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Biomarkers profile of people with sarcopenia: a cross-sectional analysis from UK Biobank

Abstract

Objective –This study aimed to characterise the biomarker profile of sarcopenic, versus non-sarcopenic men and women, using the current European Working Group on Sarcopenia in Older People (EWGSOP2) definition in the UK Biobank study.

Design – Cross-sectional study.

Setting and participants – 396,707 (68.8% women, age 38 to 73) participants from UK Biobank.

Measures – Thirty-three biomarkers, standardised to sex-specific z-scores, were included in the analysis. Associations between these biomarkers and sarcopenia, defined using EWGSOP2 criteria, were examined using multiple linear regression.

Results – Higher concentrations of rheumatoid factor, CRP, cystatin C, SHBG, GGT, ALP and total protein as well as lower concentrations of IGF-1, albumin, creatinine, sodium, and systolic blood pressure, were associated with sarcopenia both in men and women. However, some of the association differed by sex. Sarcopenia was associated with higher concentrations of phosphate, lipoprotein A and lower of diastolic blood pressure, HbA1c, urea, glucose, total bilirubin and testosterone in women only, and with higher concentrations of HDL, AST, direct bilirubin and lower values of apolipoprotein A, vitamin D, and apolipoprotein B in men only.

Conclusions and implications – Several biomarkers were associated with sarcopenia in men and women using the new EWGSOP2 statement. However, some of these associations and their magnitude differed between men and women. Considering the EWGSOP2 updated its

22 statement on the definition of sarcopenia in 2019, this study enables us to update the study
23 of the biomarkers profile of people with sarcopenia.

24

Introduction

Sarcopenia – the age-related loss of muscle mass and function – is a multifactorial disease strongly related to the lack of independence and a worse quality of life among the elderly ^{1,2}.

Sarcopenia also leads to an increased risk of falling, fractures, hospitalisations, surgical complications and a wide range of metabolic disorders ^{1,2}. Its prevalence is higher in older ages and, on top of this, a recent analysis from the UK estimated the economic consequences of sarcopenia are ~£2.5 billion/year ³. Bodyweight, nutrients intake, physical activity levels, sitting time and health status are some of the risk factors which contribute to the development and progression of sarcopenia ⁴.

Measurements of muscle mass (quantity, quality, and function) are the main clinical, functional and imaging biomarkers recognised in the diagnosis of sarcopenia ^{5,6}. However, as sarcopenia can increase the inflammatory, oxidative, and functional responses during ageing, the interest in biomarkers related to sarcopenia (as well as to other elderly syndromes) has increased in the scientific community since could represent a cost-effective and fast approach to identify and monitor the disease progression ^{5,6}. As a result, some biomarkers – such as the differentiation factor-15, C-reactive protein (CRP), and albumin – have been recognised as sarcopenia-related markers ⁶. However, these are far from being well established and accepted.

Previous studies have identified biomarkers which were associated with sarcopenia using different diagnostic criteria ⁵. However, there has been a lack of evidence for biomarker profile among people with sarcopenia since the European Working Group on Sarcopenia in Older People (EWGSOP2) updated its statement on the definition of sarcopenia in 2019 ².

Therefore, this study aimed to characterise the biomarker profile of sarcopenic versus non-sarcopenic men and women, using the current EWGSOP2 definition in the UK Biobank study.

Methods

This was a cross-sectional analysis of baseline data from the UK Biobank study. UK Biobank (www.ukbiobank.co.uk) is a very large, general population cohort study. Between April 2007 and December 2010, UK Biobank recruited over 500,000 participants (5.5% response rate), aged 37-73 years from the general population⁷. Participants attended one of 22 assessment centres across England, Wales and Scotland^{8, 9} where they completed a touch-screen questionnaire, had physical measurements taken, and provided biological samples, as described in detail elsewhere^{8, 9}.

This study is reported in adherence to the strengthening the reporting of observational studies in epidemiology (STROBE) statement¹⁰.

Sarcopenia definition

Following the diagnostic criteria of the EWGSOP2, sarcopenia was defined as low grip strength plus low muscle mass². The combination of sarcopenia plus slow gait speed was classified as severe sarcopenia. However, because of the low number of UK Biobank participants with severe sarcopenia (n=469), these two groups have been pooled together (hereafter 'sarcopenia'). Due to ethnic differences in the reference values for sarcopenia, only white European participants were included in this study.

Grip strength was measured using a Jamar J00105 hydraulic hand dynamometer. Isometric grip force was assessed from a single 3-second maximal grip effort, performed separately in the right and left arms, with the participant seated upright with their elbow by their side and

flexed at 90° so that their forearm was facing forwards and resting on an armrest. The mean of the right and left values and was derived and was expressed in absolute units (kg). The cut-off points used to define low grip strength were <27 kg in men and <16 kg in women ². Muscle mass index was derived from appendicular lean muscle mass (kg) divided by height (m) squared. To calculate the appendicular lean muscle mass, the Janssen equation was utilised ¹¹ using the total body composition measured by bioimpedance (BIA) by trained nurses. The cut-off points used to define low muscle mass were <7.0 kg/m² in men and < 5.5 kg/m² for women ². Self-reported walking speed was utilised as a proxy of measured gait speed. Participants categorised their usual walking pace as slow, average or brisk and, to derive a proxy for the EWGSOP-2019 definition of walking pace, this was then dichotomised into slow or normal (average or brisk pace).

Biomarkers

Thirty-three biomarkers, which has been previously linked to health outcomes (Table 1) were included for the analyses in this study. These biomarkers were: albumin, alkaline phosphatase [ALP], aspartate aminotransferase [AST], alanine aminotransferase [ALT], gamma-glutamyltransferase [GGT], apolipoprotein A, apolipoprotein B, direct bilirubin, total bilirubin, urea, cholesterol, HDL cholesterol, LDL direct, triglycerides, CRP, cystatin C, glucose, haemoglobin A1c [HbA1c], insulin-like growth factor 1 [IGF-1], lipoprotein A, oestradiol, testosterone, phosphate, rheumatoid factor, sex hormone-binding globulin [SHBG], total protein, urate, vitamin D, calcium, sodium, systolic blood pressure [SBP] and diastolic blood pressure [DBP]. The first 29 were analysed from serum and packed red blood cell samples, while calcium and sodium were measured in urine [15]. SBP and DBP were derived from the mean of two readings recorded in the left arm. The right arm was only used if the left was not

practical (e.g., amputee). The units for each biomarker – as well as its association with sarcopenia or ageing – are available in Table 1. Finally, missing values due to the level of biomarkers exceeding the range of detection of the test were imputed using the square-root of the lowest and the highest detectable values for all serum biomarkers and calcium.

Covariates

Age was calculated from dates of birth and baseline assessment. Area-based socioeconomic status was derived from the postcode of residence, using the Townsend score ¹². Height was measured to the nearest centimetre (cm) using a Seca 202 height measure, and a Tanita BC-418 body composition analyser was used to measure weight to the nearest 0.1 kg. Both were used to estimate the body mass index (BMI) and the WHO criteria were applied to categorise participants as underweight <18.5 kg.m⁻², normal weight 18.5-24.9 kg.m⁻², overweight 25.0-29.9 kg.m⁻² and obese ≥30.0 kg.m⁻² ¹³. Waist circumference was used to derive central or abdominal obesity, defined as ≥88 cm for women or ≥102 cm for men ¹³. Body composition (fat and fat-free mass) was measured using BIA by trained nurses. Physical activity was based on self-report using the International Physical Activity Questionnaire (IPAQ) short form ¹⁴. Total physical activity was computed as the sum of walking, moderate and vigorous activity, measured as metabolic equivalents (MET-hours/week). Cardio-respiratory fitness was estimated during a cycle ergometry on a stationary bike and is expressed in METs ¹⁵. Total time spent in sedentary behaviours was derived from the sum of self-reported time spent driving, using a computer and watching television. Self-reported smoking status was categorised as never, former or current smoker. Further details of these measurements can be found in the UK Biobank online protocol (<http://www.ukbiobank.ac.uk>).

Statistical analyses

Descriptive characteristics of the cohort by sarcopenia and sex, are presented as means with standard deviations (SD) for quantitative variables and percentages for categorical variables.

The validity of BIA-measured muscle mass was verified using Pearson's correlation coefficient and a Bland-Altman plot.

Associations between biomarkers and sarcopenia were investigated using multiple linear regression with the biomarkers being the dependent variables and sarcopenia being the independent variable. Biomarkers were expressed in two formats, as their traditional measurement unit and as sex-specific z-score (1-standard deviation [SD]). The standardisation allowed comparison between biomarkers since all of them were expressed per 1-SD change. People without sarcopenia were the reference group.

All analyses were adjusted for age, deprivation, smoking status, sleep duration, discretionary sedentary time, physical activity, waist circumference and dietary intake (alcohol, red meat and processed meat intake) at baseline. These factors were chosen because of their potential influence on both the biomarkers and sarcopenia.

STATA 16 was used to perform the statistical analyses (StataCorp; College Station, TX). A p-value lower than .05 was considered statistically significant.

Ethical Approval

UK Biobank was approved by the North West Multi-Centre Research Ethics Committee, and all participants provided written informed consent to participate in the UK Biobank study. The study protocol is available online (<http://www.ukbiobank.ac.uk/>).

Results

The descriptive characteristics by sarcopenia status and sex are presented in Table 2. In summary, the prevalence of sarcopenia was higher in women than men (0.9% versus 0.1%). However, in both sexes, people with sarcopenia were older and had a lower body weight, waist circumference, cardio-respiratory fitness and physical activity levels in comparison to those without sarcopenia. Men with sarcopenia had a higher prevalence of deprivation in comparison to men without sarcopenia. Finally, muscle mass estimated using BIA and dual-energy X-ray absorptiometry (DXA) were in good agreement ($r=0.868$, $p<0.001$; Figure A1).

Figures 1 and 2 show the association between sarcopenia and standardised biomarkers in women and men, respectively. After adjusting for potential confounders, twenty biomarkers were associated with sarcopenia in women and eighteen in men. In comparison to women without sarcopenia, sarcopenic women had higher concentrations of rheumatoid factor, CRP, SHBG, cystatin C, total protein, ALP, GGT, phosphate, and lipoprotein A, with differences ranging from 0.05 to 0.38 units of SD. In comparison to men without sarcopenia, sarcopenic men had higher concentrations of CRP, rheumatoid factor, ALP, cystatin C, GGT, SHBG, total protein, HDL, apolipoprotein A, AST, and direct bilirubin, with differences ranging from 0.24 to 0.90 units of SD (Table A1).

Compared to non-sarcopenic women, those who were sarcopenic had a lower concentration of IGF-1, creatinine, DBP, SBP, HbA1c, urea, glucose, albumin, total bilirubin, sodium, and testosterone with the magnitude of the associations ranging from -0.21 to -0.01 units of SD. In terms of men, lower concentrations of vitamin D, IGF-1, creatinine, sodium, albumin, apolipoprotein B, and SBP were associated with sarcopenia (Figures 1 and 2 and Table A1).

157 Biomarkers concentrations expressed in their traditional measurement units by sarcopenia
158 status and sex are presented in Table A2. When we compared the means of each biomarker,
159 similar results were identified.

Discussion

Sarcopenia is a complex syndrome which shares common cellular mechanisms with other diseases, such as frailty and with ageing itself ¹. Although many efforts have been carried out to characterise biomarkers in older adults, there is still a lack of evidence on the profile of biomarkers in people with sarcopenia beyond inflammatory markers and ageing ¹⁶⁻²⁷. In this study, after standardising 33 biomarkers to sex-specific z-score, higher concentrations of seven biomarkers and lower concentrations of five were associated with sarcopenia both in men and women. However, some of the associations differed by sex. These can be related to the difference in sarcopenia prevalence between men and women (only 0.1% of men had sarcopenia). This low prevalence could be due to both the classification used to define sarcopenia as well as for the average age of our sample. Women experience an earlier and major decline in sex-specific hormones that are important for muscle maintenance. Therefore, considering that UK Biobank represents an adult more than an older adult population, it is not surprising that a greater number of women had sarcopenia in this stage than men.

Research aiming to identify biomarkers for sarcopenia has increased over the years ¹⁶⁻²⁷; however, the main focus has been on muscle mass but not diagnose of sarcopenia ⁵. Nevertheless, biomarkers that classically were used to assess renal, cardiovascular, endocrine, or liver function, have shown promising results in the sarcopenia field.

Renal function markers were found to be related to muscle mass and sarcopenia. For instance, circulating creatinine concentrations – a renal biomarker – have shown some potential as a biomarker since has been associated with the total quantity of muscle mass ²⁸. As a result, it is not surprising that lower concentrations of creatinine in this study were associated with sarcopenia both in men and women. Previous studies conducted using cystatin C, another

183 renal biomarker, have also shown that sarcopenic people had a positive correlation with this
184 biomarker ²⁷. These findings are in agreement with our results.

185 Individuals with sarcopenia have shown a higher risk of cardiovascular diseases and chronic
186 diseases like hypertension and diabetes ^{23, 29}. However, we found that lower concentrations
187 of glucose and HbA1c were associated with sarcopenia in women. This result was unexpected
188 since it is recognised that higher glucose concentrations, i.e., hyperglycaemia, are a risk factor
189 for muscle mass reduction ²³.

190 Decreasing in endocrine hormones is a physiological consequence of ageing ^{21, 22, 24}. However,
191 lower levels of some endocrine biomarkers have also been associated with sarcopenia and
192 lower levels of muscle mass. In the Framingham Study, higher concentrations of IGF-1 were
193 associated with a smaller loss of fat-free mass ²². Considering that IGF-1 is related to changes
194 in lean body mass and fat-free mass, ²¹, lower concentrations of IGF-1 in sarcopenic people
195 were expected in our study. In terms of steroid hormones, lower concentrations of
196 testosterone and higher concentrations of SHBG were associated with lower levels of
197 appendicular skeletal muscle mass ²⁴. Consistent with our finding on lower testosterone level
198 in sarcopenic women, studies have shown that testosterone, as well as other sex hormones,
199 plays a role in sarcopenia onset ²¹.

200 Nutritional related biomarkers are also strongly related to muscle mass. Similar to our study,
201 lower concentrations of albumin were also related to loss of the appendicular skeletal muscle
202 mass in older people in the Health Aging and Body Composition Study ¹⁸. Furthermore, people
203 with sarcopenia and lower serum albumin concentrations have been shown previously to be
204 almost three times more risk of disability than those without sarcopenia and normal albumin
205 concentrations ¹⁶. Vitamin D has also been linked to skeletal muscle mass in terms of cell

contractility, proliferation and differentiation ²¹. In our study, lower concentrations of vitamin D was one of the strongest biomarkers negative identified in sarcopenic men. This biomarker was also associated with poor physical performance in the InCHIANTI study ¹⁷. Higher total protein concentrations – a biomarker associated with malnutrition – were identified in people with sarcopenia in contrast to previous studies ³⁰.

The literature has reported that ~70% of patients with advanced liver disease have sarcopenia, highlighting their relevance ³¹. In this context, higher concentrations of GGT, AST and ALP, as well as lower levels of ALT, could reflect smaller quantity and function of muscle mass in older people ^{19, 20}. Probably, as the muscle mass loss is associated with increased of visceral fat and fat accumulation in the liver, this could induce higher concentrations of these transaminases (Table 1)¹⁹. In our study, the concentrations of these transaminases (GGT, AST and ALP) were greater in sarcopenic people.

The prevalence of sarcopenia is elevated in people with rheumatic diseases, an autoimmune disease ²⁵. It can be one of the reasons why higher concentrations of a rheumatoid factor - an autoimmune biomarker - were associated with sarcopenia in our study ³⁰. Finally, inflammatory biomarkers such as CRP has also been associated with loss of muscle strength and mass ^{6, 26}.

Strength and Limitations

Using the UK Biobank study provided the opportunity to test our research question in a large general population cohort as well as the opportunity to work with information collected using validated and standardised methods. In addition, in this study, all serum biomarkers and calcium were imputed. This was particularly important for biomarkers with assay values that were too low, such as oestradiol and rheumatoid factor. However, UK Biobank is not

representative of the UK population in terms of lifestyle and disease prevalence³². Moreover, as in any observational study, residual confounding is possible, and due to the cross-sectional study design, temporal relationships could not be established to exclude the possibility of reverse causation. This limitation mitigates against inferring causation³³. On the other hand, DXA is the most commonly used method for deriving muscle mass because it can provide a reproducible estimation of the appendicular skeletal muscle mass in a few minutes. In UK Biobank, only 5,000 participants had data available from DXA, but we have found a strong correlation between BIA and DXA measured muscle mass ($r=0.868$, $p<0.001$; Figure A1). Furthermore, we had a low prevalence of sarcopenic men, potentially, due to the average age of the UK Biobank population. Finally, whilst we were able to study a wide range of biological markers of interest, we could not explore all. For example, we did not have data for differentiation factor-15, collagen type IV, interleukin-6 and advanced glycation end products (AGEs), shown, in other studies, to be associated with sarcopenia²². Therefore, future studies using the EGWSOP2 classification in an older population should investigate these factors.

Conclusions and implications

Several biomarkers were associated with sarcopenia in this study, such as higher levels of rheumatoid factor, CRP, cystatin C, SHBG, GGT, ALP, total protein IGF-1, albumin, creatinine and SBP in both men and women. However, some of the associations differed by sex. Considering the EWGSOP2 updated its statement on the definition of sarcopenia in 2019, this study contributes to understanding better the biological profile of individuals with sarcopenia using an extensive list of biomarkers that are related to the development and outcomes of sarcopenia. However, as these findings were derived from cross-sectional data, future studies should focus on investigating changes in biomarkers prior to the development of sarcopenia

252 and after they have developed this condition. We cannot infer causality, but our results could
253 be used to identify biomarkers that are more likely to be abnormal in people with sarcopenia
254 and, therefore, potentially inform personalised treatment in individuals with this condition.

255 **Conflict of interest**

256 None to declare.

257

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Table 1. Biomarkers and their role in sarcopenia/ageing

Biomarker (unit)	Common classification	Role in sarcopenia/ageing
Albumin (g/L)	Nutritional biomarker	Nutritional marker of physical function impairment ²¹ . Associated with malnutrition which is highly correlated with sarcopenia in older ages ¹⁶ .
Sodium (urine), (mmol/L)	Nutritional and mineral balance biomarker	Along with calcium and potassium, sodium is important for healthy muscle, having a positive effect on muscle relaxation and in muscle function ³⁴ .
Total protein (g/L)	Nutritional biomarker	Lower levels are identified in underweight individuals. In older adults, it has been recognised as a useful biomarker of malnutrition even in people with chronic inflammation ³⁰ .
Calcium (mmol/L)	Bone and nutritional biomarker	Along with sodium and potassium, calcium is important for healthy muscle, having a positive effect on muscle relaxation and in muscle function ³⁴ .
Vitamin D (nmol/L)	Bone, nutritional and mineral balance biomarker	Linked to skeletal muscle mass in terms of cell contractility, proliferation and differentiation. Vitamin D has an active role in the control of calcium transportation and protein synthesis ¹⁷ .
Alkaline phosphatase (ALP), (U/L)	Liver biomarker	Higher levels of ALP are identified in older people. Although is it not a bone-specific biomarker, higher levels have been associated with bone disorders ³⁵ .
Alanine aminotransferase (ALT), (U/L)	Liver biomarker	Older adults report lower levels of ALT. An inverse association has been reported between frailty, sarcopenia and ALT levels of ALT ³⁶ . ALT has been recognised as a novel biomarker of ageing ³⁷ .
Aspartate aminotransferase (AST), (U/L)	Liver biomarker	Higher levels have been identified in individuals with nonalcoholic fatty liver disease. Individuals with low muscle mass and sarcopenia are more likely to have this disease ³⁸ .
Direct bilirubin (µmol/L)	Liver biomarker	Protein and energy metabolic disorders associated with age could increase the risk of low muscle mass and, therefore, sarcopenia. The latter has been highly related to inflammatory diseases, such as liver disease. Direct bilirubin is a biomarker of liver status ³⁹ .
Gamma-glutamyltransferase (GGT), (U/L)	Liver biomarker	GGT has been related to metabolic risk factors associated with sarcopenia mediated by insulin resistance or chronic inflammation. In this context, higher levels of GGT may indicate sarcopenia ¹⁹ .
Total bilirubin (µmol/L)	Liver Biomarker	Protein and energy metabolic disorders associated with age could increase the risk of low muscle mass and,

		therefore, sarcopenia. The latter has been highly related to inflammatory diseases, such as liver disease. Total bilirubin is a biomarker of liver status ³⁹ .
Apolipoprotein A (g/L)	Cardiovascular biomarker	Biomarker of cardiovascular function. Ageing is associated with a higher risk of cardiovascular disease (CVD), and people with CVD have a higher risk of sarcopenia ²⁹ .
Apolipoprotein B (g/L)	Cardiovascular biomarker	Biomarker of cardiovascular function. Ageing is associated with a higher risk of cardiovascular disease . and people with CVD have a higher risk of sarcopenia ²⁹ .
Cholesterol (mmol/L)	Cardiovascular biomarker	In older adults, it has been recognised as a useful biomarker of malnutrition even in people with chronic inflammation ³⁰ .
Diastolic blood pressure (DBP), (mm Hg)	Cardiovascular biomarker	Hypertension increase with ageing and has been associated with sarcopenia in previous studies ⁴⁰ .
HDL cholesterol (mmol/L)	Cardiovascular biomarker	Biomarker of cardiovascular function. Ageing is associated with a higher risk of CVD, and people with CVD have a higher risk of sarcopenia ²⁹ .
LDL direct (nmol/L)	Cardiovascular biomarker	Biomarker of cardiovascular function. Ageing is associated with a higher risk of CVD, and people with CVD have a higher risk of sarcopenia ²⁹ .
Lipoprotein A (nmol/L)	Cardiovascular biomarker	Biomarker of cardiovascular function. Ageing is associated with a higher risk of CVD, and people with CVD have a higher risk of sarcopenia ²⁹ .
Systolic blood pressure (SBP), (mm Hg)	Cardiovascular biomarker	Hypertension increase with ageing and has been associated with sarcopenia in previous studies ⁴⁰ .
Triglycerides (mmol/L)	Cardiovascular biomarker	Biomarker of cardiovascular function. Ageing is associated with a higher risk of CVD, and people with CVD have a higher risk of sarcopenia ²⁹ .
Glucose (mmol/L)	Diabetes biomarker	Nutritional marker. A decrease in muscle mass could increase insulin resistance risk since glucose is one of the primary sources of muscle ²¹ . Insulin stimulates protein synthesis, including the synthesis of muscle ²³ .
HbA1c (mmol/mol)	Diabetes biomarker	Nutritional marker ²¹ . This biomarker is associated with lower muscle strength. Higher levels are associated with type 2 diabetes. The latter is a risk factor for functional disability and mobility limitations ²³ .
Creatinine (µmol/L)	Renal biomarker	Associated with the total quantity of muscle mass. Serum levels are proportional to muscle mass ⁵ .
Cystatin C (mg/L)	Renal biomarker	Sensitive biomarker to estimate glomerular filtration rate. A previous study showed that the glomerular filtration rate (using Cystatic C) was associated with a higher risk of frailty ⁴¹ . The creatinine/Cystatin C ratio has been positively correlated with muscle mass ²⁷ .

Phosphate (mmol/L)	Renal biomarker	Higher levels of phosphate have been associated with lower levels of muscle mass. Hyperphosphatemia led to vascular calcification which leads to muscle impairment ⁴² .
Urate (μmol/L)	Renal biomarker	Salt derived from acid uric. Higher levels of acid uric have been associated with low relative muscle mass and sarcopenia ⁴³ .
Urea (mmol/L)	Renal biomarker	Biomarker of Catabolic condition. A decrease in muscle mass could increase the urea levels due to a protein breakdown ⁴⁴ .
IGF-1 (insulin-like growth factor 1), (nmol/L)	Endocrine biomarker	Anabolic hormone which stimulates muscle growth and regeneration ²¹ .
Oestradiol (pmol/L)	Endocrine biomarker	Important for muscle maintenance. The decline in sex hormones is associated with the age decline in muscle mass ⁴⁵ .
SHBG (nmol/L)	Endocrine biomarker	Important for muscle maintenance. The decline in sex hormones is associated with the age decline in muscle mass ⁴⁵ .
Testosterone (nmol/L)	Endocrine biomarker	Participation in the maintenance of muscle homeostasis. Associated with an anti-catabolic and anabolic effect on muscle ²¹ .
C-reactive protein (mg/L)	Inflammation biomarker	Lower levels are associated with muscle mass, strength and physical function impairment ²¹ .
Rheumatoid Factor (IU/ml)	Autoimmune biomarker	Higher levels are associated with autoimmune diseases, such as rheumatoid arthritis. Muscle mass is normally reduced in people with this disease ²⁵ .

μmol: micromole; nmol: nanomole; mmol: millimole; pmol: picomole; IU: international units; L: litre; g: gramme; mm Hg: millimetre of mercury.

Table 2. Characteristics of the population according to their sarcopenia status by sex.

	Women (209,722)		Men (186,935)	
	No sarcopenia *	Sarcopenia †	No sarcopenia *	Sarcopenia †
Socio-demographics				
Total, n (%)	207,782 (99.1)	1,990 (0.9)	186,823 (99.9)	112 (0.1)
Age (years), mean (SD)	55.8 (8.0)	62.9 (5.4)	56.5 (8.1)	60.6 (7.4)
Deprivation, n (%)				
Lower	73,906 (35.6)	637 (32.0)	67,754 (36.3)	19 (17.0)
Middle	72,245 (34.8)	716 (36.0)	63,734 (34.2)	31 (27.6)
Higher	61,402 (29.6)	636 (32.0)	55,107 (29.5)	62 (55.4)
Obesity-related markers				
Body weight (kg), mean (SD)	71.0 (13.0)	59.7 (8.5)	85.8 (13.6)	64.8 (11.2)
BMI, mean (SD)	26.7 (4.7)	23.1 (3.0)	27.6 (4.0)	20.9 (3.3)
BMI Categories, n (%)				
Underweight (<18.5 kg.m ⁻²)	1,185 (0.6)	103 (5.2)	295 (0.2)	27 (24.1)
Normal weight (18.5-24.9 kg.m ⁻²)	84,107 (40.6)	1,372 (68.9)	47,624 (25.6)	73 (65.2)
Overweight (25.0 to 29.9 kg.m ⁻²)	78,947 (38.1)	486 (24.4)	94,606 (50.8)	12 (10.7)
Obese (≥30.0 kg.m ⁻²)	42,951 (20.7)	29 (1.5)	43,741 (23.5)	0
Waist Circumference (cm)	83.7 (11.7)	78.5 (9.0)	96.3 (10.7)	86.2 (9.7)
Central obesity, n (%)	69,057 (33.3)	316 (15.9)	52,933 (28.4)	7 (6.2)
% Body fat, mean (SD)	36.0 (6.7)	36.8 (6.1)	24.9 (5.6)	26.0 (7.4)
Fitness and Lifestyle				
Total PA (MET.h ⁻¹ .week ⁻¹), mean (SD)	2,754.5 (2,861.2)	2,482.7 (2,623.1)	3,306.6 (3,674.8)	2,385.6 (3,487.5)
Cardiorespiratory fitness (MET), mean (SD)	8.7 (2.3)	7.6 (1.7)	11.0 (2.7)	8.8 (2.5)
TV viewing (h.day ⁻¹), mean (SD)	2.6 (1.5)	3.3 (1.8)	2.7 (1.5)	3.6 (2.4)
Total Sedentary behaviour (h.day ⁻¹), mean (SD)	4.6 (1.9)	4.7 (2.1)	5.4 (2.4)	5.1 (2.9)
Smoking status, n (%)				
Never	122,692 (59.4)	1,145 (57.9)	92,962 (49.9)	48 (42.9)
Previous	66,657 (32.2)	633 (32.0)	71,952 (38.6)	29 (25.9)
Current	17,542 (8.4)	201 (10.1)	21,335 (11.5)	35 (31.2)

* No sarcopenia was defined as people without sarcopenia and any physical capability marker altered.

† Sarcopenia represents both sarcopenia and severe sarcopenia.

BMI: body mass index; PA: physical activity; SD: standard deviation; h: hour; MET: metabolic-equivalent-task.

Figure 1. Association between biomarkers and sarcopenia in women.

Data presented as β -coefficient and its 95% CI. No sarcopenia was considered as the reference group. All analyses were adjusted for age, deprivation, smoking status, sleep duration, discretionary sedentary time, waist circumference and dietary intake (alcohol, red meat and processed meat intake. Biomarkers were standardised and expressed as standard deviation.

Figure 2. Association between biomarkers and sarcopenia in men.

Data presented as β -coefficient and its 95% CI. No sarcopenia was considered as the reference group. All analyses were adjusted for age, deprivation, smoking status, sleep duration, discretionary sedentary time, waist circumference and dietary intake (alcohol, red meat and processed meat intake. Biomarkers were standardised and expressed as standard deviation.