



## Prospective associations of osteosarcopenia and osteodynopenia with incident fracture and mortality over 10 years in community-dwelling older adults



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### ABSTRACT

**Aim:** To determine whether older adults with low muscle mass (sarcopenia) and strength (dynapenia), in the presence of osteoporosis/osteopenia, have an increased risk of fracture and mortality over 10 years, compared to those with low muscle or low bone mass alone or with neither condition.

**Methods:** 1032 participants (52% women; mean age  $62.9 \pm 7.4$  years) were prospectively followed for 10 years. Mortality was ascertained from the death registry and fractures were self-reported. Baseline appendicular lean mass (ALM) was assessed using dual-energy X-ray absorptiometry and normalised to body mass index (BMI). Hand grip strength (HGS) was assessed by dynamometer. Osteosarcopenia and osteodynopenia were defined as having T-scores of the total hip and/or lumbar spine bone mineral density (BMD)  $< -1$  combined with being in the lowest 20% of the sex-specific distribution for ALM/BMI or HGS respectively.

**Results:** Incident fracture risk was significantly higher in participants who were osteodynopenic (RR = 2.07, 95% CI: 1.26–3.39), dynapenic alone (RR = 1.74, 95% CI: 1.05–2.87), and osteopenic alone (RR = 1.63, 95% CI: 1.15–2.31), compared to those without dynapenia or osteopenia. Mortality risk was significantly higher only in participants with osteosarcopenia (RR = 1.49, 95% CI: 1.01–2.21) compared to those without sarcopenia or osteopenia. However, osteosarcopenia and osteodynopenia did not lead to a significantly greater fracture or mortality risk compared to having these conditions on their own.

**Conclusion:** These findings suggest that the combined effect of osteopenia and sarcopenia or dynapenia on fracture and mortality risk, respectively, may not be greater than that of each individual condition.

### 1. Introduction

Ageing is associated with changes in body composition including decreases in muscle mass, strength and bone mass, with declines in each occurring at a different rate (Daly et al., 2013; Delmonico, Harris, & Visser, 2009). Loss of muscle mass and loss of bone mass (osteopenia/osteoporosis) are closely interconnected, however, both have been considered independently as risk factors for falls, fracture and mortality in older people (Brotto & Bonewald, 2015). Historically, the

interconnection between muscle and bone mass has been thought to be through the mechanostat model which postulates that a decrease in muscle function would result in a decline in mechanical loading on bone and consequently results in a decrease in bone mass (Pearson & Lieberman, 2004). However, recent evidence suggests that, beyond the mechanostat model, there is a biochemical and metabolic interconnection between muscle and bone (Binkley, Krueger, & Buehring, 2013; Levinger, Phu, & Duque, 2016). Indeed, a significant proportion of older people with low muscle function also experience osteopenia/

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osteoporosis (Levinger et al., 2016; Y. Huo, Suriyaarachchi, & Gomez, 2015). Due to the close interconnection between bone and muscle tissue, the simultaneous occurrence of osteopenia/osteoporosis and low muscle mass/strength could significantly increase the risk of fracture and mortality compared to low muscle mass/strength or osteopenia/osteoporosis alone.

Previous cross-sectional studies showed that older adults with combined low muscle and bone mass experienced higher falls, fracture and poorer quality of life compared to those with low muscle or low bone mass alone (Y. Huo et al., 2015). However, limited long-term prospective studies have described the association between the combination of low muscle and bone mass with fracture and mortality in older people (Chalhoub, Cawthon, & Ensrud, 2015). It is also unclear whether low bone mass when combined with low muscle mass has a different impact on fracture and mortality than when combined with low muscle strength. This is particularly important to investigate because muscle strength is associated with functional declines in older people independent of muscle mass (Visser & Schaap, 2011). The aim of the present study was to determine whether older adults with low muscle mass (sarcopenia) and strength (dynapenia), in the presence of osteoporosis/osteopenia, have an increased risk of fracture and mortality over 10 years, compared to those with low muscle or low bone mass alone or with neither condition. We hypothesised that fracture and mortality risk over 10 years will be significantly higher in older people with combined low muscle and bone quality compared to individuals with low muscle or low bone mass alone and those with neither condition.

## 2. Data and methods

### 2.1. Sample and study setting

The Tasmanian Older Adult Cohort (TASOAC) study is a prospective, population-based study primarily aimed at examining the causes and progression of osteoarthritis. Participants aged 50 years and above were selected using sex-stratified random sampling from the electoral roll in Southern Tasmania (population 229,000). A total of 1099 adults (response rate = 57%) consented to participate in the study and were invited to attend a clinic at the Menzies Institute for Medical Research, Hobart, Tasmania between March 2002 and September 2004. They were invited for follow-up clinic assessments at 2.5, 5, and 10 years after the initial clinic assessment. The study was approved by the Tasmanian Health and Medical Research Ethics Committee and written informed consent was obtained from all participants.

### 2.2. Outcome measures

#### 2.2.1. Fracture

At each study visit participants were asked to list, by location, any fractures they had since their previous visit. Those who experienced at least one fracture between the baseline and 10-year follow-up assessment were coded as '1' (incident fracture.) and those without any fracture were coded '0' (no incident fracture).

#### 2.2.2. Mortality

Mortality over 10 years was ascertained through national and state death registries.

#### 2.2.3. Baseline measures

**2.2.3.1. Anthropometrics.** Weight was measured to the nearest 0.1 kilogram (kg) using electronic scales (Heine, Dover, USA) with shoes and heavy clothing removed. Height was measured to the nearest 0.1 centimetre using Leicester stadiometer (Invicta, Leicester, UK), with shoes, socks and headgear removed. Body mass index (BMI) was calculated as weight (kg) divided by height (meter) squared.

**2.2.3.2. Body composition and BMD measures.** Lean mass, fat mass, right hip and lumbar spine bone mineral density (BMD) were measured using dual-energy X-ray absorptiometry (DXA; Hologic Delphi, Hologic, Waltham USA). Appendicular lean mass (ALM) calculated as the sum of lean mass in the upper and lower limbs was normalised to body mass index [BMI] (ALM/BMI) (Studenski, Peters, & Alley, 2014).

**2.2.3.3. Muscle strength.** Handgrip strength in pounds per square inch (psi) was measured using a pneumatic handheld bulb dynamometer (North Coast™ bulb dynamometer; adult 0–30 psi, model no. 70154). The mean of the right and left handgrip strength was calculated for each participant. The intra-class correlation coefficients of the first and second trial for handgrip strength measurements was 0.96 (95% CI: 0.92–0.97).

**2.2.3.4. Operational definitions of osteosarcopenia and osteodynepenia.** Low BMD (osteopenia/osteoporosis) was defined as a T-scores of the total hip and/or lumbar spine of less than –1 (Ilich, Inglis, Kelly, & McGee, 2015; World Health Organization, 1994; Y. R. Huo, Suriyaarachchi, & Gomez, 2015). Sarcopenia and dynapenia were defined as being in the lowest 20% of the sex-specific distribution of muscle mass and strength respectively of our study sample at baseline (Hairi, Cumming, & Naganathan, 2010; Newman, Kupelian, & Visser, 2003). Participants were classified into one of the following four categories based on osteopenic and sarcopenic status: (1) non-sarcopenic, non-osteopenic; (2) sarcopenic non-osteopenic; (3) osteopenic non-sarcopenic; (4) osteosarcopenic. A similar classification was made based on osteopenic and dynapenic status: (1) non-osteopenic, non-dynapenic; (2) dynapenic non-osteopenic; (3) osteopenic non-dynapenic; (4) osteodynepenic.

**2.2.3.5. Potential confounders.** Physical activity was measured over seven consecutive days using a pedometer (Omron HJ-003 & HJ-102; Omron Healthcare, Kyoto, Japan) as previously described (Scott, Blizzard, Fell, & Jones, 2011). Serum 25-hydroxyvitamin D [25(OH)D] was assayed using a liquid-phase radioimmunoassay (Immunodiagnosics Systems Ltd), which detects both 25(OH)D2 and 25(OH)D3. The intra-assay and inter-assay coefficients of variation were 1.8% and 3.3% respectively. Serum 25(OH)D was de-seasonalised as previously described (Mei, Dore, Winzenberg, Blizzard, & Jones, 2012) to account for differences in the time of the year that blood was taken. Age, sex, medical history, including a previous diagnosis of diabetes, rheumatoid arthritis, cardiovascular disease (hypertension, bronchitis/emphysema, or heart attack) were recorded using a questionnaire. Falls risk was assessed using the short form Physiological Profile Assessment (PPA) (Prince of Wales Medical Research Institute, Sydney, Australia), a valid and reliable tool used to identify individuals who are at risk of falls (Lord, Menz, & Tiedemann, 2003).

### 2.3. Data analysis

Categorical and continuous variables were compared across categories of osteopenia/sarcopenia and osteopenia/dynapenia using Chi-square tests and one-way ANOVA, respectively. Log-binomial models were used to estimate relative risk (RR) for fracture and mortality over 10 years in unadjusted and adjusted analysis. The fracture models were adjusted for age, sex, physical activity (steps/day) and 25-hydroxyvitamin-D. The mortality models were adjusted for age, sex, physical activity (steps/day) and number of chronic conditions. We assessed statistical interaction between sex and osteopenic/sarcopenic and osteopenic/dynapenic status. Additionally, we modelled fracture and mortality using continuous (hip BMD) and muscle measures (ALM/BMI and HGS) in both univariable and multivariable models. Hip BMD, HGS and ALM/BMI were standardised for comparison and the relative risk of fracture and mortality were reported as per standard deviation (SD)

**Table 1**  
Baseline descriptive characteristics according to categories of sarcopenia, dynapenia and osteopenia.

Variables	Non-sarcopenic, Non-osteopenic N = 471	Osteopenic non-sarcopenic N = 367	Sarcopenic non-osteopenic N = 108	Osteosarcopenic N = 86	Non-dynapenic, Non-osteopenic N = 468	Osteopenic non-dynapenic N = 353	Dynapenic non-osteopenic N = 111	Osteodynepenic N = 100
Age (years)	61.3 ± 6.9	63.7 ± 7.6 <sup>a</sup>	64.5 ± 7.8 <sup>a</sup>	66.5 ± 7.3 <sup>a</sup>	60.9 ± 6.6	62.9 ± 7.2 <sup>b</sup>	66.3 ± 7.9 <sup>b</sup>	68.8 ± 7.0 <sup>b</sup>
Female, (%) <sup>*</sup>	219 (47%)	213 (58%) <sup>a</sup>	50 (46%) <sup>a</sup>	50 (58%)	225 (48%)	200 (57%)	44 (40%) <sup>b</sup>	63 (63%) <sup>b</sup>
Weight (kg)	80.1 ± 13.7	70.5 ± 12.4 <sup>a</sup>	88.2 ± 14.3 <sup>a</sup>	80.1 ± 14.6	81.9 ± 14.5	72.8 ± 13.6 <sup>b</sup>	80.2 ± 12.8 <sup>b</sup>	70.7 ± 12.5 <sup>b</sup>
Height (cm)	169.5 ± 8.5	166.4 ± 8.5 <sup>a</sup>	164.1 ± 8.4 <sup>a</sup>	159.6 ± 8.7 <sup>a</sup>	168.8 ± 8.8	165.7 ± 8.9 <sup>b</sup>	167.6 ± 8.4	163.1 ± 9.2 <sup>b</sup>
BMI (kg/m <sup>2</sup> )	27.8 ± 3.9	25.4 ± 3.4 <sup>a</sup>	32.7 ± 4.6 <sup>a</sup>	31.4 ± 4.7 <sup>a</sup>	28.7 ± 4.6	26.5 ± 4.4 <sup>b</sup>	28.6 ± 4.3	26.6 ± 4.4 <sup>b</sup>
Total body fat mass (kg)	27.8 ± 8.0	24.9 ± 7.3 <sup>a</sup>	35.8 ± 9.3 <sup>a</sup>	33.9 ± 8.6 <sup>a</sup>	29.3 ± 8.8	26.4 ± 8.4 <sup>b</sup>	29.6 ± 9.1	27.6 ± 8.0
Appendicular lean mass	25.8 ± 5.4	23.1 ± 5.1 <sup>a</sup>	24.3 ± 4.7 <sup>a</sup>	22.2 ± 4.8 <sup>a</sup>	25.7 ± 5.5	23.3 ± 5.1 <sup>b</sup>	24.7 ± 4.5	21.5 ± 4.5 <sup>b</sup>
Physical activity (steps/day)	9159 ± 3301	8861 ± 3271	7029 ± 3156 <sup>a</sup>	6872 ± 3070 <sup>a</sup>	8949 ± 3404	8769 ± 3295	7974 ± 3147 <sup>b</sup>	7476 ± 3244 <sup>b</sup>
Current smoker (%) <sup>*</sup>	234 (50%)	182 (50%)	55 (51%)	47 (55%)	233 (50%)	188 (53%)	56 (50%) <sup>b</sup>	41 (41%)
Number of chronic conditions	1.03 ± 1.09	1.00 ± 1.06	1.43 ± 1.31 <sup>a</sup>	1.51 ± 1.28 <sup>a</sup>	1.04 ± 1.10	1.03 ± 1.10	1.40 ± 1.27 <sup>b</sup>	1.21 ± 1.20
25-hydroxyvitamin D	54.8 ± 17.2	52.2 ± 16.6	46.8 ± 16.2 <sup>a</sup>	47.6 ± 14.4 <sup>a</sup>	53.3 ± 17.5	51.5 ± 16.3	53.3 ± 16.4	50.5 ± 16.0
Falls risk Z-score	0.08 ± 0.82	0.23 ± 0.81	0.20 ± 0.74	0.28 ± 0.90	0.03 ± 0.76	0.15 ± 0.75	0.40 ± 0.94 <sup>b</sup>	0.56 ± 0.98 <sup>b</sup>

± Standard deviation; all tests are one-way ANOVA except \* (Chi-square test).

<sup>a</sup> Significant difference to non-sarcopenic non-osteopenic.

<sup>b</sup> Significant difference to non-dynapenic non-osteopenic.

decrease in hip BMD and per SD increase in HGS or ALM/BMI (results presented as supplementary information). Data were analyzed using Stata version 13 (StataCorp, TX, USA).

### 3. Results

A total of 1032 participants (63 ± 7.4 years; 52% female) with complete body composition and muscle strength assessments at baseline were included in the analysis. Table 1 presents the baseline characteristics of the participants stratified according to osteopenic, sarcopenic and dynapenic status. Both osteosarcopenic and osteodynepenic participants were older, shorter, had lower ALM, and engaged in lower levels of physical activity compared non-sarcopenic non-osteopenic and non-dynapenic non-osteopenic participants. There were a higher proportion of women in the osteodynepenic group compared to non-dynapenic non-osteopenic participants. The proportion of women in the osteopenic non-sarcopenic group was significantly higher than those in the non-sarcopenic non-osteopenic category. BMI and total body fat mass were significantly higher in participants with osteosarcopenia compared to those who were non-sarcopenic non-osteopenic. BMI but not total body fat mass was significantly lower in participants with osteodynepenia compared to those who were non-dynapenic non-osteopenic. Smoking status did not differ across sarcopenic, osteopenic and dynapenic categories. Participants with osteosarcopenia had a greater number of chronic conditions and lower levels of serum 25(OH) D compared to non-sarcopenic non-osteopenic participants whereas no significant differences in serum 25(OH)D or number of chronic conditions was observed between osteodynepenic and non-dynapenic non-osteopenic participants. Falls risk score did not differ across sarcopenic/osteopenic categories whereas it was significantly higher among participants with osteodynepenia compared to those who were non-dynapenic non-osteopenic.

Incident fracture and mortality over 10 years were 17% and 15% respectively. Fig. 1 shows the incidence of fracture over 10 years stratified according to osteopenic, sarcopenic and dynapenic status. Incident fracture was higher in participants who were osteosarcopenic (21%) and osteopenic non-sarcopenic (21.5%) compared to those who were sarcopenic non-osteopenic (13%) and non-sarcopenic non-osteopenic (13.5%). Fracture was more prevalent among participants who were osteodynepenic (25.4%), osteopenic non-dynapenic (20.4%), dynapenic non-osteopenic (19.5%) compared to those who were non-dynapenic non-osteopenic (12%).

Fig. 2 shows the incidence of mortality over 10 years stratified according to osteopenic, sarcopenic and dynapenic status. Mortality was more prevalent in participants who were osteosarcopenic (27.9%), and sarcopenic non-osteopenic (23.2%) compared to those who were osteopenic non-sarcopenic (15.3%) and non-sarcopenic non-osteopenic (11.3%). Mortality was also higher in participants who were osteodynepenic (22%) and dynapenic non-osteopenic (21.6%) compared to those who were osteopenic non-dynapenic (16.4%) and non-dynapenic non-osteopenic (11.5%).

#### 3.1. Associations of osteosarcopenia and osteodynepenia with incident fracture

Table 2 shows the risk ratios for self-reported fracture over 10 years according to osteopenic, sarcopenic, and dynapenic categories. Fracture risk was significantly higher among participants who were osteopenic non-sarcopenic (RR = 1.50, 95% CI: 1.07, 2.10) but not among those who were osteosarcopenic (RR = 1.48, 95% CI: 0.83, 2.64) or sarcopenic non-osteopenic (RR = 0.97, 95% CI: 0.52, 1.81), compared to non-sarcopenic non-osteopenic participants. Osteosarcopenia did not lead to a significantly greater risk of fracture compared to those with sarcopenia alone (P = 0.255) or osteopenia alone (P = 0.964).

Fracture risk was significantly higher in participants who were osteodynepenic (RR = 2.07, 95% CI: 1.26–3.39), dynapenic non-

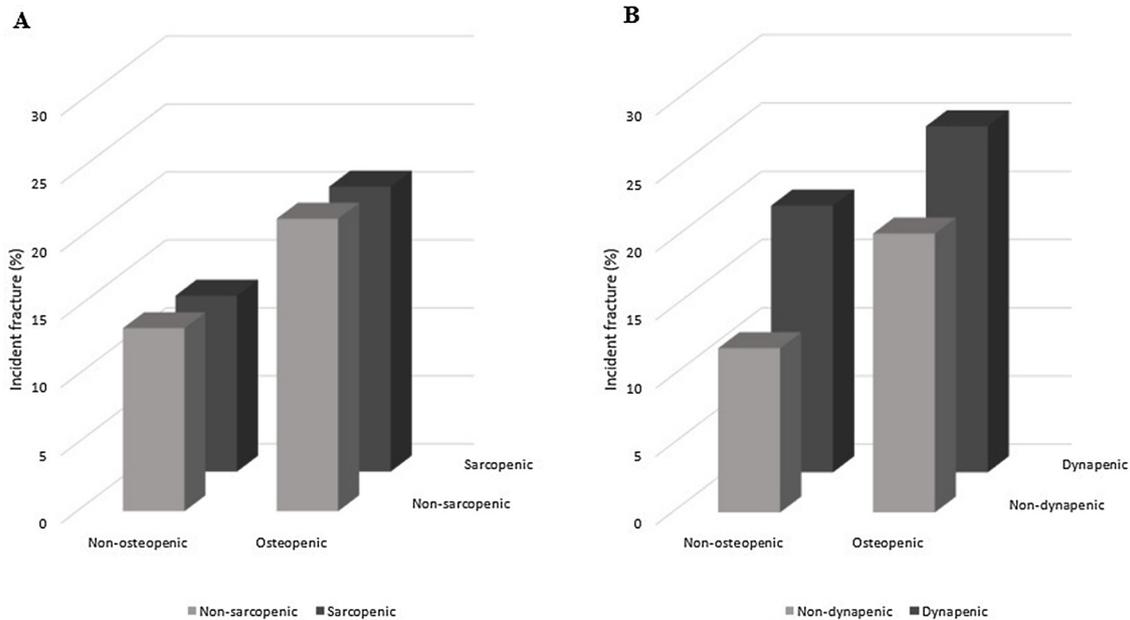


Fig. 1. Incident fracture over 10 years stratified according to sarcopenic/osteopenic (A) and dynapenic/osteopenic (B) status.

osteopenic (RR = 1.74, 95% CI: 1.05, 2.87), and osteopenic non-dynapenic (RR = 1.63, 95% CI: 1.15, 2.31), compared to those without dynapenia or osteopenia. Osteodynepenia did not lead to a significantly greater risk of fracture compared to those with dynapenia alone ( $P=0.561$ ) or osteopenia alone ( $P=0.311$ ).

There was no significant sex interaction with regards to the association between fracture risk and sarcopenic/osteopenic categories ( $P=0.889$ ) or dynapenic/osteopenic categories ( $P=0.749$ ).

### 3.2. Associations of osteosarcopenia and osteodynepenia with mortality

Table 3 shows the incident rate ratios for mortality over 10 years according to osteopenic, sarcopenic, and dynapenic categories. Mortality risk was significantly higher among participants who were osteosarcopenic (RR = 1.49, 95% CI: 1.01, 2.21) but not among those who were osteopenic non-sarcopenic (RR = 1.27, 95% CI: 0.92, 1.76) or sarcopenic non-osteopenic participants (RR = 1.30, 95% CI: 0.88,

1.91), compared to those participants who were non-sarcopenic non-osteopenic. The combination of osteosarcopenia did not lead to a significantly greater risk of mortality compared to those with sarcopenia alone ( $P=0.529$ ) or osteopenia alone ( $P=0.418$ ).

There was no evidence for increased risk of mortality for participants who were osteodynepenic (RR = 1.03, 95% CI: 0.68, 1.57), dynapenic non-osteopenic (RR = 0.91, 95% CI: 0.62, 1.34) or osteopenic non-dynapenic (RR = 1.27, 95% CI: 0.93, 1.72) compared to those who were non-dynapenic non-osteopenic. The combination of osteodynepenia did not lead to a significantly greater risk of mortality compared to those with dynapenia alone ( $P=0.602$ ) or osteopenia alone ( $P=0.318$ ). There was no significant sex interaction with regards to the association between mortality risk and sarcopenic and osteopenic categories ( $P=0.555$ ) or dynapenic and osteopenic status ( $P=0.514$ ).

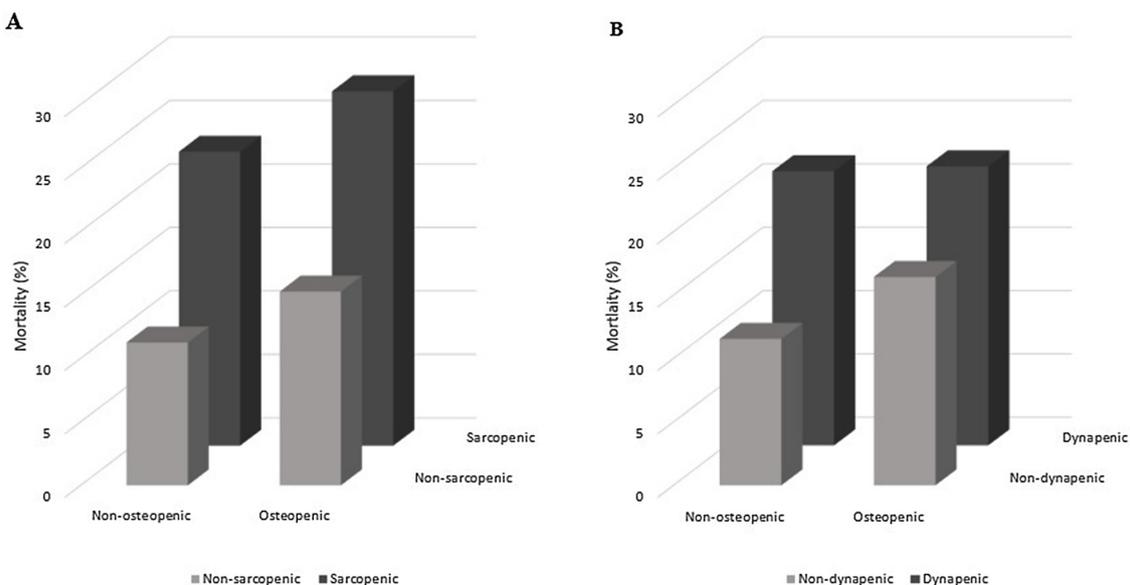


Fig. 2. Mortality over 10 years stratified according to sarcopenic/osteopenic (A) and dynapenic/osteopenic (B) status.

**Table 2**  
Relative risk (95% CI) for self-reported fracture over 10 years according to sarcopenic, dynapenic, and osteopenic categories.

	Non-sarcopenic, Non-osteopenic N = 401	Osteopenic non-sarcopenic N = 288	Sarcopenic non-osteopenic N = 85	Osteosarcopenic N = 62
Unadjusted	REF	<b>1.60 (1.15, 2.23)</b>	0.96 (0.52, 1.76)	1.56 (0.90, 2.68)
Adjusted*	REF	<b>1.50 (1.07, 2.10)</b>	0.97 (0.52, 1.81)	1.48 (0.83, 2.64)
	Non-dynapenic, Non-osteopenic N = 399	Osteopenic non-dynapenic N = 279	Dynapenic non-osteopenic N = 87	Osteodynapenic N = 71
Unadjusted	REF	<b>1.70 (1.19, 2.42)</b>	1.62 (0.98, 2.68)	<b>2.11 (1.30, 3.40)</b>
Adjusted*	REF	<b>1.63 (1.15, 2.31)</b>	<b>1.74 (1.05, 2.87)</b>	<b>2.07 (1.26, 3.39)</b>

Relative risk represents the increased risk compared to the REF (reference) group.

\* Adjusted for age, sex, physical activity (steps/day) and 25-hydroxyvitamin-D. Bold text indicates significant at P < 0.05.

**Table 3**  
Relative risk (95% CI) for mortality over 10 years according to sarcopenic, dynapenic, and osteopenic categories.

	Non-sarcopenic, Non-osteopenic N = 471	Osteopenic non-sarcopenic N = 367	Sarcopenic non-osteopenic N = 108	Osteosarcopenic N = 86
Unadjusted	REF	1.36 (0.96, 1.92)	<b>2.06 (1.34, 3.15)</b>	<b>2.48 (1.62, 3.79)</b>
Adjusted*	REF	1.27 (0.92, 1.76)	1.30 (0.88, 1.91)	<b>1.49 (1.01, 2.21)</b>
	Non-dynapenic, Non-osteopenic N = 468	Osteopenic non-dynapenic N = 353	Dynapenic non-osteopenic N = 111	Osteodynapenic N = 100
Unadjusted	REF	<b>1.42 (1.01, 2.01)</b>	<b>1.87 (1.21, 2.89)</b>	<b>1.91 (1.22, 2.98)</b>
Adjusted*	REF	1.27 (0.93, 1.72)	0.91 (0.62, 1.34)	1.03 (0.68, 1.57)

Relative risk represents the increased risk compared to the REF (reference) group.

\* Adjusted for age, sex, physical activity (steps/day) and number of chronic conditions. Bold text indicates significant at P < 0.05.

#### 4. Discussion

This long-term prospective study investigates the association of sarcopenia and dynapenia in the presence of osteopenia with fracture and mortality over 10 years in a large sample of community-dwelling older adults. We found that incident fracture over 10 years was significantly higher among older adults who were osteodynapenic, dynapenic alone and osteopenic alone compared to those without dynapenia or osteopenia. Furthermore, mortality over 10 years was significantly higher in participants with osteosarcopenia compared to those without sarcopenia or osteopenia. Notably, the combination of osteopenia with sarcopenia or dynapenia did not lead to a significantly greater mortality or fracture risk compared to having these conditions on their own. These findings suggest that the combined effect of osteopenia and sarcopenia or dynapenia on fracture and mortality risk, respectively, may not be greater than that of each individual condition.

The coexistence of low BMD and low muscle strength (osteodynapenia), but not low BMD and low muscle mass (osteosarcopenia), significantly increased the risk of fracture over 10 years. Low BMD is an established risk factor for fracture (Ensrud, 2013; Hamdy, 2016) and muscle strength exerts significant force on the bone, contributing to the maintenance of bone strength (Christen, Ito, & Ellouz, 2014). Hence, both low muscle strength and low BMD in older adults may not adequately stimulate osteogenesis thereby increasing fracture risk in the event of a fall. Furthermore, prior studies have suggested that low muscle strength (but not muscle mass) significantly increases falls risk in older people, potentially due to accelerated age-related decline in muscle strength compared to muscle mass (Balogun, Winzenberg, & Wills, 2017; Manini & Clark, 2012). This may explain why the coexistence of low BMD and low muscle strength but not low muscle mass results in a high risk of fractures. The higher risk of fracture in participants with osteodynapenia was largely driven by osteopenia as we observed significant excess risk of fracture in participants with osteopenia (with or without dynapenia) compared to those without osteopenia (Supplementary Table 1). While osteodynapenia was associated with increased fracture risk, the risk was not significantly greater compared to having osteopenia or dynapenia alone. This suggests that the combined assessment does not add additional risk for fracture in individual with either condition. When BMD, muscle mass and strength were considered as continuous variables, increasing BMD but not muscle mass or strength was associated with a lower risk of fracture (Supplementary Table 2). It was surprising that HGS (as continuous variable) was not associated with fracture risk, given it is a marker of overall muscle strength in the body. There have been several attempts to identify HGS thresholds for the identification of clinically relevant weakness (Alley, Shardell, & Peters, 2014; Cheung et al., 2012). The lowest 20% of the sex-specific distribution of HGS, as used in this study, has been shown to be predictive of fracture and poorer health outcomes in older people (Balogun et al., 2017; Hairi et al., 2010).

The coexistence of low BMD and low muscle mass (osteosarcopenia), but not low BMD and low muscle strength (osteodynapenia), significantly increased the risk of mortality over 10 years. While osteosarcopenia was associated with increased mortality risk, the risk was not significantly greater compared to having osteopenia or sarcopenia alone. Although, we did not see an increased mortality risk in those with osteopenia or sarcopenia alone compared to having neither condition. Contrary to the risk of fracture it was muscle mass (not strength) that was important for mortality. Low ALM/BMI is indicative of high body fat percentage which has been shown to be associated with mortality risk (Padwal, Leslie, Lix, & Majumdar, 2016). A prior study also showed that low BMD is predictive of mortality over 6 years, independent of comorbidities, physical activity and previous history of fractures (Johansson, Odén, & Kanis, 2011). Therefore, the coexistence of both low BMD and low ALM/BMI may confer additional risk. Low muscle mass (as opposed to low strength) combined with low BMD may increase mortality risk because muscle mass serves as a reliable protein

reserve and plays a key role in recovery from illness or trauma, including fracture healing (Stini, 1991). Indeed, survival following fracture is lower in older adults with low muscle mass compared to those with normal muscle mass (Deren et al., 2017). For instance, in a sample of 192 older adults admitted to the hospital following acetabular fracture, mortality over one year was 28.6% in those with low muscle mass compared with 12.3% in those with normal muscle mass (Deren et al., 2017). The higher risk of mortality in participants with osteosarcopenia was mainly driven by sarcopenia as we observed significant excess risk of mortality in participants with sarcopenia (with or without osteopenia) compared to those without sarcopenia (Supplementary Table 3). Notably, mortality risk in individuals with osteosarcopenia was not significantly different from those with osteopenia or sarcopenia alone. Interestingly, no significant relationships were observed among muscle and BMD as continuous variables, and mortality after adjusting for covariates (Supplementary Table 4). This finding is consistent with prior studies providing evidence for a non-linear relationship between muscle mass, BMD and mortality (Cawthon, Peters, & Shardell, 2014; Johansson et al., 2011).

It is clear that improvements are needed when clinically identifying older people at risk of poor musculoskeletal health outcomes (Binkley et al., 2013; Hill, Farrier, Russell, & Burton, 2017). Basing risk prediction on a single risk factor such as sarcopenia, dynapenia or osteoporosis alone may be too narrow and may exclude subgroups of older people who have combined risk factors and may be at a greater risk of adverse health outcomes (Hill et al., 2017). We examined whether the combination of osteopenia and sarcopenia/dynapenia significantly increases the risk of fracture and mortality compared to these conditions alone. However, other authors have recommended the combination of a more diverse range of conditions (Binkley et al., 2013; Cruz-Jentoft, Baeyens, & Bauer, 2010). For instance, Binkley et al. (2013) recommended the combination of six common risk factors including low lean mass, low handgrip strength, osteoporosis, obesity/high fat mass, falls in the preceding year and slow gait speed (Binkley et al., 2013). Older adults with three or more of the six conditions are said to have a dysmobility syndrome (Binkley et al., 2013). Several authors have shown that dysmobility syndrome increases the risk of fracture and mortality (Binkley et al., 2013; Lee et al., 2017; Looker, 2015). However, further studies are required to clarify whether the risk of fracture and mortality observed among older people with dysmobility syndrome is significantly different from those with each individual risk factor. Ascertaining whether dysmobility syndrome significantly increases the risk of fracture and mortality compared to each individual risk factor alone may facilitate the uptake of this approach in clinical settings.

The strength of this study includes the 10-year follow-up period and the use of a population-based sample which increases its generalizability. In addition, body composition was assessed using DXA, a gold standard for diagnosing osteopenia/osteoporosis and a valid instrument for measuring muscle mass. However, this study has a number of limitations. Firstly, there was 19% missing data for incident fracture. Such missing data is not unexpected in a long-term prospective study involving older people. We performed sensitivity analysis for missing data using inverse probability weighting to assess the robustness of the fracture models. The results of the analyses were similar to the complete case analyses (Supplementary Tables 5 and 6). Secondly, incidence of fracture was self-reported and may be subject to recall bias. However, inaccuracy of fracture recall is unlikely as fractures are a major life event (Ivers, Cumming, Mitchell, & Peduto, 2002). Thirdly, we were unable to perform cause-specific analysis for mortality as data on the specific cause of death was not available for all the participants. Furthermore, we did not assess the association of both sarcodynapenia (coexistence of sarcopenia and dynapenia) and osteopenia with fracture and mortality as only 2.6% ( $n = 27/1032$ ) of our sample had both sarcodynapenia and osteopenia. Lastly, established definitions for sarcopenia were not used in this study as only 4 participants (men = 4; women = 0) were classified as having sarcopenia according to the

established cut-points for ALM/BMI by the Foundation for National Institute of Health (FNIH) sarcopenia project. In contrast we defined cut-points in the lowest 20% of the sex-specific distribution of muscle mass and strength, which has previously been used as a diagnostic measure for sarcopenia (Newman et al., 2003; World Health Organization, 1994). Despite this we were able to find important associations using this diagnostic measure for low muscle mass and strength.

In conclusion, low BMD combined with low muscle mass or strength does not significantly increase the risk of fracture or mortality compared to having low BMD or low muscle mass/strength alone, suggesting that combined assessments may not add additional risk for fracture and mortality.

### Conflict of interest

The authors have no conflicts of interest to declare

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### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.archger.2019.01.015>.

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