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Authors

Cawthon, Peggy M
Blackwell, Terri L
Cauley, Jane
et al.

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Evaluation of the Usefulness of Consensus Definitions of Sarcopenia in Older Men: Results from the Observational Osteoporotic Fractures in Men Cohort Study

Peggy M. Cawthon, PhD, MPH,[a] Terri L. Blackwell, MA,[a] Jane Cauley, DrPH,[b] Deborah M. Kado, MD, MS,[c] Elizabeth Barrett-Connor, MD,[c] Christine G. Lee, MD,[d] Andrew R. Hoffman, MD,[e] Michael Nevitt, PhD, MPH,[f] Marcia L. Stefanick, PhD,[e] Nancy E. Lane, MD,[g] Kristine E. Ensrud, MD,[hi] Steven R. Cummings, MD,[a] and Eric S. Orwoll, MD[j]

OBJECTIVE: To evaluate the associations between definitions of sarcopenia and clinical outcomes and the ability of the definitions to discriminate those with a high likelihood of having these outcomes from those with a low likelihood.

DESIGN: Osteoporotic Fractures in Men Study.

SETTING: Six clinical centers.

PARTICIPANTS: Community-dwelling men aged 65 and older (N = 5,934).

MEASUREMENTS: Sarcopenia definitions from the International Working Group, European Working Group on Sarcopenia in Older Persons, Foundation for the National Institutes of Health Sarcopenia Project, Baumgartner, and Newman were evaluated. Recurrent falls were defined as two or more self-reported falls in the year after baseline (n = 694, 11.9%). Incident hip fractures (n = 207, 3.5%) and deaths (n = 2,003, 34.1%) were confirmed according to central review of medical records over 9.8 years. Self-reported functional limitations were assessed at baseline and 4.6 years later. Logistic regression or proportional hazards models were used to estimate associations between sarcopenia and falls, hip fractures, and death. The discriminative ability of the sarcopenia definitions (vs reference models) for these outcomes was evaluated using area under the receiver operating characteristic curve or C-statistics. Referent models included age alone for falls, functional limitations and mortality, and age and bone mineral density for hip fractures.

RESULTS: The association between sarcopenia according to the various definitions and risk of falls, functional limitations, and hip fractures was variable; all definitions were associated with greater risk of death, but none of the definitions materially changed discrimination based on the AUC and C-statistic when compared with reference models (change ≤1% in all models).

CONCLUSION: Sarcopenia definitions as currently constructed did not consistently improve prediction of clinical outcomes in relatively healthy older men. **J Am Geriatr Soc 2015.**

Key words: sarcopenia; falls; fractures; mortality; functional limitation

Several operational definitions for sarcopenia have recently been proposed.[1–7] Conceived initially as the loss of lean body mass accompanying aging,[8] early operational definitions of sarcopenia were based solely on appendicular lean mass (ALM) from dual-energy X-ray absorptiometry (DXA) standardized to height,[9] but the relationship between muscle or lean mass and functional decline and disability is uncertain.[10–16] Thus, more recently proposed consensus definitions of sarcopenia have broadened the criteria for diagnosis to include components of strength and physical performance. The predictive validity of these more-recent definitions has not been established.

Before sarcopenia is defined as a clinical syndrome, a biomarker, a risk factor, or an outcome in clinical trials,

From the [a]Research Institute, San Francisco Coordinating Center, California Pacific Medical Center, San Francisco, California; [b]Department of Epidemiology, University of Pittsburgh, Pittsburgh, Pennsylvania; [c]Department of Family and Preventive Medicine, University of California at San Diego, San Diego, California; [d]Portland Veterans Affairs Medical Center, Portland, Oregon; [e]Department of Medicine, Stanford University, Stanford; [f]Department of Epidemiology, University of California at San Francisco, San Francisco; [g]Medical Center, University of California at Davis, Sacramento, California; [h]Department of Medicine, University of Minnesota; [i]Minneapolis Veterans Affairs Health System, Minneapolis, Minnesota; and [j]School of Medicine, Oregon Health & Science University, Portland, Oregon.

Address correspondence to Peggy M. Cawthon, California Pacific Medical Center Research Institute, San Francisco Coordinating Center, 550 16th Street, 2nd floor, Box #0560, San Francisco, CA 94158. E-mail: pcawthon@sfcc-cpmc.net

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Table 1. Criteria and Prevalence for Consensus Definitions of Sarcopenia in the Osteoporotic Fractures in Men Study

	Slowness		Weakness		Low Lean Mass		Summary Definition	
Definition	Definition	n (%)	Definition	n (%)	Definition	n (%)	Definition	n (%)
International Working Group	Gait speed <1.0 m/s	1,034 (17.4)	Not included	N/A	ALM/ht^2 ≤7.23 kg/m^2	1,239 (20.9)	Sarcopenia: slowness and low lean mass	277 (4.7)
EWGSOP	Gait speed ≤0.8 m/s	262 (4.4)	Grip strength <30 kg	474 (8.0)	ALM/ht^2 ≤7.23 kg/m^2	1,239 (20.9)	(1) Sarcopenia: low lean mass plus slowness or weakness	(1) 257 (4.3)
							(2) Severe sarcopenia: all three criteria[a]	(2) 26 (0.4)
FNIH Sarcopenia Project primary definition	Gait speed ≤0.8 m/s	262 (4.4)	Grip strength <26 kg	233 (3.9)	ALM/body mass index <0.789[b]	1,025 (17.3)	(1) Weakness and low lean mass	(1) 88 (1.5)
							(2) Slowness with weakness and low lean mass	(2) 18 (0.3)
Baumgartner	Not included	N/A	Not included	N/A	ALM/ht^2 ≤7.23 kg/m^2	1,239 (20.9)	Low lean mass	1,239 (20.9)
Newman	Not included	N/A	Not included	N/A	Residual of actual ALM–predicted ALM from equation[c]	1,186 (20.0)	Low lean mass	1,186 (20.0)

[a]Because prevalence of European Working Group on Sarcopenia in Older Persons (EWGSOP) severe sarcopenia was low, sarcopenia and severe sarcopenia were analyzed together.

[b]The Foundation for the National Institutes of Health (FNIH) Sarcopenia Project also proposed an alternative definition using appendicular lean mass (ALM) <19.75 kg for low lean mass (n = 525, 8.9%). Using the alternative definition, prevalence of "weakness and low lean mass" was 67 (1.1%), and prevalence of "slowness with weakness and low lean mass" was 16 (0.3%).

[c]The equation used to calculate residuals was ALM (kg) = −22.48 + 24.14 × height(m) + 0.21 × total fat mass (kg) as derived for men in the Health, Aging and Body Composition study (17); the cut-point for the residual was −0.204 kg/m^2.

N/A = not applicable.

its utility should be evaluated. To establish the utility of a novel measure, several conditions must be met. First, the measure must increase the likelihood of development of other adverse outcomes, independent of age and potentially other known clinical factors (e.g., body mass index (BMI)). Second, the measure should improve ability to discriminate individuals who go on to develop outcomes from those who do not. Third, the measure should appropriately and significantly reclassify people in terms of risk of development of adverse outcomes.

Therefore, the associations between five definitions of sarcopenia were evaluated[1,2,5–7,9,17] using four adverse outcomes (recurrent falls, hip fractures, functional limitations, mortality). The discriminative ability and reclassification of the definitions for likelihood of these outcomes were also determined. Analyses were completed in the Osteoporotic Fractures in Men (MrOS) Study, a prospective cohort of community-dwelling older men.

METHODS

Study Population

From 2000 to 2002, 5,994 ambulatory community-dwelling men aged 65 and older without bilateral hip replacement were enrolled in MrOS, a multicenter cohort study of aging and osteoporosis.[18,19] All men provided written informed consent, and the institutional review board at each center approved the study.

Clinical Measurements

Weight was measured using a balance beam or digital scale and height using wall-mounted stadiometers. BMI was calculated as weight (kg)/height^2 (m^2). ALM and total hip bone mineral density (BMD) were assessed using DXA (Hologic 4500, Waltham, MA) as previously described.[20] Gait speed was measured over a 6-m course, using the average of two trials (m/s).[21] Grip strength (kg) from two tests of each hand was assessed using Jamar handheld dynamometers; the maximum value obtained on all tests was analyzed. Ability and time to complete five repeated chair stands was assessed. Men self-reported a physician's diagnosis of a number of medical conditions (Table 2 footnote); the number of these conditions was summed. Participants also self-reported activity level (Physical Activity Scale for the Elderly),[22] race, alcohol use, smoking status, health status (excellent, good vs fair, poor, very poor), and history of fracture before the baseline visit.

Sarcopenia Definitions

Published operational definitions for sarcopenia include Baumgartner's;[9] Newman's;[17] the International Working

Group (IWG);[2] the European Working Group on Sarcopenia in Older Persons (EWGSOP);[1] the European Society for Clinical Nutrition and Metabolism Special Interest Group on cachexia-anorexia in chronic wasting diseases (ESPEN);[3] the Society of Sarcopenia, Cachexia, and Wasting Disorders (SCWD);[4]and the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project[6] (Table 1). The ESPEN and SCWD recommendations were similar to those of the EWGSOP and IWG, respectively, and therefore were not analyzed separately. The consensus definitions are similar in that all combine lean mass assessed using DXA with a strength or physical performance component; the Newman and Baumgartner definitions rely on lean mass estimates alone. The definitions also overlap to some extent. For lean mass, the EWGSOP and IWG definitions used the Baumgartner criteria as the lean mass component, and the EWGSOP and FNIH definitions define slowness as gait speed of 0.8 m/s or less.

Outcomes

Men answered mailed questionnaires about falls and fractures three times per year; response to these questionnaires exceeded 99%. When a participant did not return a questionnaire in a timely fashion, clinic staff contacted him or his next of kin. Men who reported two or more falls in the year after baseline were considered recurrent fallers, and those who reported no or one fall were not considered recurrent fallers. Fractures and deaths were centrally adjudicated using physician review of radiology reports, death certificates, and hospital discharge summaries when available. Men were queried about self-reported functional limitation (inability to walk 2–3 blocks, climb 10 steps without resting, prepare meals, shop, or do heavy housework) at baseline and the second clinic visit questionnaire 4.6 years later.

Statistical Analyses

Of the 5,994 men at baseline, 60 were missing gait speed, grip strength, or lean mass data, leaving 5,934 eligible for inclusion in follow-up analyses. Analysis of each outcome included a different number of participants; 106 men were missing follow-up data for recurrent falls, leaving 5,828 in analyses; all 5,934 men had follow-up data for hip fracture; 1,200 men were classified as having a functional limitation at baseline, 19 were missing this data at baseline, and 989 were missing follow-up data for functional limitations at Visit 2 (including those who died or terminated before the visit), leaving 3,726 in the functional limitations analyses; and 65 were missing final adjudication of vital status (because of a missing or pending collection of death certificate), leaving 5,869 men in mortality analyses.

Characteristics of participants were compared according to presence or absence of each sarcopenia definition using *t*-tests, Wilcoxon tests, and chi-square tests as appropriate.

Proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for hip fracture and mortality, and the proportionality assumption was tested and was not found to be violated. Logistic regression models were used to estimate odds ratios (ORs) and 95% CIs for recurrent falls and functional limitations. All models were age adjusted; hip fracture models were also adjusted for femoral neck BMD.

To quantify the discriminative ability of each sarcopenia definition for the study outcomes, the area under the receiver operating characteristic curve (AUC) was calculated from logistic models and the analogous Harrell C-statistic[23] from proportional hazards models. The AUC or C-statistic was calculated in the reference models and in models that additionally included the sarcopenia definition. The difference and 95% CI in the AUC or C-statistic and between these two models were calculated. Reference models for falls, functional limitations, and mortality included age alone; for hip fractures, the reference model included age and BMD.

The net reclassification improvement (NRI) statistic was used to quantify the amount of reclassification attributable to addition of each sarcopenia definition to the reference model.[24] A no-category approach to calculating the NRI was used, because established risk thresholds for study outcomes are not widely used in clinical settings. Risk estimates were calculated as the predicted probability of the event from logistic regression models or 1 minus the survivor function estimate from proportional hazard models. For example, for mortality, two proportions were determined for those who died: the proportion for whom addition of the sarcopenia definition to the referent model increased predicted probability (representing appropriate reclassification) and the proportion for whom addition of the sarcopenia definition to the referent model decreased their risk estimate (representing inappropriate reclassification). To ensure that small changes in predicted probability between the old and new models was not driving the NRI values, each individual's predicted probability must have changed by at least 1%; otherwise their predicted probability change was considered to be 0. The proportion that was inappropriately reclassified was then subtracted from the proportion that was appropriately reclassified, resulting in the net reclassification of those who died. For those who did not die, the proportion with appropriate reclassification (the proportion whose risk estimates decreased with the addition of the sarcopenia definition to the reference model) was also calculated, and the proportion with inappropriate reclassification (the proportion whose risk estimate increased with the addition of the sarcopenia definition to the reference model) was subtracted from this, resulting in the net reclassification of those who did not die. To calculate the overall NRI, the net reclassification values for those who died were then added to the reclassification values for those who did not die. The overall NRI ranges from –2 to 2, with negative values indicating inappropriate reclassification and positive values indicating appropriate reclassification. CIs were calculated from standard errors described previously.[24]

Analyses were conducted using SAS version 9.2 (SAS Institute, Inc., Cary, NC) or Stata version 12.1 (Stata Corp, College Station, TX).

RESULTS

The prevalence of sarcopenia was low to moderate overall (Table 1). Characteristics of participants according to the

Table 2. Characteristics of Osteoporotic Fractures in Men Study Participants According to Consensus Definitions of Sarcopenia

	Baumgartner		Newman		European Working Group for Sarcopenia in Older Persons		International Working Group		Foundation for the National Institutes of Health Sarcopenia Project			
									Definition 1		Definition 2	
Characteristic	No Sarcopenia, n = 4,633	Sarcopenia, n = 1,301[a]	No Sarcopenia, n = 4,748	Sarcopenia, n = 1,186[b]	No Sarcopenia, n = 5,677	Sarcopenia, n = 257[c]	No Sarcopenia, n = 5,657	Sarcopenia, n = 277[d]	No Sarcopenia, n = 5,846	Sarcopenia, n = 88[e]	No Sarcopenia, n = 5,916	Sarcopenia, n = 18[f]
Age, mean ± SD	72.9 ± 5.5[g]	76.2 ± 6.4[g]	73.1 ± 5.7[g]	75.7 ± 6.2[g]	73.4 ± 5.7[g]	79.9 ± 6.5[g]	73.4 ± 5.7[g]	79.3 ± 6.7[g]	73.6 ± 5.8[g]	78.1 ± 6.6[g]	73.6 ± 5.8[g]	82.8 ± 5.2[g]
White, n (%)	4,148 (89.5)[g]	1,160 (89.2)[g]	4,219 (88.9)[g]	1,089 (91.8)[g]	5,082 (89.5)	226 (87.9)	5,065 (89.5)	243 (87.7)	5,225 (89.4)	83 (94.3)	5,291 (89.4)	17 (94.4)
Height, cm, mean ± SD	174.3 ± 6.8[g]	173.5 ± 6.9[g]	174.0 ± 6.8[g]	174.7 ± 6.7[g]	174.3 ± 6.7[g]	170.1 ± 6.7[g]	174.3 ± 6.8[g]	172.0 ± 6.8[g]	174.3 ± 6.7[g]	165.4 ± 4.7[g]	174.2 ± 6.8[g]	164.6 ± 5.5[g]
Weight, kg, mean ± SD	86.1 ± 12.6[g]	72.4 ± 8.9[g]	84.0 ± 13.2[g]	79.6 ± 12.4[g]	83.7 ± 13.0[g]	70.2 ± 9.3[g]	83.6 ± 13.1[g]	72.5 ± 9.6[g]	83.2 ± 13.2[g]	76.6 ± 12.3[g]	83.1 ± 13.2[g]	77.0 ± 15.5[g]
BMI, kg/m^2, mean ± SD	28.3 ± 3.6[g]	24.0 ± 2.3[g]	27.7 ± 3.8[g]	26.1 ± 3.6[g]	27.5 ± 3.8[g]	24.2 ± 2.5[g]	27.5 ± 3.8[g]	24.5 ± 2.5[g]	27.4 ± 3.8	28.0 ± 3.9	27.4 ± 3.8	28.4 ± 5.1
Gait speed, m/s, mean ± SD	1.21 ± 0.22[g]	1.16 ± 0.23[g]	1.21 ± 0.23[g]	1.15 ± 0.23[g]	1.21 ± 0.22[g]	0.96 ± 0.27[g]	1.22 ± 0.22[g]	0.84 ± 0.14[g]	1.20 ± 0.23	1.01 ± 0.25	1.20 ± 0.23[g]	0.64 ± 0.1[g]
Grip strength, kg, mean ± SD	42.9 ± 8.3[g]	37.3 ± 7.6[g]	42.7 ± 8.4[g]	37.6 ± 7.7[g]	42.2 ± 8.1[g]	28.2 ± 6.6[g]	42.0 ± 8.4[g]	33.7 ± 7.3[g]	41.9 ± 8.3[g]	21.7 ± 3.4[g]	41.7 ± 8.4[g]	21.1 ± 4.3[g]
Chair stands inability, n (%)	97 (2.1)	67 (5.2)	86 (1.8)[g]	78 (6.6)[g]	124 (2.2)[g]	40 (15.6)[g]	117 (2.1)[g]	47 (17.0)[g]	148 (2.5)[g]	16 (18.4)[g]	153 (2.6)[g]	11 (64.7)[g]
ALM, kg, mean ± SD	25.3 ± 3.1[g]	20.5 ± 2.0[g]	25.0 ± 3.3[g]	21.2 ± 2.5[g]	24.5 ± 3.4[g]	19.3 ± 1.8[g]	24.5 ± 3.4[g]	19.9 ± 1.9[g]	24.3 ± 3.5[g]	20.3 ± 3.0[g]	24.3 ± 3.5[g]	20.3 ± 3.7[g]
ALM/ht2, kg/m^2, mean ± SD	8.3 ± 0.8[g]	6.8 ± 0.4[g]	8.2 ± 0.8[g]	6.9 ± 0.6[g]	8.0 ± 0.9[g]	6.7 ± 0.4[g]	8.0 ± 0.9[g]	6.7 ± 0.4[g]	8.0 ± 0.9[g]	7.4 ± 1.1[g]	8.0 ± 0.9	7.5 ± 1.4
ALM/BMI, mean ± SD	0.90 ± 0.11[g]	0.86 ± 0.11[g]	0.91 ± 0.11[g]	0.82 ± 0.11[g]	0.90 ± 0.10[g]	0.80 ± 0.10[g]	0.90 ± 0.10[g]	0.82 ± 0.10[g]	0.89 ± 0.11[g]	0.73 ± 0.05[g]	0.89 ± 0.11[g]	0.72 ± 0.06[g]
≥1 medical conditions, n (%)[h]	2,277 (49.2)[g]	746 (57.3)[g]	2,324 (49.0)[g]	699 (58.9)[g]	2,845 (50.1)[g]	178 (69.3)[g]	2,833 (50.1)[g]	190 (68.6)[g]	2,965 (50.7)[g]	58 (65.9)[g]	3,012 (50.9)[g]	11 (61.1)[g]
Excellent or good health, n (%)	4,009 (86.6)[g]	1,089 (83.8)[g]	4,132 (87.2)[g]	966 (81.5)[g]	4,910 (86.5)[g]	188 (73.2)[g]	4,899 (86.6)[g]	199 (71.8)[g]	5,035 (86.2)[g]	63 (71.6)[g]	5,087 (86.0)[g]	11 (61.1)[g]
Smoking, n (%)												
Never	1,714 (37.0)[g]	510 (39.2)[g]	1,797 (37.9)	427 (36.0)	2,121 (37.4)	103 (40.1)	2,128 (37.6)[g]	96 (34.7)[g]	2,190 (37.5)[g]	34 (38.6)[g]	2,219 (37.5)[g]	5 (27.8)[g]
Past	2,771 (59.8)[g]	734 (56.4)[g]	2,797 (58.9)	708 (59.7)	3,361 (59.2)	144 (56.0)	3,343 (59.1)[g]	162 (58.5)[g]	3,455 (59.1)[g]	50 (56.8)[g]	3,493 (59.1)[g]	12 (66.7)[g]
Current	147 (3.2)[g]	57 (4.4)[g]	153 (3.2)	51 (4.3)	194 (3.4)	10 (3.9)	185 (3.3)[g]	19 (6.9)[g]	200 (3.4)[g]	4 (4.6)[g]	203 (3.4)[g]	1 (5.6)[g]
Alcohol use, drinks/wk, n (%)												
0–2	2,762 (59.7)	781 (60.1)	2,842 (60.0)	701 (59.2)	3,360 (59.3)[g]	183 (71.2)[g]	3,364 (59.5)[g]	179 (64.9)[g]	3,481 (59.6)[g]	62 (70.5)[g]	3,528 (59.7)[g]	15 (83.3)[g]
3–13	1,333 (28.8)	362 (27.9)	1,366 (28.8)	329 (27.8)	1,647 (29.1)[g]	48 (18.7)[g]	1,630 (28.9)[g]	65 (23.6)[g]	1,677 (28.7)[g]	18 (20.5)[g]	1,693 (28.7)[g]	2 (11.1)[g]
≥14	531 (11.5)	157 (12.1)	533 (11.2)	155 (13.1)	662 (11.7)[g]	26 (10.1)[g]	656 (11.6)[g]	32 (11.6)[g]	680 (11.7)[g]	8 (9.1)[g]	687 (11.6)[g]	1 (5.6)[g]
Physical Activity Scale for the Elderly score, mean ± SD	151.2 ± 68.0[g]	131.7 ± 66.2[g]	151.6 ± 68.2	128.1 ± 64.5	148.9 ± 67.8[g]	104.0 ± 61.5[g]	148.9 ± 67.7[g]	107.8 ± 64.5[g]	147.7 ± 68.0[g]	99.6 ± 61.3[g]	147.2 ± 68.0[g]	66.2 ± 60.4[g]

(Continued)

Table 2 (Contd.)

Characteristic	Baumgartner		Newman		European Working Group for Sarcopenia in Older Persons		International Working Group		Foundation for the National Institutes of Health Sarcopenia Project			
									Definition 1		Definition 2	
	No Sarcopenia, n = 4,633	Sarcopenia, n = 1,301[a]	No Sarcopenia, n = 4,748	Sarcopenia, n = 1,186[b]	No Sarcopenia, n = 5,677	Sarcopenia, n = 257[c]	No Sarcopenia, n = 5,657	Sarcopenia, n = 277[d]	No Sarcopenia, n = 5,846	Sarcopenia, n = 88[e]	No Sarcopenia, n = 5,916	Sarcopenia, n = 18[f]
Femoral neck bone mineral density, g/cm2, mean ± SD	0.800 ± 0.127[g]	0.728 ± 0.114[g]	0.794 ± 0.128[g]	0.747 ± 0.119[g]	0.789 ± 0.127[g]	0.693 ± 0.109[g]	0.788 ± 0.127[g]	0.710 ± 0.117[g]	0.785 ± 0.128[g]	0.746 ± 0.129[g]	0.784 ± 0.128[g]	0.703 ± 0.121[g]
Nonspine fracture after age 50, n (%)	1,069 (23.1)	315 (24.2)	1,088 (22.9)	296 (5.0)	1,305 (23.0)[g]	79 (30.7)[g]	1,301 (23.0)[g]	83 (30.1)[g]	1,361 (23.3)[g]	23 (26.1)[g]	1,376 (23.3)[g]	8 (44.4)[g]

[a]Low lean mass (appendicular lean mass (ALM)/ht^2 ≤7.23 kg/m^2).

[b]The equation used to calculate residuals was ALM (kg) = −22.48 + 24.14 × height (m) + 0.21 × total fat mass (kg) (17); the cut-point was −0.204 kg/m.[29]

[c]Slowness (gait ≤0.8 m/s) plus low lean mass (ALM/ht^2 ≤7.23 kg/m^2) or weakness (grip <30 kg).

[d]Slowness (gait <1.0 m/s) and low lean mass (ALM/ht^2 ≤7.23 kg/m^2).

[e]Weakness (grip <26 kg) and low lean mass (ALM/body mass index (BMI) <0.789).

[f]Slowness (gait ≤0.8 m/s), weakness (grip <26 kg), and low lean mass (ALM/BMI <0.789).

[g]Pair-wise differences within definitions $P < .05$. *P*-values for continuous variables from a t-test if normally distributed, a Wilcoxon rank-sum test if skewed; for categorical variables from a chi-square test.

[h]Stroke, diabetes mellitus, hyper- or hypothyroidism, Parkinson's disease, myocardial infarction, congestive heart failure, chronic obstructive pulmonary disease, or nonskin cancer.

SD = standard deviation.

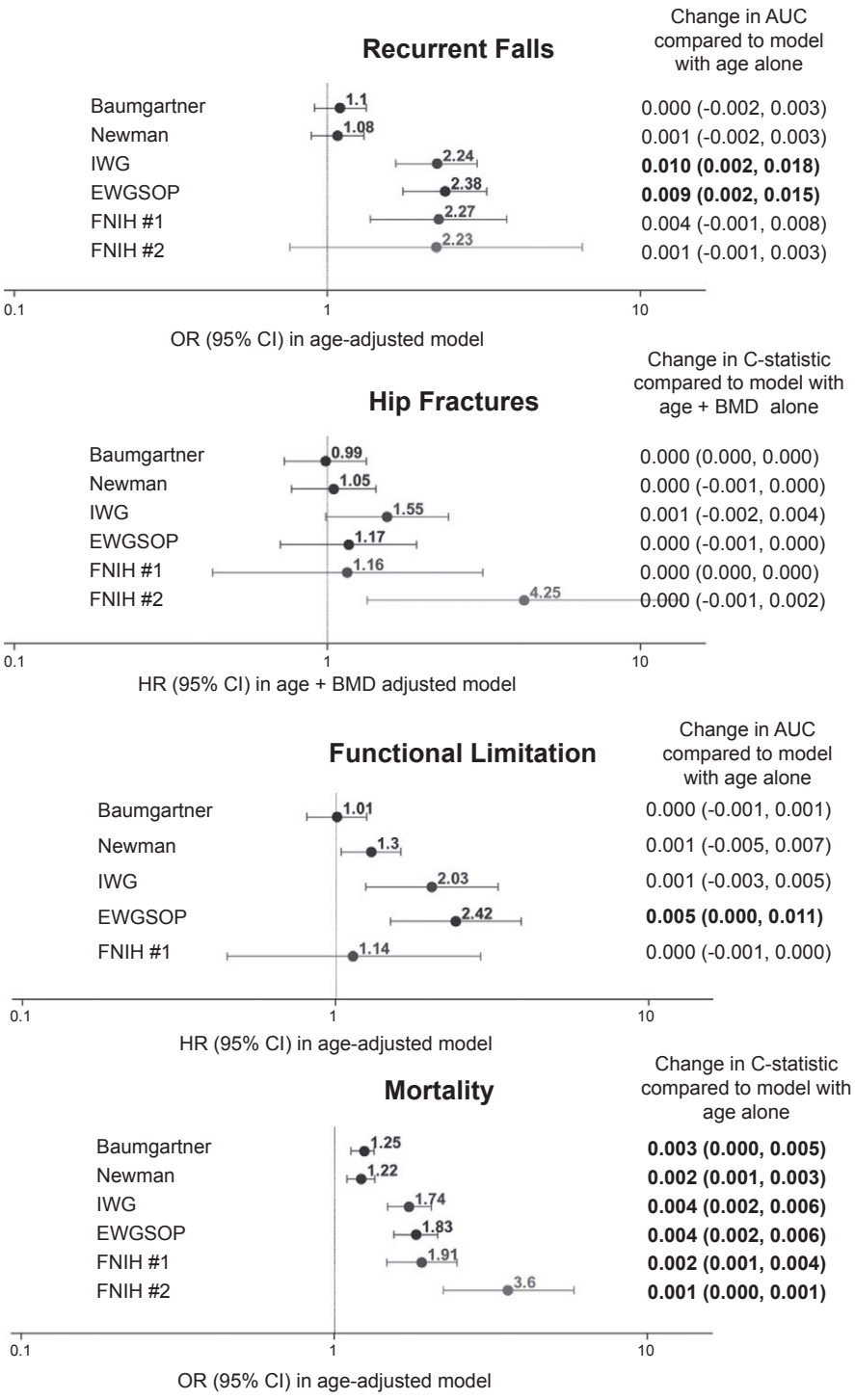

Figure 1. Association between and discrimination of sarcopenia definitions and recurrent falls, hip fractures, functional limitations, and mortality in older men. Area under the receiver operating characteristic curve (AUC) for model with age alone for falls was 0.577. C-statistic for model with age and bone mineral density (BMD) alone for hip fractures was 0.806. AUC for model with age alone for functional limitations was 0.632. C-statistic for model with age alone for mortality was 0.684. Bold indicates $P < .05$. Definitions of sarcopenia: International Working Group (IWG): slowness (gait <1.0 m/s) and low lean mass (appendicular lean mass (ALM0/ht^2 ≤7.23 kg/m^2). European Working Group for Sarcopenia in Older Persons (EWGSOP): slowness (gait ≤0.8 m/s) plus low lean mass (ALM/ht^2 ≤7.23 kg/m^2) or weakness (grip <30 kg). Foundation for the National Institutes of Health Sarcopenia Project (FNIH) Definition 1: weakness (grip <26 kg) and low lean mass (ALM/body mass index (BMI) <0.789); Definition 2: slowness (gait ≤0.8 m/s), weakness (grip <26 kg), and low lean mass (ALM/BMI <0.789). OR = odds ratio; CI = confidence interval; HR = hazard ratio.

presence or absence of sarcopenia for each definition are presented in Table 2. In general, those classified as having sarcopenia (according to any definition) were older and weaker and had lower lean mass, more comorbid conditions, worse self-rated health, lower activity level, and lower BMD than those classified as not having sarcopenia. Associations between sarcopenia classification and smoking, alcohol use, BMI, and history of fracture varied according to the definition used.

Six hundred ninety-four men (11.9%) were classified as recurrent fallers in the year after the baseline examination. Neither the Baumgartner nor Newman definition was associated with recurrent falls. The likelihood of recurrent falls was two to three times as great in men with sarcopenia according to definitions that incorporated weakness or slowness as in men without sarcopenia, but the FNIH Definition 2 did not reach statistical significance, perhaps because so few met the definition (Figure 1). Overall, when compared with the reference model with age alone, differences in the AUCs with the addition of each sarcopenia definition that included slowness or weakness mirrored the significance of the associations (the ORs) but tended to be small in absolute magnitude, with the greatest difference in the AUC of only 0.01 (for the IWG definition). For all sarcopenia definitions that included weakness or slowness, the NRI showed better reclassification for men without an event (0.03 to 0.35), but there was also substantial reclassification in the inappropriate direction for those with events (–0.05 to –0.33), resulting in no overall reclassification improvement (–0.05 to 0.01) (Table 3). The Baumgartner and Newman definitions appropriately reclassified events but inappropriately reclassified nonevents, resulting in no change in the overall NRI.

During follow-up (9.8 ± 3.0 years), 207 men (3.5%) experienced a hip fracture. There was no association between sarcopenia (IWG, EWGSOP, Newman, or Baumgartner) or "weakness and low lean mass" according to the FNIH (Definition 1) and hip fracture risk (Figure 1). The risk of hip fracture was four times as great in men with "slowness with weakness and low lean mass" according to the FNIH (Definition #2) as in those without, although the CIs were wide. The addition of none of the sarcopenia definitions to the reference model with age and BMD resulted in significant changes in the C-statistic. None of the sarcopenia definitions significantly improved the reclassification of participants over the reference model (overall NRI –0.06 to 0.01, $P > .05$ for all) (Table 3).

During follow-up (4.6 ± 0.4 years), 590 (15.8%) men had a new functional limitation. Men who met the Newman, IWG, or EWGSOP definition had a greater likelihood of functional limitation. There was no association between the Baumgartner definition or the FNIH "weakness and low lean mass" definition (Definition 1) and development of a functional limitation. The association between the FNIH definition "slowness with weakness and low lean mass" (Definition 2) and functional limitation could not be estimated because only one of the participants in this subset (those free of functional limitations at baseline) met the criteria for FNIH Definition 2.

During follow-up (9.8 ± 3.0 years), 2,003 men (34.1%) died. Men who met any definition of sarcopenia had a greater risk of mortality than those without these conditions (Figure 1). Changes in the C-statistic with the addition of all sarcopenia definitions to the reference model with age alone were statistically significant but small (0.001 to 0.004, $P < .05$ for all).For sarcopenia definitions that included a weakness or slowness component, the NRI showed better reclassification for men without an event (0.05 to 0.26), but frequent reclassification in the inappropriate direction for those with events (0.18 to 0.41) resulted in overall reclassification in the inappropriate direction (–0.07 to –0.16) (Table 3). The Baumgartner and Newman definitions that include lean mass alone demonstrated significant overall reclassification in the appropriate direction (0.20 and 0.15) for mortality. This reclassification was primarily due to correct reclassification of a large number of men without events (0.40 and 0.38) that inappropriate reclassification in nonevents partly offset (–0.20 and –0.23).

The FNIH alternative definitions were evaluated (Table 4) and did not materially change estimates for falls, hip fracture, functional limitations, and mortality from those determined using the primary FNIH definitions. Neither of the FNIH alternative summary definitions significantly changed the AUC from that of the reference model, with the exception of the alternative Definition 1 and a small change in the C-statistic for mortality. In addition, overall NRI for these outcomes was not significant or was in the inappropriate direction.

DISCUSSION

These results suggest that these proposed definitions of sarcopenia as currently constructed would be of limited clinical utility in healthy community-dwelling men. Despite differences between the definitions in cut-points for gait speed, grip strength, and lean mass, the risk estimates for falls, fracture, and mortality increased and were fairly similar across the definitions. The proposed sarcopenia definitions do not appear to materially change discrimination based on AUC and C-statistic analyses for falls, hip fracture, functional limitations, or mortality from that of simple models. Overall, only the Baumgartner and Newman definitions significantly improved reclassification in the appropriate direction for mortality; none of the other definitions significantly reclassified men in the expected direction in terms of risk of recurrent falls, hip fractures, functional limitations, or mortality from simple models.

One challenge for evaluating usefulness of a definition of sarcopenia is that selection of the outcome against which to evaluate candidate definitions is not obvious. It is likely that age-related decline in muscle function is related to various outcomes including falls, fractures, functional limitation, hospitalization, disability, and mortality. For example, physical performance, particularly slow gait speed, is related to falls, hip fracture, disability, and mortality.[21,25–28] Thus, no single outcome can serve as a criterion standard against which to evaluate potential clinical definitions of sarcopenia. A few reports have evaluated individual consensus definitions against single outcomes such as mortality[29–31] but have not undertaken more-complete analyses comparing the predictive validity of multiple proposed definitions of sarcopenia with the risk of several adverse outcomes simultaneously, as was done in the current study.

Table 3. Reclassification of Osteoporotic Fractures in Men Study Participants After Addition of Other Definitions of Sarcopenia to a Simple Model with Age (for Recurrent Falls, Functional Limitations, and Mortality) or Age and Bone Mineral Density (for Hip Fractures)

Characteristic	Baumgartner	Newman	IWG	EWG	FNIH Definition 1	FNIH Definition 2
Recurrent falls over 1 year						
With event, n = 694						
Appropriately reclassified, n (%)	143 (21)	117 (17)	70 (10)	68 (10)	22 (3)	5 (1)
Inappropriately reclassified, n (%)	61 (9)	66 (10)	298 (43)	298 (43)	101 (15)	37 (5)
No change, n (%)	490 (71)	511 (74)	326 (47)	328 (47)	571 (82)	652 (94)
NRI (95% CI), events	0.12 (0.08–0.16)[a]	0.07 (0.04–0.11)[a]	−0.33 (−0.38 to −0.28)[a]	−0.33 (−0.38 to −0.28)[a]	−0.11 (−0.14 to −0.08)[a]	−0.05 (−0.06 to −0.03)[a]
Without event, n = 5,134						
Appropriately reclassified, n (%)	285 (6)	284 (6)	1,934 (38)	1,947 (38)	416 (8)	154 (3)
Inappropriately reclassified, n (%)	916 (18)	675 (13)	195 (4)	176 (3)	61 (1)	12 (0)
No change, n (%)	3,933 (77)	4,175 (81)	3,005 (59)	3,011 (59)	4,657 (91)	4,968 (97)
NRI (95% CI), nonevents	−0.12 (−0.14 to −0.11)[a]	−0.08 (−0.09 to −0.06)[a]	0.34 (0.32–0.35)[a]	0.35 (0.33–0.36)[a]	0.07 (0.06–0.08)[a]	0.03 (0.02–0.03)[a]
Overall NRI (95% CI)	0 (−5 to 4)	0 (−4 to 4)	0.01 (−0.04 to 0.06)	0.01 (−0.04 to 0.06)	−0.05 (−0.08 to −0.01)	−0.02 (−0.04 to 0.00)
Hip fractures over 9.8 years						
With event, n = 207						
Appropriately reclassified, n (%)	4 (2)	12 (6)	20 (10)	12 (6)	3 (1)	3 (1)
Inappropriately reclassified, n (%)	3 (1)	5 (2)	41 (20)	11 (5)	2 (1)	12 (6)
No change, n (%)	200 (97)	190 (92)	146 (71)	184 (89)	202 (98)	192 (93)
NRI (95%CI), events	0.00 (−0.02 to 0.03)	0.03 (0.0–0.07)	−0.10 (−0.17 to −0.03)[a]	0.00 (−0.04 to 0.05)	0.00 (−0.02 to 0.03)	−0.04 (−0.08 to −0.01)[a]
Without event, n = 5,727						
Appropriately reclassified, n (%)	39 (1)	159 (3)	497 (9)	175 (3)	39 (1)	197 (3)
Inappropriately reclassified, n (%)	41 (1)	180 (3)	231 (4)	132 (2)	38 (1)	47 (1)
No change, n (%)	5,647 (99)	5,388 (94)	4,999 (87)	5,420 (95)	5,650 (99)	5,483 (96)
NRI (95% CI), nonevents	0.00 (0.00–0.00)	0.00 (−0.01 to 0.00)	0.05 (0.04–0.06)[a]	0.01 (0.00–0.01)[a]	0.00 (0.00–0.00)	0.03 (0.02–0.03)[a]
Overall NRI (95% CI)	0.00 (0.02–0.03)	0.03 (−0.01 to 0.07)	−0.06 (−0.13 to 0.02)	0.01 (−0.03 to 0.06)	0.01 (−0.02 to 0.03)	−0.02 (−0.05 to 0.02)
Functional limitations over 4.6 years						
With event, n = 590						
Appropriately reclassified, n (%)	38 (6)	133 (23)	28 (5)	31 (5)	6 (1)	[b]
Inappropriately reclassified, n (%)	0 (0)	236 (40)	181 (31)	242 (41)	0 (0)	
No change, n (%)	552 (94)	221 (37)	381 (65)	317 (54)	584 (99)	
NRI (95% CI), events	0.06 (0.04–0.08)[a]	−0.17 (−0.24 to −0.11)[a]	−0.26 (−0.30 to −0.22)[a]	−0.36 (−0.40 to −0.31)[a]	0.01 (0.00–0.02)	
Without event, n = 3,136						
Appropriately reclassified, n (%)	1 (0)	982 (31)	581 (19)	807 (26)	0 (0)	
Inappropriately reclassified, n (%)	147 (5)	495 (16)	51 (2)	46 (1)	20 (1)	
No change, n (%)	2,988 (95)	1,659 (53)	2,504 (80)	2,283 (73)	3,116 (99)	
NRI (95% CI), nonevents	−0.05 (−0.05 to −0.04)[a]	0.16 (0.13–0.18)[a]	0.17 (0.15–0.18)[a]	0.24 (0.23–0.26)[a]	−0.01 (−0.01 to 0.00)	
Overall NRI (95% CI)	0.02 (0.00–0.04)	−0.02 (−0.09 to 0.05)	−0.09 (−0.14 to −0.04)[a]	−0.11 (−0.16 to −0.07)	0.00 (0.00–0.01)	

(Continued)

Table 3 (Contd.)

Characteristic	Baumgartner	Newman	IWG	EWG	FNIH Definition 1	FNIH Definition 2
Deaths over 9.8 years						
With event, n = 2003						
Appropriately reclassified, n (%)	543 (27)	474 (24)	193 (10)	192 (10)	58 (3)	22 (1)
Inappropriately reclassified, n (%)	938 (47)	930 (46)	1,001 (50)	1,009 (50)	602 (30)	377 (19)
No change, n (%)	522 (26)	599 (30)	809 (40)	802 (40)	1,343 (67)	1,604 (80)
NRI (95% CI), events	−0.20 (−0.23 to −0.16)[a]	−0.23 (−0.26 to −0.19)[a]	−0.40 (−0.43 to −0.38)[a]	−0.41 (−0.44 to 0.38)[a]	−0.27 (−0.29 to −0.25)[a]	−0.18 (−0.20 to −0.16)[a]
Without event, n = 3,866						
Appropriately reclassified, n (%)	2,220 (57)	2,109 (55)	1,392 (36)	1,382 (36)	811 (21)	306 (8)
Inappropriately reclassified, n (%)	687 (18)	646 (17)	393 (10)	420 (11)	45 (1)	103 (3)
No change, n (%)	959 (25)	1,111 (29)	2,081 (54)	2,064 (53)	3,010 (78)	3,457 (89)
NRI (95% CI), nonevents	0.40 (0.37–0.42)[a]	0.38 (0.35–0.40)[a]	0.26 (0.24–0.28)[a]	0.25 (0.23–0.27)[a]	0.20 (0.19–0.21)[a]	0.05 (0.04–0.06)[a]
Overall NRI (95% CI)	0.20 (0.16–0.24)[a]	0.15 (0.11–0.19)[a]	−0.15 (−0.18 to −0.11)[a]	−0.16 (−0.19 to −0.12)[a]	−0.07 (−0.10 to −0.05)[a]	−0.13 (−0.15 to −0.10)[a]

For events, appropriate reclassification occurs when estimated risk increases when the additional factor is added to the model; inappropriate reclassification occurs when estimated risk decreases when the additional factor is added to the model.

For nonevents, appropriate reclassification occurs when estimated risk decreases when the additional factor is added to the model; inappropriate reclassification occurs when estimated risk increases when the additional factor is added to the model.

Definitions of sarcopenia; International Working Group (IWG): slowness (gait <1.0 m/s) and low lean mass (appendicular lean mass (ALM)/ht^2 ≤7.23 kg/m^2). European Working Group for Sarcopenia in Older Persons (EWGSOP): slowness (gait ≤0.8 m/s) plus low lean mass (ALM/ht^2 ≤7.23 kg/m^2) or weakness (grip <30 kg). Foundation for National Institutes of Health Sarcopenia Project (FNIH) Definition 1: weakness (grip <26 kg) and low lean mass (ALM/body mass index (BMI) <0.789). FNIH definition #2: slowness (gait ≤0.8 m/s), weakness (grip <26 kg), and low lean mass (ALM/BMI <0.789).

[a] $P < .05$.

[b] There were no incident functional limitations in men who met the FNIH Definition 2, so these models could not be run.

NRI = net reclassification improvement; CI = confidence interval.

Table 4. Association, Discrimination, and Reclassification for Foundation for National Institutes of Health Sarcopenia Project (FNIH) Alternative Sarcopenia Definitions with Falls, Functional Limitation, Hip Fractures, and Mortality in Older Men

Outcome	FNIH Alternative Sarcopenia Classification	
Recurrent falls	**Definition 1**	**Definition 2**
Association and discrimination		
OR (95% CI) in model with age alone	2.33 (1.32–4.10)[a]	2.37 (0.79–7.07)
Difference in AUC (95% CI) vs model with age alone	0.003 (−0.001 to 0.007)	0.000 (−0.001 to 0.001)
Reclassification		
In those with event, n = 694		
Appropriately reclassified, n (%)	18 (3)	5 (1)
Inappropriately reclassified, n (%)	105 (15)	40 (6)
No change, n (%)	571 (82)	649 (94)
NRI (95% CI), events	−0.13 (−0.16 to −0.10)[a]	−0.05 (−0.07 to −0.03)[a]
In those without event, n = 5,134		
Appropriately reclassified, n (%)	433 (8)	159 (3)
Inappropriately reclassified, n (%)	45 (1)	11 (0)
No change, n (%)	4,656 (91)	4,964 (97)
NRI (95% CI), nonevents	0.08 (0.07–0.08)[a]	0.03 (0.02–0.03)[a]
Overall NRI (95% CI)	−0.05 (−0.08 to −0.02)[a]	−0.02 (−0.04 to 0.00)[a]
Hip fracture		
Association and discrimination		
HR (95% CI) in model with age + BMD	1.68 (0.74–3.81)	5.46 (1.71–17.46)[a]
Difference in C-statistic (95% CI) vs model with age and BMD	−0.001 (−0.001 to 0.000)	0.000 (−0.001 to 0.000)
Reclassification		
In those with event, n = 207[a]		
Appropriately reclassified, n (%)	6 (3)	3 (1)
Inappropriately reclassified, n (%)	11 (5)	17 (8)
No change, n (%)	190 (92)	187 (90)
NRI (95% CI), events	−0.02 (−0.06 to 0.01)	−0.07 (−0.11 to −0.03)[a]
In those without event, n = 5,727[b]		
Appropriately reclassified, n (%)	185 (3)	213 (4)
Inappropriately reclassified, n (%)	60 (1)	53 (1)
No change, n (%)	5,482 (96)	5,461 (95)
NRI (95% CI), nonevents	0.02 (0.02–0.03)[a]	0.03 (0.02–0.03)[a]
Overall NRI (95% CI)	0.00 (−0.04 to 0.04)	−0.04 (−0.08 to 0.00)[a]
Functional limitations		
Association and discrimination		
OR (95% CI) in model with age alone	1.01 (0.81–1.23)	1.30 (1.04–1.65)[a]
Difference in AUC (95% CI) vs model with age alone	0.000 (−0.001 to 0.001)	0.001 (−0.005 to 0.007)
Reclassification		
In those with event, n = 590[a]		
Appropriately reclassified, n (%)	38 (6)	133 (23)
Inappropriately reclassified, n (%)	0 (0)	236 (40)
No change, n (%)	552 (94)	221 (37)
NRI (95% CI), events	0.06 (0.04–0.08)[a]	−.17 (−0.24 to −0.11)[a]
In those without event, n = 3,136[b]		
Appropriately reclassified, n (%)	1 (0)	982 (31)
Inappropriately reclassified, n (%)	147 (5)	495 (16)
No change, n (%)	2,988 (95)	1,659 (53)
NRI (95% CI), nonevents	−0.05 (−0.05 to −0.04)[a]	0.16 (0.13–0.18)[a]
Overall NRI (95% CI)	0.02 (0.00–0.04)	−0.02 (−0.09 to 0.05)
Mortality		
Association and discrimination		
HR (95% CI) in model with age alone	2.03 (1.51–2.73)[a]	3.49 (2.01–6.05)[a]
Difference in C-statistic (95% CI) vs model with age and BMD	0.002 (0.001–0.003)[a]	0.001 (0.000–0.002)
Reclassification		
In those with event, n = 2,003[a]		
Appropriately reclassified, n (%)	52 (3)	22 (1)
Inappropriately reclassified, n (%)	551 (28)	306 (15)
No change, n (%)	1,400 (70)	1,675 (84)
NRI (95% CI), events	−0.25 (−0.27 to −0.23)[a]	−0.14 (−0.16 to −0.13)[a]

(Continued)

Table 4 (Contd.)

Outcome Recurrent falls	FNIH Alternative Sarcopenia Classification	
	Definition 1	Definition 2
In those without event, n = 3,866[b]		
Appropriately reclassified, n (%)	641 (17)	222 (6)
Inappropriately reclassified, n (%)	123 (3)	130 (3)
No change, n (%)	3,102 (80)	3,514 (91)
NRI (95% CI), nonevents	0.13 (0.12−0.15)[a]	0.02 (0.01−0.03)[a]
Overall NRI (95% CI)	−0.12 (−0.14 to −0.09)[a]	−0.12 (−0.14 to −0.10)[a]

For recurrent falls, area under the receiver operating characteristic curve (AUC) for model with age alone was 0.577.
For hip fractures, C-statistic for model with age and bone mineral density (BMD) was 806.
For functional limitations, AUC for model with age alone was 0.632.
For mortality, C-statistic for model with age alone was 0.684.
FNIH definition 1: weakness (grip <26 kg) and low lean mass (appendicular lean mass (ALM) <19.75 kg).
FNIH definition 2: slowness (gait ≤0.8 m/s), weakness (grip <26 kg) and low lean mass (ALM <19.75 kg).
For events, appropriate reclassification occurs when estimated risk increases when the additional factor is added to the model; inappropriate reclassification occurs when estimated risk decreases when the additional factor is added to the model.
For nonevents, appropriate reclassification occurs when estimated risk decreases when the additional factor is added to the model; inappropriate reclassification occurs when estimated risk increases when the additional factor is added to the model.
[a] $P < .05$.
NRI = net reclassification improvement; CI = confidence interval.

Recent analyses have supported an association between the FNIH components (the low lean mass criterion using ALM and BMI and the weakness criterion) or the composite definition with disability, limitations in walking, and poor physical performance in older adults,[32–34] although these reports did not evaluate discrimination or reclassification of the FNIH sarcopenia definition or its components. One report in older adults in Hong Kong found that none of several sarcopenia definitions considered predicted incident physical limitations and that AUCs for the various definitions were similarly low.[35] With regard to hip fracture, the current study found that the C-statistic for a simple model with age and BMD alone was 0.806 and that none of the sarcopenia definitions significantly improved the C-statistic from that of this simple model. The discriminative ability of the FRAX algorithm[36] for fracture risk has been previously evaluated in MrOS; the AUCs in those models that accounted for the competing risk of mortality were 0.77 for the FRAX algorithm that included BMD and 0.69 for the FRAX algorithm that did not include BMD.[37]

It was initially postulated that a clinical diagnosis of sarcopenia would identify those at high risk of these adverse outcomes, because poor physical performance and strength (and to a lesser extent low lean mass) have been previously associated with falls, hip fractures, disability, and mortality,[21,25,27,28] but the results do not support this hypothesis. There are several possible reasons for these findings. First, the proposed operational definitions may not correctly identify the underlying condition. Refinement of the definition of sarcopenia, with omission of some criteria and addition of others, may more accurately identify those at risk. For example, although slow gait speed appears to increase the risk of many health outcomes,[26,28] alternative measures, such as inability to rise from chair, may better stratify those at risk of poor outcomes. Previous analyses in MrOS found that men unable to rise from a risk of hip fracture was eight times as great as that of men with the fastest (best) performance on the repeat chair stand test.[21] However, the reclassification and discriminative ability of chair rise performance for the outcomes examined in the present analyses have not been evaluated. Similarly, although assessment of grip strength is highly reproducible[38] and is associated with falls, hip fractures, disability, and mortality,[21,25,39,40] it is possible that lower extremity strength is a more clinically relevant measure in terms of risk stratification. Nevertheless, lower extremity strength is more difficult to measure accurately in a clinical setting than is grip strength. Also, muscle power includes strength and velocity; alternative definitions of sarcopenia with a criterion based on power may improve discriminative ability, but again, measures of lower extremity power are difficult to assess in clinical settings. In addition, lean mass according to DXA is only a surrogate measure of muscle mass,[41] and more-direct and -precise assessment of muscle mass could lead to different results. In addition, aside from the Newman definition, none of the sarcopenia definitions take into account fat mass. Criteria that include the relative amount of lean mass to fat mass, as well as physical function, have not been developed and may provide better predictive validity than current measures that do not account for fat. Another possibility is that sarcopenia, as currently conceptualized, is nota true clinical syndrome, in that the presence of this condition does not increase the risk of subsequent poor outcomes regardless of the operational definition used.

MrOS is a large, well-characterized cohort with little loss to follow-up and excellent assessment of endpoints, although a few limitations must be noted. First, the MrOS cohort was relatively healthy, well functioning, and overweight and had a low prevalence of sarcopenia at baseline, especially for the definitions of sarcopenia that include low lean mass and a functional component. The results of these analyses may differ in a less-healthy population with a higher prevalence of sarcopenia or with higher or lower body weight, although if these definitions of sarcopenia are found to be more discriminative in terms of risk of

poor outcomes in less-healthy populations, such evidence would not necessarily support the use of the definitions in a general clinic population. Second, the MrOS cohort is all male and mostly white. Therefore, extrapolation of these results to other groups may not be warranted. Separate criteria for sarcopenia for nonwhite individuals have been suggested, for example for Asians,[42] but these criteria are not data driven, and the predictive and discriminative ability of these race-specific criteria have not been evaluated. Further evaluation or development of sarcopenia definitions in nonwhite populations is warranted. Third, MrOS data were included in the pooled analyses that were used, in part, to develop the FNIH sarcopenia definitions. Thus, it was initially expected that the FNIH definitions (and their alternatives) might perform better (in terms of discrimination and reclassification) than the other definitions that did not directly employ MrOS data in their construction, but none of the definitions of sarcopenia performed well, so inclusion of the MrOS data in the previous analyses was unlikely to influence the conclusions. Fourth, sarcopenia measures from only a single visit were evaluated. The extent to which sarcopenia status changes over time and whether fluctuating sarcopenia status confers risk of clinical outcomes has not been determined. Finally, the use of the NRI to evaluate a new marker has been criticized for several reasons,[43,44] mostly notably because the NRI statistic does not weigh the importance of reclassification based on clinical consequences; that is, the importance of reclassification of individuals with events is given equal weight to reclassification in those without events. Nevertheless, even when the data are interpreted without the calculation of the overall NRI, the conclusions are unchanged. The goal of adding new information about sarcopenia to a clinical assessment is to better identify those at risk of poor outcomes, rather than excluding those at lower risk. In this study, adding information about sarcopenia resulted in lower estimated risk of the outcome in those who went on to have an event, which would result in correctly identifying fewer, not more, men at risk of adverse outcomes. Thus, even without relying on the overall NRI, the sarcopenia definitions do not help identify men who are at risk of adverse outcomes.

Although sarcopenia according to any of the definitions used was associated with greater likelihood of recurrent falls and greater risk of mortality (and less consistently associated with risk of hip fracture and functional limitation), the definitions do not improve on age alone in terms of discrimination and reclassification of risk of important adverse outcomes in community-dwelling older men. Thus, in their current state, these definitions are unlikely to be clinically useful in a general population of older men. Before any sarcopenia definition is implemented in clinical practice, it should be shown to be useful in predicting geriatric outcomes of interest and providing good discrimination and reclassification of risk of these outcomes. Future studies should investigate the utility of these criteria in populations at higher risk of adverse outcomes.

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Author Contributions: PMC monitored data collection for the whole study, wrote the statistical analysis plan, drafted and revised the paper. She is guarantor. TLB analyzed the data and drafted and revised the paper. JC, EB-C, MLS, KEE, and ESO enrolled study participants at their clinical sites and revised the paper. SRC oversaw the study design at the study coordinating center and revised the paper. DMK, CGL, ARH, MMN, and NEL revised the draft paper. All authors designed the study.

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