ORIGINAL ARTICLE

Pretiree lifestyles in relation to musculoskeletal health: cross-sectional data from the Geelong Osteoporosis Study

Julie A. Pasco[1,2,3,4], Kara L Holloway-Kew[1], Natalie K Hyde[1], Monica C Tembo[1], Pamela G Rufus[1], Sophia X Sui[1], Michael Berk,[1,3,5] Mark A Kotowicz[1,2,3]

1 Deakin University, School of Medicine, Geelong, Australia; **2** Department of Medicine-Western Health, The University of Melbourne, St Albans, Australia; **3** Barwon Health, Geelong, Australia; **4** Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia; **5** Orygen, The Centre of Excellence in Youth Mental Health, the Department of Psychiatry and the Florey Institute of Neuroscience and Mental Health, The University of Melbourne, Melbourne, Australia

Abstract

Aims What happens in the early-elderly 'pretiree' period potentially influences the divergent paths of healthy or unhealthy ageing. In this cross-sectional study, we aimed to profile musculoskeletal health and lifestyle behaviours for men and women in their late-fifties and sixties.

Methods and results For 482 participants from the Geelong Osteoporosis Study, we measured DXA-derived relative appendicular lean mass (rALM), bone mineral density (BMD) at the femoral neck and percentage body fat mass (%BF). Low-rALM and low-BMD referred to sex-specific T-scores<-1.0. Associations between exposures and low-rALM and/or low-BMD were explored using multivariable logistic regression. Three-quarters of participants had high %BF, 98(20.3%) had low-rALM, 202(41.9%) had low-BMD and 63(13.1%) had both low-rALM and low-BMD. Eight-two (17.0%) were very active and one-third participated in sports/recreational activities. Most [n=416(87.8%)] met the recommended daily intake (RDI) for protein; only 119(25.1%) met the RDI for calcium. Less than 10% smoked and one-third exceeded recommended alcohol intakes. Independent of age, weight and sex, greater %BF and sedentary behaviour increased the likelihood of low-rALM; high-alcohol consumption increased the likelihood of low-BMD; and greater %BF increased the likelihood of low-rALM and low-BMD combined.

Conclusions One-half of participants had rALM and BMD in the normal range. Only a few were involved in resistance-training or weight-bearing exercise, despite having the capacity to be physically active. As sedentary lifestyles, excessive adiposity and high alcohol use were associated with low-rALM and/or low-BMD, we propose that these adverse factors be potential targets among pretirees to minimise their risk of entering old age with poor musculoskeletal health.

Address for correspondence: Prof Julie A Pasco, Epi-Centre for Healthy Ageing, IMPACT Strategic Research Centre, School of Medicine, Deakin University, PO Box 281 (Barwon Health) , Geelong VIC, Australia; Email: juliep@barwonhealth.org.au; Tel: +61 3 42153331; Fax: +61342153491
Keywords: Ageing, Body composition, Lean mass, Osteoporosis, Sarcopenia, Osteosarcopenia

Introduction

Across the contemporary world, including Australia, the population is older than ever before, with growth in both the number and proportion of older people [1, 2]. Increased longevity affords the opportunity for the emergence of morbid conditions that markedly increase in prevalence and impact with advancing age. Disorders of the musculoskeletal system are exemplars, notably sarcopenia and osteoporosis, and these are poised to rise markedly as the population ages even more.

Age-related loss of skeletal muscle mass and impaired muscle function that characterise sarcopenia, frequently underpin a number of the key features of geriatric frailty, such as unintentional weight loss, weakness, exhaustion, gait disorders, poor balance and physical inactivity [3], other adverse health outcomes such as disability, falls, cognitive decline and reduced survival times [4, 5]. Sarcopenia also may have additional detrimental effects on those non-communicable disorders whose risks are reduced by exercise [6, 7]. Several mechanisms that contribute to the pathophysiology of sarcopenia include genetics, the cumulative effects of co-morbidities, hormonal changes and factors associated with lifestyle [4]. Also associated with ageing is a loss of bone mass and deterioration of bone quality that lead to osteoporosis, increased bone fragility and the likelihood of fracture.

There is cross-talk between muscle and bone tissue; the connections are more than just mechanical, and involve inflammatory, metabolic and endocrine interactions [8]. The co-occurrence of osteoporosis and sarcopenia (osteosarcopenia [9]) exacerbates the harmful consequences of each disorder and predisposes individuals to increased risk of falls and subsequent fractures [9-11] and early mortality [12].

Establishing and maintaining functional ability is a fundamental foundation for healthy ageing [1]. While the foundations for such a trajectory build across the life course, timely reinforcement of public health messages during the early-elderly period is likely to be beneficial before the onset of old age. We have previously described individuals in this early-elderly period as 'pretirees', as this group straddles work and retirement, and reported that being physically active during this period was associated with better quality of life [13]. Imprudent life choices and behaviour patterns in the pretiree stage of life can exacerbate considerable risks for unhealthy ageing, whereas optimising these factors can set the stage for a healthier trajectory into old age. Lifestyles geared to maintaining musculoskeletal health are important for slowing or preventing loss of functional ability and preserving autonomy.

As muscle and bone mass deficits are key factors in defining sarcopenia and osteoporosis, we aimed to describe the characteristics and health behaviours associated with low muscle mass and low bone mineral density (BMD) for participants of the Geelong Osteoporosis Study, aged 55-69 years.

Methods

Participants

This is a cross-sectional analysis of data collected as part of the prospective cohort study known as the Geelong Osteoporosis Study, which was designed to describe the epidemiology of osteoporosis in Australia and to identify risk factors for fracture [14]. At baseline, age-stratified samples of 1,540 men and 1,494 women were selected at random from electoral rolls for the Barwon Statistical Division in south-eastern Australia. Registration on the Australian electoral roll is compulsory, providing a comprehensive listing of the adult population. Since baseline, participants have been re-assessed every few years and the current analysis utilises data collected at the 5-year follow-up for men (2007-2011) and the 15-year follow-up for women (2011-2014). Details of study design, participation and retention have been described elsewhere [14]. From a potential 742 participants (383 men and 359 women) assessed at baseline and who would have been in this analysis at follow-up, 27 (3.6%) had died (13 men, 14 women), 33 (4.4%) had left the region (13 men, 20 women), 48 (6.5%) had lost contact (27 men, 21 women), and 107 (14.4%) had declined (48 men, 59 women). A further 36 (4.9%) were excluded (17 men, 19 women) as they had not provided whole body and/or hip densitometry, leaving 491 (66.2%) eligible for this analysis (265 men, 226 women). There were no detectable differences between baseline characteristics for participants and non-participants at follow-up in terms of age, weight, height, adiposity, lean tissue mass or bone mineral density (BMD; Table 1). Written, informed consent was obtained from all participants. This study was approved by the Barwon Health Human Research Ethics Committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Table 1 Baseline characteristics for participants and non-participants at follow-up.

Data are shown as mean (± standard deviation) or median (interquartile range).

(a)Men

	Participants		Non-participants		p
	n		n		
Age (yr)	265	56.9 (53.3-61.0)	118	56.2 (51.0-61.7)	0.282
Weight (kg)	262	85.9 (±13.6)	107	87.1 (±13.8)	0.462
Height (m)	262	1.74 (±0.06)	107	1.76 (±0.06)	0.105
%BF	259	25.8 (±6.3)	107	26.9 (±6.1)	0.128
rALM (kg/m^2)	259	8.78 (±0.80)	107	8.70 (±0.87)	0.216
BMD (g/cm^2)	261	0.993 (±0.120)	102	1.001 (±0.155)	0.666

(b)Women

	Participants		Non-participants		p
	n		n		
Age (yr)	226	45.1 (41.4-49.3)	181	44.4 (38.2-50.0)	0.064
Weight (kg)	226	71.0 (±14.7)	181	71.9 (±16.1)	0.530
Height (m)	226	1.63 (±0.05)	181	1.62 (±0.06)	0.192
%BF	226	38.3 (±8.0)	179	38.7 (±8.2)	0.619
rALM (kg/m^2)	225	6.69 (±0.82)	178	6.80 (±0.87)	0.216
BMD (g/cm^2)	226	0.975 (±0.136)	180	0.977 (±0.139)	0.890

Data

Body composition was assessed by dual energy x-ray absorptiometry (DXA; Lunar Prodigy, Madison, WI, USA) thereby providing measures of lean tissue, bone and fat mass. Lean tissue assessed by whole body DXA technology comprises non-bone and non-fat tissue and serves as a proxy measure of muscle mass. Appendicular lean mass (ALM, in kg) was determined by summing lean mass measures for the arms and legs; relative ALM (rALM) was determined by expressing ALM relative to height (kg/m^2). For this study, low-rALM was recognised as T-scores < -1.0 [15]. BMD measures of the femoral neck were used to identify low-BMD as T-score < -1.0 [16, 17]. The rALM and BMD T-score cut-points were drawn from data of our own cohort, as previously described [15-17]. We made the a priori decision to use T-scores < -1.0 for classifying rALM and BMD as low, rather than using lower cut-points, in order to identify individuals with moderate deficits and at risk of progressing to more severe deficits. However, for descriptive and illustrative purposes, we have also identified participants in the lowest, mid and highest ranges of rALM (lowest T-score < -2.0, mid T-score between -1.9 and -1.0 and highest T-score ≥ -1.0) and BMD (lowest T-score ≤ -2.5, mid T-score between -2.5 and -1.0 and highest T-score ≥ -1.0). Body fat mass was expressed as a percentage of body weight (%BF) and high %BF was defined as >25% for men and >35% for women. We used the timed up-&-go (TUG) test over a distance of 3m as a measure of balance and muscle performance [18]. Body weight and height were measured to the nearest 0.1 kg and 0.001 m, respectively, and body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Based on World Health Organization (WHO) criteria, overweight corresponded to BMI 25.0-29.9 kg/m^2 and obesity to BMI ≥ 30.0 kg/m^2 [19].

Participants provided information about mobility, sports and recreational activities, falls, diet and lifestyle via self-reported questionnaires. For this analysis, mobility was categorised for 265 men and 225 women as very active, active and sedentary (which included limited activity and inactivity; there were no participants who were chair/bed-ridden or bedfast). The descriptors provided in the question related to mobility were: very-active 'moves, walks and works energetically and participates in vigorous activity'; active 'walks at brisk pace, does normal housework or other work and engages in light exercise; sedentary 'walks reasonable distances, does light housework, shopping or equivalent, and normal activities of day-to-day living but no appreciable exercise'; limited 'little walking outside home, but prepares meals and does very light housework or equivalent'; inactive 'sits in chair or lies in bed most of the time, walks independently from bed to chair to toilet but requires assistance for greater movement'; chair or bed-ridden 'cannot walk from bed to chair to toilet without considerable assistance'; bedfast 'not able to walk' [14]. Sports and recreational activities were documented according to physical activity questionnaires [20, 21]. These activities were subsequently considered in analyses if the intensity was equivalent to middle level (such as racquet sports, bike-riding/cycling, dancing, swimming) with an average energy expenditure of 1.26 megajoules per hour (MJ)/hr), and/or high level (such as basketball, football, rowing) with an average energy expenditure of 1.76 MJ/hr [20] and sustained for at least 2 hr/week. Fallers were those who reported at least one fall during the previous 12 months. Food and alcohol intakes were documented for 257 men and 222 women via a food frequency questionnaire developed by the Cancer Council (Victoria) [22]. Age-appropriate recommended dietary intakes (RDIs) for calcium were 1,000 mg/d for men and 1,300 mg/d for women [23] and for protein, 64 g/d for men and 46 g/d for women [23]. Mean energy intake was expressed in megajoules per day MJ/d. Individual mean daily alcohol consumption was expressed in grams per day (g/d) and amounts exceeding 20 g/d were considered above recommended levels [24]. Participants reported how many cigarettes they had each day, and current smoking referred to at least one per day.

Statistics

Intergroup differences for continuous data were compared using Student's t-test for parametric data and Mann-Whitney test for non-parametric data, and the chi-square test was used for categorical data. We used histograms to visually appraise the distribution of the variables. Agreement between classification for concomitant deficits in rALM and BMD was tested using Cohen's kappa coefficient (κ). Best models for predicting low-rALM, low-BMD and a combination of low-rALM and low-BMD were identified using multivariable logistic regression techniques; backwards elimination employed $p<0.05$ in the decision to retain variables in models. All models were tested for effect modification. Analyses were performed using Minitab (version 17, Minitab, State College, PA, USA).

Results

Participant characteristics and lifestyle behaviours

Table 2 lists participant characteristics. Data are shown for all men and women, and according to categories of normal vs low-rALM and/or low-BMD. Overall, mean BMI was in the overweight category and 81 (30.6%) men and 87 (38.5%) women had BMI in the obese range ($\geq$30.0 kg/m^2). There were 190 (71.7%) men and 185 (81.9%) women with high %BF. While only 99 (38.5%) men and 20 (9.0%) women met the RDI for calcium, most men (n=221, 87.8%) and women (n=200, 90.1%) met the RDI for dietary protein, 30 (11.3%) men and 16 (7.1%) women smoked, and 111 (43.2%) men and 39 (17.6%) women exceeded recommended alcohol intakes. Mobility for participants was either in the very-active (42 (15.9%) men, 41 (18.2%) women) or active (162 (61.1%) men, 123 (54.7%) women) category, and 39 (14.7%) men and 63 (27.9%) women had fallen in the past year.

Approximately one-half of participants reported involvement in recreational activities. The most popular activity for men was walking/bushwalking (n=57; 21.5%), followed by golf (n=50; 18.9%), bike-riding/cycling (n=19; 7.2%), lawn bowls (n=17; 6.4%), gym/weights (n=16; 6.0%), racquet sports (n=12; 4.5%), swimming (n=10; 3.8%), running/jogging (n=5; 1.9%); others included ten-pin bowling, sailing, kayaking, surfing, dancing, table tennis, indoor soccer, cricket and fishing. For women, the most common activities were walking (n=48; 21.2%) and gym/aerobics/yoga/Pilates (n=48; 21.2%), followed by golf (n=19; 8.4%), bike-riding/cycling (n=11; 4.9%), water aerobics (n=11; 4.9%), dancing (n=9; 4.0%), racquet sports (n=9; 4.0%), lawn/indoor bowls (n=7; 3.1%); others included running, sailing, swimming, dancing, badminton, netball, horseriding and fishing.

Sports or recreational activities that were of middle and/or high intensity and performed for at least 2 hr/wk, were reported by 98 (20.0%) participants (52 (19.6%) men, 46 (20.4%) women). The proportion of individuals who participated in these actives was greater in the whole group with normal rALM compared to low-rALM; this pattern was observed in the sex-specific groups, but the difference was not significant for women.

Table 2. Participant characteristics for (a) men and (b) women, for all and by deficits in relative appendicular lean mass (rALM), bone mineral density (BMD), and combined rALM and BMD. Data are presented as mean (± standard deviation), median (interquartile range) or number (%).

(a) Men

	All	rALM			BMD			Combined low-rALM and low-BMD		
	n=265	Normal n=214	Low n=51	p	Normal n=191	Low n=74	P	No n=240	Yes n=25	p
Age (yr)	61.9 (58.5-66.1)	61.7 (58.4-66.1)	63.1 (58.6-66.3)	0.366	61.6 (57.7-65.9)	63.4 (59.8-66.9)	0.060	61.8 (58.5-66.0)	62.5 (58.2-67.7)	0.504
Height (m)	1.74 (±0.06)	1.75 (±0.06)	1.73 (±0.06)	0.192	1.75 (±0.06)	1.73 (±0.07)	0.120	1.74 (±0.06)	1.73 (±0.07)	0.207
Weight (kg)	86.9 (±13.8)	89.5 (±13.5)	75.8 (±9.1)	<0.001	88.3 (±13.6)	83.3 (±13.9)	0.010	88.0 (±13.8)	76.1 (±8.8)	<0.001
BMI (kg/m^2)	28.6 (±4.2)	29.4 (±4.1)	25.3 (±2.6)	<0.001	28.9 (±4.1)	27.8 (±4.3)	0.050	28.9 (±4.2)	25.6 (±2.7)	<0.001
%BF	28.7 (±6.3)	28.9 (±6.2)	27.7 (±6.9)	0.270	28.9 (±6.3)	28.1 (±6.4)	0.342	28.7 (±6.2)	28.0 (±7.1)	0.596
ALM (kg)	26.2 (±3.2)	27.1 (±2.7)	22.4 (±1.9)	<0.001	26.6 (±3.1)	25.1 (±3.1)	0.001	26.6 (±3.0)	22.4 (±1.8)	<0.001
rALM (kg/m^2)	8.62 (±0.85)	8.90 (±0.68)	7.45 (±0.31)	<0.001	8.72 (±0.83)	8.37 (±0.84)	0.002	8.74 (±0.80)	7.51 (±0.27)	<0.001
BMD f0 (g/cm^2)	0.968 (±0.117)	0.978 (±0.117)	0.925 (±0.110)	0.003	1.018 (±0.095)	0.838 (±0.049)	<0.001	0.981 (±0.115)	0.842 (±0.042)	<0.001
TUG (s)	7.8 (7.0-8.7)	7.7 (7.0-8.6)	8.2 (6.7-8.9)	0.314	7.8 (6.9-8.6)	7.7 (7.1-8.8)	0.559	7.7 (7.0-8.6)	8.0 (6.7-8.8)	0.647
Calcium (mg/d)*	945 (±355)	951 (±356)	920 (±353)	0.569	963 (±365)	897 (±324)	0.164	950 (±357)	895 (±333)	0.448
Protein (mg/d)*	91 (75-111)	93 (77-115)	88 (68-101)	0.039	92 (77-112)	87 (72-111)	0.303	92 (77-112)	82 (63-101)	0.098
Alcohol (g/d)*	17.6 (4.3-30.3)	17.8 (4.3-29.7)	17.2 (2.4-34.1)	0.723	15.5 (4.3-28.3)	20.8 (4.3-34.0)	0.285	17.3 (4.3-28.4)	24.4 (2.0-41.8)	0.478
Energy (kJ/d)*	9041 (±3371)	9194 (±3573)	8411 (±2277)	0.057	9203 (±3624)	8610 (±2548)	0.144	9110 (±3436)	8377 (±2626)	0.217
Mobility				0.275			0.223			0.228
very active	42 (15.9%)	37 (17.3%)	5 (9.8%)		34 (17.8%)	8 (10.8%)		41 (17.1%)	1 (4.0%)	
active	162 (61.1%)	131 (61.2%)	31 (60.8%)		111 (58.1%)	51 (68.9%)		145 (60.4%)	17 (68.0%)	
sedentary	61 (23.0%)	46 (21.5%)	15 (29.4%)		46 (24.1%)	15 (20.3%)		54 (22.5%)	7 (28.0%)	-
Sport	52 (19.6%)	47 (22.0%)	5 (9.8%)	0.049	40 (20.9%)	12 (16.2%)	0.385	50 (20.8%)	2 (8.0%)	0.092
Falls	39 (14.7%)	31 (14.5%)	8 (15.7%)	0.828	25 (13.1%)	14 (18.9%)	0.229	35 (14.6%)	4 (16.0%)	0.772
Smoke	30 (11.3%)	20 (9.4%)	10 (19.6%)	0.038	20 (10.5%)	10 (13.5%)	0.483	24 (10.0%)	6 (24.0%)	0.047

*Missing data: dietary data n=8

(b) Women

	All	rALM			BMD			Combined low-rALM and low-BMD		
	n=226	Normal n=177	Low n=49	p	Normal n=90	Low n=136	p	No n=186	Yes n=40	p
Age (yr)	62.0 (58.6-66.3)	61.8 (58.6-66.0)	63.1 (58.4-66.7)	0.353	61.7 (58.1-66.2)	62.7 (58.6-66.4)	0.572	61.7 (58.4-65.8)	63.5 (59.1-67.0)	0.100
Height (m)	1.62 (±0.06)	1.62 (±0.06)	1.62 (±0.06)	0.538	1.62 (±0.06)	1.62 (±0.05)	0.750	1.62 (±0.06)	1.62 (±0.06)	0.561
Weight (kg)	76.3 (±16.1)	80.5 (±15.1)	61.3 (±9.5)	<0.001	82.9 (±15.2)	71.9 (±15.3)	<0.001	79.7 (±15.2)	60.5 (±9.8)	<0.001
BMI (kg/m^2)	29.2 (±6.2)	30.8 (±5.7)	23.3 (±3.7)	<0.001	31.7 (±5.7)	27.6 (±5.9)	<0.001	30.5 (±5.8)	23.0 (±3.6)	<0.001
%BF	42.4 (±8.1)	43.6 (±7.2)	37.9 (±9.3)	<0.001	45.2 (±6.3)	40.5 (±8.6)	<0.001	43.6 (±7.3)	36.9 (±9.2)	<0.001
ALM (kg)	17.6 (±2.5)	18.4 (±2.1)	14.9 (±1.5)	<0.001	18.6 (±2.6)	17.0 (±2.2)	<0.001	18.2 (±2.2)	14.9 (±1.5)	<0.001
rALM (kg/m^2)	6.72 (±0.84)	7.02 (±0.67)	5.65 (±0.35)	<0.001	7.08 (±0.85)	6.49 (±0.74)	<0.001	6.96 (±0.72)	5.64 (±0.38)	<0.001
BMD f0 (g/cm^2)	0.873 (±0.126)	0.894 (±0.118)	0.794 (±0.123)	<0.001	0.994 (±0.081)	0.793 (±0.076)	<0.001	0.898 (±0.116)	0.756 (±0.100)	<0.001
TUG (s)*	7.9 (6.5-9.2)	8.0 (6.6-9.3)	7.8 (6.2-8.9)	0.580	8.6 (6.9-9.3)	7.7 (6.2-8.9)	0.035	7.9 (6.3-9.2)	8.0 (6.9-9.0)	0.761
Calcium (mg/d)*	884 (±318)	897 (±322)	838 (±303)	0.246	868 (±321)	895 (±317)	0.547	889 (±322)	859 (±298)	0.579
Protein (mg/d)*	74 (56-92)	74 (56-94)	73 (52-86)	0.348	73 (58-87)	74 (54-95)	0.648	74 (56-93)	73 (55-87)	0.597
Alcohol (g/d)*	2.0 (0.3-13.1)	1.3 (0.2-13.1)	5.2 (0.5-15.3)	0.073	0.9 (0.0-10.0)	2.5 (0.3-15.6)	0.036	1.3 (0.2-12.9)	6.0 (0.9-16.8)	0.075
Energy (kJ/d)*	6524 (±2342)	6572 (±2400)	6343 (±2130)	0.525	6276 (±2237)	6693 (±2405)	0.187	6512 (±2396)	6581 (±2092)	0.856
Mobility*				0.256			0.163			0.333
very active	41 (18.2%)	35 (19.8%)	6 (12.5%)		11 (12.2%)	30 (22.2%)		36 (19.4%)	5 (12.8%)	
active	123 (54.7%)	98 (55.4%)	25 (52.1%)		53 (58.9%)	70 (51.9%)		103 (54.5%)	20 (51.3%)	
sedentary	61 (27.1%)	44 (24.9%)	17 (35.4%)		26 (28.9%)	35 (25.9%)		47 (25.3%)	14 (35.9%)	
Sport	46 (20.4%)	39 (22.0%)	7 (14.3%)	0.219	13 (14.4%)	33 (24.3%)	0.068	40 (21.5%)	6 (15.0%)	0.354
Falls	63 (27.9%)	45 (25.4%)	18 (36.7%)	0.118	26 (28.9%)	37 (27.2%)	0.782	47 (25.3%)	16 (40.0%)	0.067
Smoke	16 (7.1%)	13 (7.3%)	3 (6.1%)	0.999	9 (10.0%)	7 (5.2%)	0.164	13 (7.0%)	3 (7.5%)	0.910

*Missing data: dietary data n=4; mobility n=1.

Musculoskeletal health

As shown in Table 2, 51 (19.2%) men and 49 (21.7%) women had low-rALM, 74 (27.9%) men and 136 (60.2%) women had low-BMD; 25 (9.4%) men and 40 (15.1%) women had combined low-rALM and low-BMD (men κ 0.22, women κ 0.16). Compared to participants with normal-rALM, those with low-rALM weighed less and had a lower BMI and %BF; the pattern was similar for those with low-BMD vs normal-BMD, except that the difference in %BF for men was not significant. Men with low-rALM vs normal-rALM consumed less dietary protein and energy, but no such differences were detected for women. There were no differences found in dietary calcium intakes for low-BMD vs normal-BMD in either sex. Similarly, participants with combined low-rALM and low-BMD weighed less, had lower BMI and lower %BF (women only). There was a tendency for individuals with combined low-rALM and low-BMD to be older, but this difference was not significant. Figure 1 shows that, within the low-rALM group, four (1.5%) men and eight (3.5%) women had rALM T-scores $\leq$ -2.0 and within the low-BMD group, four (1.5%) men and 15 (6.6%) women had BMD T-scores $\leq$ -2.5. No men and four women had concomitant rALM T-score $\leq$ -2.0 and BMD T-score $\leq$ -2.5.

Multivariable regression models

Independent of age, weight and sex, greater %BF and sedentary behaviour increased the likelihood for low-rALM; high alcohol consumption (>20g/d) increased the likelihood for low-BMD; and greater %BF increased the likelihood for combined low-rALM and low-BMD, while involvement in sport/recreational activities of at middle-to-high intensity for at least 2 hr/wk were protective (Table 3). No other factors contributed to the models and no effect modifiers were identified.

Figure 1

Prevalence of individuals in the lowest, mid and highest ranges of rALM (lowest T-score ≤ -2.0, mid T-score between -2.0 and -1.0, and highest T-score ≥ -1.0); and BMD (lowest T-score ≤ -2.5, mid T-score between -2.5 and -1.0, and highest T-score ≥ -1.0).

Data are shown for (a) all participants, (b) men, and (c) women.

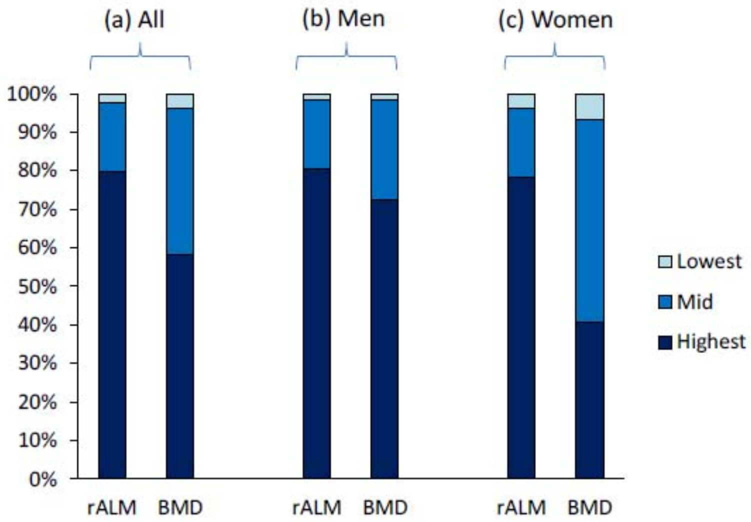

Table 3 Multivariable logistic regression models showing best predictors for low relative appendicular lean mass (low-rALM), low bone mineral density (low-BMD) and combined low-rALM and low-BMD.

Outcome*	Exposure		OR	95%CI
Low-rALM	Body fat (%)		1.23	1.15, 1.31
	Mobility	very active	1	-
		active	2.28	0.99, 5.26
		sedentary	4.74	1.82, 12.30
Low-BMD	Alcohol (>20g/d)		1.70	1.07, 2.70
Combined low-rALM and low-BMD	Body fat (%)		1.13	1.06, 1.20
	Sport**		0.41	0.17, 0.97

*Models adjusted for age, weight and sex.
**mid-high intensity for at least 2 hr/wk

Discussion

Adiposity, high alcohol intakes and physical inactivity were identified as modifiable factors associated with increased likelihood for poor musculoskeletal health. Only one-half of the participants assessed in this study had both lean mass and bone mass in the normal range (T-scores ≥ -1). Thus, this early-elderly age group as a whole would likely benefit from adopting lifestyle behaviours that might reduce the likelihood of progressing to sarcopenia and/or osteoporosis.

Skeletal muscle mass is determined by the number and size of muscle fibres. Most adults reach peak muscle mass in the fifth age-decade followed by a marked age-related decline in muscle mass and strength [15, 25], mainly as a consequence of muscle fibre loss and weakening of residual fibres [26]. Similarly, an age-related decline in BMD occurs from the third or fourth decade of life [16, 17]. This is a consequence of cortical bone loss which begins in mid-life for women and later for men, and trabecular bone loss which begins during younger adulthood in both sexes and continues with advancing age, with accelerated loss in women during menopause [27].

Biological ageing is characterised by persistent oxidative stress and low-grade inflammation, which involves redox disturbance and the release of inflammatory cytokines/chemokines [28-31]. In ageing men and women, waning productions of estrogens and androgens reduce defences against oxidative stress. Ageing muscle cells also produce more reactive oxygen species (ROS) [32] and become less efficient at maintaining homeostasis, so excess ROS accumulates, contributing to muscle cell death. Excess ROS also disrupts bone metabolism by affecting osteoclasts, osteoblasts and osteocytes, thereby uncoupling bone turnover and contributing to bone loss [31, 33]. Many health behaviours that promote healthy ageing, such as habitual physical activity, good nutrition, avoidance of smoking and limitation of alcohol consumption, work through increasing anti-oxidant defences, minimising ROS and restoring redox balance, and shifting away from a pro-inflammatory and towards an anti-inflammatory state.

There is evidence to suggest that appropriate nutrition and exercise provide anabolic stimuli for skeletal muscle, offsetting the rate of muscle protein synthesis in comparison with breakdown. Low protein intakes were not common among participants in our study, as almost 90% of participants met or exceeded the sex-specific RDIs for Australia. This is a positive finding, because among participants of the Health, Aging, and Body Composition study in the USA, aged in their seventies, those in the highest quintile of protein intake, compared with the lowest quintile, lost approximately 40% less lean mass and appendicular lean mass over a three-year period [34]. Similarly, in a study of 2,726 men and women aged 65 years and older from Hong Kong, participants in the highest quartile of vegetable protein intake lost less appendicular skeletal muscle mass over four years than those in the lowest quartile [35]. The authors noted that no differences in the decline of muscle mass or indices of physical performance were observed when total or animal protein intakes were considered, so whether high vegetable protein intakes are a proxy for diet quality or suggest a direct effect, remains unclear. In our study, men with lower-rALM had a lower median protein intake but no difference was detected for women. Moreover, having protein intakes above the RDI did not contribute to the multivariable model for low-rALM or combined low-rALM and low-BMD and perhaps this is because only about one-tenth of our participants had protein intakes below the RDI. There is also extant evidence that fish oil-derived omega-3 fatty acids slow the decline in muscle mass and function in older adults [36], and that low vitamin D [37], cigarette smoking [38] and high alcohol consumption [39] exacerbate skeletal muscle deterioration. What is unclear if these factors operate directly or are indicative of lifestyle behaviours or of social or economic determinants of health.

Public health messages for building and maintaining healthy bones also stress the importance of appropriate exercise, a healthy diet that includes sufficient dietary calcium, adequate vitamin D nutrition, avoiding tobacco smoking and limiting alcohol intakes [40]. The majority of our participants had calcium intakes below the RDI, but we did not detect an association between calcium intakes and BMD. There is also evidence that high dietary intakes of protein are positively associated with BMD, despite the opposing effects of protein-related acid load on urinary excretion of calcium [41]. We did not observe an association between protein intakes and BMD in our study.

Resistance training improves muscle strength and power, and induces skeletal muscle hypertrophy. In young adults, within two hours of acute high-intensity resistance exercise, increases have been observed in leg muscle protein synthesis of 52% in men and 47% in women [42]. In older individuals in their mid-sixties, a three days per week resistance training program over a 16-week period resulted in a mean 23% increase in type II fibre size in leg muscle, thereby restoring myofibre size equivalent to those found in adults about 35 years younger [43]. Furthermore, ingestion of essential amino acids or whole proteins following resistance exercise augmented the rate of muscle protein synthesis [44, 45].

Multicomponent exercise programs that involve progressive resistance training and weight-bearing activities are recommended for both bone health and muscle health, and again may have benefits for a range of non-communicable disorders [46-48]. In a recent randomised controlled trial in Australia involving 162 men and women aged at least 60 years and at risk for falls or low BMD, a 12-month multimodal exercise intervention improved BMD, muscle strength, muscle power and balance [49]. In contrast to observed standard care self-management for the control group, the intervention group participated in high-velocity progressive resistance training and educational programs. Mean compliance to the exercise program was 59%, suggesting that the regimen was feasible, at least to some older individuals living in the community. In our study of pretirees, very few reported involvement in resistance-training, even though for many it was apparent they had the capacity to be physically active. Indeed, the benefits of resistance training may need to be more widely publicised.

Obesity is linked to both systemic inflammation and oxidative stress [50, 51]. A combination of sarcopenia and obesity, known as sarcopenic obesity and characterised by fat infiltration into muscle, markedly diminishes muscle strength and causes poorer outcomes in terms of health and wellbeing [5, 52]. A positive relationship is observed between body weight and BMD [53] and, while the mass of adipose tissue contributes to this relationship, there are also multiple endocrine and neural pathways that link fat and bone tissue [54]. In our study, we observed that high levels of adiposity were associated with low-rALM and low-BMD. Our multivariable models, which were adjusted for age, weight and height, indicated an inverse relationship between low-rALM and adiposity. This highlights the limitations of using BMI to identify sarcopenic obesity, as a given body weight-for-height will not provide insight into the relative proportions of fat and lean tissue [55].

We acknowledge that our study has several strengths and limitations. A major strength is that our participants were drawn from the general population and were not selected on the basis of disease. Moreover, indices of body composition were objectively measured. We also acknowledge, however, that we relied on self-reported data for assessing health behaviours. We have not considered all factors and health behaviours that might influence musculoskeletal health, such as secondary osteoporosis, parental fracture, glucocorticoid intake, polyarthritis, nor the participants' dietary intakes of omega-3 fatty acids or vitamin D status. However, we have previously reported that nearly all (97%) female participants in the Geelong Osteoporosis Study have low mean omega-3 fatty acid intakes (<0.5 g/d) [56] and that vitamin D levels display marked seasonal variation such that 30% of women have serum 25-hydroxyvitamin D levels below 50 nmol/L during summer, rising to 43.2% during winter [57], placing them below recommended levels [40]. Data on exercise frequency would have provided further insight into this project, as the minimum effective dose of exercise frequency for addressing fracture risk appears to vary between 2.1 and 2.5 sessions per week [58]. Our findings would likely have been different if different cut-points had been used for identifying deficits in rALM and BMD. Moreover, we have not included assessments of muscle strength or gait speed which are also important for defining sarcopenia [59]. Finally, as the majority of our sample was Caucasian (white), the findings may not be generalisable to other populations.

Early detection, when individuals are still able to implement targeted lifestyle interventions, is an important element in developing public health policies for delaying or preventing muscle and bone loss. As sedentary lifestyles, excessive adiposity and high alcohol use were associated with low muscle mass and/or low bone mass, we propose that these adverse factors could be potential targets among pretirees to minimise their risk of entering old age with poor musculoskeletal health.

Acknowledgements

JAP, MB and MAK conceived and designed this study. All authors contributed to data acquisition, coding and/or interpretation of the data. JAP analysed the data and drafted the work, and all authors revised it critically for important intellectual content. All authors approved the final version for submission and take responsibility for all aspects of the work. The Geelong Osteoporosis Study was funded by the National Health and Medical Research Council (NHMRC) Australia (project 628582) but they played no role in study design; in the collection, analysis and interpretation of data; in the writing of the report; nor in the decision to submit the paper for publication.

Conflict of interest

KLH-K and NKH are supported by Alfred Deakin Postdoctoral Research Fellowships; MCT, PRG and SXS are supported by postgraduate scholarships from Deakin University; MB is supported by a NHMRC Senior Principal Research Fellowship (1059660). JAP and MAK have no competing interests, including specific financial interests, relationships or affiliations relevant to the subject matter or materials discussed in the manuscript.

References

1. Beard JR, Officer A, de Carvalho IA, Sadana R, Pot AM, Michel JP, Lloyd-Sherlock P, Epping-Jordan JE, Peeters GMEEG, Mahanani WR, Thiyagarajan JA, Chatterji S. The World report on ageing and health: a policy framework for healthy ageing. Lancet 2016;387:2145-2154.
2. Australian Bureau of Statistics. Australian Demographic Statistics, Dec 2014. Cat no. 3101.0. Canberra: ABS, 2015.
3. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-156.
4. Dodds RM, Roberts HC, Cooper C, Sayer AA. The epidemiology of sarcopenia. J Clin Densitom 2015;18:461-466.
5. Pasco JA, Sui SX, Tembo MC, Holloway-Kew KL, Rufus PG, Kotowicz MA. Sarcopenic obesity and falls in the elderly. J Gerontology Geriatr Res 2017;7:2.
6. Pasco JA, Williams LJ, Jacka FN, Henry MJ, Coulson CE, Brennan SL, Leslie E, Nicholson GC, Kotowicz MA, Berk M. Habitual physical activity and the risk for depressive and anxiety disorders among older men and women. Int Psychogeriatr 2011;23:292-298.
7. Pasco JA, Jacka FN, Williams LJ, Brennan SL, Leslie E, Berk M. Don't worry, be active: positive affect and habitual physical activity. Aust N Z J Psychiatry 2011;45:1047-1052.
8. Tagliaferri C, Wittrant Y, Davicco MJ, Walrand S, Coxam V. Muscle and bone, two interconnected tissues. Ageing Res Rev 2015;21:55-70.
9. Huo YR, Suriyaarachchi P, Gomez F, Curcio CL, Boersma D, Muir SW, Montero-Odasso M, Gunawardene P, Demontiero O, Duque G. Phenotype of osteosarcopenia in older individuals with a history of falling. J Am Med Dir Assoc 2015;16:290-295.
10. Cederholm T, Cruz-Jentoft AJ, Maggi S. Sarcopenia and fragility fractures. Eur J Phys Rehabil Med 2013;49:111-117.
11. Levinger I, Phu S, Duque G. Sarcopenia and osteoporotic fractures. Clinic Rev Bone Miner Metab 2016;14:38-44.
12. Pasco JA, Mohebbi M, Holloway KL, Brennan-Olsen SL, Hyde NK, Kotowicz MA. Musculoskeletal decline and mortality: prospective data from the Geelong Osteoporosis Study. J Cachexia Sarcopenia Muscle 2017;8:482-489.
13. Pasco JA, Holloway KL, Stuart AL, Williams LJ, Brennan-Olsen SL, Berk M. The subjective wellbeing profile of the 'pretiree' demographic: A cross-sectional study. Maturitas 2018;110:111-117.
14. Pasco JA, Nicholson GC, Kotowicz MA. Cohort profile: Geelong

Osteoporosis Study. Int J Epidemiol 2012;41:1565-1575.
15. Gould H, Brennan SL, Kotowicz MA, Nicholson GC, Pasco JA. Total and appendicular lean mass reference ranges for Australian men and women: the Geelong Osteoporosis Study. Calcif Tissue Int 2014;94:363-372.
16. Henry MJ, Pasco JA, Pocock NA, Nicholson GC, Kotowicz MA. Reference ranges for bone densitometers adopted Australia-wide: Geelong Osteoporosis Study. Australas Radiol 2004;48:473-475.
17. Henry MJ, Pasco JA, Korn S, Gibson JE, Kotowicz MA, Nicholson GC. Bone mineral density reference ranges for Australian men: Geelong Osteoporosis Study. Osteoporos Int 2010;21:909-917.
18. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142-148.
19. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation on Obesity. Geneva, 3-5 June 1997. Geneva: WHO, 1998.
20. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. Am J Clin Nutr 1982;36:936-942.
21. Voorrips LE, Ravelli AC, Dongelmans PC, Deurenberg P, Van Staveren WA. A physical activity questionnaire for the elderly. Med Sci Sports Exerc 1991;23:974-979.
22. Giles GG, Ireland PD. Dietary Questionnaire for Epidemiological Studies (Version 2), Melbourne: The Cancer Council Victoria, 1996.
23. National Health and Medical Council of Australia. Nutrient references values for Australia and New Zealand, Canberra, Australia, 2006.
24. National Health Medical Research Council. Australian guidelines to reduce health risks from drinking alcohol. Canberra, Australia, 2009.
25. Leong DP, Teo KK, Rangarajan S, Kutty VR, Lanas F, Hui C, Quanyong X, Zhenzhen Q, Jinhua T, Noorhassim I, AlHabib KF, Moss SJ, Rosengren A, Akalin AA, Rahman O, Chifamba J, Orlandini A, Kumar R, Yeates K, Gupta R, Yusufali A, Dans A, Avezum Á, Lopez-Jaramillo P, Poirier P, Heidari H, Zatonska K, Iqbal R, Khatib R, Yusuf S. Reference ranges of handgrip strength from 125,462 healthy adults in 21 countries: a prospective urban rural epidemiologic (PURE) study. J Cachexia Sarcopenia Muscle 2016;7:535-546
26. Marzetti E, Lees HA, Wohlgemuth SE, Leeuwenburgh C. Sarcopenia of aging: underlying cellular mechanisms and protection by calorie restriction. Biofactors 2009;35:28-35.
27. Riggs BL, Melton LJ, Robb RA, Camp JJ, Atkinson EJ, McDaniel L, Amin S, Rouleau PA, Khosla S. A population-based assessment of rates of bone loss at multiple skeletal sites: evidence for substantial trabecular bone loss in young adult women and men. J Bone Miner Res 2008;23:205–214
28. Kennedy BK, Berger SL, Brunet A, Campisi J, Cuervo AM, Epel ES, Franceschi C, Lithgow GJ, Morimoto RI, Pessin JE, Rando TA, Richardson A, Schadt EE, Wyss-Coray T, Sierra F. Geroscience: linking aging to chronic disease. Cell 2014;159:709-713
29. De la Fuente M, Miquel J. An update of the oxidation-inflammation theory of aging: the involvement of the immune system in oxi-inflamm-aging. Curr Pharm Des 2009;15:3003-3026.
30. Franceschi C, Campisi J. Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. J Gerontol A Biol Sci Med Sci 2014;69:S4-9.
31. Zhou Q, Zhu L, Zhang D, Li N, Li Q, Dai P, Mao Y, Li X, Ma J, Huang S. Oxidative stress-related biomarkers in postmenopausal osteoporosis: A systematic review and meta-analyses. Dis Markers 2016;2016:7067984.
32. Palomero J, Vasilaki A, Pye D, McArdle A, Jackson MJ. Aging increases the oxidation of dichlorohydrofluorescein in single isolated skeletal muscle fibers at rest, but not during contractions. Am J Physiol Regul Interg Comp Physiol 2013;305:R351-358.
33. Manolagas SC. From estrogen-centric to aging and oxidative stress: a revised perspective of the pathogenesis of osteoporosis. Endocr Rev 2010;31:266-300.
34. Houston DK, Nicklas BJ, Ding J, Harris TB, Tylavsky FA, Newman AB, Lee JS, Sahyoun NR, Visser M, Kritchevsky SB; Health ABC Study. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. Am J Clin Nutr 2008;87:150-155.
35. Chan R, Leung J, Woo J, Kwok T. Associations of dietary protein intake on subsequent decline in muscle mass and physical functions over four years in ambulant older Chinese people. J Nutr Health Aging 2014;18:171-177.
36. Smith GI, Julliand S, Reeds DN, Sinacore DR, Klein S, Mittendorfer B. Fish oil-derived n-3 PUFA therapy increases muscle mass and function in healthy older adults. Am J Clin Nutr 2015;102:115-122.
37. Rosendahl-Riise H, Spielau U, Ranhoff AH, Gudbrandsen OA, Dierkes J. Vitamin D supplementation and its influence on muscle strength and mobility in community-dwelling older persons: a systematic review and meta-analysis. J Hum Nutr Diet 2017;30:3-15.
38. Steffl M, Bohannon RW, Petr M, Kohlikova E, Holmerova I. Relation between cigarette smoking and sarcopenia: meta analysis. Physiol Res 2015;64:419-426.
39. Kwon YJ, Lim HJ, Lee YJ, Lee HS, Linton JA, Lee JW, Kang HT. Associations between high-risk alcohol consumption and sarcopenia among postmenopausal women. Menopause 2017;24:1022-1027.
40. Ebeling PR, Daly RM, Kerr DA, Kimlin MG. An evidence-informed strategy to prevent osteoporosis in Australia. Med J Aust 2013;198:90-91
41. Cao JJ. High dietary protein intake and protein-related acid load on bone health. Curr Osteoporos Rep 2017;15:571-576.
42. Dreyer HC, Fujita S, Glynn EL, Drummond MJ, Volpi E, Rasmussen BB. Resistance exercise increases leg muscle protein synthesis and mTOR signalling independent of sex. Acta Physiol (Oxf) 2010;199:71-81.
43. Kosek DJ, Kim JS, Petrella JK, Cross JM, Bamman MM. Efficacy of 3 days/wk resistance training on myofiber hypertrophy and myogenic mechanisms in young vs. older adults. J Appl Physiol (1985) 2006;101:531–544.
44. Dreyer HC, Drummond MJ, Pennings B, Fujita S, Glynn EL, Chinkes DL, Dhanani S, Volpi E, Rasmussen BB. Leucine-enriched essential amino acid and carbohydrate ingestion following resistance exercise enhances mTOR sgnaling and protein synthesis in human muscle. Am J Physiol Endocrinol Metab 2008;294:E392-400.
45. Reitelseder S, Agergaard J, Doessing S, Helmark IC, Lund P, Kristensen NB, Frystyk J, Flyvbjerg A, Schjerling P, van Hall G, Kjaer M, Holm L. Whey and casein labeled with L-[1-13C]leucine and muscle protein synthesis: effect of resistance exercise and protein ingestion. Am J Physiol Endocrinol Metab 2011;300:E231-242.
46. Gianoudis J, Bailey CA, Sanders KM, Nowson CA, Hill K, Ebeling PR, Daly RM. Osteo-cise: strong bones for life: protocol for a community-based randomised controlled trial of a multi-modal exercise and osteoporosis education program for older adults at risk of falls and fractures. BMC Musculoskelet Disord 2012;13:78.
47. Marques EA, Mota J, Machado L, Sousa F, Coelho M, Moreira P, Carvalho J. Multicomponent training program with weight-bearing exercises elicits favorable bone density, muscle strength, and balance adaptations in older women. Calcif Tissue Int 2011;88:117-129
48. Kukuljan S, Nowson CA, Bass SL, Sanders K, Nicholson GC, Seibel MJ, Salmon J, Daly RM. Effects of a multi-component exercise program and calcium-vitamin-D3-fortified milk on bone mineral density in older men: a randomised controlled trial. Osteoporos Int 2009;20:1241-1251

49. Gianoudis J, Bailey CA, Ebeling PR, Nowson CA, Sanders KM, Hill K, Daly RM. Effects of a targeted multimodal exercise program incorporating high-speed power training on falls and fracture risk factors in older adults: a community-based randomized controlled trial. J Bone Miner Res 2014;29:182-191.
50. de Heredia FP, Gomez-Martinez S, Marcos A. Obesity, inflammation and the immune system. Proc Nutr Soc 2012;71:332–338.
51. Pou KM, Massaro JM, Hoffmann U, Vasan RS, Maurovich-Horvat P, Larson MG, Keaney JF Jr, Meigs JB, Lipinska I, Kathiresan S, Murabito JM, O'Donnell CJ, Benjamin EJ, Fox CS. Visceral and subcutaneous adipose tissue volumes are cross-sectionally related to markers of inflammation and oxidative stress: the Framingham Heart Study. Circulation 2007;116:1234-1241
52. Stenholm S, Harris TB, Rantanen T, Visser M, Kritchevsky SB, Ferrucci L. Sarcopenic obesity: definition, cause and consequences. Curr Opin Clin Nutr Metab Care 2008;11:693-700.
53. Henry MJ, Pasco JA, Nicholson GC, Seeman E, Kotowicz MA. Prevalence of osteoporosis in Australian women: Geelong Osteoporosis Study. J Clin Densitom 2000;3:261-268
54. Baldock P. Reciprocal regulation of bone and energy metabolism. Horm Res Paediatr 2011;76:7-11
55. Pasco JA, Nicholson GC, Brennan SL, Kotowicz MA. Prevalence of obesity and the relationship between the body mass index and body fat: cross-sectional, population-based data. PLoS One 2012;7:e29580.
56. Jacka FN, Pasco JA, Henry MJ, Kotowicz MA, Nicholson GC, Berk M. Dietary omega-3 fatty acids and depression in a community sample. Nutr Neurosci 2004;7:101-106.
57. Pasco JA, Henry MJ, Nicholson GC, Sanders KM, Kotowicz MA. Vitamin D status of women in the Geelong Osteoporosis Study: association with diet and casual exposure to sunlight. Med J Aust 2001;175:401-405.
58. Kemmler W, von Strengel S, Kohl M. Exercise frequency and fracture risk in older adults - how often is enough? Curr Osteoporos Rep 2017;15:564-570.
59. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinková E, Vandewoude M, Zamboni M; European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39: 412-4