

Muscle Strength and BMI as Predictors of Major Mobility Disability in the Lifestyle Interventions and Independence for Elders Pilot (LIFE-P)

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Background. Muscle weakness and obesity are two significant threats to mobility facing the increasing number of older adults. To date, there are no studies that have examined the association of strength and body mass index (BMI) on event rates on a widely used performance measure of major mobility disability.

Methods. This study was a secondary analysis of a randomized controlled trial in which sedentary functionally limited participants (70–89 years, Short Physical Performance Battery ≤ 9) who were able to complete a 400-m walk test at baseline were randomized to a physical activity or health education intervention and reassessed for major mobility disability every 6 months for up to 18 months. We evaluated whether baseline grip strength and BMI predicted failure to complete the 400-m walk test in 15 minutes or less (major mobility disability).

Results. Among $N = 406$ participants with baseline measures, lower grip strength was associated with an increased risk for developing major mobility disability, with and without covariate adjustment ($p < .01$): The hazard ratio (95% confidence interval) for the lowest versus high sex-specific quartile of grip strength was 6.11 (2.24–16.66). We observed a U-shaped relationship between baseline BMI and the risk of developing major mobility disability, such that the risk for participants with a BMI of 25–29 kg/m² was approximately half that of participants with BMI less than 25 or 30 kg/m² or more ($p = .04$ in fully adjusted analyses).

Conclusions. Our data highlight the importance of muscle weakness, low BMI, and obesity as risk factors for major mobility disability in older adults. Being overweight may be protective for major mobility disability.

Key Words: Physical disability—Physical activity—Older adults.

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THE rapid growth in the population of older adults in the United States has led to considerable interest in the risk factors and processes underlying physical disablement (1–3). Rantanen and colleagues (4) have demonstrated that muscle weakness is a critical risk factor for becoming functionally limited or disabled in the future. Muscle strength is also a strong predictor of 400-m walk performance (5). Equally important are accumulating data suggesting that elevated body mass index (BMI) poses increased risk for functional limitations and disability (6,7).

The literature is replete with studies of either muscle strength or obesity and their association with functional limitations, but only a few studies have examined the association of both muscle weakness and obesity on mobility limitation or gait speed in older adults (8–10). In these studies, limitations in walking or mobility were assessed with self-report of difficulty walking 400–500 m (sometimes in combination with climbing a flight of stairs), using a gait speed below 1.2 m/s or examining decline in gait speed over time. To date, no studies have examined the association of muscle

strength and obesity on event rates in a widely used performance measure of mobility in older adults at high risk for mobility disability.

The Lifestyle Interventions and Independence for Elders pilot (LIFE-P) was a single-blind, multicenter, randomized controlled trial of a physical activity intervention compared with a successful aging intervention in sedentary functionally limited older adults (aged 70–89 years, Short Physical Performance Battery score ≤ 9) who were able to complete a 400-m walk test (400-MWT) in 15 minutes or less (11). Major mobility disability was defined as the inability to complete the 400-MWT in 15 minutes or less (12,13) and was reassessed every 6 months for up to 18 months. The current study was a secondary analysis of the LIFE-P study. The goals of the current study were to evaluate how baseline strength and BMI predicted incidence of major mobility disability and changes in gait speed across 18 months after controlling for intervention assignment and a number of risk factors previously linked to disability.

METHODS

Study Design, Recruitment, and Participants

The study design, eligibility criteria, and recruitment procedures of LIFE-P have been described in detail previously (12,14). Participants were eligible for LIFE-P if they were aged 70–89 years, had a sedentary lifestyle (<20 min/wk spent in structured physical activity during the past month), were able to walk 400 m in 15 minutes or less without sitting and without using an assistive device, and were functionally limited (Short Physical Performance Battery score ≤ 9). Participants were ineligible if they had uncontrolled or severe chronic disease or illnesses that would likely interfere with physical activity or a Mini-Mental State Examination score less than 21. Written informed consent was obtained; the National Institutes of Health and Institutional Review Boards for all participating institutions approved the protocol and consent forms.

Between April 2004 and February 2005, 424 participants were enrolled. Follow-up was planned for 12–18 months, depending on the date of randomization and included semi-annual clinic visits for data collection. All standard assessments were conducted by trained research staff blinded to intervention assignment.

Measurements

Four hundred-meter walk test.—For the 400-MWT, participants were asked to walk 10 laps of a 40-m course (20 m out and 20 m back) at their usual pace. Participants were allowed to stop and rest in a standing position for a maximum of 60 seconds per stop, but they were not allowed to sit. Major mobility disability was defined as the inability to complete the 400-MWT in 15 minutes or less without

sitting. If the 400-MWT could not be assessed at follow-up, a committee of investigators masked to intervention group adjudicated the outcome. Available information at follow-up was reviewed, and major mobility disability was determined to be present if 4-m walking speed was slower than 0.4 m/s at a home or clinic assessment, the participant was unable to walk across a room without assistance from another person or assistive device as evident from observation or self- or proxy-report collected in-person or over the telephone or medical records documented that the participant was unable to walk (eg, bed or wheelchair bound). The major mobility disability outcome was defined as indeterminate if information was insufficient to adjudicate the outcome. Persistent major mobility disability was defined to be failure of the 400-m walk at two successive scheduled visits at any time during follow-up. Deaths were verified from proxies, death certificates, and medical records.

Grip strength.—Right and left handgrip strength was measured in kilograms using a handheld dynamometer (Jamar Handheld Dynamometer; J.A. Preston Corporation, Clifton, NJ). If the participant reported current flare-up of pain in the wrist or hand or had undergone fusion, arthroplasty, tendon repair, synovectomy, or other related surgery of the hand or wrist in the past 3 months, the affected side was not tested. Prior to data collection, a practice session was conducted to acquaint participants with the instrument and adjust it appropriately. Each measurement was made with the participant seated, elbow slightly flexed, wrist in a neutral position, and the interphalangeal joint of the index finger at a 90° angle. The participant was instructed to squeeze the handle with maximal effort for 3–5 seconds. The measurement was repeated after a 10-second pause for recovery. The average of the two trials from the stronger hand was used in the analyses. We compared individuals in the lowest and highest sex-specific quartiles with those in the middle of our grip strength distribution. For women, the lowest and highest quartiles were defined by 18 and 26 kg, respectively; for males, these cut-points were 28 and 41 kg, respectively.

Body mass index.—Body mass was measured to the nearest 0.1 kg using a calibrated scale with the participants wearing light clothes and no shoes. Body height was measured to the nearest millimeter using a wall-mounted stadiometer. BMI was calculated as body mass (kg) divided by height (m) squared (kg/m^2). In our analyses, we used the standard BMI cut-points of less than 25, 25–29.9, and 30 kg/m^2 or more.

Covariates.—Baseline risk factors included as covariates in our analyses were determined, as follows. Sex, age, ethnicity, and education were based on self-report. Global cognitive function was based on the Mini-Mental State Examination (15). Depressive symptoms were based on the Center for Epidemiological Studies–Depression Scale (16).

The prevalence of comorbid clinical conditions was determined using self-reported physician-diagnosed disease information.

Statistical Methods

Analyses were limited to the 406 (96%) of the LIFE-P cohort for whom baseline measures of grip strength and BMI were available.

Distributions of population characteristics for anthropometric measures, body composition, and measures of physical function were expressed as means and standard deviations for continuous variables and frequency and percentage for categorical variables.

Proportional hazards regression was used to assess the association between muscle strength and BMI, respectively, and the development of major mobility disability. Persistent mobility disability was defined to be failure of the 400-m walk at two successive scheduled visits at any time during follow-up. Time was measured from randomization; participants were censored at the time of their last on-study measurement. Intervention assignment was included as a covariate in all models. Sex, race, and education were included as categorical covariates; the comorbidity index, Center for Epidemiological Studies–Depression, and Mini-Mental State Examination were included as continuous covariates. Two degrees of freedom tests were used to assess differences among the three groups defined by levels of grip strength and by levels of BMI. We examine the consistency of relationships between women and men using tests of interaction.

The associations between muscle strength, BMI, and the interventions and 400-m walk gait speed over time (among those able to complete the walk) were assessed with general linear models.

RESULTS

The demographic and health characteristics of the LIFE-P sample are shown in Table 1. Participants with lower grip strength tended to be older and were less likely to be African American. Participants with higher BMI tended to be younger but had more comorbidities. Grip strength and BMI were positively related ($p = .005$). Random intervention assignment was balanced across levels of grip strength; however, participants with BMI more than 30 kg/m² were more likely to have been assigned to the physical activity intervention than those with lower BMI. Detailed descriptions of the baseline characteristics of the LIFE-P sample have been previously published (14). To summarize this study, the mean age of the sample was ~77 years and 67% reported education beyond high school. Nearly one third of the sample was male, and approximately one quarter reported a race or ethnicity other than white. The majority of the sample was overweight or obese with a mean BMI of 30.3 kg/m². Only 6 participants had BMI less than 20 kg/m² and 29 participants

had BMI more than 40 kg/m². Most participants (82%) reported their health as good or better.

Persistent mobility disability was observed for 17.4% of the individuals in the lowest sex-specific quartile of grip strength (and was not observable in 5.1% due to termination of follow-up). In the middle two and highest quartiles, the rates were 3.9% (9.8% nonobservable) and 3.9% (6.8% nonobservable), respectively. A chi-square test to compare the rates among observable individuals yields $p < .001$. Persistent mobility disability was observed for 8.2% of the individuals in the lowest BMI group (and was not observable in 8.2% due to termination of follow-up). In the middle and highest BMI groups, the rates were 4.6% (7.0% nonobservable) and 9.2% (8.7% nonobservable), respectively, with $p = .22$.

In Table 2, we present hazard ratios associated with sex-specific categories of grip strength, adjusted for covariates. Adjustment for covariates did not change the nature of the association between grip strength and risk of major mobility disability. The striking finding from these data is the steep linear gradient of risk across the grip strength categories. In fully adjusted analyses, individuals in the lowest sex-specific quartile of grip strength at baseline had six times the risk of developing major mobility disability as compared with those in the highest sex-specific quartile at baseline.

In Table 3, we present hazard ratios associated with BMI categories, adjusted for covariates. Adjustment for covariates did not change the nature of the association between BMI and risk of major mobility disability. These data suggest that there may be a U-shaped relationship between BMI and the development of major mobility disability. That is, the risk of major mobility disability for participants with a BMI of 25–29 kg/m² was approximately half that of participants in the lower and higher categories of BMI.

When both grip strength and BMI group were included in a model with covariate adjustment for intervention assignment, grip strength was significantly related to the hazard for mobility disability ($p < .001$) but BMI was not ($p = .11$). A formal test for an interaction between the effects of grip strength and BMI found no evidence for synergism in the effects ($p = .87$). The associations that grip strength and BMI had with the hazard of mobility disability were reasonably similar between intervention groups based on tests of interactions, $p = .15$ and $p = .96$, respectively.

Individuals assigned to the physical activity intervention, compared with successful aging, averaged (*SE*) 0.03 (0.01) m/s greater gait speeds for the 400-m walk across time (based on a general linear model that included sex as a covariate). Grip strength was measured at 6 and 12 months and BMI at 12 months postrandomization. The physical activity intervention had little effect on changes in grip strength ($p = .22$) or BMI ($p = .45$) from baseline at these follow-up times. For each intervention arm, grip strength and gait speed were highly correlated ($p < .001$) at 6 and 12 months, respectively, after covariate adjustment for gender. Similarly, at 12 months, BMI had significant cross-sectional

Table 1. Baseline Characteristics of Participants Grouped by Sex-Specific Grip Strength Percentiles and BMI: Comparisons Are Based on Chi-Squared Tests for Categorical Variables and Analyses of Variance for Continuous Variables

Risk Factor	Lower Quartile, <i>N</i> = 94	Middle Two Quartiles, <i>N</i> = 218	Upper Quartile, <i>N</i> = 94	<i>p</i> Value
Grip strength				
Age (y)	78.5 (4.0)	76.8 (4.1)	75.1 (3.9)	<.001
Sex				
Female	67 (71%)	150 (69%)	65 (69%)	.91
Male	27 (29%)	68 (31%)	29 (31%)	
Race/ethnicity				
African American	11 (12%)	35 (16%)	29 (31%)	.001
White	71 (76%)	171 (78%)	58 (62%)	
Other	12 (13%)	12 (6%)	7 (5%)	
Education				
HS or less	27 (29%)	64 (29%)	32 (34%)	.80
College or more	47 (50%)	100 (46%)	39 (42%)	
Missing	20 (21%)	54 (25%)	22 (24%)	
Comorbidity index	1.5 (1.1)	1.8 (1.2)	1.6 (1.1)	.19
CES-D	7.6 (5.4)	7.3 (6.6)	6.5 (6.7)	.45
MMSE score	27.2 (2.4)	27.3 (2.3)	27.5 (1.9)	.69
Intervention assignment				
Successful aging	46 (49%)	107 (49%)	48 (51%)	.94
Physical activity	48 (51%)	111 (51%)	46 (49%)	
BMI, kg/m ²	29.4 (6.7)	30.1 (5.5)	32.2 (7.8)	.005
Risk factor	<25 kg/m ² , <i>N</i> = 61	25–29 kg/m ² , <i>N</i> = 172	≥30 kg/m ² , <i>N</i> = 173	<i>p</i> Value
BMI				
Age (year)	78.3 (4.3)	77.4 (4.1)	75.7 (3.9)	<.001
Sex				
Female	45 (74%)	118 (69%)	119 (69%)	.73
Male	16 (26%)	54 (31%)	54 (31%)	
Race/ethnicity				
African American	6 (10%)	31 (18%)	38 (22%)	.11
White	52 (85%)	130 (76%)	118 (68%)	
Other	3 (5%)	11 (6%)	17 (10%)	
Education				
HS or less	16 (26%)	56 (33%)	51 (29%)	.58
College	26 (43%)	76 (44%)	84 (49%)	
Post college	19 (31%)	39 (23%)	38 (22%)	
Comorbidity index	1.3 (1.1)	1.7 (1.1)	1.8 (1.2)	.01
CES-D	7.3 (6.8)	7.2 (6.2)	7.1 (6.5)	.96
MMSE score	27.3 (2.1)	27.3 (2.3)	27.4 (2.2)	.89
Intervention assignment				
Control	33 (54%)	95 (55%)	73 (42%)	.04
Physical activity	28 (46%)	77 (45%)	100 (58%)	
Grip strength (kg)	22.9 (7.2)	25.1 (9.6)	26.2 (8.3)	.01

Note: Provided are means (*SD*) and prevalences (percents). For women, the lowest and highest quartiles were defined by 18 and 26 kg, respectively; for males, these cut-points were 28 and 41 kg, respectively. BMI = body mass index; CES-D = Center for Epidemiological Studies–Depression; HS = high school; MMSE = Mini-Mental State Examination.

relationships with gait speed in both the successful aging ($p = .004$) and physical activity ($p = .04$) cohorts, with the slowest mean gait speeds being recorded among individuals with BMI more than 30 kg/m². There was no association between baseline grip strength and subsequent changes in gait speed overall (and in either intervention arm).

DISCUSSION

The aim of this study was to evaluate whether muscle strength and BMI at baseline predicted major mobility disability across 18 months while controlling for a number of risk factors previously linked to disability and the treatment effect in sedentary functionally limited older adults. We

also examined whether changes in gait speed were related to baseline strength and BMI. The major results of this study were (i) muscle strength, assessed with a simple handgrip test, was an important predictor of mobility disability and (ii) overweight appeared to be protective for mobility disability as compared with normal or obese categories of BMI. We did not find any evidence for an interaction between muscle strength and obesity. Also, the associations of grip strength and BMI with mobility disability were distinct from the associations with changes in gait speed, for which we found no significant relationships.

In our study, grip strength was a significant predictor of risk for major mobility disability. From a screening perspective, grip strength has much appeal (17). The sharp

Table 2. Risk of Major Mobility Disability After 6, 12, and 18 Months and Baseline Grip Strength

Model	Grip Strength			<i>p</i> Value
	Lower Quartile	Middle Quartiles	Upper Quartile	
Number of participants	94	218	94	
Numbers of events	27	25	5	
Total years of follow-up	109.8	252.8	115.8	
Rate of failure (events per person-year)	0.25/pyr	0.10/pyr	0.04/pyr	
	Relative hazard ratio (95% confidence intervals)			
Adjustment for intervention assignment	6.47 (2.40–6.47)	2.39 (0.91–6.28)	1.00	<.001
Additionally adjusted for age	5.77 (2.17–15.34)	2.23 (0.84–5.91)	1.00	<.001
Additionally adjusted for sex, ethnicity, and education	5.97 (2.21–16.10)	2.26 (0.85–6.02)	1.00	<.001
Additionally adjusted for comorbidities and CES-D score	6.55 (2.40–17.88)	2.12 (0.79–5.68)	1.00	<.001
All of above and MMSE	6.11 (2.24–16.66)	1.95 (0.72–5.24)	1.00	<.001

Note: CES-D = Center for Epidemiological Studies–Depression; MMSE = Mini-Mental State Examination.

increase in risk for mobility disability observed for participants with grip strength scores in the lowest sex-specific quartiles (18 kg for women and 26 kg for men) suggests that these values might be used in a clinical setting for risk stratification. It is interesting to compare these values with the cut-points for mobility limitations (defined as gait speed < 0.8 m/s and self-reported inability to walk for 1 km) of 20 kg in women and 30 kg in men identified by Lauretani and colleagues (18) and cut-points for mobility limitation (defined as self-reported difficulty walking 500 m or climbing one flight of stairs) for women (21 kg) and men (37 kg) identified by Sallinen and colleagues (19). The consistency across different studies using different outcomes is remarkable and lends support for the use of this simple test in clinical practice.

We observed a U-shaped relationship between BMI and risk of mobility disability. A potential *protective* effect of an overweight BMI in older adults has been reported in a number of studies that have data across the entire spectrum of BMI, from underweight (BMI < 18 kg/m²) to morbid obesity [BMI ≥ 40 kg/m² (20–23)]. Outcomes in these studies have included self-reported activity of daily living disability,

self-reported *functional illness*, self-reported ability to walk without assistance, (i) across a small room, (ii) up and down stairs, and (iii) half a mile, and disability-free life expectancy. Our study is unique in showing this U-shaped relationship for BMI and failure on an objective test of physical function.

The effect of obesity on mobility has become an important question because of the increasing number of overweight and obese older adults. Although existing data suggest that overweight and Class 1 obesity confer reduced risk for mortality (24), living longer with overweight and obesity may be problematic if one has to contend with reduced mobility and poorer health as a result of excess fat mass (7,25). Our data clearly show that obesity increases the risk of mobility disability in older adults.

The role of obesity as compared with muscle strength in the disablement process is not clear primarily because the majority of studies have examined these two factors in isolation or examined muscle mass as opposed to strength (26–30). In the current study, the hazard ratios associated with lower muscle strength were considerably greater than those for categories of obesity. Interestingly, Misisic and

Table 3. Risk of Major Mobility Disability After 6, 12, and 18 Months and Baseline BMI

Model	BMI			<i>p</i> Value
	<25 kg/m ²	25–29.9 kg/m ²	≥30 kg/m ²	
Number of participants	61	172	173	
Numbers of events	10	17	30	
Total years of follow-up	72.0	203.6	205.7	
Rate of failure (events per person-year)	0.14/pyr	0.08/pyr	0.15/pyr	
	Relative hazard ratio (95% confidence intervals)			
Adjustment for intervention assignment	1.00 (0.49–2.06)	0.54 (0.29–0.98)	1.00	.09
Additionally adjusted for age	0.80 (0.38–1.67)	0.46 (0.25–0.86)	1.00	.04
Additionally adjusted for sex, ethnicity, and education	0.78 (0.36–1.66)	0.45 (0.24–0.84)	1.00	.03
Additionally adjusted for comorbidities and CES-D score	0.95 (0.44–2.06)	0.50 (0.26–0.92)	1.00	.06
All of above and MMSE	0.97 (0.45–2.08)	0.48 (0.26–0.90)	1.00	.04

Note: BMI = body mass index; CES-D = Center for Epidemiological Studies–Depression; MMSE = Mini-Mental State Examination.

colleagues (31) reported that muscle quality was a much stronger predictor of lower extremity function as compared with fat mass. In contrast, Zoico and colleagues (32,33) reported that fat mass was more important than muscle mass or strength as a predictor of disability. However, they used a modified activity of daily living scale to assess disability. Muscle mass and strength may not be as relevant to the performance of activities of daily living compared with the 400-MWT. Similarly, in cross-sectional analyses, Lebrun and colleagues (34) concluded that fat mass was more important than muscle strength as a risk factor for poorer physical performance and disability in postmenopausal women. Our data suggest that the risk of major mobility disability as a result of poor strength may be greater than that posed by having a normal or obese BMI. However, an important consideration in evaluating the consequences of obesity on function is the nature of the physical task. For example, obesity might not be particularly detrimental to limited movement within the home or walking short distances on level ground. However, walking for longer distances or raising the body center of mass from a chair or up a flight of stairs may be considerably compromised by a high BMI.

An obvious question of interest is whether an interaction existed between strength and obesity, for example, whether the associations between mobility disability and obesity were less pronounced among individuals with greater grip strength. We tested the interaction between grip strength and BMI, and it was not significant ($p = .87$). Stenholm and colleagues (8) showed a gradient of greater prevalence of walking limitation with lower handgrip strength within all three body fat percentage categories but the interaction between fat percentage and handgrip strength was not significant ($p = .43$). More recently, in a longitudinal analysis from the InCHIANTI Study, Stenholm and colleagues (10) reported that obese participants with low muscle strength (isometric strength of the knee extensors) had a higher risk of developing mobility disability (defined using self-report of the ability to walk 400 m or climb one flight of stairs) over the 6-year follow-up compared with those without obesity or low muscle strength. Similar to the earlier study, they found no significant interaction between muscle strength and obesity, which they suggested was indicative of an additive as opposed to a multiplicative effect on mobility disability. In this study, they also reported that obese older adults with low muscle strength had a steeper decline in gait speed over the 6-year follow-up, but this effect was substantially attenuated in those over 80 years. Our data are consistent with this result because we did not find any significant associations between grip strength, BMI, and gait speed in our sample of older adults who had an average age of 77 years. Also, our follow-up of 1 year may have limited the opportunity for declines in gait speed.

There are several limitations inherent in the current study. We used BMI, which is an imperfect measure of body composition. However, Zoico and colleagues (33) reported

that high body fat as well as high BMI was associated with greater probability of developing functional limitations, and Stenholm and colleagues (8) found similar results whether they used BMI or body fat. Also, the use of grip strength rather than the strength of a lower extremity muscle group such as the quadriceps muscles might be seen as a limitation. The strong association observed between grip strength and the risk of major mobility disability suggests that grip strength might be an indicator of general body strength, but grip strength was not sensitive to the physical activity intervention. A strong association between handgrip strength and the strength of other muscle groups (18,35,36) has been reported. Recently, Newman and colleagues (37) reported that muscle strength, but not muscle mass, was related to mortality and also showed that isometric grip strength provided risk estimates very similar to quadriceps strength measured on an isokinetic dynamometer. Our findings are based on data from volunteers for a physical activity clinical trial, which may not generalize to other populations. It is also possible for mobility disability status to change, that is, individuals can recover. We did not account for lifelong or recent changes in body mass or composition in our analyses. The analyses we presented on persistent mobility disability are consistent with our hazard ratio results and suggest that recovery is poorest in those with the lowest grip strength and normal or obese BMI. Therefore, our results were not affected by changes in mobility disability status. Finally, a major issue for future research in this area is the clear delineation of what is meant by mobility disability and major mobility disability. For example, mobility disability has been defined in several ways (4,10,11,38–41). Adoption of standard definitions would assist efforts to integrate and understand the relationships between muscle strength, BMI, and mobility.

Ferrucci and colleagues (42) have argued that the complex nature of disability presents a challenge when trying to identify a single risk factor on which to intervene. They suggested targeting common factors that increase the risk of disability regardless of specific causes. It is encouraging that recent evidence shows that weight loss and physical activity can significantly improve physical function in obese older adults (43,44). Our data underscore the importance of muscle strength and BMI as risk factors for mobility disability and provide support for studies of caloric restriction and resistance exercise training designed to target these risk factors. However, overweight in older adults at risk for mobility disability may be protective for major mobility disability. Finally, failure on a performance measure of physical function appears to provide a unique assessment of functional decline in older adults distinct from assessment of gait speed.

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REFERENCES

1. Loneragan ET, Krevans JR. A national agenda for research on aging. *N Engl J Med*. 1991;324(25):1825–1828.
2. Fried LP, Guralnik JM. Disability in older adults: evidence regarding significance, etiology, and risk. *J Am Geriatr Soc*. 1997;45(1):92–100.
3. Manton KG. Recent declines in chronic disability in the elderly U.S. population: risk factors and future dynamics. *Annu Rev Public Health*. 2008;29:91–113.
4. Rantanen T, Guralnik JM, Foley D, et al. Midlife hand grip strength as a predictor of old age disability. *JAMA*. 1999;281(6):558–560.
5. Marsh AP, Miller ME, Saikin AM, et al. Lower extremity strength and power are associated with 400-meter walk time in older adults: the InCHIANTI study. *J Gerontol A Biol Sci Med Sci*. 2006;61(11):1186–1193.
6. Rejeski WJ, Marsh AP, Chmelo E, Rejeski JJ. Obesity, intentional weight loss and physical disability in older adults. *Obes Rev*. 2010;11(9):671–685.
7. Alley DE, Chang VW. The changing relationship of obesity and disability, 1988–2004. *JAMA*. 2007;298(17):2020–2027.
8. Stenholm S, Rantanen T, Heliovaara M, Koskinen S. The mediating role of C-reactive protein and handgrip strength between obesity and walking limitation. *J Am Geriatr Soc*. 2008;56(3):462–469.
9. Stenholm S, Sainio P, Rantanen T, et al. High body mass index and physical impairments as predictors of walking limitation 22 years later in adult Finns. *J Gerontol A Biol Sci Med Sci*. 2007;62(8):859–865.
10. Stenholm S, Alley D, Bandinelli S, et al. The effect of obesity combined with low muscle strength on decline in mobility in older persons: results from the InCHIANTI study. *Int J Obes (Lond)*. 2009;33(6):635–644.
11. The LIFE Study Investigators. Effects of a physical activity intervention on measures of physical performance: results of the Lifestyle Interventions and Independence for Elders Pilot (LIFE-P) Study. *J Gerontol A Biol Sci Med Sci*. 2006;61(11):1157–1165.
12. Rejeski WJ, Fielding RA, Blair SN, et al. The lifestyle interventions and independence for elders (LIFE) pilot study: design and methods. *Contemp Clin Trials*. 2005;26(2):141–154.
13. Espeland MA, Gill TM, Guralnik J, et al. Designing clinical trials of interventions for mobility disability: results from the lifestyle interventions and independence for elders pilot (LIFE-P) trial. *J Gerontol A Biol Sci Med Sci*. 2007;62(11):1237–1243.
14. Katula JA, Kritchevsky SB, Guralnik JM, et al. Lifestyle Interventions and Independence for Elders pilot study: recruitment and baseline characteristics. *J Am Geriatr Soc*. 2007;55(5):674–683.
15. Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189–198.
16. Radloff LS. The CES-D scale. A self-report depression scale for research in the general population. *Applied Psychol Meas*. 1977;1:385–401.
17. Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. *J Geriatr Phys Ther*. 2008;31(1):3–10.
18. Lauretani F, Russo CR, Bandinelli S, et al. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol*. 2003;95(5):1851–1860.
19. Sallinen J, Stenholm S, Rantanen T, Heliovaara M, Sainio P, Koskinen S. Hand-grip strength cut points to screen older persons at risk for mobility limitation. *J Am Geriatr Soc*. 2010;58(9):1721–1726.
20. Galanos AN, Pieper CF, Cornoni-Huntley JC, Bales CW, Fillenbaum GG. Nutrition and function: is there a relationship between body mass index and the functional capabilities of community-dwelling elderly? *J Am Geriatr Soc*. 1994;42(4):368–373.
21. Ferraro KF, Booth TL. Age, body mass index, and functional illness. *J Gerontol B Psychol Sci Soc Sci*. 1999;54(6):S339–S348.
22. Mendes de Leon CF, Hansberry MR, Bienias JL, Morris MC, Evans DA. Relative weight and mobility: a longitudinal study in a biracial population of older adults. *Ann Epidemiol*. 2006;16(10):770–776.
23. Al Snih S, Ottenbacher KJ, Markides KS, Kuo YF, Eschbach K, Goodwin JS. The effect of obesity on disability vs mortality in older Americans. *Arch Intern Med*. 2007;167(8):774–780.
24. Janssen I. Morbidity and mortality risk associated with an overweight BMI in older men and women. *Obesity (Silver Spring)*. 2007;15(7):1827–1840.
25. Seidell JC. The impact of obesity on health status: some implications for health care costs. *Int J Obes Relat Metab Disord*. 1995;19(suppl 6):S13–S16.
26. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. *J Am Geriatr Soc*. 2002;50(5):889–896.
27. Janssen I, Baumgartner RN, Ross R, Rosenberg IH, Roubenoff R. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. *Am J Epidemiol*. 2004;159(4):413–421.
28. Visser M, Harris TB, Langlois J, et al. Body fat and skeletal muscle mass in relation to physical disability in very old men and women of the Framingham Heart Study. *J Gerontol A Biol Sci Med Sci*. 1998;53(3):M214–M221.
29. Zamboni M, Turcato E, Santana H, et al. The relationship between body composition and physical performance in older women. *J Am Geriatr Soc*. 1999;47(12):1403–1408.
30. Visser M, Langlois J, Guralnik JM, et al. High body fatness, but not low fat-free mass, predicts disability in older men and women: the Cardiovascular Health Study. *Am J Clin Nutr*. 1998;68(3):584–590.
31. Misis MM, Rosengren KS, Woods JA, Evans EM. Muscle quality, aerobic fitness and fat mass predict lower-extremity physical function in community-dwelling older adults. *Gerontology*. 2007;53(5):260–266.
32. Zoico E, Di FV, Guralnik JM, et al. Physical disability and muscular strength in relation to obesity and different body composition indexes in a sample of healthy elderly women. *Int J Obes Relat Metab Disord*. 2004;28(2):234–241.
33. Zoico E, Di FV, Mazzali G, et al. High baseline values of fat mass, independently of appendicular skeletal mass, predict 2-year onset of disability in elderly subjects at the high end of the functional spectrum. *Aging Clin Exp Res*. 2007;19(2):154–159.
34. Lebrun CE, van der Schouw YT, de Jong FH, Grobbee DE, Lamberts SW. Fat mass rather than muscle strength is the major determinant of physical function and disability in postmenopausal women younger than 75 years of age. *Menopause*. 2006;13(3):474–481.
35. Rantanen T, Pertti E, Kauppinen M, Heikkinen E. Maximal isometric muscle strength and socioeconomic status, health, and physical activity in 75-year-old persons. *J Aging Phys Act*. 1994;2:206–220.
36. Payette H, Hanusaik N, Boutier V, Morais JA, Gray-Donald K. Muscle strength and functional mobility in relation to lean body mass in free-living frail elderly women. *Eur J Clin Nutr*. 1998;52(1):45–53.
37. Newman AB, Kupelian V, Visser M, et al. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. *J Gerontol A Biol Sci Med Sci*. 2006;61(1):72–77.
38. Onder G, Penninx BW, Ferrucci L, Fried LP, Guralnik JM, Pahor M. Measures of physical performance and risk for progressive and

- catastrophic disability: results from the Women's Health and Aging Study. *J Gerontol A Biol Sci Med Sci*. 2005;60(1):74–79.
39. Guralnik JM, Ferrucci L, Balfour JL, Volpato S, Di IA. Progressive versus catastrophic loss of the ability to walk: implications for the prevention of mobility loss. *J Am Geriatr Soc*. 2001;49(11):1463–1470.
 40. Melzer D, Gardener E, Guralnik JM. Mobility disability in the middle-aged: cross-sectional associations in the English Longitudinal Study of Ageing. *Age Ageing*. 2005;34(6):594–602.
 41. Fried LP, Bandeen-Roche K, Chaves PH, Johnson BA. Preclinical mobility disability predicts incident mobility disability in older women. *J Gerontol A Biol Sci Med Sci*. 2000;55(1):M43–M52.
 42. Ferrucci L, Penninx BW, Leveille SG, et al. Characteristics of nondisabled older persons who perform poorly in objective tests of lower extremity function. *J Am Geriatr Soc*. 2000;48(9):1102–1110.
 43. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. *N Engl J Med*. 2011;364(13):1218–1229.
 44. Rejeski WJ, Brubaker PH, Goff DC Jr., et al. Translating weight loss and physical activity programs into the community to preserve mobility in older, obese adults in poor cardiovascular health. *Arch Intern Med*. 2011;171(10):880–886.

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