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

Anthony P. Marsh,¹ W. Jack Rejeski,¹ Mark A. Espeland,² Michael E. Miller,² Timothy S. Church,³ Roger A. Fielding,⁴ Thomas M. Gill,⁵ Jack M. Guralnik,⁶ Anne B. Newman,⁷,⁸ and Marco Pahor⁹; for the LIFE Study Investigators (see Appendix 1)

¹Department of Health and Exercise Science, Wake Forest University, Winston-Salem, North Carolina.
²Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, North Carolina.
³Pennington Biomedical Research Center, Baton Rouge, Louisiana.
⁴Nutrition, Exercise, Physiology, and Sarcopenia Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, Massachusetts.
⁵Department of Medicine, Yale University School of Medicine, New Haven, Connecticut.
⁶Division of Gerontology, Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore.
⁷Department of Epidemiology and ⁸Department of Medicine, Graduate School of Public Health, University of Pittsburgh, Pennsylvania.
⁹Department of Aging and Geriatric Research, Institute on Aging, University of Florida, Gainesville.

Address correspondence to Anthony P. Marsh, PhD, Department of Health and Exercise Science, Wake Forest University, Winston-Salem, NC 27109-7868. Email: marshap@wfu.edu

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.

Received September 7, 2010; Accepted August 7, 2011

Decision Editor: Luigi Ferrucci, MD, PhD

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 semiannual 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/m²). In our analyses, we used the standard BMI cut-points of less than 25, 25–29.9, and 30 kg/m² 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/m$^2$ 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 $\sim 77$ 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 $30.3 \text{ kg/m}^2$. Only 6 participants had BMI less than $20 \text{ kg/m}^2$ and 29 participants had BMI more than $40 \text{ kg/m}^2$. 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/m$^2$ 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
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/m$^2$. 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).
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/m$^2$) to morbid obesity [BMI $\geq$ 40 kg/m$^2$ (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, Misic and

<table>
<thead>
<tr>
<th>Grip Strength</th>
<th>Lower Quartile</th>
<th>Middle Quartiles</th>
<th>Upper Quartile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>94</td>
<td>218</td>
<td>94</td>
</tr>
<tr>
<td>Numbers of events</td>
<td>27</td>
<td>25</td>
<td>5</td>
</tr>
<tr>
<td>Total years of follow-up</td>
<td>109.8</td>
<td>252.8</td>
<td>115.8</td>
</tr>
<tr>
<td>Rate of failure (events per person-year)</td>
<td>0.25/pyr</td>
<td>0.10/pyr</td>
<td>0.04/pyr</td>
</tr>
</tbody>
</table>

Relative hazard ratio (95% confidence intervals) $p$ Value

- Adjustment for intervention assignment: 6.47 (2.40–16.47) $p < 0.001$
- Additionally adjusted for age: 5.77 (2.17–15.34) $p < 0.001$
- Additionally adjusted for sex, ethnicity, and education: 5.97 (2.21–16.10) $p < 0.001$
- Additionally adjusted for comorbidities and CES-D score: 6.55 (2.40–17.88) $p < 0.001$
- All of above and MMSE: 6.11 (2.24–16.66) $p < 0.001$

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

<table>
<thead>
<tr>
<th>BMI</th>
<th>&lt;25 kg/m$^2$</th>
<th>25–29.9 kg/m$^2$</th>
<th>$\geq$30 kg/m$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>61</td>
<td>172</td>
<td>173</td>
</tr>
<tr>
<td>Numbers of events</td>
<td>10</td>
<td>17</td>
<td>30</td>
</tr>
<tr>
<td>Total years of follow-up</td>
<td>72.0</td>
<td>203.6</td>
<td>205.7</td>
</tr>
<tr>
<td>Rate of failure (events per person-year)</td>
<td>0.14/pyr</td>
<td>0.08/pyr</td>
<td>0.15/pyr</td>
</tr>
</tbody>
</table>

Relative hazard ratio (95% confidence intervals) $p$ Value

- Adjustment for intervention assignment: 1.00 (0.49–2.06) $p = 0.9$
- Additionally adjusted for age: 0.80 (0.38–1.67) $p = 0.4$
- Additionally adjusted for sex, ethnicity, and education: 0.78 (0.36–1.66) $p = 0.03$
- Additionally adjusted for comorbidities and CES-D score: 0.95 (0.44–2.06) $p = 0.06$
- All of above and MMSE: 0.97 (0.45–2.08) $p = 0.04$

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.

**Funding**

A.P.M., W.J.R., and M.E.M. are supported by the Wake Forest University Claude D. Pepper Center National Institutes for Aging (P30 AG021332).
J.M.G. is supported in part by the Intramural Research Program, National Institute on Aging, National Institutes of Health (NIH). The Lifestyle Interventions and Independence for Elders (LIFE-P) Pilot Study is funded by a National Institutes of Health/National Institute on Aging Cooperative Agreement #U01 AG22376 and sponsored in part by the Intramural Research Program, National Institute on Aging, NIH.

Acknowledgment
T.M.G. is the recipient of an National Institute on Aging Midcareer Investigator Award in Patient-Oriented Research (K24AG021507).

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APPENDIX 1. RESEARCH INVESTIGATORS FOR PILOT PHASE OF LIFE

Cooper Institute, Dallas, TX: Steven N. Blair, PED—Field Center Principal Investigator; Timothy Church, MD, PhD, MPH—Fielding Center Co-Principal Investigator; Jamie A. Ashmore, PhD; Judy Dubreuil, MS; Georita Frierson, PhD; Alexander N. Jordan, MS; Gina Morss, MA; Ruben Q. Rodarte, MS; Jason M. Wallace, MPH.

National Institute on Aging: Jack M. Guralnik, MD, PhD—Co-Principal Investigator of the Study; Evan C. Hadley, MD; Sergei Romashkan, MD, PhD.

Stanford University, Palo Alto, CA: Abby C. King, PhD—Field Center Principal Investigator; William L. Haskell, PhD—Field Center Co-Principal Investigator; Leslie A. Pruitt, PhD; Kari Abbott-Pilolla, MS; Karen Bolen, MS; Stephen Fortmann, MD; Ami Laws, MD; Carolyn Prosak, RD; Kristin Wallace, MPH.

Tufts University: Roger Fielding, PhD; Miriam Nelson, PhD. Dr. Fielding’s contribution is partially supported by the U.S. Department of Agriculture, under agreement No. 58-1950-4-401. Any opinions, findings, conclusion, or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect the view of the U.S. Dept of Agriculture.

University of California, Los Angeles, Los Angeles, CA: Robert M. Kaplan, PhD, MA.

VA San Diego Healthcare System and University of California, San Diego, San Diego, CA: Erik J. Groessl, PhD.

University of Florida, Gainesville, FL: Marco Pahor, M.D.—Principal Investigator of the Study; Michael Perri, PhD; Connie Caudle, MPH; Sarah Hayden; Lotiona Holmes; Cinzia Maraldi, MD; Crystal Quirin. Dr. Pahor is partially supported by the Geriatric Research, Education and Clinical Center (GRECC) of the Malcom Randall Veteran’s Affairs Medical Center, North Florida/ South Georgia Veterans Health System, Gainesville, FL.

University of Pittsburgh, Pittsburgh, PA: Anne B. Newman, MD, MPH—Field Center Principal Investigator; Stephanie Studenski, MD, MPH—Field Center Co-Principal Investigator; Bret H. Goodpaster, PhD, MS; Nancy W. Glynn, PhD; Erin K. Aiken, BS; Steve Anthony, MS; Sarah Beck (for recruitment papers only); Judith Kadosh, BSN, RN; Piera Kost, BA; Mark Newman, MS; Jennifer Rush, MPH (for recruitment papers only); Roberta Spanos (for recruitment papers only); Christopher A. Taylor, BS; Pam Vincent, CMA. The Pittsburgh Field Center was partially supported by the Pittsburgh Claude D. Pepper Center P30 AG024827.

Wake Forest University, Winston-Salem, NC: Stephen B. Kritchevsky, PhD—Field Center Principal Investigator; Peter Brubaker, PhD; Jamieh Demons, MD; Curt Furberg, MD, PhD; Jeffrey A. Katula, PhD, MA; Anthony Marsh, PhD; Barbara J. Nicklas, PhD; Jeff D. Williamson, MD, MPH; Rose Fries, LPM; Kimberly Kennedy; Karin M. Murphy, BS, MT (ASCP); Shruti Nagaria, MS; Katie Wickley-Krupel, MS.

Data Management, Analysis and Quality Control Center (DMAQC): Michael E. Miller, PhD—DMAQC Field Principal Investigator; Mark Espeland, PhD—DMAQC Co-Principal Investigator; Fang-Chi Hsu, PhD; Walter J. Rejeski, PhD; Don P. Babcock, Jr., PE; Lorraine Costanza; Lea N. Harvin; Lisa Kaltenbach, MS; Wei Lang, PhD; Wesley A. Roberson; Julia Rushing, MS; Scott Rushing; Michael P. Walkup, MS. The Wake Forest University Field Center is, in part, supported by the Claude D. Older American Independence Pepper Center #1 P30 AG21332.

Yale University: Thomas M. Gill, MD. Dr. Gill is the recipient of a Midcareer Investigator Award in Patient-Oriented Research (K24AG021507) from the National Institute on Aging.