyle data left 12,128 participants eligible for inclusion in the linear regression analysis (Figure S2).

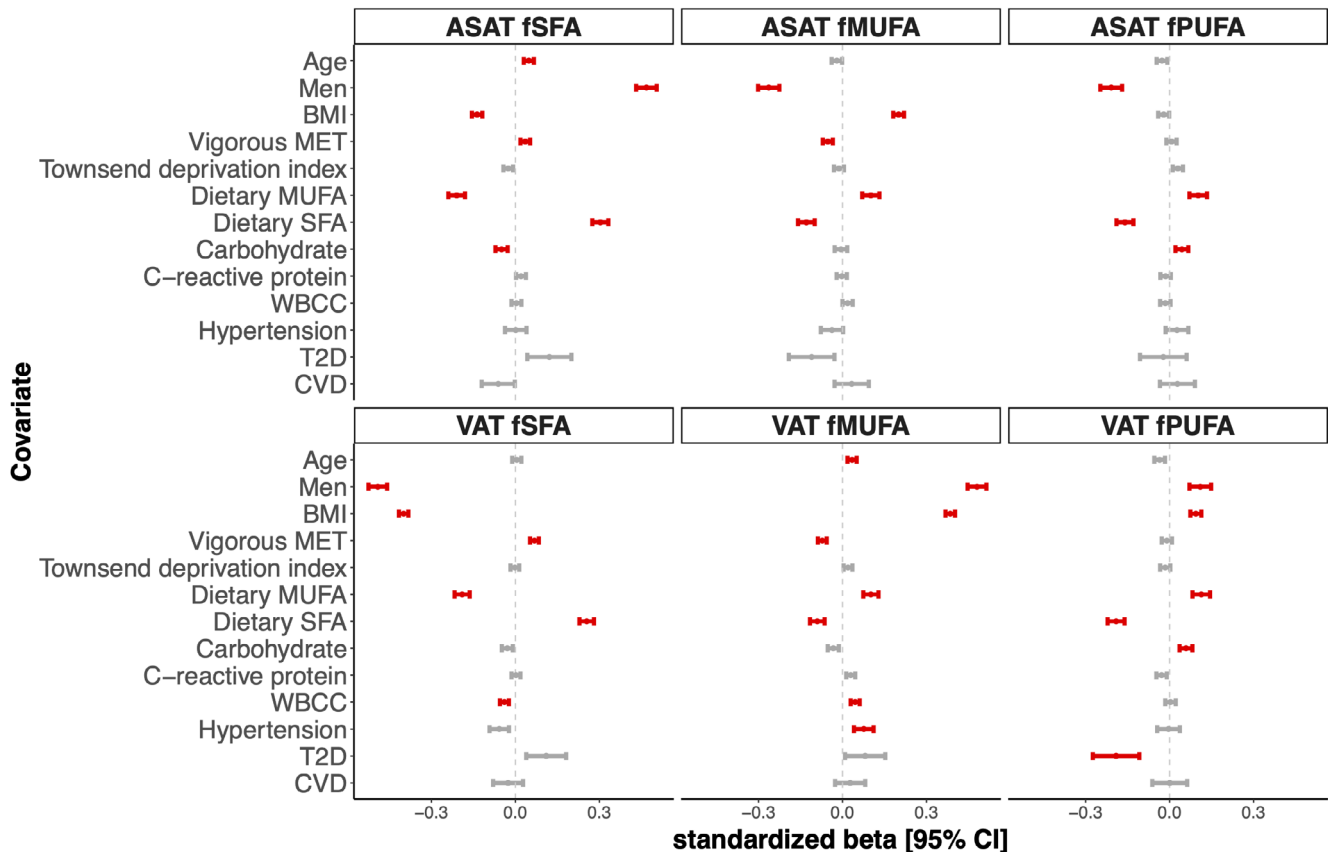
fSFA in ASAT and fMUFA in VAT were positively associated with age (*p* < 0.00016). In ASAT, fSFA was positively associated with age and men, whereas fMUFA and fPUFA were negatively associated with men (fSFA:  $\beta$  = 0.468; fMUFA:  $\beta$  = -0.264; fPUFA:  $\beta$  = -0.209; *p* < 0.00016). In VAT, these measures were inversely associated (*p* < 0.00016). BMI was negatively associated with fSFA but positively associated with fMUFA in both ASAT and VAT (*p* < 0.00016). fSFA in both ASAT and VAT was significantly positively associated with vigorous MET, whereas fMUFA was negatively associated. Dietary MUFA was negatively associated with fSFA and positively associated with fMUFA and fPUFA in both ASAT and VAT. However, dietary SFA was positively associated with fSFA and negatively associated with fMUFA and fPUFA in ASAT and VAT (*p* < 0.00016). ASAT fSFA was negatively associated with carbohydrate intake, whereas fPUFA in both fat depots was positively associated with dietary carbohydrate intake (*p* < 0.00016).

In VAT, WBCC showed a significant negative association with fSFA and a positive association with fMUFA (fSFA:  $\beta$  = -0.039; fMUFA:  $\beta$  = 0.045; *p* < 0.00016). In the context of associations with disease, in VAT, fMUFA exhibited a positive association with hypertension ( $\beta$  = 0.076; *p* < 0.00016), whereas fPUFA in VAT was negatively associated with T2D ( $\beta$  = -0.191; *p* < 0.00016). It is worth noting that *R*<sup>2</sup> values were relatively low, reflecting a poor fit in the linear regression models for all three FA compositions in both ASAT and VAT, with the highest *R*<sup>2</sup> values being for fSFA and fMUFA in VAT (0.29 and 0.28, respectively).

## DISCUSSION

In the present study, we estimated the FA composition of ASAT and VAT from abdominal MRI acquired from 33,823 UK Biobank participants. The increasing inclusion of abdominal MRI within national biobanks and large cohorts presents an ideal opportunity to extract maximum information from these valuable datasets. Because the UK Biobank does not collect tissue biopsies, validating our MRI findings against GLC was impossible. Therefore, we tested our overall findings by assessing our ability to detect well-established diet-related differences in adipose tissue composition, in particular, those related to participants habitually following a vegan or omnivore diet. Obtaining results consistent with prior studies using <sup>13</sup>C MRS, a technique validated against GLC, which demonstrated higher fPUFA and lower fSFA in the adipose tissue of participants following a vegan diet [7], gave us confidence in the reliability of our findings, enabling subsequent analyses relating to associations among diet, anthropometric, inflammatory, lifestyle, and disease traits.

Although numerous small human studies relating dietary fat to adipose tissue fat composition have been undertaken using GLC, very few have used MRI [14]. Trinh et al. [27] reported that differences in habitual saturated fat intake are closely reflected in the FA composition of VAT and ASAT. In the present study, we confirm these findings, with dietary saturated and monounsaturated fats being positively associated with fSFA and negatively associated with fMUFA



**FIGURE 2** Summary of linear regression coefficients of the FA composition in ASAT and VAT representing the associations with the most relevant baseline characteristics in the full cohort. Standardized  $\beta$  coefficients are displayed with 95% CI. Significant associations for  $p$  values below the Bonferroni correction ( $p = 0.00016$ ) are shown in red, and nonsignificant associations are shown in gray. ASAT, abdominal subcutaneous adipose tissue; fMUFA, monounsaturated fatty acid fraction; fPUFA, polyunsaturated fatty acid fraction; fSFA, saturated fatty acid fraction; VAT, visceral adipose tissue.

and fPUFA, respectively, in both fat depots. These results also align well with previous murine studies, in which high dietary SFA has resulted in VAT containing significantly less MUFA and PUFA but more SFA than a diet composed primarily of PUFA [28].

In our study, we further found that ASAT fSFA was negatively associated, whereas fPUFA was positively associated, with dietary carbohydrates in both ASAT and VAT. This aligns with a previous human study indicating a negative correlation between carbohydrate intake and SFA in adipose tissue composition [29]. Moreover, studies in mice have suggested that high dietary carbohydrate intake is related to increased PUFA in SAT [30]. A high-carbohydrate diet would be expected to drive de novo lipogenesis, thereby increasing adipose tissue fSFA [31]. However, given the relatively high dietary fat intake in the UK Biobank, it is doubtful that de novo lipogenesis significantly impacts adipose tissue composition. Furthermore, research is needed to provide further insights into these dietary associations with FA composition in different fat depots and help clarify how long-term diet affects the FA profile of adipose tissue and its potential influence on metabolic outcomes.

We sought to determine the influence of sex and age on the FA composition of adipose tissue. We found that ASAT was more unsaturated in women than in men, with higher levels of fMUFA and fPUFA, whereas

VAT was more saturated in women than in men. In agreement with our overall findings, Machann et al. [16], using  $^1\text{H}$  MRS, reported ASAT to be significantly more unsaturated than VAT. However, they reported a non-significant trend for a more unsaturated adipose tissue profile in men than in women. However, the same authors reported a negative association between VAT PUFA and total VAT volume [32], suggesting that men with a larger VAT depot would have a more saturated VAT FA profile. Given that the differences we observed were small, the power of the large number of participants in our study may be an important factor. In our analysis of FA composition across different adipose tissues, VAT was more saturated than ASAT, whereas ASAT was more enriched in MUFA than VAT, and this was consistently observed in both men and women, aligning with previous studies that have investigated FA composition differences among different human fat depots [33]. However, it is worth noting that previous studies have provided conflicting results, showing more MUFA and less SFA in VAT than in ASAT [30]. Further research may offer additional insights into these adipose tissue-specific differences.

Direct comparison of MRI results with the GLC literature is not straightforward; for instance, Lohner et al. [34], in a large meta-analysis, found that levels of certain PUFA such as linoleic acid (18:2n-6) and dihomo- $\gamma$ -linolenic acid (20:3n-6) were elevated in the

adipose tissue of women, whereas others such as  $\gamma$ -linolenic acid (C18:3n-6) and arachidonic acid (C20:4n-6) and n-3 PUFA were higher in men. There is evidence that there are sex differences in the ability to synthesize n-3 FA from precursors such as  $\alpha$ -linolenic acid, and sex hormones also play a role, with estrogen stimulating and testosterone inhibiting conversion of essential FA into long-chain FA [35]. It is unclear why the sex differences between ASAT and VAT depots are inconsistent. A confounding factor may relate to the interaction between sex and age, which have both been shown to influence adipose tissue FA composition [36]. In the present study, we found a significant positive association between age and adipose tissue composition only for ASAT fSFA and VAT fMUFA. The variability in these patterns emphasizes the sex-specific differences in ASAT and VAT regulation of the FA pathways.

In addition to diet, sex, and aging, multiple factors influence the FA composition of adipose tissue. We found a significant negative association between BMI and fSFA and a positive association with fMUFA in both ASAT and VAT. The reasons for these observations are unclear but may be related to various factors, including fat cell size [37], which is known to be positively associated with increasing adiposity [38].

Chronic low-grade adipose tissue inflammation is a well-known factor in individuals with overweight and obesity. It has been causally linked to metabolic disease, with adipose tissue FA composition linked to the inflammatory profile [39]. In our study, we found that inflammatory biomarkers, including WBCC, also showed negative associations with fSFA and positive associations with fMUFA in VAT. Previous studies have suggested that SFA intake produces proinflammatory gene expression in adipose tissue, whereas MUFA intake reduces inflammatory activity [40]. However, recent findings on inflammatory activity, FA intake, and red blood cell FA in healthy humans revealed unexpected findings, highlighting an inverse association between inflammation and total red blood cell SFA and a positive relationship with MUFA, attributed to an increase in a rate-limiting enzyme responsible for desaturation of both SFA and MUFA [41].

Elevated serum palmitoleic acid has previously been associated with increased systolic blood pressure [42]. We found that VAT fMUFA was positively associated with hypertension. We also found a negative association between VAT fPUFA and T2D. VAT is known for its metabolic activity and association with features of the metabolic syndrome such as hyperinsulinemia [43]. Previous studies have shown that adipose tissue PUFA levels in mice reduce obesity-related insulin resistance [44]. Further research involving longitudinal data could explore the FA composition tracking dietary and lifestyle changes, their impact on disease outcomes, and their effects on adipose tissue.

Although the study offers valuable insights, it is crucial to recognize its constraints. The UK Biobank, a substantial cross-sectional study, may be influenced by selection bias because it represents a "healthier" group compared with the broader UK population and excludes younger individuals and cases of severe disease. Moreover, because the UK Biobank population is predominantly White, future work is needed to investigate diverse race and ethnicity population data. Another potential limitation of this study is that the dietary parameters and inflammatory markers used were reported

approximately 6.8 (1.5) years and 9 (1.7) years before the MRI acquisition, respectively. Finally, the relatively low  $R^2$  values suggest that many other factors contribute to FA composition; owing to the observational nature of this analysis, relevant measurements such as adipocyte size, for instance, were not possible.

## CONCLUSION

Our large-scale MRI-based analysis of the FA composition of ASAT and VAT shows valuable insights into their associations with diet, anthropometrics, lifestyle, inflammation factors, and disease. Our findings underscore the significance of assessing adipose tissue composition in relationship to lifestyle and disease traits, paving the way for future research focusing on longitudinal and intervention studies to elucidate the impact of genetics and the exposome on adipose tissue composition and disease outcomes.  $\text{\textcircled{O}}$

## AUTHOR CONTRIBUTIONS

Jimmy D. Bell, E. Louise Thomas, and Marjola Thanaj conceived the study. Jimmy D. Bell, Brandon Whitcher, E. Louise Thomas, and Marjola Thanaj designed the study. Marjola Thanaj, Brandon Whitcher, and Nicolas Basty implemented the methods. Marjola Thanaj performed the data and statistical analysis. E. Louise Thomas, Brandon Whitcher, Marjola Thanaj, Jimmy D. Bell, and Nicolas Basty drafted the manuscript. All authors read and approved the manuscript.

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## CONFLICT OF INTEREST STATEMENT

The authors declared no conflict of interest.

## DATA AVAILABILITY STATEMENT

Our research was conducted using UK Biobank data. Under the standard UK Biobank data sharing agreement, we (and other researchers) cannot directly share raw data obtained or derived from the UK Biobank. However, under this agreement, all of the data generated, and methodologies used in this paper, are returned by us to the UK Biobank, where they will be fully available. Access is obtained directly from the UK Biobank to all bona fide researchers upon submitting a health-related research proposal to the UK Biobank (<https://www.ukbiobank.ac.uk>).

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## REFERENCES

1. Gesta S, Tseng Y-H, Kahn CR. Developmental origin of fat: tracking obesity to its source. *Cell*. 2007;131:242-256.



2. Acosta-Montaño P, García-González V. Effects of dietary fatty acids in pancreatic Beta cell metabolism, implications in homeostasis. *Nutrients*. 2018;10:10.
3. Bazzano LA, Green T, Harrison TN, Reynolds K. Dietary approaches to prevent hypertension. *Curr Hypertens Rep*. 2013;15:694-702.
4. Fattore E, Massa E. Dietary fats and cardiovascular health: a summary of the scientific evidence and current debate. *Int J Food Sci Nutr*. 2018;69:916-927.
5. Hodson L, Skeaff CM, Fielding BA. Fatty acid composition of adipose tissue and blood in humans and its use as a biomarker of dietary intake. *Prog Lipid Res*. 2008;47:348-380.
6. Hamilton G, Schlein AN, Middleton MS, et al. In vivo triglyceride composition of abdominal adipose tissue measured by H MRS at 3T. *J Magn Reson Imaging*. 2017;45:1455-1463.
7. Thomas EL, Frost G, Barnard ML, et al. An in vivo <sup>13</sup>C magnetic resonance spectroscopic study of the relationship between diet and adipose tissue composition. *Lipids*. 1996;31:145-151.
8. Thomas EL, Hanrahan JD, Ala-Korpela M, et al. Noninvasive characterization of neonatal adipose tissue by <sup>13</sup>C magnetic resonance spectroscopy. *Lipids*. 1997;32:645-651.
9. Thomas EL, Taylor-Robinson SD, Barnard ML, et al. Changes in adipose tissue composition in malnourished patients before and after liver transplantation: a carbon-<sup>13</sup> magnetic resonance spectroscopy and gas-liquid chromatography study. *Hepatology*. 1997;25:178-183.
10. Hamilton G, Yokoo T, Bydder M, et al. In vivo characterization of the liver fat 1H MR spectrum. *NMR Biomed*. 2011;24:784-790.
11. Bydder M, Girard O, Hamilton G. Mapping the double bonds in triglycerides. *Magn Reson Imaging*. 2011;29:1041-1046.
12. Leporq B, Lambert SA, Ronot M, Vilgrain V, Van Beers BE. Simultaneous MR quantification of hepatic fat content, fatty acid composition, transverse relaxation time and magnetic susceptibility for the diagnosis of non-alcoholic steatohepatitis. *NMR Biomed*. 2017;30:e3766.
13. Peterson P, Månsson S. Simultaneous quantification of fat content and fatty acid composition using MR imaging. *Magn Reson Med*. 2013;69:688-697.
14. Nemeth A, Segrestin B, Leporq B, et al. 3D chemical shift-encoded MRI for volume and composition quantification of abdominal adipose tissue during an overfeeding protocol in healthy volunteers. *J Magn Reson Imaging*. 2019;49:1587-1599.
15. Martel D, Honig S, Monga A, Chang G. Analysis of muscle, hip, and subcutaneous fat in osteoporosis patients with varying degrees of fracture risk using 3T chemical shift encoded MRI. *Bone Rep*. 2020;12:100259.
16. Machann J, Stefan N, Wagner R, et al. Intra- and interindividual variability of fatty acid unsaturation in six different human adipose tissue compartments assessed by 1H-MRS in vivo at 3 T. *NMR Biomed*. 2017;30:e3744.
17. Iggman D, Arnlöv J, Vessby B, Cederholm T, Sjögren P, Risérus U. Adipose tissue fatty acids and insulin sensitivity in elderly men. *Diabetologia*. 2010;53:850-857.
18. Yeung DKW, Griffith JF, Antonio GE, Lee FKH, Woo J, Leung PC. Osteoporosis is associated with increased marrow fat content and decreased marrow fat unsaturation: a proton MR spectroscopy study. *J Magn Reson Imaging*. 2005;22:279-285.
19. Iggman D, Arnlöv J, Cederholm T, Risérus U. Association of adipose tissue fatty acids with cardiovascular and all-cause mortality in elderly men. *JAMA Cardiol*. 2016;1:745-753.
20. Littlejohns TJ, Holliday J, Gibson LM, et al. The UK Biobank imaging enhancement of 100,000 participants: rationale, data collection, management and future directions. *Nat Commun*. 2020;11:2624.
21. Liu Y, Bastly N, Whitcher B, et al. Genetic architecture of 11 organ traits derived from abdominal MRI using deep learning. *Elife*. 2021;10:10.
22. O'Donnell J, Smith-Byrne K, Velardo C, et al. Self-reported and objectively measured physical activity in people with and without chronic heart failure: UK Biobank analysis. *Open Heart*. 2020;7(7):e001099.
23. Ren J, Dimitrov I, Sherry AD, Malloy CR. Composition of adipose tissue and marrow fat in humans by 1H NMR at 7 tesla. *J Lipid Res*. 2008;49:2055-2062.
24. Watling CZ, Schmidt JA, Dunneram Y, et al. Risk of cancer in regular and low meat-eaters, fish-eaters, and vegetarians: a prospective analysis of UK Biobank participants. *BMC Med*. 2022;20:73. doi:10.1186/s12916-022-02256-w
25. Peterson P, Trinh L, Månsson S. Quantitative 1H MRI and MRS of fatty acid composition. *Magn Reson Med*. 2021;85:49-67.
26. Ho FK, Gray SR, Welsh P, et al. Associations of fat and carbohydrate intake with cardiovascular disease and mortality: prospective cohort study of UK Biobank participants. *BMJ*. 2020;368:m688.
27. Trinh L, Stenkula KG, Olsson LE, et al. Favorable fatty acid composition in adipose tissue in healthy Iraqi- compared to Swedish-born men - a pilot study using MRI assessment. *Adipocyte*. 2022;11:153-163.
28. Leporq B, Lambert SA, Ronot M, et al. Hepatic fat fraction and visceral adipose tissue fatty acid composition in mice: quantification with 7.0T MRI. *Magn Reson Med*. 2016;76:510-518.
29. Alsharari ZD, Leander K, Sjögren P, et al. Association between carbohydrate intake and fatty acids in the de novo lipogenic pathway in serum phospholipids and adipose tissue in a population of Swedish men. *Eur J Nutr*. 2020;59:2089-2097.
30. Yew Tan C, Virtue S, Murfitt S, et al. Adipose tissue fatty acid chain length and mono-unsaturation increases with obesity and insulin resistance. *Sci Rep*. 2015;5:18366. doi:10.1038/srep18366
31. Colleins JM, Neville MJ, Pinnick KE, et al. De novo lipogenesis in the differentiating human adipocyte can provide all fatty acids necessary for maturation. *J Lipid Res*. 2011;52:1683-1692.
32. Machann J, Stefan N, Schabel C, et al. Fraction of unsaturated fatty acids in visceral adipose tissue (VAT) is lower in subjects with high total VAT volume—a combined 1H MRS and volumetric MRI study in male subjects. *NMR Biomed*. 2013;26:232-236.
33. Garaulet M, Pérez-Llamas F, Pérez-Ayala M, et al. Site-specific differences in the fatty acid composition of abdominal adipose tissue in an obese population from a Mediterranean area: relation with dietary fatty acids, plasma lipid profile, serum insulin, and central obesity. *Am J Clin Nutr*. 2001;74:585-591.
34. Lohner S, Fekete K, Marosvölgyi T, Decsi T. Gender differences in the long-chain polyunsaturated fatty acid status: systematic review of 51 publications. *Ann Nutr Metab*. 2013;62:98-112.
35. Childs CE, Romeu-Nadal M, Burdge GC, Calder PC. Gender differences in the n-3 fatty acid content of tissues. *Proc Nutr Soc*. 2008;67:19-27.
36. Bolton-Smith C, Woodward M, Tavendale R. Evidence for age-related differences in the fatty acid composition of human adipose tissue, independent of diet. *Eur J Clin Nutr*. 1997;51:619-624.
37. Garaulet M, Hernandez-Morante JJ, Lujan J, Tebar FJ, Zamora S. Relationship between fat cell size and number and fatty acid composition in adipose tissue from different fat depots in overweight/obese humans. *Int J Obes (Lond)*. 2006;30:899-905.
38. Tchoukalova YD, Koutsari C, Karpayak MV, Votruba SB, Wendland E, Jensen MD. Subcutaneous adipocyte size and body fat distribution. *Am J Clin Nutr*. 2008;87:56-63.
39. Fisk HL, Childs CE, Miles EA, et al. Modification of subcutaneous white adipose tissue inflammation by omega-3 fatty acids is limited in human obesity—a double blind, randomised clinical trial. *EBioMedicine*. 2022;77:103909.
40. Rodríguez-Pacheco F, Gutierrez-Repiso C, Garcia-Serrano S, et al. The pro-/anti-inflammatory effects of different fatty acids on visceral adipocytes are partially mediated by GPR120. *Eur J Nutr*. 2017;56:1743-1752.

41. Berg J, Seyedsadjadi N, Grant R. Saturated fatty acid intake is associated with increased inflammation, conversion of kynurenine to tryptophan, and Delta-9 desaturase activity in healthy humans. *Int J Tryptophan Res.* 2020;13:1178646920981946.
42. Simon JA, Fong J, Bernert JT Jr. Serum fatty acids and blood pressure. *Hypertension.* 1996;27:303-307.
43. Chait A, den Hartigh LJ. Adipose tissue distribution, inflammation and its metabolic consequences, including diabetes and cardiovascular disease. *Front Cardiovasc Med.* 2020;7:22.
44. Zhu P, Zhang J-J, Cen Y, et al. High endogenously synthesized N-3 polyunsaturated fatty acids in Fat-1 mice attenuate high-fat diet-induced insulin resistance by inhibiting NLRP3 inflammasome activation via Akt/GSK-3 $\beta$ /TXNIP pathway. *Molecules.* 2022;27:6384.

## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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