Development of a New Patient-Reported Outcome Measure in Sarcopenia

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Objective: The objective of this study was to develop a patient-reported outcome (PRO) to assess reduced muscle strength in sarcopenia.

Design: Qualitative research study.

Setting: University of Arkansas for Medical Sciences.

Participants: Subjects with sarcopenia.

Measurements: Adults aged 55 years and older with sarcopenia (n = 12) attended open-ended, concept elicitation interviews to characterize the functional effects of reduced muscle strength on their lives. The resulting qualitative data were analyzed using a qualitative analysis software program (Atlas.ti [Atlas.ti GmbH, Berlin, Germany]) and a common set of codes was developed to summarize the data. Subsequently, the initial PRO measure was drafted. Cognitive interviews were then conducted with additional sarcopenia subjects (n = 12) to refine the measure.

Results: Qualitative interviews identified key concepts (eg, impacts) in the areas of activities of daily living, emotions, social activities, energy, balance, coordination, sleep, and strength. Based on data from the cognitive debriefing interviews (eg, understandability, relevance, suggestions to reword items), the PRO measure development team came to consensus on which items or parts of the instructions to retain, revise, or delete. The final measure included 14 items.

Conclusion: The final PRO measure, the Age-Related Muscle Loss Questionnaire, can be used in both clinical practice and clinical trial settings to assess functional impacts of reduced muscle strength in sarcopenia. **(J Am Med Dir Assoc 2011; 12: 226–233)**

Keywords: Patient-reported outcome; sarcopenia; muscle wasting

Sarcopenia is the loss of skeletal muscle mass and strength that occurs with aging.[1] When muscle loss reaches a critical threshold, individuals may experience functional impairments, physical disability, and reduction in health-related quality of life. Data from the Third National Health and Nutrition Examination Survey found that the likelihood of functional impairment (eg, difficulty climbing stairs, lifting/carrying 10 pounds, performing household chores) was approximately doubled in older men and tripled in older women with severe sarcopenia compared with controls with a normal skeletal mass index.[2] Sarcopenia is also associated with self-reported physical disability in older adults, independent of gender, ethnicity, age, comorbidities, obesity, income, and health behaviors.[3] Both the use of assistive walking devices and number of falls have been found to be higher in individuals with sarcopenia compared with those with normal muscle mass.[3] Furthermore, weak strength, poor function, and low muscle density are associated with greater risk of hospitalization in older adults.[4]

Not only is sarcopenia associated with physical disability[3] and functional impairment[2] in older adults, but it creates a societal burden in terms of national health care spending. A decade ago, direct health care costs related to sarcopenia were estimated to be $18.5 billion in the United States, accounting for 1.5% of total health care expenditures.[5]

The importance of subjects' points of view on their health status and use of health care is widely recognized.[6] Patient-reported outcomes (PROs) provide subjects' perspectives on impacts of a disease and therapies used to treat it.[7–9]

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Funding for this study was provided by Amgen. C-F.C., S.G. are employed by Amgen and hold stocks in Amgen. W.J.E. and W.D. received funds for recruitment of study participants. W.D. received a grant for data collection from Amgen. D.L.P. received honorarias for his consulting services from Amgen. C.J.E., K.A.F., W.J.E., B.R.F., W.D., L.P.F., B.D-S., and D.L.P. provided consulting services to Amgen.

The authors have no conflicts of interest.

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DOI:10.1016/j.jamda.2010.09.010

Table 1. *Inclusion and Exclusion Criteria for Study Participants*

Inclusion Criteria	Exclusion Criteria
1. 55 years or older; 2. gait speed of less than 0.9 meters/second; 3. body mass index ≤ 30.0; 4. A score on the Short Physical Performance Battery* assessment between 4 and 9; 5. Able to speak, read, and write English well enough to fill out questionnaires on their own and participate in discussions during a focus group or interview; and 6. Capable of participating in a 1-hour interview.	1. History of primary muscle disease or myopathy; 2. History of major trauma to the legs requiring casting or immobilization within the past 6 months; 3. Current malignancy other than nonmelanomatous skin cancers or in situ cervical cancer or on chemotherapy; 4. History of prostate cancer and is being treated with Androgen Deprivation Therapy; 5. History of breast cancer and is being treated with estrogen blockade; 6. Rheumatoid arthritis; 7. History of bilateral knee replacement; 8. History of stroke or heart failure; 9. Currently receiving renal replacement therapy (hemodialysis or peritoneal dialysis); 10. History of vitamin D deficiency; 11. Severe obstructive pulmonary disease and is receiving medical oxygen; 12. Human immunodeficiency virus positive; 13. Currently participating in another research study or clinical trial that includes the use of investigational medications for muscle wasting; 14. Cognitive impairment that would interfere with him/her participating in a focus group or interview; and 15. Severe psychiatric comorbidity that would interfere with him/her participating in a focus group or interview.

* Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85–M94.

Existing measures (eg, Subclinical Status in Functional Limitation and Disability,[10] World Health Organization Disability Assessment Schedule II[11]) evaluate functional assessment and limitations but are not specific to muscle loss. A PRO measure covering loss in muscle strength specific to sarcopenia would complement objective measures while assessing areas (eg, household activities, endurance) individuals feel are important.

There are a limited number of relevant disease-specific measures applicable to a population with sarcopenia; however, most assess specific aspects, such as dementia,[12] depression,[13] and urological problems.[14] Generic measures relevant to this population, such as the Instrumental Activities of Daily Living Scale,[15] were developed solely from clinician input and lack specific relevance to sarcopenia. A review of existing literature yielded no readily available, psychometrically sound measure to capture PROs associated with loss of muscle strength in sarcopenia. This study aimed to address this gap by developing a measure that assesses the burden of muscle loss in sarcopenia.

METHODS

Conceptual Framework

A preliminary conceptual framework was developed based on a literature review and input from experts in muscle wasting-related research (L.P.F., W.J.E., W.D., B.R.F.). The framework listed relevant PRO concepts and potential items (eg, an item measuring difficulty lifting objects would measure the concept of upper body activities). The preliminary framework was revised, and a final conceptual framework emerged after cognitive debriefing interviews.

Subject Interviews

Twelve sarcopenia subjects were interviewed to understand the effect of muscle weakness on their daily lives. An investigator (W.J.E.) at the University of Arkansas for Medical Sciences (UAMS) identified eligible subjects based on age, gait speed, body mass index, and Short Physical Performance Battery (SPPB) results[16] from his subject caseload and review of medical records (see Table 1 for inclusion and exclusion criteria). Potential subjects were provided information about the study, asked to sign a written informed consent form, and screened by study site staff for eligibility. All study documents, including protocol, interview guide, demographic form, RAND-36 questionnaire, screening form, and informed consent, were approved by the UAMS Institutional Review Board in September 2007.

A semi-structured concept elicitation interview guide was developed to obtain unprompted and prompted subject input on effects of muscle wasting on outcomes subjects considered relevant. Subject-reported concepts were considered spontaneous if reported by subjects without interviewer probing, whereas probed concepts emerged following interviewer prompting. An approach consistent with grounded theory was used for data collection and applied for the analysis. Grounded theory methods seek to produce rich descriptions and theoretical explanations of phenomena under investigation.[17] Concepts thus emerge from the data, allowing the

voice of the subject to be heard rather than applying a priori concepts or hypotheses.[17–19]

All interviews were audio-recorded and transcribed. Transcripts were coded and analyzed using Atlas.ti software, versions 5.0 and 6.0 (Atlas.ti GmbH, Berlin, Germany), into a range of areas to get an initial conceptualization of the data and determine which themes were common across subjects. Atlas.ti is designed for qualitative analysis of textual, graphical, audio, and video data.[20]

An iterative approach was used to compare concepts across subjects to determine if new concepts were elicited as data analysis neared completion and, ultimately, whether concept saturation, the point where further data collection produces minimal or no new information, was met.[21]

Following analysis, a face-to-face meeting of the authors was held for item generation and construction of the sarcopenia PRO measure. During this process, consideration was given to the recent US Food and Drug Administration guidance for the development of PRO measures.[22,23] Additionally, 7 general principles guided selection of appropriate items. Each item should:

1. Evaluate impact of muscle wasting on an individual's life;
2. Represent a single impact, rather than a multidimensional concept;
3. Be relevant to most people with sarcopenia most of the time, determined by frequency of concept mentions (eg, at least 5 subjects) and importance ranking (eg, the top 10 impact rankings);
4. Be easily understood;
5. Measure a concept likely to change with successful treatment of the condition, determined by clinical input;
6. Be unlikely to be vulnerable to ceiling or floor effects; and
7. Be likely to have semantic (or at least conceptual) equivalence with other languages.

Concepts subjects mentioned spontaneously were given preference in item selection.

Using these criteria, the team reviewed the preliminary list of concepts and decided which to retain. Items representative of each retained concept that best matched subject quotes from the transcripts were selected. Because physical functioning and activities of daily living were the chief complaints mentioned, and because several relevant and valid measures already exist for emotional/social impact of disease (eg, Beck Depression Inventory,[24] Hospital Anxiety and Depression Scale[25,26]), it was decided to focus the PRO on physical effects of weakness resulting from muscle wasting. An item-tracking matrix was used to document changes or deletions and reasons for changes. Item format, response options, and recall period were determined in accordance with the US Food and Drug Administration guidance at this stage of measure development.[23]

A cognitive debriefing exercise was then conducted with 12 sarcopenia subjects in 3 waves (6 subjects in the first wave, 3 subjects each in the second and third). Subjects for cognitive debriefing were recruited in the same manner (ie, site, inclusion/exclusion criteria) as concept elicitation subjects. During the interviews, subjects were asked to complete the draft questionnaire and provide feedback using a "think aloud" technique.[27] Subjects reviewed the questionnaire item-by-item to evaluate clarity, ease of comprehension, and other components of face and content validity. Subjects' ability to accurately recall the information requested was evaluated via queries about the time frame they were considering when answering questions and their opinion on recall period in the instrument. Last, subjects were questioned on possible missing concepts and opinions on the instructions and response options.

After each wave of interviews, results were tabulated and discussed among the authors. Data from each wave were used to modify items for the subsequent wave. The questionnaire was finalized after discussion following the third wave of interviews.

RESULTS

Concept Elicitation Interviews

Twelve subjects participated in concept elicitation interviews: 9 females and 3 males ranging from 64 to 89 years old. Most of the subjects were white (75.0%) and had attended some college or had a college or graduate degree (66.7%). The most common comorbid condition was hypertension (41.7%), followed by diabetes mellitus (16.7%). Most subjects had a RAND-36 vitality score in the range of 40.1 to 60.0 (83.3%). RAND-36 physical function scores were more widely distributed. Two subjects had scores ranging from 20.0 to 30.0 (16.7%); 3 subjects each had scores in the ranges of 30.1 to 40.0 (25.0%), 50.1 to 60.0 (25.0%), and 60.1 to 70.0 (25.0%); and 1 subject had a score between 80.1 and 90.0 (8.3%). Most subjects scored between 8.00 and 9.00 on their SPPB[16] (66.7%).

Subjects were asked how their lack of muscle strength affected activities of daily living. Subjects reported impacts to the following: walking, running, or jogging (n = 11); lifting, carrying, moving, or pushing activities (n = 10); hand function (n = 9); household activities (n = 9); getting up from, out of, or on various objects (eg, chairs) or positions (eg, kneeling) (n = 8); getting up from sitting position (n = 7); standing (n = 7); bending or kneeling (n = 6); self-care (n = 6); and sitting or squatting (n = 5).

Lack of muscle strength was reported by 9 subjects to have affected overall balance. Nine subjects reported that their endurance was affected, 8 subjects reported that their coordination was affected, and 2 subjects reported loss of strength. Six subjects reported reduced stamina.

Most subjects (n = 11) reported that lack of muscle strength affected their energy level: tiredness (n = 9), reduced energy (n = 9), and loss of sleep (n = 4), including difficulty with sleep continuation, sleeping longer than usual, and lack of physically restorative sleep.

Most subjects (n = 10) reported experiencing emotional impacts because of lack of muscle strength. Eight subjects reported feelings of frustration, 3 reported feeling anxious, and 2 mentioned feeling embarrassed, angry, nervous, and depressed. Two subjects reported feeling discouraged or upset because of lack of muscle strength. Two subjects reported

Table 2. *Impacts of Muscle Loss Reported in Concept Elicitation*

Impacts	Examples of Verbatim Interview Quotes
Activities of daily living	I think maybe mainly when I noticed it is if I do try to walk any distance at all. And the muscles are tired. My leg muscles, I guess is where that would be.
	I'm not sure how to describe it except I'm not as strong. I'm not as strong as I was. It's harder to lift things up than it used to be.
	But if I have very many books to transport I'd take my little flat cart and roll them. I don't carry them…
	And the strength in my hands and my wrists, I don't have as much. I cannot open jars and bottles like I used to.
	For a long period, I probably would have some problems. For a short period, probably not. Standing on an unbalanced area, too, like on a hillside too…. And we were on the levee, we were on the banks of the river, and it sloped down. And I could - I had my cane, but I could feel myself getting tired…
	Well, it's not [difficult to get up from a sitting position] if I've got something to put my hands on. But it's tough trying to get out of a chair if ain't got no arms… I push - I get out of a chair if I put my arm and hand on it like that.
	I can't bend over to do any good.
Strength	I thought of something about the upper body. I was used to fixing my own curls for years, and now just to roll with curlers in my hair I find to be exhausting. *Q: Is it exhaust - How is it exhausting?* A: Reaching up. Loss of strength, I guess, in my arms. I don't know, but it's nice to have a beauty operator in the same building. One reason I wanted to go ahead and come this morning is because I usually go to her on Friday morning.
Energy	I live on the sixth floor of a high rise. I can walk the length of the building, down the stairs, length of the building, down the stairs, and so forth. I can do that all the way down and all the way up. Now last night I tried coming back up. When I got to the third floor I decided I'd better get back on the elevator… *Q: …Why did you stop?* A: I got tired.
	I guess I just got 50% of the energy too. I don't overdo nothing.
Balance	I was standing up. And I staggered around and fell backwards… I didn't fall down, but I hit tables and stuff…But just standing up.
	Well, I just noticed when I'm walking, like I'm walking down a hall - I'm in the center of the hall - and then as I go along, I may get closer to one wall or the other. So I don't know why, that's just the way it is. And I feel like I can't walk as straight. Because of that, that's made me think I don't walk as straight as I did and I'd like to do better.
Endurance	Well, if I'm doing yard work, I need to take a break more often. I used to be able to do it most of the morning.
	…walking, if I don't pace myself, then I get tired too fast. I have to make myself walk slow.
Coordination	I can't pick up anything with my thumbs… But I don't know whether that's strength - or what it is… Because when I go to pick up anything I get both hands before I get my fingers around… I can't pick up a coffee cup. I get my fingers lined up, the mugs, I get my fingers through it… But my thumbs don't work good. And I can't button a shirt… But that's on account of my thumbs.
	Like stumbling or dropping something occasionally. Twice in one day.
Sleep	Mentally well rested. I kind of have to work into feeling physically well rested… Because I'm mentally alert, and when I wake up, I'm immediately saying what I have to do today, or what do I desire to do today? But then I think back in the back of my mind, OK, am I physically feeling like doing all these things? And I compromise.
Emotional	Well, it's discouraging when you can't lift things. I guess it does make me upset, I just know I have to do it more slowly or go back for another - go back, make more trips.
	It's depressing. Because I cannot do the things I used to be able to do so easily.
Social	I don't volunteer in the library anymore because I can't pick up heavy books and put them up on the shelf.
	Well, I dabbled in needlework and things like that. If I work too long, then my hands cramp up.

experiencing a lack of motivation. One subject each reported feeling bothered, resentful, and sad.

All subjects (n = 12) reported social effects. An effect on general social life activities because of lack of muscle strength was reported by 4 subjects. Four subjects reported having difficulty shopping. Three subjects each reported that dancing, exercising, participating in athletic activities, traveling, and relationships with family and friends were affected. Knitting, swimming, and participating in volunteer work were indicated by 2 subjects each. Other impacts on social life reported by 1 subject each included attending sporting events, working, riding bicycles or horses, canoeing, playing tennis, gardening, and using a computer. See Table 2 for examples of verbatim quotes for the most commonly mentioned impacts.

Subjects ranked activities affected by lack of muscle strength by degree of importance. Walking was ranked among the 5 most important activities by 9 subjects. Five subjects each ranked getting in and out of cars and getting up from a sitting position among the 5 most important activities. Four subjects each ranked standing for extended periods of

time and going up and down stairs among the 5 most important activities. Additionally, 3 subjects each ranked gripping or grasping, bending, and lifting or carrying among the 5 most important activities. Two subjects each ranked dressing and getting up from a kneeling position among the 5 most important activities.

Analysis of the 12 concept elicitation interviews determined that concept saturation had been achieved within the sample, confirming sample size adequacy.[28] The initial paper-pen, interviewer-administered questionnaire, called the Age-Related Muscle Loss Questionnaire (ARMLQ), consisted of 14 items using a 24-hour recall period. It was determined that each questionnaire item would begin with "Considering your loss of muscle strength…" because unlike other muscle-wasting conditions, weight loss is not necessarily associated with sarcopenia, and most individuals are not aware of the existence of sarcopenia. Because older, sarcopenic subjects frequently use assistive devices in their daily activities, it was further decided that "without assistance from anyone else" be included at the end of each item. Response options are on an 11-point numeric rating scale.

Cognitive Debriefing Interviews

An additional 12 subjects, 3 males and 9 females, participated in cognitive debriefing interviews aimed at testing the face and content validity of 3 versions of the ARMLQ. The age of the subjects ranged from 66 to 89 years, and most of the subjects were white (91.7%). Many of the subjects indicated that they had attended either some college or a certificate program or had earned at least a college or university degree (58.3%). The most common comorbidity was hypertension (41.7%). Most subjects had a RAND-36 vitality score in the range of 40.1 to 70.0 (83.3%). Four subjects had RAND-36 physical function scores ranging from 30.1 to 40.0 (33.3%) and 6 subjects had scores ranging from 60.1 to 70.0 (25.0%). Six subjects (50.0%) scored a 6 on the SPPB[16] and the remainder of the subjects' scores ranged from 4 to 5 and 7 to 8.

During the cognitive debriefing interviews, subjects provided feedback on the ARMLQ. During the first wave, most subjects needed further clarification regarding how to answer questions about assistive devices; therefore, the instructions for these questions were revised. Additionally, most of the subjects in the first wave recommended increasing the recall period; 3 subjects explained that they had not performed many of the activities within the past 24 hours (eg, shopping), but they did do them over a slightly longer period. Before the second wave, the recall period was modified to "the most recent day in the past 7 days that you were up and about" to capture impacts from activities not performed in the past 24 hours. The revised recall period was restricted to the past 7 days to reduce the risk of inaccurate recall. Most of the subjects understood the response choices and all were satisfied with the questionnaire format. Problematic items included balance, endurance, and social activities. Based on feedback, appropriate revisions were made to the items and instructions and a second and third wave of debriefing interviews were conducted. The final interviewer-administered version of the ARMLQ is shown in Appendix 1.

Based on subject feedback, the following revisions were made to the final version of the ARMLQ. Text specifying jars "that have never been opened" was added to question 9 (difficulty opening jars) because subjects reported that opening old and new jars is different, the latter being more difficult. The example of "going out to eat with others" was added to question 14 (difficulty doing social activities outside your home) because it was a reported social activity and is presumably applicable to all subjects (unlike going to church, and so forth). Additionally, a self-administered version was created based on the interviewer-administered version to reduce study management burden and resources required for clinical trials.

DISCUSSION

The aging of the population in industrialized countries suggests the burden of sarcopenia will increase substantially. With a few notable exceptions, current investigations focus on clinical aspects of sarcopenia (eg, knee extensor, grip strength[1]) rather than the impact the condition has on aspects of functioning and health-related quality of life that subjects consider most important. Loss of muscle size and strength, characteristic of the sarcopenia population, has a substantial impact on subjects' lives. Based on concept elicitation interviews, the ARMLQ covers all the concepts (household activities, upper-body strength activities, lower-body strength activities, ambulation, activities requiring dexterity, endurance, balance, and social activities) relevant to sarcopenia subjects in a well-developed, easily administered questionnaire. Additionally, the ARMLQ provides information that complements traditional performance-based outcome measures, such as gait speed and SPPB.[16] As a disease-specific measure, it provides more specific information on treatment outcomes than generic measures, such as the Medical Outcomes Study 36-Item Short-Form Health Survey, which measures health status by assessing various concepts including limitations in physical activities because of health problems.[29]

Given the nature of the older subject population, it was decided that a relatively short recall period (the past 7 days) was most appropriate. To reduce subject burden and difficulty completing the questionnaire, an interviewer-administered mode was determined to be most appropriate. Despite the convenience of capturing data digitally (eg, using a personal digital assistant), it was also decided that a paper format would be best because of the demographics of the sarcopenia population. Potential challenges for this population include dexterity issues using a personal digital assistant keypad and lack of familiarity with electronics.

There are some limitations to our findings. Although conceptual saturation was achieved (saturation of the concepts within the preliminary conceptual framework), research exploring sarcopenia as a disease is ongoing. When more is learned about sarcopenia as a unique medical condition, additional impacts relevant to sarcopenia subjects may be revealed. Another limitation is that the study population did not represent individuals with sarcopenia on the younger end of the age spectrum (ages 55 to 63). Additionally, the

study sampled sarcopenia subjects from only one setting, UAMS. Because of the subjects' affiliation with the university's Reynolds Institute on Aging, the study population may have been in better physical condition than a community-based sample. However, this recruitment strategy permitted inclusion of those identified as having sarcopenia under well-defined criteria. The authors would not consider sample size a limitation because the goal was to reach saturation, not a particular quota for gender, age, or race. It was considered unethical to burden subjects with additional interviews, because after 12 interviews, saturation had been reached. Finally, using a single site and investigator for recruitment was also not considered a limitation or cause for bias because the investigator was not aware of the attributes of a potential molecule for treatment of muscle loss in sarcopenia.

The findings from this research are likely to be applicable to other conditions where muscle loss is prevalent. Muscle loss is important in disuse atrophy, cancer cachexia, prostate cancer subjects treated with androgen deprivation therapy, steroid-induced myopathy, muscular dystrophy, cardiac failure, obstructive pulmonary disease, and human immunodeficiency virus/acquired immunodeficiency syndrome. In cachexia, for instance, loss of muscle is associated with reduced survival, impaired functional status, and poor health-related quality of life.[30] As with sarcopenia, impact of muscle loss on subject-defined endpoints is not well investigated. It is hoped that this research can form a basis for measuring PROs in these areas to more fully characterize the burden of muscle loss.

CONCLUSION

The ARMLQ is a well-developed measure that adheres to principles of good qualitative survey research design and instrument development and current regulatory guidance on PROs. It is anticipated that the measure can be used in clinical trials and potentially in routine clinical practice. There is also a need for measurements of reduced muscle strength sarcopenia in nursing home residents,[31] and the ARMLQ could be used in this setting as well. Additionally, recent nutritional recommendations for the management of sarcopenia[32] could be assessed using the ARMLQ, among other measures. Subsequent psychometric testing is planned, including validation of the ARMLQ compared with performance-based measures.

ACKNOWLEDGMENTS

The authors acknowledge Denise Globe and Joel Kallich of Amgen; Jay Magaziner of the University of Maryland School of Medicine; and Jonathan Stokes, Benjamin Banderas, and Andrea Zeytoonjian of Mapi Values.

REFERENCES

1. Doherty T. Invited review: aging and sarcopenia. J Appl Physiol 2003;95:1717–1727.
2. Janssen I, Heymsfield SB, Ross R. Low relative muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc 2002;50:889–896.
3. Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of sarcopenia among elderly in New Mexico. Am J Epidemiol 1998;147:755–763.
4. Cawthon PM, Fox KM, Gandra SR, et al. Do muscle mass, muscle density, strength, and physical function similarly influence risk of hospitalization in older adults? J Am Geriatr Soc 2009;57:1411–1419.
5. Janssen I, Shepard DS, Katzmarzyk PT, et al. The healthcare costs of sarcopenia in the United States. J Am Geriatr Soc 2004;52:80–85.
6. Marquis P, Arnould B, Acquardo C, et al. Patient-reported outcomes and health-related quality of life in effectiveness studies: pros and cons. Drug Dev Res 2006;67:198–201.
7. Leidy NI, Revicki DA, Genesté B. Recommendations for evaluating the validity of quality of life claims for labeling and promotion. Value Health 1999;2:113–127.
8. Revicki DA, Osoba D, Fairclough D, et al. Recommendations on health-related quality of life research to support labeling and promotional claims in the United States. Qual Life Res 2000;9:887–900.
9. Willke RJ, Burke LB, Erickson P. Measuring treatment impact: A review of patient-reported outcomes and other efficacy endpoints in approved product labels. Control Clin Trials 2004;25:535–552.
10. Wolinksy FD, Miller DK, Andresen EM, et al. Further evidence for the importance of subclinical functional limitation and subclinical disability assessment in gerontology and geriatrics. J Gerontol B Pyschol Sci Soc Sci 2005;60:S146–S151.
11. World Health Organization. World Health Organization Disability Assessment Schedule II (WHO DAS II). Available at: http://www.who.int/icidh/whodas/index.html. Accessed April 1, 2010.
12. Weiner MF, Martin-Cook K, Svetlik DA, et al. The quality of life in late-stage dementia (QUALID) scale. J Am Med Dir Assoc 2000;1:114–116.
13. Yesavage JA. Geriatric Depression Scale. Psychopharmacol Bull 1988;24:709–711.
14. Barry MJ, Fowler FJ, O'Leary MP, et al. The American Urological Association Symptom Index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol 1992;148:1549–1557. discussion 1564.
15. Lawton MP, Brody EM. Assessment of older people: Self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179–186.
16. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85–M94.
17. Charmaz K. Grounded theory. In: Smith JA, Harre R, Van Langenhove L, editors. Rethinking Methods in Psychology. London: Sage; 1995. p. 27–49.
18. Glaser BG, Strauss A. The Discovery of Grounded Theory: Strategies for Qualitative Research. Chicago: Aldine; 1967.
19. Strauss A, Corbin J. Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory. London: Sage; 1998.
20. Muhr T, Friese S. User's Manual for Atlas.ti 5.0, 2nd ed. Berlin: 2004.
21. Guest G, Bunce A, Johnson L. How many interviews are enough? An experiment with data saturation and variability. Field Methods 2006;18:59–82.
22. Patrick DL, Burke LB, Powers JH, et al. Patient-reported outcomes to support medical product labeling claims: FDA perspective. Value Health 2007;10:S125–S137.
23. US Department of Health and Human Services. Draft guidance for industry patient-reported outcome measures: Use in medical product development to support labeling claims. Available at: http://www.fda.gov/ohrms/DOCKETS/98fr/06d-0044-gdl0001.pdf. Accessed April 13, 2010.
24. Beck AT, Steer RA, Brown GK. BDI®-II Manual. San Antonio, TX: The Psychological Corporation; 1996.
25. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361–370.
26. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale—a review of validation data and clinical results. J Psychosom Res 1997;42:17–41.
27. Presser S, Rothgeb J, Coopler M, et al. Methods for Testing and Evaluating Survey Questionnaires. Hoboken (NJ): John Wiley & Sons, Inc; 2004.
28. Mays M, Pope C. Rigor and qualitative research. Br Med J 1995;311:109–112.

29. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992; 30:473–483.
30. Morley JE, Thomas DR, Wilson MM. Cachexia: Pathophysiology and clinical relevance. Am J Clin Nutr 2006;83:735–743.
31. Bauer JM, Kaiser MJ, Sieber CC. Sarcopenia in nursing home residents. J Am Med Dir Assoc 2008;9:545–551.
32. Morley JE, Argiles JM, Evans WJ, et al. Nutritional recommendations for the management of sarcopenia. J Am Med Dir Assoc 2010;11: 391–396.

APPENDIX 1

Age-Related Muscle Loss Questionnaire

Interviewer-Administered Version

INSTRUCTIONS

This questionnaire includes 14 questions about your health. In particular, it asks how the loss of your muscle strength has affected how you do things that require physical effort.

Note to Interviewer: Please read each device on the list below one at a time and ask the subject to answer "yes" or "no" for each device. If the subject answers "yes" to using a particular device, please check (☒) the corresponding box. If the subject answers "no" to using a particular device, please skip the question.

Do you currently use:

☐1	Devices for dressing, such as a button hook, zipper pull, etc.
☐2	Special or built-up chair
☐3	Built-up or special utensils
☐4	Cane
☐5	Walker
☐6	Crutches
☐7	Wheelchair
☐8	Other (please specify) ———

Next, I will ask you to rate 14 questions about your strength on a scale of 0 to 10. Zero means you have no difficulty and 10 means you have extreme difficulty. For example, if you had a little difficulty doing an activity, you would choose "3" on the scale and if you had a lot of difficulty you would choose "8" on the scale.

If you routinely use devices or aids, please consider your use of those aids when answering the questions; however, please do *not* consider help from anyone else when answering the questions. There are no right or wrong answers to any of the questions.

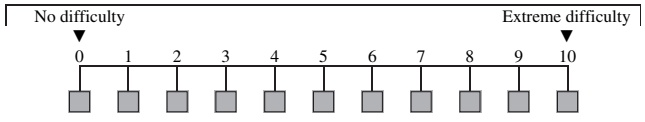
Please consider the ***loss of your muscle strength*** when answering the questions.

Think about the most recent day in the past 7 days when you were up and about. What day was that? _____

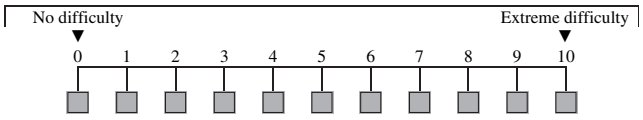
Note to interviewer: If the subject states that he/she did not do the activity included in the question within the past 7 days, then the question should be left blank.

Please choose the number that best describes how you have felt on that day:

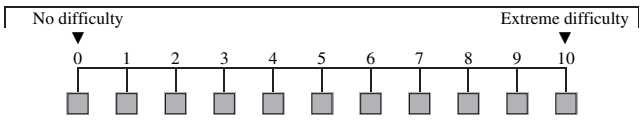
1. How much difficulty did you have **walking at your usual speed**?



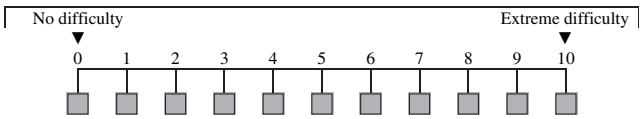
2. How much difficulty did you have **walking a distance, for example, walking 100 yards or the length of a football field**?



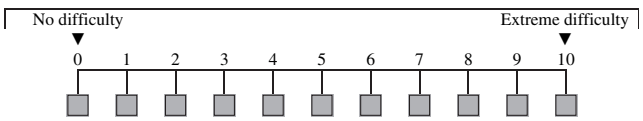
3. How much difficulty did you have **walking in a straight line, for example, down a hallway**?



4. How much difficulty did you have **walking without stumbling**?



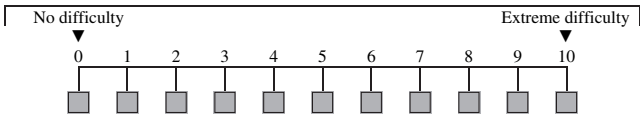
5. How much difficulty did you have **going up and down stairs (a flight of stairs or 12 steps)**?



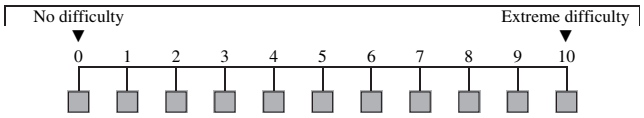
Please consider the ***loss of your muscle strength*** when answering the questions.

If you routinely use devices or aids, please consider your use of those aids when answering the questions; however, please do *not* consider help from anyone else when answering the questions.

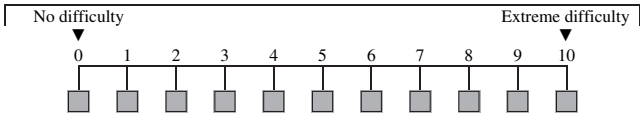
6. How much difficulty did you have **standing for 15 minutes without a break**?



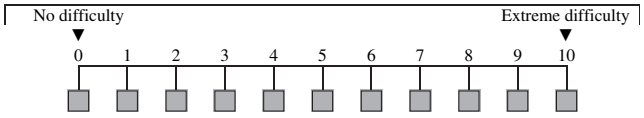
7. How much difficulty did you have **getting up from a sitting position**?



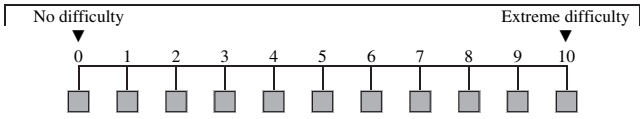
8. How much difficulty did you have **bending to pick up an object off the floor from a standing position**?



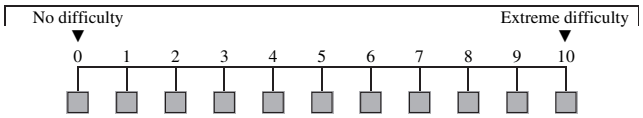
9. How much difficulty did you have **opening jars that have never been opened**?



10. How much difficulty did you have ***lifting* objects that weigh about 10 pounds, for example, a gallon of milk**?



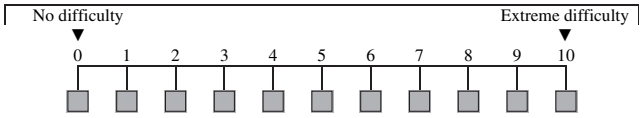
11. How much difficulty did you have ***carrying* objects that weigh about 10 pounds, for example, a gallon of milk**?



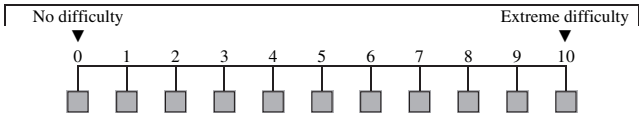
Please consider the ***loss of your muscle strength*** when answering the questions.

If you routinely use devices or aids, please consider your use of those aids when answering the questions; however, please do *not* consider help from anyone else when answering the questions.

12. How much difficulty did you have **doing your usual household activities without resting**?



13. How much difficulty did you have **completing a physical activity without resting**?



14. How much difficulty did you have **doing social activities outside your home, such as going out to eat with others**?