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Agreement and Predictive Validity Using Less Conservative FNIH Sarcopenia Project Weakness Cutpoints

Nancy Chiles Shaffer, Ph.D.[1], **Luigi Ferrucci, M.D**[1], **Michelle Shardell, Ph.D.**[1], **Eleanor M. Simonsick, Ph.D.**[1], and **Stephanie Studenski, M.D.**[1]

[1]Longitudinal Studies Section, Translational Gerontology Branch, National Institute on Aging, National Institutes of Health, Baltimore, MD, 21225

Abstract

OBJECTIVES—The FNIH Sarcopenia Project derived conservative definitions for weakness and low lean mass, resulting in low prevalence and low agreement with prior definitions. The FNIH Project also estimated a less conservative cutpoint for low grip strength, potentially yielding a cutpoint for low lean mass more consistent with the European Working Group on Sarcopenia in Older People (EWGSOP). We derived lean mass cutpoints based on the less conservative cutpoint for grip strength ($Weak_I$), and assessed agreement with EWGSOP and prediction of incident slow walking and mortality.

Address Correspondence To: Nancy Chiles Shaffer, Ph.D., National Institute on Aging, MedStar Harbor Hospital, 3001 S. Hanover Street, 5th Floor, Baltimore, MD 21225, Office: 410-350-3971, Fax: 410-350-7304, nancy.chiles@nih.gov.

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Royalties		X		X		X		X		X
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DESIGN, SETTING, PARTICIPANTS, MEASUREMENTS—Longitudinal analysis of 287 men and 258 women from the Baltimore Longitudinal Study of Aging aged >65 years, with 2–10 years followup. Weakness was determined via hand dynamometer, appendicular lean mass (ALM) via DEXA, and slow walking by 6m usual pace walk <0.8m/s. Analyses used classification and regression tree analysis, Cohen's Kappa, and Cox models.

RESULTS—Cutpoints derived from $Weak_I$ for ALM (ALM_I) and ALM adjusted for body mass index (ALM/BMI_I) were (ALM_I) <21.4kg (men) and <14.1kg (women); and (ALM/BMI_I) <0.725 (men) and <0.591 (women). Kappas with EWGSOP were ($ALM_{I);}$ 0.65 (men) and 0.75 (women) and $ALM/BMI_{I;}$ 0.34 (men) and 0.47 (women). In men, the hazard ratio for incident slow walking by $Weak_I$ + ALM_I was 2.44 (95% CI:1.02–5.82) versus 2.91 (95% CI:1.11–7.62) by EWGSOP. Neither approach predicted incident slow walking in women.

CONCLUSION—The ALM_I cutpoints agree with EWGSOP and predict slow walking in men. Future studies should explore sex differences in the relationship between body composition and physical function and the impact of change in muscle mass on muscle strength and physical function.

Keywords

Aging; Sarcopenia; Weakness; Muscle

INTRODUCTION

Sarcopenia, the age-associated loss of muscle and strength, may contribute to functional decline. Recently, multiple research groups developed definitions and criteria for sarcopenia, including the European Working Group on Sarcopenia in Older People (EWGSOP), and the Foundations for National Institutes of Health (FNIH) Sarcopenia Project. Although the measures of muscle mass and muscle strength overlap, the cutpoints differ. Recent comparisons among definitions have shown low levels of agreement, limiting the ability to begin to apply these criteria to research studies and clinical care[1–3]. The classic definition of sarcopenia established by Baumgartner et al was based on low lean mass, because mass itself was assumed to strongly affect muscle function[4]. More recently, age-related strength decline has been shown to exceed lean mass decline and to correlate more strongly with poor lower extremity function[5,6]. Thus contemporary definitions of sarcopenia include both muscle mass and strength. The EWGSOP first used this approach to recommended that sarcopenia definitions include both low lean mass and low muscle function, and defined function as either strength or performance[6]. They proposed three stages of sarcopenia: presarcopenia is low lean mass without low muscle function, sarcopenia is low lean mass with either low muscle strength or low performance , and severe sarcopenia is low muscle mass with low muscle strength and low performance. Grip strength cutpoints for EWGSOP were <30kg for men and <20 kg for women[6]. The mass cutpoints were derived from a population distribution, similar to Baumgartner et al, with an appendicular lean mass adjusted for height (RALM) less than two standard deviations below the sex-specific means of young reference groups (Men: 7.26 kg/m^2, Women: 5.50 kg/m^2)[6].

Given the varying definitions of the term, “sarcopenia”, the FNIH Sarcopenia Project avoided it, and proposed cutpoints for “clinically meaningful” low muscle strength (weakness) and low lean mass based on their ability to predict slow walking speed (<0.8 m/s) and weakness, respectively[5]. The Project team suggested that these cutpoints could provide a “differential diagnosis”, distinguishing muscle weakness as a result of low muscle mass from muscle weakness due to other causes, or even low lean mass in the absence of weakness. The cutpoints for low lean mass and weakness were empirically determined using pooled data from several data sets and were intended to be very conservative with high specificity and low false positive rates.

The FNIH cutpoints were developed through recursive partitioning, a method that splits data into mutually exclusive and collectively exhaustive groups. The FNIH weakness cutpoint was based on the group with the lowest cutpoint for grip strength predictive of slow walking speed, and the cutpoint for low mass based on the group with the lowest cutpoint for muscle mass predictive of weakness[5]. The recursive partitioning approach also yielded an intermediate cutpoint for weakness[7] ($Weak_I$); however, no intermediate cutpoints for low lean mass were derived. Less stringent cutpoints for low lean mass and weakness would likely lead to a higher prevalence and better agreement with other criteria. The FNIH studies suggested that body mass index (BMI) adjustment might be an important factor in determining the relationship between mass, strength and function, so new cutpoints would need to be assessed with and without BMI adjustment.

The original FNIH cutpoints for weakness and low lean mass showed poor agreement with the EWGSOP and yielded lower prevalence rates[3]. Thus, we expect the new lean mass cutpoints, derived from and used in conjunction with the less conservative FNIH weakness cutpoint, to improve agreement with EWGSOP and yield more similar prevalence estimates.

This study developed new cutpoints for appendicular lean mass (ALM), with and without BMI adjustment, based on the reported less conservative FNIH strength cutpoints using data from the Baltimore Longitudinal Study of Aging (BLSA). We assessed agreement with the EWGSOP definition and ability to predict incident slow walking and mortality.

METHODS

Study Sample

The BLSA is a longitudinal study of normative aging established in 1958 and currently administered by the Intramural Research Program of the National Institute on Aging. This observational study continuously enrolls initially healthy participants over age 20 for biological, behavioral, physical, and psychological assessments to help determine changes that occur with aging, factors associated with healthy aging, and factors associated with age-related diseases. The study protocol is IRB approved and all participants gave informed consent. More detailed descriptions of the BLSA study design have been previously reported[8].

Analytic Sample

This analysis included participants aged 65 years and older with at least 2 years of follow up and measures of muscle strength, muscle mass, and walking speed. The sample consisted of 286 men and 257 women, with an average follow-up of 5 years (range: 2 to 9).

Measurements for Muscle Strength, Muscle Mass, and Physical Function

Muscle strength was assessed using grip strength, measured using a Jamar Hydraulic Hand Dynamometer and defined as the maximum of three consecutive trials from either hand (kilograms, kg). ALM, the sum of lean mass in both arms and legs (kg), was assessed via dual-energy X-ray absorptiometry (DXA) (Lunar Prodigy Advance with GE EnCore 2006 version 10.51.0006, General Electric, Madison, WI). Slow walking was determined from the average of two trials of usual 6m gait speed. Participants unable to attend a clinic visit had gait speed assessed in the home. Usual gait speed less than 0.80 m/s was defined as slow[5,6]. All participants who were slow at baseline were excluded from the longitudinal analyses. Mortality was ascertained from family report and corroborated or supplemented by the Social Security Death Index (SSDI).

Weakness and Low Lean Mass Classifications

Based on the less conservative (intermediate) FNIH grip strength cutpoint ($Weak_I$), the new lean mass cutpoints (ALM_I and ALM/BMI_I), and the EWGSOP cutpoints, three classes of weakness and low lean mass were created: 1) FNIH $Weak_I$ and ALM_I, 2) FNIH $Weak_I$ and ALM/BMI_I, 3) and EWGSOP weakness and low RALM. Within each classification, participants were subclassified as either being: 1) not weak with normal lean mass, 2) not weak with low lean mass, 3) weak with normal lean mass, or 4) weak with low lean mass. Derivation of ALM_I and ALM/BMI_I is described below.

Statistical Analyses

Analyses were performed using SAS version 9.3 (SAS Institute Inc. Cary, NC). All analyses were stratified by sex. Descriptive statistics for participant characteristics were based on the index visit. Similar to Cawthon et al, classification and regression tree (CART) analysis was used to derive appropriate ALM_I and ALM/BMI_I cutpoints for the study sample[9]. Recursive partitioning was performed using R software (version 3.1.2) with the rpart package. ALM and ALM/BMI were individually used in CART models to predict FNIH $Weak_I$ (31.83 kg for men and 19.99 kg for women). To prevent over-fitting, the tree was pruned by minimizing cross-validation error via internal leave 10% out cross-validation, wherein the data were divided into 10 mutually exclusive data sets, with each set excluding 10% of the original sample and classification error repeatedly estimated within the remaining 90% of the data (leaving out a different 10% each time). The final model was selected as the most parsimonious model with a cross-validated classification error within one standard deviation of the minimum classification error.

To compare the FNIH and EWGSOP classifications, positive percent agreement (analogous to sensitivity) and negative percent agreement (analogous to specificity) were calculated with EWGSOP treated as the gold standard, as well as Cohen's Kappa statistics, as in

previous FNIH analyses[3]. For these cross-sectional comparisons, weakness and low lean mass were classified at a participant's most recent visit.

Cox proportional hazards models were fit to assess risk of developing incident slow walking over time by each sarcopenia subclass, separately for men and women. Sarcopenia was modeled as a time-varying covariate, which involved updating sarcopenia status at each assessment[10]. For these analyses, sarcopenia status was modeled to predict incident slow walking at the subsequent visit. Initial models were unadjusted, followed by an adjustment for age at baseline. No additional confounders were included to be comparable to published analyses[11]. The same analyses were used to predict mortality.

RESULTS

The characteristics of the study population (287 men and 258 women) are presented in Table 1. Mean follow-up was 5.7 (2.2) and 5.6 (2.2) years for men and women, respectively. Overall, 8.5% of men and 3.9% of women died over the follow-up period.

Based on the reported FNIH less conservative grip strength cutpoints of 31.83 for men and 19.99 for women, the cutpoints derived from CART analyses for ALM_I were 21.38 kg for men and 14.12 kg for women, and the ALM/BMI_I cutpoints were 0.725 m^2 for men and 0.591 m^2 for women.

Prevalence of each weakness and low lean mass definition are also shown in Table 1. For men, the prevalence of weakness using the new FNIH cutpoint was higher than when using EWGSOP, while ALM/BMI_I was less common than ALM_I. The EWGSOP definition of low mass (low RALM <7.23 kg/m^2) had the highest prevalence of low lean mass. The subclass "weak with low lean mass" was most prevalent by the FNIH $Weak_I$ + ALM_I classification and least by the FNIH $Weak_I$ + ALM/BMI_I.

In women, the prevalence of weakness was similar in EWGSOP and FNIH $Weak_I$, while the prevalence of ALM/BMI_I was higher than low RALM and ALM_I. The highest prevalence of "weak with low lean mass" was observed with the FNIH $Weak_I$ + ALM/BMI_I classification and lowest for EWGSOP.

Agreement improved using the new FNIH cutpoints. In men, while both intermediate FNIH definitions had high negative percent agreements with EWGSOP (FNIH $Weak_I$ + ALM_I: NPA=92%; FNIH $Weak_I$ + ALM/BMI_I: NPA=96.2%), only FNIH $Weak_I$ + ALM_I had a high positive percent agreement and a kappa statistic indicating good agreement with EWGSOP (PPA 83.9%, κ=0.65). High agreement was due to similar grip strength cutpoints between the less conservative FNIH and EWGSOP (Men: FNIH $Weak_I$ 31.83 kg, EWGSOP 30.00 kg). In women, both FNIH definitions yielded high negative percent agreements with EWGSOP (FNIH $Weak_I$ + ALM_I: NPA=97.7%; FNIH $Weak_I$ + ALM/BMI_I: NPA=89.5%). The FNIH intermediate and EWGSOP grip strength cutpoints were similar (FNIH $Weak_I$ 19.99 kg, EWGSOP 20.00 kg) and both FNIH $Weak_I$ + ALM_I (PPA=88.2%) and FNIH $Weak_I$ + ALM/BMI_I (PPA=82.4%) had high positive percent agreement with EWGSOP. Additionally, kappa statistics indicated fair (FNIH $Weak_I$ + ALM/BMI_I: κ=0.47) or excellent (FNIH $Weak_I$ + ALM_I: κ=0.79) agreement.

For men, the incidence of slow walking by sarcopenia definition and group is displayed in Table 2, along with the hazard ratio within each group compared to normal (not weak + normal lean mass). Using the FNIH $Weak_I$ and ALM_I definition, those not weak with low lean mass, weak with normal lean mass and weak with low lean mass had a higher incidence of slow walking. After age adjustment, the weak with low lean mass group still had a higher incidence of slow walking. In both unadjusted and adjusted analyses for ALM/BMI_I, only weak men with normal lean mass had a higher incidence of slow walking compared to men with normal strength and mass. Using the EWGSOP definition in unadjusted analyses in men, all subgroups had a higher incidence rate of slow walking than the normal group. After age-adjustment, both the not weak and low lean mass group and the weak with low lean mass group had higher incident slow walking over time.

Results in women are shown in Table 3. Using the FNIH $Weak_I$ and ALM/BMI_I definition, only those with weakness and low lean mass had a higher incidence of slow walking relative to the normal group, which became non-significant after age adjustment. Weakness with normal lean mass was associated with a lower incidence of slow walking after age adjustment. No associations were observed using the EWGSOP cutpoints.

Supplementary Tables S1 and S2 describe incident mortality per 100 person-years, as well as the hazard ratio for mortality in men and women. Neither the FNIH intermediate definitions nor EWGSOP was associated with mortality in unadjusted or adjusted models.

DISCUSSION

We derived new lean mass cutpoints based on previously described less conservative, intermediate FNIH $Weak_I$ cutpoints[7]. The FNIH intermediate definitions showed stronger agreement with EWGSOP than the original weakness and low lean mass cutpoints, and better agreement without BMI adjustment[3]. Both intermediate cutpoints (with and without BMI adjustment) and the EWGSOP predicted incident slow walking in men, but not in women.

Recognition and treatment of sarcopenia would be facilitated by greater uniformity across definitions[1–3]. Several reports have compared definitions of sarcopenia and found varying prevalence ranges[1–3] and poor agreement[3,12]. Comparisons of EWGSOP and the original FNIH reported prevalence from 1.6–20.4% in men and 2.5–26.2% in women[2]. Comparing definitions using mass or grip separately also resulted in broad prevalence ranges - 0–45.2% and 0–25.8% in men and women respectively[1]. Improving agreement across definitions may help increase applicability for clinical care and research. The very conservative values for the FNIH definition contribute to the low agreement with other definitions. The less conservative, intermediate weakness and resultant lean mass cutpoints described here help improve agreement, and may indicate that the FNIH intermediate and EWGSOP identify a mild/moderate degree of sarcopenia while the original FNIH definition identifies those with severe sarcopenia.

For clinical application, it is important to fully understand how sarcopenia definitions distinguish older adults. A longitudinal analysis in men that compared several definitions of

sarcopenia and their predictive and discriminative ability for multiple clinical outcomes found many of the definitions, including the FNIH and EWGSOP, were associated with increased risk of clinical outcomes[13]. The definitions, however, did not discriminate better than age alone. To meet its intended purpose, definitions of sarcopenia should distinguish this geriatric syndrome from declines of normal aging.

While the intermediate definitions of weakness and resultant low lean mass seem suitable for assessment in men, our results showed no associations with higher incidence of slow walking in women. Weakness with normal lean mass, after adjusting for age, trended in the direction of lower incidence of slow walking with each definition, even reaching significance in the FNIH $Weak_I$ and ALM/BMI_I definition. In the original FNIH Sarcopenia Project pooled cohort, weakness regardless of low lean mass was associated with a higher odds of future slow walking relative to being not weak with normal lean mass in men[11]. In women, being weak and/or having low lean mass was associated with higher odds of future slow walking compared to being not weak with normal lean mass[11]. These differences in association may be due to sample differences. Compared to the original FNIH pooled cohort[11], the BLSA women at baseline are younger (mean age 73.1 vs 76.5) and have a higher mean grip strength (23.6 vs. 22.1). The BLSA men at baseline were more comparable to the FNIH pooled cohort in age (mean 74.4 vs. 74.0) and BLSA men had a lower mean grip strength at baseline (38.1 vs. 41.3), both of which may explain why we found associations with higher incidence of slow walking in men but not women. Additionally, the $Weak_I$ cutpoint may be too liberal for women in the BLSA due to the above-mentioned differences, which may explain why FNIH $Weak_I$ and ALM/BMI_I was associated counter-intuitively with a lower incidence of slow walking.

The strengths of this study include multiple assessments of muscle mass, strength, and walking speed over time, as well as inclusion of data on walking speed from home assessments. Additionally, the time-varying analysis allowed for change in status over time. The primary limitation is the relatively good health of BLSA participants who had a lower incidence of slow walking and mortality than other cohorts. Lower outcome rates coupled with a smaller sample size may have limited our power to observe expected associations.

These results indicate that using the less conservative FNIH weakness cutpoints improves agreement while still identifying men at risk of future slow walking. Caution, however, should be taken in using the lean mass cutpoints derived from the BLSA in other cohorts. The ALM_I cutpoint derived in women in this sample and the ALM/BMI_I cutpoint derived in men in this sample are lower than those derived in the original FNIH study (ALM_I: 14.12 kg vs. 15.02 kg, ALM/BMI_I: 0.725 m^2 vs. 0.789 m^2). These lower cutpoints may also be due to sample differences, as described earlier. When comparing baseline gait speed in the BLSA participants to the original FNIH sarcopenia project cohort, there is a lower prevalence of gait speed less than or equal to 1.0 m/s in BLSA men (21.2% vs. 28.7%) and women (32.1% vs. 66.5%). This may explain why lower lean mass cutpoints were necessary to identify participants at risk of slowness in the BLSA compared to other cohorts.

Conceptually, sarcopenia is an important state, but challenges with operational definitions remain. Future research should focus beyond between- person effects, to the trajectory and

timeline of loss of muscle mass and strength, as well as the impact of muscle quality. In addition, future work should address the causes of the strikingly different relationships between mass, strength and future function among men and women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Participant Characteristics

	Men n=287	Women n=258
	Mean (SD) or %	Mean (SD) or %
Age, years	79.2 (7.2)	77.7 (7.3)
Height, m	1.7 (0.1)	1.6 (0.1)
BMI, kg/m^2	27.2 (3.8)	27.0 (5.2)
Grip Strength, kg	34.4 (8.5)	21.9 (6.1)
ALM, kg	24.0(3.6)	16.9 (2.6)
ALM/BMI, m^2	0.9 (0.2)	0.6 (0.1)
RALM, kg/m^2	8.0 (1.0)	6.5 (0.9)
Average Gait Speed, m/s	1.1 (0.2)	1.1 (0.2)
FNIH Intermediate Weak (%)	33.5	30.1
EWGSOP Weak (%)	23.9	30.1
Intermediate Low ALM (%)	22.7	12.3
Intermediate Low ALM/BMI (%)	20.8	42.9
Low RALM (%)	21.6	15.7
FNIH Intermediate Weak[a] + Low ALM[b]		
Not weak, normal ALM (%)	60.4	66.1
Not weak, low ALM (%)	6.2	3.8
Weak, normal ALM (%)	16.9	21.6
Weak, low ALM (%)	16.5	8.5
FNIH Intermediate Weak[a] + Low ALM/BMI[c]		
Not weak, normal ALM/BMI (%)	61.2	48.3
Not weak, low ALM/BMI (%)	5.4	21.6
Weak, normal ALM/BMI (%)	26.5	14.4
Weak, low ALM/BMI (%)	6.9	15.7
EWGSOP Weak[d] + Low RALM[e]		
Not weak, normal RALM (%)	65.3	61.3
Not weak, low RALM (%)	10.8	8.5
Weak, normal RALM (%)	13.1	23.0
Weak, low RALM (%)	10.8	7.2
Died over follow-up (%)	8.5	3.9
Mean follow-up time	5.7 (2.2)	5.6 (2.2)

BMI = body mass index, ALM = appendicular lean mass, RALM = relative appendicular lean mass (ALM/height squared), FNIH=Foundation for the National Institutes of Health, EWGSOP = European Working Group on Sarcopenia in Older People.

[a] FNIH Intermediate Weak = grip strength <31.83 kg (men), <19.99 kg (women);

[b] Intermediate ALM = <21.38 kg (men), <14.12 kg (women);

[c] Intermediate ALM/BMI = <0.725 m^2 (men), <0.591 m^2 (women);

[d] EWGSOP Weak = grip strength <30 kg (men), <20 kg (women);

[e] Low RALM = <7.26 kg/m^2 (men), <5.50 kg/m^2 (women).

Table 2

Hazard of Incident Slow Walking by Weakness and Low Lean Mass Definition, Men

	Men				
	Incident Slow Walking by Group	**Person Years**	**Incidence Rate per 100 pys**	**Unadjusted**	**Baseline Age adjusted**
	n			**HR (95% CI)**	**HR (95% CI)**
FNIH Intermediate Weak[a] + Low ALM[b]					
Not weak, normal ALM	12	586	2.1	1.0	1.0
Not weak, low ALM	5	94	5.3	3.0 (1.0, 8.4) *	2.0 (0.7, 5.8)
Weak, normal ALM	10	144	6.9	3.2 (1.4, 7.5) *	2.3 (0.96, 5.4)
Weak, low ALM	12	132	9.1	4.6 (2.0, 10.2) *	2.4 (1.0, 5.8) *
FNIH Intermediate Weak[a] + Low ALM/BMI[c]					
Not weak, normal ALM/BMI	15	627	2.4	1.0	1.0
Not weak, low ALM/BMI	2	53	3.8	1.3 (0.3, 5.8)	1.1 (0.2, 4.8)
Weak, normal ALM/BMI	18	218	8.3	3.5 (1.8, 7.0) *	2.3 (1.1, 4.6) *
Weak, low ALM/BMI	4	58	6.9	2.2 (0.7, 6.7)	1.2 (0.4, 3.8)
EWGSOP Weak[d] + Low RALM[e]					
Not weak, normal RALM	12	599	2.0	1.0	1.0
Not weak, low RALM	12	161	7.5	3.7 (1.6, 8.2) *	2.6 (1.1, 6.0) *
Weak, normal RALM	7	100	7.0	3.1 (1.2, 8.0) *	1.8 (0.7, 4.8)
Weak, low RALM	8	94	8.5	5.1 (2.1, 12.7) *	2.9 (1.1, 7.6) *

Pys = person years, BMI = body mass index, ALM = appendicular lean mass, RALM = relative appendicular lean mass (ALM/height squared), FNIH=Foundation for the National Institutes of Health, EWGSOP = European Working Group on Sarcopenia in Older People.

[a] FNIH Intermediate Weak = grip strength <31.83 kg (men), <19.99 kg (women);

[b] Intermediate ALM = <21.38 kg (men), <14.12 kg (women);

[c] Intermediate ALM/BMI = <0.725 m^2 (men), <0.591 m^2 (women);

[d] EWGSOP Weak = grip strength <30 kg (men), <20 kg (women);

[e] Low RALM = <7.26 kg/m^2 (men), <5.50 kg/m^2 (women).

* p-value <0.05

Table 3

Hazard of Incident Slow Walking by Weakness and Low Lean Mass Definition, Women

	Women				
	Incident Slow Walking by Group	**Person Years**	**Incidence Rate per 100 pys**	**Unadjusted**	**Baseline Age adjusted**
	n			**HR (95% CI)**	**HR (95% CI)**
FNIH Intermediate Weak[a] + Low ALM[b]					
Not weak, normal ALM	24	522	4.6	1.0	1.0
Not weak, low ALM	4	58	6.9	1.8 (0.6, 5.2)	1.2 (0.4, 3.4)
Weak, normal ALM	9	165	5.5	1.1 (0.5, 2.5)	0.7 (0.3, 1.5)
Weak, low ALM	7	82	8.5	2.2 (0.96, 5.2)	1.1 (0.5, 2.7)
FNIH Intermediate Weak[a] + Low ALM/BMI[c]					
Not weak, normal ALM/BMI	20	409	4.9	1.0	1.0
Not weak, low ALM/BMI	8	171	4.7	1.0 (0.4, 2.2)	1.0 (0.4, 2.2)
Weak, normal ALM/BMI	2	127	1.6	0.3 (0.1, 1.2)	0.2 (0.04, 0.7) *
Weak, low ALM/BMI	14	120	11.7	3.3 (1.6, 6.5) *	1.8 (0.9, 3.8)
EWGSOP Weak[d] + Low RALM[e]					
Not weak, normal RALM	24	491	4.9	1.0	1.0
Not weak, low RALM	4	88	4.6	1.6 (0.6, 4.6)	1.5 (0.5, 4.4)
Weak, normal RALM	10	181	5.5	1.2 (0.6, 2.5)	0.7 (0.3, 1.5)
Weak, low RALM	6	66	9.1	2.3 (0.9, 5.6)	1.2 (0.5, 3.1)

Pys = person years, BMI = body mass index, ALM = appendicular lean mass, RALM = relative appendicular lean mass (ALM/height squared), FNIH=Foundation for the National Institutes of Health, EWGSOP = European Working Group on Sarcopenia in Older People.

[a] FNIH Intermediate Weak = grip strength <31.83 kg (men), <19.99 kg (women);

[b] Intermediate ALM = <21.38 kg (men), <14.12 kg (women);

[c] Intermediate ALM/BMI = <0.725 m^2 (men), <0.591 m^2 (women);

[d] EWGSOP Weak = grip strength <30 kg (men), <20 kg (women);

[e] Low RALM = <7.26 kg/m^2 (men), <5.50 kg/m^2 (women).

* p-value <0.05