Cross-sectional associations of objectively measured physical activity and sedentary time with sarcopenia and sarcopenic obesity in older men

Daniel A. Aggio MSc, a,b,*, Claudio Sartini MSc, a,b, Olia Papacosta MSc, a, Lucy T. Lennon MSc, a, Sarah Ash, a, Peter H. Whincup PhD, FRCP, FFPH b, S. Goya Wannamethee PhD, FFPH a,b, Barbara J. Jefferis MSc, PhD a,b

a UCL Department of Primary Care & Population Health, UCL Medical School, Rowland Hill Street, London NW3 2PF, UK
b UCL Physical Activity Research Group, UK
b Population Health Research Institute, St George’s University of London, Cranmer Terrace, London. SW17 0RE, UK

Keywords:
Muscle mass
Sarcopenic obesity
Sarcopenia
Physical activity

Article history:
Received 1 June 2016
Received in revised form 23 August 2016
Accepted 25 August 2016
Available online 26 August 2016

1. Introduction

Normal aging involves important changes to body composition, including decreased muscle mass and increased fat mass (Zamboni et al., 2008). The age-related loss of muscle mass combined with loss of muscular strength and/or function is referred to as sarcopenia and occurs in up to 25% of community-dwelling older adults (Cruz-Jentoft et al., 2014). Sarcopenia is associated with an increased risk of frailty, disability and mortality in older adults (Waters et al., 2010; Landi et al., 2013). The occurrence of sarcopenia and obesity, defined as sarcopenic obesity, may heighten effects on health outcomes (Atkins et al., 2014a; Dominguez & Barbagallo, 2007; Zamboni et al., 2008). As physical activity (PA) is associated with lower fat mass and increased muscular strength and function (Bann et al., 2015; Shephard et al., 2013; Kuh et al., 2005), it may significantly reduce the risk of sarcopenia and sarcopenic obesity, making it one of the most important modifiable risk factors. Resistance training is particularly beneficial for improving muscular strength and function in the elderly (Cruz-Jentoft et al., 2014).

A number of cross-sectional and longitudinal studies have investigated the association between PA and sarcopenia using predominantly self-reported measures of PA. These studies have consistently shown that higher overall levels of PA are associated with a reduced risk of sarcopenia and sarcopenic obesity (Ryu et al., 2013; Kim et al., 2013; Atkins et al., 2014a; Hughes et al., 2001). One study reported that the risk of sarcopenia and sarcopenic obesity can be reduced by up to 74% and 73% in regularly active men, respectively (Ryu et al., 2013). Although self-report measures provide useful information on context of PA, objective measures allow more reliable estimates of volume and intensity. While studies using objective measures are few (Shephard et al., 2013; Bann et al., 2014; Park et al., 2010) they appear to confirm previous findings using self-reported PA. A recent prospective study showed that high levels of objectively measured walking approximately halved the risk of sarcopenia (Shephard et al., 2013). The authors also observed additional reductions in risk with PA at a moderate-to-vigorous intensity. Other studies report positive associations between PA and the individual components of sarcopenia, including muscle mass (Abe et al., 2012; Bann et al., 2014), muscular strength and function...
Valid data required

100

threshold values for older adults of "ute (CPM). Time (minutes per day) spent sedentary and in different in-

axis were integrated into 60 s epochs and used to derive counts per min-

when the accelerometer was not being worn. Raw data from the vertical

30 min before and after that interval, allowing for accidental movement

si

(Wannamethee et al., 2002). Men were grouped as inactive, occasional

participation in sports. A total PA score was derived based on the fre-

often they make journeys by foot or by bike, recreational activities and

3.2. Self-reported PA data

Participants self-reported their habitual PA levels, including how

frequent sporting exercise or frequent sporting exercise plus other recre-

ational activities). An additional question asked respondents to report

their engagement in muscular strength/endurance training. This includ-

lifing weights, doing push-ups and using exercise machines. Particip-

ants were classified as participating or not participating in muscular

strength and endurance training.

Participants also completed a six-item version of the Duke Activity

Status Index (DASI), which was used as a measure of general fitness. The

DASI was developed to measure functional capacity and strongly

correlates with peak oxygen uptake (r = 0.80) (Halmy et al., 1989). The

index comprised of questions regarding ability to participate in six

activities of increasing intensity, weighted according to the MET value

for each activity. A total score was calculated by adding the weighted

scores for the six items.

4. Outcome measures

4.1. Anthropometric measures

Height (cm), weight (kg), waist circumference (WC) (cm), mid-

upper arm circumference and triceps skinfold thickness (mm) were

measured as previously described (Wannamethee et al., 2007). WC

was used as a measure of obesity using a sex-specific cut point

(A02 cm) (Anon, 1998). Muscle mass was derived from the mid-

upper arm muscle circumference (MAMC) using the formula mid-

upper arm circumference − (0.3142 × triceps skinfold thickness)

(Miller et al., 2002).

4.2. Physical function and strength

Gait speed (m/s) was derived from a 3-metre walking test and was

used as a measure of physical function. Grip strength (kg) was used as

a marker of muscular strength and was measured using a Jamar Hydramui-

lic Hand Dynamometer. Participants had three attempts for each hand

and the highest score was used.

4.3. Definitions of sarcopenia and sarcopenic obesity

Sarcopenia and severe sarcopenia were defined using the European

Working Group on Sarcopenia in Older People (EWGSP) definition

(Cruz-Jentoft et al., 2010). Both conditions required (i) low muscle

mass (participants in the lowest two-fifths of the MAMC distribution

were classified as having low muscle mass) and either (ii) low grip

strength (<30 kg) or (iii) low gait speed (≤0.8 m/s) (Cruz-Jentoft et al.,

2010). Severe sarcopenia required the presence of all three conditions

(Cruz-Jentoft et al., 2010). To determine sarcopenia-obesity groups,

men with sarcopenia and severe sarcopenia were collapsed into an

overall sarcopenic group. They were then categorised into four groups:

non-sarcopenic non-obese (WC ≤102 cm, not sarcopenic), sarcopenic

non-obese (WC ≤102 cm, sarcopenic), non-sarcopenic obese (WC

>102 cm, not sarcopenic), or sarcopenic obese (WC >102 cm, sarcopenic).

5. Covariates

Men self-reported the following: social class, derived from longest

held occupation; doctor diagnosis of medical conditions including angi-

na, heart attack, heart failure, other heart conditions, bronchitis, depres-

sion, emphysema, osteoporosis, Parkinson’s disease, cancer (excluding

skin cancers), arthritis and stroke; cigarette smoking habits and alcohol

intake. Number of medical conditions was categorised as low (<3) or

high (≥3) according to the above medical conditions. Cigarette smoking

was classified as current or recent smokers (given up in the last ten

years), ex-smokers (gave up >10 years ago) and never smokers. Alcohol

intake was classified as high (>15) or low (≤15 units of alcohol per

week).
6. Statistical analysis

Descriptive statistics of demographic, physical health and PA variables selected a priori were calculated firstly for sarcopenia groups and then for sarcopenic obese groups. Differences between groups were examined using one-way ANOVA and chi-square tests. Mean and standard deviation (SD) of PA levels were calculated for quintiles of MAMC, WC, grip strength and gait speed. Quintiles were generated based on participants with available data on the variable of interest after excluding participants without valid accelerometer data and those living in care homes (sample size, n = 1521). Tests for linear trend were conducted by entering each component of sarcopenia/sarcopenic obesity (muscle mass, MAMC [cm]; obesity, WC [cm]; physical performance, gait speed [m/s]; muscular strength, grip strength [kg]) continuously into regression models, adjusting for age and WC. Multinomial logistic regression was used to examine the association between PA and sarcopenia categories. Exposure measures were objectively measured PA variables (sedentary time [min/day], number of breaks in sedentary time per hour, LPA [min/day], MVPA [min/day]) and strength training (y/n). The primary outcomes were (i) sarcopenia, (ii) severe sarcopenia and (iii) sarcopenic obesity. The “non-sarcopenic” and “non-sarcopenic non-obese” groups were selected as reference categories in respective analyses. In an additional analysis including just obese men, we compared the non-sarcopenic obese group with the sarcopenic obese group by selecting the former as the reference category. Analyses were initially adjusted for age (years), wear time, season and region (model 1); and then for occupational social class, number of medical conditions, smoking, alcohol and height (model 2). Model 2 also controlled for WC in analyses investigating risk of sarcopenia and severe sarcopenia. Final models (model 3) also controlled for the other intensities of PA i.e. MVPA was included as a covariate when examining associations of sedentary time, breaks in sedentary time and LPA. All analyses were carried out using STATA version 12 (Stata Corp, College Station, TX).

6.1. Sensitivity analyses

We repeated models excluding men with heart attack, heart failure or stroke (n = 206). MVPA was positively skewed so we repeated models using square-root-transformed MVPA to normalise the distribution. We also repeated analyses using self-reported PA and DASI fitness scores as exposures.

7. Results

1655/3137 (52.8%) of survivors agreed to take part in the physical examination and wear an accelerometer. After excluding men who were confined to a wheelchair or resident in a care home (n = 7), 1521 (48.5%) men provided valid PA data, of whom 1286 (41.0%) had complete data from the physical examination, functional tests and questionnaire (Fig. 1). Participants not attending this wave of data collection based on participants with available data on the variable of interest after excluding participants without valid accelerometer data and those living in care homes (sample size, n = 1521). Tests for linear trend were conducted by entering each component of sarcopenia/sarcopenic obesity (muscle mass, MAMC [cm]; obesity, WC [cm]; physical performance, gait speed [m/s]; muscular strength, grip strength [kg]) continuously into regression models, adjusting for age and WC. Multinomial logistic regression was used to examine the association between PA and sarcopenia categories. Exposure measures were objectively measured PA variables (sedentary time [min/day], number of breaks in sedentary time per hour, LPA [min/day], MVPA [min/day]) and strength training (y/n). The primary outcomes were (i) sarcopenia, (ii) severe sarcopenia and (iii) sarcopenic obesity. The “non-sarcopenic” and “non-sarcopenic non-obese” groups were selected as reference categories in respective analyses. In an additional analysis including just obese men, we compared the non-sarcopenic obese group with the sarcopenic obese group by selecting the former as the reference category. Analyses were initially adjusted for age (years), wear time, season and region (model 1); and then for occupational social class, number of medical conditions, smoking, alcohol and height (model 2). Model 2 also controlled for WC in analyses investigating risk of sarcopenia and severe sarcopenia. Final models (model 3) also controlled for the other intensities of PA i.e. MVPA was included as a covariate when examining associations of sedentary time, breaks in sedentary time and LPA. All analyses were carried out using STATA version 12 (Stata Corp, College Station, TX).

Table 3 presents participant PA levels by quintiles of MAMC, WC, grip strength and gait speed. None of the PA variables were associated with MAMC after adjustments. WC was inversely associated with MVPA, LPA, breaks in sedentary time and participation in muscle strengthening/endurance exercises and positively associated with sedentary time after adjusting for age. Gait speed and grip strength were positively associated with MVPA and inversely associated with sedentary time. Gait speed was also positively associated with LPA and breaks in sedentary time. Participation in muscle strengthening/endurance exercises was associated with higher grip strength but this did not remain significant after adjusting for WC and age.

Table 4 presents the risk of sarcopenic obesity categories by PA levels. Sedentary time was associated with an increased risk of sarcopenic obesity independent of MVPA. Sedentary breaks, LPA and MVPA were associated with reduced risk of sarcopenic obesity in final adjusted models. Similar associations were observed between PA variables and the risk of non-sarcopenic obesity. Strength training was associated with a reduced risk of non-sarcopenic obesity and non-obese sarcopenia, although the association with non-obese sarcopenia was of borderline significance (p = 0.06). Associations between strength training and sarcopenic obesity were also uninterpretable due to low numbers participating in strength training. In an additional analysis including just obese men, the non-sarcopenic obese category was selected as the reference category and compared with the sarcopenic obese group (Supplementary Table 1). After adjusting for social, health and lifestyle factors, sedentary time was associated with an increased risk of sarcopenic obesity (RR 1.16, 95% confidence interval [CI] 1.02, 1.33) and MVPA was associated with a reduced risk (RR 0.60, 95% CI 0.39, 0.95). Associations were not significant after adjusting for other PA intensities.

7.1. Sensitivity analyses

Excluding men with heart attack, heart failure or stroke and using square-root-transformed MVPA did not alter our conclusions (data not shown). Self-reported PA and DASI fitness scores were also associated with severe sarcopenia, non-sarcopenic obesity and sarcopenic obesity. They were also associated with the sarcopenic and sarcopenic non-obese groups in final adjusted models (Supplementary Tables 2-3).

8. Discussion

In this sample of free-living older British men, MVPA was associated with a reduced risk of severe sarcopenia, independent of sedentary time and WC. Similarly, MVPA and to a lesser extent LPA and sedentary breaks were independently associated with a reduced risk of sarcopenic obesity. Conversely, sedentary time was associated with an increased...
risk of sarcopenic obesity independent of MVPA. Analyses between PA and the individual components of sarcopenia and sarcopenic obesity showed that PA was not associated with muscle mass alone, suggesting that PA may be more important for preserving a healthy weight, physical performance and muscular strength in older men.

Prevalence of sarcopenia and sarcopenic obesity was lower than that of previous studies with this cohort when they were younger (Atkins et al., 2014a). However, the prevalence of sarcopenia and sarcopenic obesity was comparable with previous waves data when we used the same definition (data not shown) (Atkins et al., 2014a), suggesting that the discrepancies mainly reflect our use of the EWGSOP diagnostic criteria for sarcopenia (Cruz-Jentoft et al., 2010), including objective measures of gait speed and grip strength that were previously unavailable. Nevertheless, sarcopenia was still common in the present sample and comparable with the prevalence in other cohorts of a similar age (Kim et al., 2013; Gianoudis et al., 2015).

To our knowledge, this is the first study to explore associations of PA with sarcopenia, severe sarcopenia and sarcopenic obesity using objectively measured rather than self-reported PA. Higher MVPA was associated with significant reductions in the risk of severe sarcopenia and sarcopenic obesity. Our conclusions appear consistent with previous studies using self-report and objective measures of PA (Ryu et al., 2013; Atkins et al., 2014b; Shephard et al., 2013). In our study, each additional 30 min per day of MVPA was associated with a 47% reduction in severe sarcopenia risk. This is comparable to a recent longitudinal study also using objectively measured PA; older Japanese men taking >9000 steps per day had approximately half the risk of sarcopenia compared to men taking <6700, with additional reduction in risk for PA >3 METS (Shephard et al., 2013). However, direct comparisons between these studies are difficult due to the different definitions used for sarcopenia and different devices used to measure PA. A number of studies defining sarcopenia with muscle mass alone have demonstrated an association between PA and sarcopenia (Atkins et al., 2014b; Ryu et al., 2013; Shephard et al., 2013). In this population, only when muscle mass was combined with low muscular strength and low physical performance (severe sarcopenia) were associations observed. Furthermore, none of the PA variables were associated with muscle mass alone, but there were associations with gait speed, grip strength and WC. Our findings are consistent with a recent study that also showed no association between PA and muscle mass in men (Kim et al., 2015) and a number of other studies showing positive associations between PA and muscular strength in older populations (Hamer & Stamatakis, 2013; Kuh et al., 2005). Potentially PA may be more important for preserving muscular strength and physical function than muscle mass in elderly men. Moreover, there is a body of evidence suggesting that muscular strength is more important than muscle mass for cardiometabolic health and physical function (Stephen & Janssen, 2009; Visser et al., 2000). An alternative explanation may be that participants who had sarcopenia at previous waves are more likely to have dropped out of the study due to the increased risk of mortality, as previously reported in this cohort (Atkins et al., 2014a). Thus our sample may be unrepresentative of the lower end of muscle mass distribution and therefore reducing our power to detect associations between physical activity and muscle mass.
### Table 1
Participant characteristics of subjects with sarcopenia, severe sarcopenia and without sarcopenia defined according to MAMC, gait speed and grip strength – BRHS, 2010–12.

| Characteristic                                      | N   | Non-sarcopenic  | Sarcopenia       | Severe sarcopenia | Between group differences (p value) |
|----------------------------------------------------|-----|----------------|------------------|-------------------|-----------------------------------|
| N, (%, n)                                           | 1286| 80.3% (1013)    | 14.2% (183)      | 5.4% (70)         |                                   |
| **Sociodemographics**                              |     |                |                  |                   |                                   |
| Age, mean ± SD                                      | 1286| 77.6 ± 4.1      | 79.7 ± 4.7       | 83.1 ± 5.2        | p < 0.001                         |
| Current/recent smoker, (%, n)                       | 1286| 7.6 (78)        | 9.8 (18)         | 7.1 (5)           | 0.556                             |
| Moderate or heavy drinkers, (%, n)                  | 1286| 14.0 (145)      | 9.8 (18)         | 15.7 (11)         | 0.266                             |
| Manual workers, (%, n)                              | 1286| 44.8 (463)      | 44.8 (82)        | 57.1 (40)         | 0.255                             |
| **Physical health**                                 |     |                |                  |                   |                                   |
| Breaks in sedentary time per hour                  |     |                |                  |                   |                                   |
| Time sedentary (min/day)                            | 1286| 1280.6 (1279.4) | 1276.5 (1274.6) | 1284.5 (1282.6)   | p = 0.001                         |
| Time sedentary (mins per day)                       | 1286| 611.0 (606.0, 615.7) | 614.1 (602.1, 626.1) | 650.6 (632.0, 669.2) | p < 0.001                         |
| Time in LPA (min/day)                               | 1286| 201.9 (198.1, 205.6) | 196.4 (187.1, 205.7) | 169.2 (152.5, 185.9) | p < 0.001                         |
| Time in MVPA (min/day)                              | 1286| 858.9 (853.8, 864.0) | 850.4 (840.7, 860.1) | 849.3 (843.0, 855.6) | p < 0.001                         |
| Participation in muscle strengthening/endurance exercises, (%, n) | 1090| 12.9% (115)     | 15.4% (11)      | 17.5% (32)        | 0.105                             |
| **Physical health**                                 |     |                |                  |                   |                                   |
| Chronic conditions ≥ 3, (%, n)                      | 1286| 11.5 (119)      | 17.5 (32)        | 16.8 (33)         | p < 0.05                          |

### Table 2
Participant characteristics according to Sarcopenic Obesity Groups – BRHS, 2010–12.

| Characteristic                                      | N   | Non-sarcopenic non-obese | Sarcopenic non-obese | Non-sarcopenic obese | Sarcopenic obese | Between group differences (p value) |
|----------------------------------------------------|-----|--------------------------|----------------------|---------------------|----------------|-----------------------------------|
| N, (%, n)                                           | 1286| 46.0% (591)              | 14.7% (189)         | 34.4% (442)         | 5.0% (64)      |                                   |
| **Sociodemographics**                              |     |                          |                      |                     |                |                                   |
| Age, mean ± SD                                      | 1286| 77.4 ± 4.7               | 80.8 ± 5.2          | 77.5 ± 4.2          | 80.0 ± 4.6    | p < 0.001                         |
| Current/recent smoker, (%, n)                       | 1286| 6.8 (40)                 | 9.0 (17)            | 8.6 (38)           | 9.4 (6)       | 0.005                             |
| Moderate or heavy drinkers, (%, n)                  | 1286| 12.9 (76)                | 10.1 (19)           | 15.6 (69)          | 15.6 (10)     | 0.255                             |
| Manual workers, (%, n)                              | 1286| 40.8 (241)               | 41.3 (78)           | 50.2 (222)         | 68.8 (44)     | p < 0.001                         |
| **Physical health**                                 |     |                          |                      |                     |                |                                   |
| Breaks in sedentary time per hour                  |     |                          |                      |                     |                |                                   |
| Time sedentary (min/day)                            | 1286| 7.3 (7.2, 7.4)           | 7.3 (7.0, 7.6)     | 6.6 (6.0, 7.1)     | 7.6 (6.4)     | p = 0.05                          |
| Time in LPA (min/day)                               | 1286| 850.8 (858.0, 858.8)     | 848.4 (833.3, 858.5) | 839.5 (821.1, 857.9) | 0.105         |
| Time in MVPA (min/day)                              | 1286| 15.6 (80)                | 17.5 (33)           | 15.4 (68)          | 18.8 (12)     | p < 0.05                          |
| **Physical health**                                 |     |                          |                      |                     |                |                                   |
| Chronic conditions ≥ 3, (%, n)                      | 1286| 15.4 (91)                | 20.1 (38)           | 15.6 (69)          | 12.5 (8)      | 0.368                             |
| Height (m), mean ± SD                               | 1286| 171.5 ± 6.2              | 169.0 ± 7.0         | 173.0 ± 6.5        | 170.0 ± 6.3   | p < 0.001                         |
| Weight (kg), mean ± SD                              | 1286| 74.4 ± 7.3               | 68.0 ± 8.5          | 90.9 ± 10.2        | 86.6 ± 8.7    | p < 0.001                         |
| BMI (kg/m²), mean ± SD                              | 1286| 25.3 ± 2.2               | 23.8 ± 2.5          | 30.4 ± 3.2         | 30.0 ± 2.8    | p < 0.001                         |
| Waist circumference (cm), mean ± SD                 | 1286| 93.6 ± 6.1               | 90.6 ± 7.1          | 110.6 ± 7.0        | 109.3 ± 6.4   | p < 0.001                         |
| Hand grip (kg), mean ± SD                           | 1286| 32.5 ± 9.7               | 26.8 ± 10.2         | 32.0 ± 10.1        | 27.2 ± 7.9    | p < 0.001                         |
| Gait speed (m/s), mean ± SD                         | 1286| 0.99 ± 0.2               | 0.79 ± 0.2          | 0.91 ± 0.2         | 0.72 ± 0.2    | p < 0.001                         |
| Chronic conditions ≥ 3, (%, n)                      | 1286| 8.6 (51)                 | 17.5 (33)           | 15.4 (68)          | 18.8 (12)     | p < 0.05                          |

### CHD, coronary heart disease; BMI, body mass index; MAMC, mid-upper arm muscle circumference; MVPA, moderate-to-vigorous physical activity; LPA, light physical activity; CPM, counts per minute.

a $x^2$ for percentages, analysis of variance for means.
b Men with CHD consisted of men reporting a doctor diagnosis of a heart attack heart failure or stroke.
c Smaller sample size due to lower response on self-reported data.
| Quintiles of sarcopenia and sarcopenic obesity components | MAMC (cm) | ≤22.11 (n = 258) | 22.11–24.21 (n = 264) | 24.21–25.74 (n = 254) | 25.74–27.34 (n = 253) | ≥27.34 (n = 257) |
|----------------------------------------------------------|-----------|------------------|---------------------|---------------------|---------------------|-------------------|
| Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) | B (95% CI) | p value for trend (unadjusted) | B (95% CI) | p value for trend (unadjusted) | B (95% CI) | p value for trend (unadjusted) |
| Time sedentary (min/day) | 611.3 (84.5) 614.3 (87.5) 611.3 (80.0) 616.7 (78.9) 614.9 (79.5) | 0.02 (−0.04, 0.08) | 0.580 | −0.01 (−0.06, 0.05) | 0.821 |
| Breaks in sedentary time/hour | 7.5 (2.1) 7.4 (2.1) 7.3 (2.0) 7.1 (1.9) 7.2 (2.0) | −0.12 (−0.20, −0.03) | <0.05 | −0.02 (−0.10, 0.05) | 0.558 |
| Time in LPA (min/day) | 200.3 (46.0) 200.2 (60.1) 194.6 (61.0) 201.2 (62.9) | −0.01 (−0.07, 0.06) | 0.474 | 0.04 (−0.04, 0.11) | 0.351 |
| Participation in muscle strengthening/endurance exercises (%) | 12.3 12.2 12.9 10.2 13.8 | 0.15 (−0.38, 0.09) | 0.574 | 0.17 (−0.32, 0.05) | 0.503 |
| Waist circumference (cm) | ≤91.15 (n = 264) | | | | | |
| Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) | B (95% CI) | p value for trend (unadjusted) | B (95% CI) | p value for trend (unadjusted) | B (95% CI) | p value for trend (unadjusted) |
| Time sedentary (min/day) | 613.4 (87.5) 619.0 (88.7) 621.5 (80.7) 636.5 (75.2) | 0.64 (0.42, 0.86) | <0.001 | 0.74 (0.52, 0.96) | <0.001 |
| Breaks in sedentary time/hour | 7.4 (2.0) 7.4 (2.0) 7.1 (1.9) 6.4 (1.8) | −1.37 (−1.66, −1.09) | <0.001 | −1.51 (−1.80, −1.22) | <0.001 |
| Time in LPA (min/day) | 205.4 (61.8) 199.0 (63.1) 173.8 (55.8) | −1.13 (−1.41, −0.85) | <0.001 | −1.29 (−1.57, −1.01) | <0.001 |
| Participation in muscle strengthening/endurance exercises (%) | 44.6 (52.0) 37.7 (37.1) 22.1 (32.8) | −1.03 (−1.26, −0.80) | <0.001 | −1.36 (−1.60, −1.11) | <0.001 |
| Gait speed (m/s) | ≤0.73 (n = 249) | | | | | |
| Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) | B (95% CI) | p value for trend (unadjusted) | B (95% CI) | p value for trend (unadjusted) | B (95% CI) | p value for trend (unadjusted) |
| Time sedentary (min/day) | 624.2 (81.4) 613.4 (83.8) 603.2 (71.0) 590.2 (76.4) | −0.02 (−0.02, −0.01) | <0.001 | −0.01 (−0.02, −0.01) | <0.001 |
| Breaks in sedentary time/hour | 7.0 (2.0) 7.4 (1.8) 7.7 (1.9) 7.8 (2.0) | −0.14 (0.02, 0.03) | <0.001 | 0.02 (0.01, 0.02) | <0.001 |
| Time in LPA (min/day) | 203.5 (55.9) 211.1 (57.7) 202.2 (56.4) | 0.03 (0.03, 0.04) | <0.001 | 0.02 (0.02, 0.03) | <0.001 |
| Participation in muscle strengthening/endurance exercises (%) | 46.6 (52.0) 37.6 (40.9) 47.7 (36.4) | 0.04 (0.03, 0.04) | <0.001 | 0.03 (0.02, 0.03) | <0.001 |
| Grip strength (kg) | ≤22 (n = 253) | | | | | |
| Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) Mean (SD) | B (95% CI) | p value for trend (unadjusted) | B (95% CI) | p value for trend (unadjusted) | B (95% CI) | p value for trend (unadjusted) |
| Time sedentary (min/day) | 622.8 (80.1) 607.8 (78.8) 610.8 (81.5) 599.2 (71.7) | −0.35 (−0.56, −0.14) | <0.05 | −0.20 (−0.41, 0.01) | 0.062 |
| Breaks in sedentary time/hour | 7.1 (2.1) 7.1 (2.0) 7.4 (1.9) 7.5 (1.9) | 0.31 (0.03, 0.58) | <0.05 | 0.14 (−0.14, 0.42) | 0.329 |
| Time in LPA (min/day) | 193.8 (63.8) 202.2 (62.3) 202.6 (60.7) 212.1 (61.5) | 0.41 (0.15, 0.67) | <0.05 | 0.21 (−0.06, 0.48) | 0.125 |
| Participation in muscle strengthening/endurance exercises (%) | 249 (37.9) 35.4 (41.6) 37.5 (38.6) 46.2 (39.1) | 0.79 (0.57, 1.00) | <0.001 | 0.58 (0.34, 0.82) | <0.001 |

MAMC, moderate-to-vigorous physical activity; CPM, counts per minute; LPA, light physical activity.

\(^a\) Linear trend regression coefficient. For regression analyses time sedentary, in light and in MVPA was converted to units of 30 min/day.

\(^b\) Values expressed as median and interquartile range; MVPA was transformed by square rooting for regression analyses.
Models 1 and 2 included only one activity variable as an exposure per regression whereas model 3 also controlled for other intensities of physical activity.

MVPA, moderate-to-vigorous physical activity; LPA, light physical activity; CPM, counts per minute; RR, risk ratio.

For the first time we demonstrated an association between objectively measured PA and a reduced risk of sarcopenic obesity. This is consistent with studies using self-reported PA (Ryu et al., 2013) and fitness measures (Pedrero-Chamizo et al., 2015). Notably, we showed that even LPA and sedentary breaks were associated with a reduced risk of sarcopenic obesity, which appears to be driven by higher gait speed and lower WC. Higher sedentary time was associated with increased risk of sarcopenic obesity, independent of MVPA, which is broadly consistent with other studies that have shown independent associations between sedentary behaviour with obesity (Healy et al., 2008; Jakes et al., 2003) and sarcopenia (Gianoudis et al., 2015) as individual outcomes. As expected, PA was strongly associated with a reduced risk of obesity (Atkins et al., 2014a). PA was also associated with a reduced risk of sarcopenic obesity when compared to those with just obesity, suggesting that the presence of both conditions heightens associations with PA. Importantly, the ‘non-sarcopenic non-obese’ reference group demonstrate healthier behaviours than the ‘non-sarcopenic’ reference group, which may explain why associations between PA and sarcopenic obesity are more pronounced than those with sarcopenia and severe sarcopenia.

### Tables

#### Table 4

Multinomial logistic regression analysis of sarcopenia and severe sarcopenia risk according to physical activity levels (reference: non-sarcopenic group) – BRHS, 2010–12.

|                         | Non-sarcopenic | Sarcopenic | Severe sarcopenic |
|-------------------------|----------------|------------|-------------------|
|                         | RR (95% CI)    | RR (95% CI)| RR (95% CI)       |
| Model 1*                |                |            |                   |
| Sedentary time (30 min/day) | 1.00          | 0.99 (0.92, 1.05) | 1.19 (1.06, 1.35) |
| Breaks in sedentary time (breaks/hour) | 1.00          | 1.05 (0.96, 1.14) | 0.92 (0.80, 1.05) |
| Light PA time (30 min/day) | 1.00          | 1.02 (0.93, 1.11) | 0.85 (0.73, 0.99) |
| MVPA time (30 min/day) | 1.00          | 1.03 (0.87, 1.21) | 0.49 (0.32, 0.76) |
| Strength training (no/yes)* | 1.00          | 0.89 (0.50, 1.59) |                   |
| Model 2**               |                |            |                   |
| Sedentary time (30 min/day) | 1.00          | 1.03 (0.96, 1.11) | 1.22 (1.07, 1.38) |
| Breaks in sedentary time (breaks/hour) | 1.00          | 0.97 (0.89, 1.06) | 0.88 (0.76, 1.02) |
| Light PA time (30 min/day) | 1.00          | 0.98 (0.89, 1.07) | 0.84 (0.72, 0.98) |
| MVPA time (30 min/day) | 1.00          | 0.92 (0.77, 1.10) | 0.45 (0.29, 0.72) |
| Strength training (no/yes)* | 1.00          | 0.82 (0.45, 1.50) |                   |
| Model 3                 |                |            |                   |
| Sedentary time (30 min/day)** | 1.00          | 1.01 (0.92, 1.12) | 1.07 (0.91, 1.26) |
| Breaks in sedentary time (breaks/hour)** | 1.00          | 0.99 (0.90, 1.08) | 0.96 (0.83, 1.12) |
| Light PA time (30 min/day)** | 1.00          | 0.99 (0.90, 1.09) | 0.93 (0.79, 1.10) |
| MVPA time (30 min/day)** | 1.00          | 0.93 (0.73, 1.19) | 0.53 (0.30, 0.93) |

Models 1 and 2 included only one activity variable as an exposure per regression whereas model 3 also controlled for other intensities of physical activity.

MVPA, moderate-to-vigorous physical activity; LPA, light physical activity; CPM, counts per minute; RR, risk ratio.

* Model 1 adjusted for age, wear time, season and region.

** Model 2 additionally adjusted for social class, number of chronic conditions, smoking, alcohol, height and waist circumference.

* Model 3 further adjusted for MVPA.

* Model 3 further adjusted for sedentary time.

* Risk ratios were not interpretable due to low participation in strength training in the severe sarcopenic group.

#### Table 5

Multinomial logistic regression analysis of sarcopenia risk according to physical activity levels (reference: non-sarcopenic non-obese group) – BRHS, 2010–12.

|                         | Non-sarcopenic non-obese | Sarcopenic non-obese | Non-sarcopenic obese | Sarcopenic obese |
|-------------------------|--------------------------|----------------------|----------------------|------------------|
|                         | RR (95% CI)              | RR (95% CI)          | RR (95% CI)          | RR (95% CI)      |
| Model 1*                |                          |                      |                      |                  |
| Sedentary time (30 min/day) | 1.00                    | 1.04 (0.96, 1.12)    | 1.23 (1.16, 1.30)    | 1.43 (1.26, 1.62) |
| Breaks in sedentary time (breaks/hour) | 1.00                    | 1.00 (0.91, 1.09)    | 0.79 (0.74, 0.85)    | 0.71 (0.61, 0.83) |
| Light PA time (30 min/day) | 1.00                    | 0.97 (0.89, 1.07)    | 0.83 (0.77, 0.89)    | 0.71 (0.60, 0.82) |
| MVPA time (30 min/day) | 1.00                    | 0.91 (0.76, 1.09)    | 0.58 (0.50, 0.67)    | 0.33 (0.21, 0.51) |
| Strength training (no/yes)* | 1.00                    | 0.50 (0.26, 0.99)    | 0.56 (0.36, 0.85)    |                  |
| Model 2**               |                          |                      |                      |                  |
| Sedentary time (30 min/day)** | 1.00                    | 1.02 (0.95, 1.10)    | 1.22 (1.16, 1.30)    | 1.40 (1.23, 1.59) |
| Breaks in sedentary time (breaks/hour)** | 1.00                    | 1.00 (0.92, 1.09)    | 0.80 (0.74, 0.86)    | 0.73 (0.63, 0.85) |
| Light PA time (30 min/day)** | 1.00                    | 0.99 (0.90, 1.09)    | 0.83 (0.77, 0.89)    | 0.73 (0.62, 0.85) |
| MVPA time (30 min/day)** | 1.00                    | 0.95 (0.79, 1.13)    | 0.58 (0.50, 0.68)    | 0.34 (0.21, 0.53) |
| Strength training (no/yes)** | 1.00                    | 0.52 (0.26, 1.03)    | 0.54 (0.35, 0.83)    |                  |
| Model 3                 |                          |                      |                      |                  |
| Sedentary time (30 min/day)** | 1.00                    | 1.00 (0.90, 1.11)    | 1.11 (1.02, 1.20)    | 1.18 (0.99, 1.40) |
| Breaks in sedentary time (breaks/hour)** | 1.00                    | 1.02 (0.92, 1.12)    | 0.86 (0.80, 0.93)    | 0.84 (0.71, 0.99) |
| Light PA time (30 min/day)** | 1.00                    | 1.00 (0.90, 1.11)    | 0.91 (0.84, 0.98)    | 0.85 (0.72, 1.01) |
| MVPA time (30 min/day)** | 1.00                    | 0.94 (0.74, 1.21)    | 0.69 (0.57, 0.84)    | 0.47 (0.27, 0.84) |

Models 1 and 2 included only one activity variable as an exposure per regression whereas model 3 also controlled for other intensities of physical activity.

MVPA, moderate-to-vigorous physical activity; LPA, light physical activity; CPM, counts per minute; RR, risk ratio.

* Model 1 adjusted for age, wear time, season and region.

** Model 2 additionally adjusted for social class, number of chronic conditions, smoking, alcohol, height and waist circumference.

* Model 3 further adjusted for MVPA.

* Model 3 further adjusted for sedentary time.

* Risk ratios were not interpretable due to low participation in strength training in the severe sarcopenic obese group.
Self-reported strength training was associated with a reduced risk of non-obese sarcopenia and non-sarcopenic obesity. Participation in strength training was most strongly associated with WC and grip strength. Previous studies in similar populations have also shown positive associations between PA and grip strength (Kuh et al., 2005; Hamer & Stamatakis, 2013). A recent systematic review showed that resistance training interventions are particularly effective for improving muscular strength in aging adults (Cruz-Jentoft et al., 2014). Participation in strength training was low in this sample, which may have reduced our power to detect these associations.

One of the main strengths of this study is the use of objective measures of PA. This allowed us to investigate whether sedentary time, breaks in sedentary time and LPA were associated with these conditions. Our findings contribute evidence to the discussion about whether PA guidelines for older people should also encourage sedentary breaks and LPA. Whilst MVPA may be most strongly related to outcomes, even increasing LPA and sedentary breaks may be beneficial and also more feasible in this population. Another strength is the use of muscle mass, muscular strength and physical performance to define sarcopenia. According to the EWGSOP criteria these are essential components in the diagnosis of sarcopenia (Cruz-Jentoft et al., 2010). Although there are more precise measures of muscle mass such as dual X-ray absorptiometry, MAMC is a practical and easy clinical measure of muscle mass that is readily available in primary care settings and is recognised as a valid measure by the American Heart Association (Cornier et al., 2011). Our sample is from a large cohort of community-dwelling men rather than an at-risk population, increasing the generalisability of the results. However, our findings may not be generalizable to women and non-white ethnic groups. Sarcopenia and sarcopenic obesity have also been associated with increased risk of all-cause mortality in this cohort (Atkins et al., 2014a). Consequently participants who had sarcopenia at previous waves are more likely to have dropped out, potentially leading to underestimation of the true associations with activity levels. Further, our sample generally displayed healthier behaviours than those excluded from the analysis and therefore may have been more active than the general population, potentially attenuating observed associations. The cut points we used for defining MVPA are well established and have been validated in older adults (Copeland & Esliger, 2009). Actigraph accelerometers are less accurate at differentiating between sedentary behaviour and LPA. Therefore, some sedentary time may include standing time. Nevertheless, Actigraph-measured sedentary time correlates strongly with ActivPal measured sitting time (r = 0.76) (Healy et al., 2011), which is a reliable measure for sitting. Finally, this investigation is a cross-sectional study, and causality cannot be definitely determined.

9. Conclusion

Objectively measured PA was associated with a reduced risk of severe sarcopenia and sarcopenic obesity, PA at a moderate-to-vigorous intensity may be the most favourable for reducing risk; however, LPA and breaking up prolonged periods of sedentary behaviour may also reduce the risk of sarcopenic obesity. Further longitudinal studies are required to determine the causality of these associations.

Author contributions

DA analysed the data and drafted the initial manuscript. BJ conceived the idea and design of the manuscript, raised funding for the study and participated in its design and data acquisition. CS and OP contributed to making the database. SGW and PHW raised funding for the study and participated in its conception, design, data acquisition, coordination and interpretation. SA and LL collected and downloaded the data and helped interpret the results. All authors made contributions to the interpretation and drafting of the final article.

Transparency Document

The Transparency Document associated with this article can be found, in the online version.

Acknowledgments

All authors declare that there are no competing interests. DA is funded by a British Heart Foundation PhD studentship. This research was also supported by an NIHR Post-Doctoral Fellowship awarded to BJ (2010–03–023) and by a British Heart Foundation project grant (PG/13/86/30546) to BJ. The British Regional Heart Study is supported by British Heart Foundation grants (RG/13/16/30528 and RG/08/013/25942) and a British Heart Foundation Project Grant for the 30-year re-examination (PG09/024). This paper presents independent research funded by the National Institute for Health Research (NIHR) [see http://bjsm.bmj.com/content/49/24/1591.full]. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, the Department of Health or BHF.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ypmed.2016.08.040.

References

Abe, T., Mitsukawa, N., Thiebaud, R.S., Loenneke, J.P., Loftin, M., Ogawa, M., 2012. Lower body-site-specific sarcopenia and accelerometer-determined moderate and vigorous physical activity: the HIREGASAKI study. Aging Clin. Exp. Res. 24 (6), 657–662.
Anon, 1998. Clinical guidelines on the identification, evaluation, and treatment of over-weight and obesity in adults: executive summary. Expert panel on the identification, evaluation, and treatment of overweight in adults. Am. J. Clin. Nutr. 68 (4), 899–917.
Atkins, J.L., Whincup, P.H., Morris, R.W., Lennon, L.T., Papaogastra, O., Wannamethee, S.G., 2014a. Sarcopenic obesity and risk of cardiovascular disease and mortality: a population-based cohort study of older men. J. Am. Geriatr. Soc. 62 (2), 253–260.
Atkins, J.L., Whincup, P.H., Morris, R.W., Wannamethee, S.G., 2014b. Low muscle mass in older men: the role of lifestyle, diet and cardiovascular risk factors. J. Nutr. Health Aging 18 (1), 26–33.
Bann, D., Kuh, D., Wills, A.K., Adams, J., Brage, S., Cooper, R., et al., 2014. Physical activity across adulthood in relation to fat and lean body mass in early old age: findings from the medical research council national survey of health and development, 1946–2010. Am. J. Epidemiol. 179 (10), 1197–1207.
Bann, D., Hare, D., Manini, T., Cooper, R., Botoseneanu, A., McDermott, M.M., et al., 2015. Light intensity physical activity and sedentary behavior in relation to body mass index and grip strength in older adults: cross-sectional findings from the lifestyle interventions and independence for elders (LIFE) study. PLoS One 10 (2), e0110058.
Choi, L., Liu, Z., Matthews, C.E., Buchowski, M.S., 2011. Physical Activity: Process Physical Activity Accelerometer Data (0.1-1). http://cran.r-project.org.
Copeland, J.L., Esliger, D.W., 2009. Accelerometer assessment of physical activity in active, healthy older adults. J. Aging Phys. Act. 17 (1), 17–30.
Cornier, M.A., Desprez, J.P., Davis, N., Grossnicklaus, D.A., Klein, S., Lamarche, B., et al., 2011. Assessing adiposity: a scientific statement from the American Heart Association. Circulation 124 (18), 1996–2019.
Cruz-Jentoft, A.J., Baeyens, J.P., Bauer, J.M., Boirie, Y., Cederholm, T., Landi, F., et al., 2010. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. Age Ageing 39 (4), 412–423.
Cruz-Jentoft, A.J., Landi, F., Schneider, S.M., Zuniga, C., Arac, H., Boirie, Y., et al., 2014. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age Ageing 43 (6), 748–759.
Dominguez, L.J., Barbagallo, M., 2007. The cardiometabolic syndrome and sarcopenic obesity in elderly persons. J. Cardiometab. Syndr. 2 (3), 183–189.
Eibich, P., Buchmann, N., Kroh, M., Wagner, G.G., St Heinzen-Thiessen, E., Demuth, L., et al., 2015. Exercise at Different Ages and Appendicular Lean Mass and Strength in Later Life: Results From the Berlin Aging Study II. J. Gerontol. A. Biol. Sci. Med. Sci.
Gianoudis, J., Bailey, C.A., Dally, R.M., 2015. Associations between sedentary behaviour and body composition, muscle function and sarcopenia in community-dwelling older adults. Osteoporos. Int. 26 (2), 571–579.
Hamer, M., Stamatakis, E., 2013. Screen-based sedentary behavior, physical activity, and muscle strength in the English longitudinal study of ageing. PLoS One 8 (6), e66222.
Healy, G.N., Wijndaele, K., Dunstan, D.W., Shaw, J.E., Salomou, J., Zimmet, P.Z., et al., 2008. Objectively measured sedentary time, physical activity, and metabolic risk the Australian diabetes, obesity and lifestyle study (AusDiab). Diabetes Care 31 (2), 360–371.
Healy, G.N., Clark, B.K., Winkler, E.A., Gardiner, P.A., Brown, W.J., Matthews, C.E., 2011. Measurement of adults’ sedentary time in population-based studies. Am. J. Prev. Med. 41 (2), 216–227.
Hlatky, M.A., Boineau, R.E., Higginbotham, M.B., Lee, K.L., Mark, D.B., Califf, R.M., et al., 1989. A brief self-administered questionnaire to determine functional capacity (the Duke activity status index). Am. J. Cardiol. 64 (10), 651–654.

Hughes, V.A., Frontera, W.R., Wood, M., Evans, W.J., Dallal, G.E., Rouhennoff, R., et al., 2001. Longitudinal muscle strength changes in older adults: influence of muscle mass, physical activity, and health. J. Gerontol. Biol. 56 (5), 8209–8217.

Jakes, R.W., Day, N.E., Khaw, K.T., Luben, R., Oakes, S., Welch, A., et al., 2003. Television viewing and low participation in vigorous recreation are independently associated with obesity and markers of cardiovascular disease risk: EPIC-Norfolk population-based study. Eur. J. Clin. Nutr. 57 (9), 1089–1096.

Jefferis, B.J., Sartini, C., Lee, I.M., Choi, M., Annuzi, A., Gutierrez, C., et al., 2014. Adherence to physical activity guidelines in older adults, using objectively measured physical activity in a population-based study. BMC Public Health 14.

Kim, S.H., Kim, T.H., Hwang, H.J., 2013. The relationship of physical activity (PA) and walking with sarcopenia in Korean males aged 60 years and older using the Fourth Korean National Health and nutrition examination survey (KNHANES IV-2, 3), 2008–2009. Arch. Gerontol. Geriatr. 56 (3), 472–477.

Kim, J., Lee, Y., Kye, S., Chung, Y.S., Kim, K.M., 2015. Association between healthy diet and exercise and greater muscle mass in older adults. J. Am. Geriatr. Soc. 63 (5), 886–892.

Kuh, D., Bassey, E.J., Butterworth, S., Hardy, R., Wadsworth, M.E., Musculoskeletal, S.T., 2005. Grip strength, postural control, and functional leg power in a representative cohort of British men and women: associations with physical activity, health status, and socioeconomic conditions. J. Gerontol. A Biol. Sci. Med. Sci. 60 (2), 224–231.

Landi, F., Cruz-Jentoft, A.J., Liperoti, R., Russo, A., Giovannini, S., Tosato, M., et al., 2013. Sarcopenia and mortality risk in frail older persons aged 80 years and older: results from the SIRENTE study. Age Ageing 42 (2), 203–209.

Miller, M.D., Crotty, M., Giles, L.C., Bannerman, E., Whitehead, C., Cobiac, L., et al., 2002. Corrected arm muscle area: an independent predictor of long-term mortality in community-dwelling older adults? J. Am. Geriatr. Soc. 60 (5), 896–899.

Park, H., Park, S., Shephard, R.J., Aoyagi, Y., 2010. Yearlong physical activity and sarcopenia in older adults: The Nakanojo study. Eur. J. Appl. Physiol. 109 (5), 953–961.

Pedrero-Chamizo, R., Gomez-Cabello, A., Melendez, A., Vila-Maldonado, S., Espino, L., Gusi, N., et al., 2013. Higher levels of physical fitness are associated with a reduced risk of suffering sarcopenic obesity and better perceived health among the elderly. The EXERNET multi-center study. J. Nutr. Health Aging 19 (2), 211–217.

Ryu, M., Jo, J., Lee, Y., Chung, Y.S., Kim, K.M., Baek, W.C., 2013. Association of physical activity with sarcopenia and sarcopenic obesity in community-dwelling older adults: the Fourth Korea National Health and nutrition examination survey. Age Ageing 42 (6), 734–740.

Shephard, R.J., Park, H., Park, S., Aoyagi, Y., 2013. Objectively measured physical activity and progressive loss of lean tissue in older Japanese adults: longitudinal data from the Nakanojo study. J. Am. Geriatr. Soc. 61 (11), 1887–1893.

Stephen, W.C., Janssen, I., 2009. Sarcopenic-obesity and cardiovascular disease risk in the elderly. J. Nutr. Health Aging 13 (5), 460–466.

Visser, M., Newman, A.B., Nevitt, M.C., Kritchevsky, S.B., Stamn, E.B., Goodpaster, B.H., et al., 2000. Reexamining the sarcopenia hypothesis – muscle mass versus muscle strength. Ann. N. Y. Acad. Sci. 904, 456–461.

Wannamethee, S.G., Lowe, G.D., Whincup, P.H., Rumley, A., Walker, M., Lennon, L., 2002. Physical activity and hemostatic and inflammatory variables in elderly men. Circulation 105 (15), 1785–1790.

Wannamethee, S.G., Shaper, A.G., Lennon, L., Whincup, P.H., 2007. Decreased muscle mass and increased central adiposity are independently related to mortality in older men. Am. J. Clin. Nutr. 86 (5), 1339–1346.

Waters, D.L., Baumgartner, R.N., Caray, P.J., Vellas, B., 2010. Advantages of dietary, exercise-related, and therapeutic interventions to prevent and treat sarcopenia in adult patients: an update. Clin. Interv. Aging 5, 259–270.

Zamboni, M., Mazzoli, G., Fantin, F., Rossi, A., Di Francesco, V., 2008. Sarcopenic obesity: a new category of obesity in the elderly. Nutr. Metab. Cardiovasc. Dis. 18 (5), 388–395.