Adiposity, Muscle Mass, and Muscle Strength in Relation to Functional Decline in Older Persons

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Aging is associated with changes in body composition and muscle strength. This review aimed to determine the relation between different body composition measures and muscle strength measures and functional decline in older men and women. By use of relevant databases (PubMed, Embase, and CINAHL) and keywords in a search from 1976 to April 2012, 50 articles were reviewed that met the inclusion criteria (written in English, a prospective, longitudinal design, involving older persons aged 65 years or more, and at least one of the measures that follow: body mass index (BMI), waist circumference, waist/hip ratio, midarm circumference, fat mass, muscle fat infiltration, muscle mass, or strength as independent variables and a measure of functional decline as outcome measure). Meta-analyses were performed and revealed that BMI ≥30 and low muscle strength were associated with functional decline (pooled odds ratio (OR) = 1.60, 95% confidence interval (CI): 1.43, 1.80, for BMI ≥30 and OR = 1.86, 95% CI: 1.32, 2.64, for muscle strength). Low muscle mass was not significantly associated with functional decline (pooled OR = 1.19, 95% CI: 0.98, 1.45). Future intervention research should focus on positive changes in body composition to prevent onset or worsening of functional decline in old age.

adiposity; aging; body composition; muscles; muscle strength; obesity

Abbreviations: ADL, activities of daily living; BIA, bioelectrical impedance analysis; BMI, body mass index; CI, confidence interval; DXA, dual-energy x-ray absorptiometry; Health ABC, Health, Aging, and Body Composition; IADL, instrumental activities of daily living; MeSH, medical subject heading; OR, odds ratio.

INTRODUCTION

The population of older persons is rapidly growing in size and proportion. The number of people aged 65 years or more will dramatically increase in the years to come, from 690 million in 2010 to nearly 1.5 billion by 2050, with the proportion of older people aged 65 years or more almost doubling, from 9% to 16% (1). As aging is strongly associated with decline in physical functioning and subsequent decline in quality of life (2), the health-care costs for society are likely to rise in the upcoming years.

Aging is strongly associated with changes in body composition. The percentage of body fat increases until 80 years and then seems to reach a plateau. The increase in percentage body fat is due to an increase in body fat as well as a decrease in lean mass (3). Even in weight-stable persons, an increase in fat mass and body fat percentage can be observed because of the loss of skeletal muscle mass (4, 5). Furthermore, the distribution of body fat changes with age, including a reduction in appendicular fat and an increase in trunk fat (6–9). Also, an increasing fat infiltration into nonfat tissues can be observed with aging (7, 8). Parallel to the loss of muscle mass, there is a loss of muscle strength with aging as well (8). Moreover, muscle strength declines at a much greater rate than muscle mass (10).

Results of several studies suggest that age-related changes in body composition and muscle strength are associated with functional decline. In this systematic review and meta-analysis, we aim to describe current evidence of the associations of adiposity, muscle mass, and muscle strength with functional decline in older persons by using results of high-quality longitudinal studies. A complete understanding...
of the association of adiposity, muscle mass, and muscle strength with functional decline is needed to identify possible interventions to prevent disability or increase functioning in old age.

MATERIALS AND METHODS

Data sources

Potentially relevant articles were obtained by performing a search in 3 databases (PubMed; National Center for Biotechnology Information, US National Library of Medicine, Bethesda, Maryland), Embase (Elsevier, Amsterdam, the Netherlands), and Cumulative Index to Nursing and Allied Health Literature (CINAHL; EBSCO Publishing, Ipswich, Massachusetts) from 1976 to April 2012. The study population was specified by the Medical Subject Heading (MeSH) term “aged” and “aged, 80 and over.” Adiposity, muscle mass, and strength indicators were searched by including terms such as “skeletal muscle,” “fat mass,” “weight,” “body mass index,” “waist circumference,” “adipose tissue,” “obesity,” “sarcopenia,” “muscle strength,” “dynapenia,” and related MeSH terms combined with the conjunction “or” (“OR”). Physical functioning was specified by terms such as “activities of daily living,” “disability evaluation,” “mobility limitation,” “physical impairment,” “physical performance,” “gait,” “balance,” and related MeSH terms combined with “OR.” To specify the study design, we combined terms such as “cohort study,” “longitudinal” and “prospective studies,” and related MeSH terms with “OR.” The searches for study population, body composition or strength, physical functioning, and study design were combined with “AND,” resulting in a final search. Articles were eligible for inclusion if they met the following criteria: 1) written in English; 2) a prospective, longitudinal design; 3) involving older persons (mean age at 65 years or more); 4) at least one adiposity, muscle mass, or strength measure as independent variable; and 5) a measure of functional decline (such as incident disability, incident mobility limitations, or change in mobility performance) as outcome measure. Studies that focused only on persons with specific diseases such as arthritis, stroke, or diabetes were excluded from the review. All retrieved articles were first reviewed on the basis of the title. Next, potentially relevant articles were reviewed on the basis of the abstract by 2 independent reviewers (L. A. S. and A. K.). In the third phase of the selection process, full-text articles were retrieved and reviewed. Of all included articles, the reference lists were checked for any suitable articles that were not initially found in the literature search, and a hand search was performed. Relevant studies that met all inclusion criteria were also included in the review.

Quality assessment

The selected articles were evaluated on their methodological quality according to a checklist based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (11) in combination with a previously published quality checklist for observational studies (12). Studies were scored on the basis of 9 quality criteria on a binary scale, including clearly described characteristics of the study population, assessment of determinants and outcomes, confounding, and if there were any important flaws. Examples of important flaws are incorrect statistical analyses and lack of description of determinants or outcomes. The scores of each item were summed, and quality was considered poor (scores 0–4), moderate (scores 5–6), or good (scores 7–9). Articles with poor quality were excluded from the review (refer to the Web Appendix available at http://aje.oxfordjournals.org/).

Statistical methods

A meta-analysis was carried out for all studies that presented at least one relative risk for one category of a determinant compared with a reference group (e.g., obesity compared with normal weight) and when outcome data were presented as odds ratios, hazard ratios, or regression coefficients. The results of the models with the largest number of potential confounders are used in the meta-analyses. At least 5 studies examining a certain determinant with functional decline were needed to perform a meta-analysis. Some studies stratified results for age, sex, or body mass index (BMI) levels. These results were put into the meta-analyses separately. The results of the studies were pooled by using the random effects model that resulted in forest plots. We evaluated the heterogeneity by the $I^2$ statistic, which expresses the percentage of variation attributable to between-study heterogeneity. Roughly, an $I^2$ of 50% or higher may represent substantial heterogeneity. Meta-analyses were performed by using Review Manager 5.1 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark; http://www.cc-ims.net/RevMan, last accessed on November 28, 2012). All $P$ values were 2 tailed ($\alpha = 0.05$). Some studies could not be included in the meta-analysis because of differences in statistical methods or because of missing data. The results of these articles are described in the text and are taken into account when formulating conclusions about the strength of the associations with functional decline. Sensitivity analyses were performed by excluding papers that reported results from the same cohort, leaving one paper (usually the latest paper with the longest follow-up data presented) per cohort in the meta-analysis.

RESULTS

Literature search

Figure 1 demonstrates the flow of the literature search performed for this review. The literature search identified 1,857 articles. By screening of the title, we excluded 1,680 articles. Of the remaining 178 articles, 114 articles were excluded on the basis of review of the abstract. The main reasons for exclusion were the design of the study (not prospective and longitudinal), lack of a measure of functional decline, or lack of measures of adiposity, muscle mass, or muscle strength. After reading the full texts of the 64 remaining articles, we excluded 22 articles on the basis of the exclusion criteria, leaving 42 articles suitable for inclusion in this review. After a screening of the reference lists
of the included articles and a hand search of the literature, another 10 articles could be identified, resulting in 52 articles of which the quality could be assessed. One study did not describe the measurement of obesity (13), which was recognized as an important flaw (item 10 of the quality assessment form), and was excluded from this review. Another study (14) was graded “poor” and therefore excluded. All other articles scored between 6 (moderate quality) and 9 (good quality). Most articles scored poorly on the description of the study population and persons lost to follow-up (Web Table 1). Finally, 50 articles were eligible to be included in this review.

Description of included studies

Table 1 presents the characteristics of the included articles. The length of follow-up showed a high variation and ranged from 1 to 13 years. The population sizes of the studies varied between 110 and 20,975. Most studies were conducted in the United States (n = 34; 67%). Eight studies (15–22) included persons who were younger than 65 years, but all were aged at least 55 years.

Different measures of functional decline were used across the studies. Many studies measured aspects of activities of daily living (ADL) disability, such as difficulty or inability doing activities of daily life, which are all self-reported measures. Other studies measured aspects of functional limitation, such as (self-reported or performance based) walking difficulty or difficulty climbing stairs. Also, several studies used both types of functional decline. Few studies examined worsening of the outcome.

Many studies investigated BMI (date range 1994–2011) as a determinant of physical decline (n = 26), often categorized into groups of normal weight, overweight, and obese.
<table>
<thead>
<tr>
<th>First Author, Year (Reference No.)</th>
<th>Follow-up</th>
<th>Country</th>
<th>Study*</th>
<th>Sample Size</th>
<th>Mean Age, Years</th>
<th>Male, %</th>
<th>Setting</th>
<th>Outcome Measure</th>
<th>Body Composition Measure</th>
<th>Strength Measure</th>
<th>Quality Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al Snih, 2004 (23)</td>
<td>7 years</td>
<td>United States</td>
<td>EPESE</td>
<td>2,493</td>
<td>72</td>
<td>42.1</td>
<td>Population based, Mexican Americans</td>
<td>Self-reported ADL disability</td>
<td>BMI</td>
<td>Handgrip strength</td>
<td>8</td>
</tr>
<tr>
<td>Al Snih, 2005 (50)</td>
<td>5 years</td>
<td>United States</td>
<td>EPESE</td>
<td>1,737</td>
<td>74</td>
<td>42.2</td>
<td>Population based, Mexican Americans</td>
<td>Self-reported ADL limitation, objectively measured walking limitation</td>
<td>BMI</td>
<td>Handgrip strength</td>
<td>8</td>
</tr>
<tr>
<td>Bannerman, 2002 (24)</td>
<td>2 years</td>
<td>Australia</td>
<td>ALSA</td>
<td>1,272</td>
<td>78</td>
<td>54.0</td>
<td>Population based</td>
<td>Self-reported limitation of physical function and mobility limitation</td>
<td>BMI, WC, WHR</td>
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<td>6</td>
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<td>Baumgartner, 2004 (49)</td>
<td>8 years</td>
<td>United States</td>
<td>NMAPS</td>
<td>451</td>
<td>73</td>
<td>44.0</td>
<td>Population based</td>
<td>Self-reported IADL disability</td>
<td>Lean body mass, body fat (DXA)</td>
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<tr>
<td>Broadwin, 2001 (20)</td>
<td>4 years</td>
<td>United States</td>
<td>Rancho Bernardo Study</td>
<td>1,051</td>
<td>70</td>
<td>39.7</td>
<td>Population based</td>
<td>Self-reported functional disability and lower body disability</td>
<td>Fat mass and fat-free mass (BIA)</td>
<td></td>
<td>7</td>
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<tr>
<td>Cawthon, 2011 (51)</td>
<td>6 years</td>
<td>United States</td>
<td>Health ABC</td>
<td>2,484</td>
<td>74</td>
<td>49.0</td>
<td>Population based, 2 clinical centers</td>
<td>Self-reported ADL disability, needing equipment to ambulate, and mobility disability</td>
<td>Weight, leg lean mass, percent body fat (DXA), thigh muscle density (CT)</td>
<td>Knee extensor strength</td>
<td>6</td>
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<tr>
<td>Delmonico, 2007 (46)</td>
<td>5 years</td>
<td>United States</td>
<td>Health ABC</td>
<td>2,976</td>
<td>74</td>
<td>48.0</td>
<td>Population based, 2 clinical centers</td>
<td>Self-reported lower extremity limitation, lower extremity performance</td>
<td>Appendicular lean mass (DXA), Sarcopenia defined as appendicular lean mass/height² in the lowest 20% and appendicular lean mass adjusting for fat mass and height (residuals) using 20th percentile of the distribution</td>
<td></td>
<td>7</td>
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<td>Fantin, 2007 (25)</td>
<td>5.5 years</td>
<td>Italy</td>
<td></td>
<td>159</td>
<td>71</td>
<td>39.0</td>
<td>Patients randomly selected from 11 general practitioners, well-functioning and healthy at baseline</td>
<td>Self-reported disability</td>
<td>Height, weight, BMI, WC, total body fat, appendicular, leg, and total fat-free mass (DXA)</td>
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<td>Ferrucci, 2002 (52)</td>
<td>3 years</td>
<td>United States</td>
<td>WHAS</td>
<td>620</td>
<td>78</td>
<td>0</td>
<td>Cohort study on women with moderate to severe disability</td>
<td>Self-reported mobility disability, ADL disability, Severe walking limitation (4-m walking speed &lt; 0.4 m/second)</td>
<td>Maximum isometric strength of the knee extensor muscles</td>
<td></td>
<td>7</td>
</tr>
</tbody>
</table>

Table continues
<table>
<thead>
<tr>
<th>First Author, Year (Reference No.)</th>
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<th>Male, %</th>
<th>Setting</th>
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<th>Body Composition Measure</th>
<th>Strength Measure</th>
<th>Quality Score</th>
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<td>Forrest, 2006 (44)</td>
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<td>United States</td>
<td>SOF</td>
<td>5,178</td>
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<td>Walking speed, time to complete 5 chair stands</td>
<td>Height, weight, WHR</td>
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<td>Giampaoli, 1999 (53)</td>
<td>4 years</td>
<td>Finland, Italy, Netherlands</td>
<td>FINE</td>
<td>140</td>
<td>76</td>
<td>100</td>
<td>Population-based survey</td>
<td>Self-reported disability and mobility</td>
<td>Handgrip strength</td>
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<td>Gill, 2009 (54)</td>
<td>57 months</td>
<td>United States</td>
<td>Precipitating Events Project</td>
<td>722</td>
<td>78</td>
<td>34.8</td>
<td>Population based, nondisabled at baseline</td>
<td>Self-reported disability</td>
<td>Grip strength</td>
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<tr>
<td>Guallar-Castillon, 2007 (15)</td>
<td>2 years</td>
<td>Spain</td>
<td>InCHIANTI</td>
<td>934</td>
<td>74</td>
<td>44.9</td>
<td>Population based</td>
<td>Gait speed and self-reported mobility disability</td>
<td>BMI, WC</td>
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<td>Hicks, 2012 (55)</td>
<td>3 years</td>
<td>Italy</td>
<td>InCHIANTI</td>
<td>934</td>
<td>74</td>
<td>44.9</td>
<td>Population based</td>
<td>Self-reported disability</td>
<td>Knee extensor strength, grip strength</td>
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<td>Himes, 2012 (26)</td>
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<td>United States</td>
<td>HRS</td>
<td>9,589</td>
<td>74</td>
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<td>Self-reported ADL disability</td>
<td>BMI</td>
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<td>Ho, 1997 (27)</td>
<td>1.5 years</td>
<td>Hong Kong</td>
<td></td>
<td>1,483</td>
<td>?</td>
<td>50.4</td>
<td>70 year olds, oversampling of men and older ages</td>
<td>Self-reported mobility decline</td>
<td>BMI, WHR</td>
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<td>Hughes, 1997 (22)</td>
<td>2 years</td>
<td>United States</td>
<td></td>
<td>485</td>
<td>78</td>
<td>27.0</td>
<td>Longitudinal study among community-dwelling, chronically homebound, and residents of a continuing care retirement community</td>
<td>Objective measure of manual performance</td>
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<td>Ishizaki, 2000 (28)</td>
<td>3 years</td>
<td>Japan</td>
<td>LISA</td>
<td>583</td>
<td>71</td>
<td>44.1</td>
<td>Population based, ambulatory persons</td>
<td>Self-reported BADL and ADL</td>
<td>BMI</td>
<td>Handgrip strength</td>
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<td>Izawa, 2010 (29)</td>
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<td>Japan</td>
<td>LISA</td>
<td>543</td>
<td>80</td>
<td>38.4</td>
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<td>Self-reported ADL disability</td>
<td>BMI, midarm circumference</td>
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<td>Janssen, 2006 (47)</td>
<td>8 years</td>
<td>United States</td>
<td>CHS</td>
<td>3,694</td>
<td>?</td>
<td>46.8</td>
<td>Population based, 15.7% black</td>
<td>Self-reported disability (IADLs)</td>
<td>Whole-body muscle mass (BIA) normalized by height</td>
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<td>Jenkins, 2004 (43)</td>
<td>3 years</td>
<td>United States</td>
<td>AHEAD</td>
<td>2,460–3,373</td>
<td>78</td>
<td>37.8</td>
<td>Population-based survey</td>
<td>Self-reported impairment with upper body mobility, lower body mobility, ADL</td>
<td>BMI</td>
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Table continues
<table>
<thead>
<tr>
<th>First Author, Year (Reference No.)</th>
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<th>Country</th>
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<th>Mean Age, Years</th>
<th>Male, %</th>
<th>Setting</th>
<th>Outcome Measure</th>
<th>Body Composition Measure</th>
<th>Strength Measure</th>
<th>Quality Score</th>
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<tbody>
<tr>
<td>Jensen, 2002 (30)</td>
<td>3–4 years</td>
<td>United States</td>
<td></td>
<td>2,634</td>
<td>71</td>
<td>46.2</td>
<td>Medicare managed-risk program participants</td>
<td>Self-reported functional decline (ADLs and IADLs)</td>
<td>BMI</td>
<td>8</td>
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<td>Koster, 2008 (31)</td>
<td>6.5 years</td>
<td>United States</td>
<td>Health ABC</td>
<td>2,982</td>
<td>74</td>
<td>48.0</td>
<td>Population-based, 2 clinical centers</td>
<td>Self-reported mobility limitation</td>
<td>BMI, total percent fat (DXA), WC</td>
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<td>Koster, 2007 (32)</td>
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<td>United States</td>
<td>Health ABC</td>
<td>3,022</td>
<td>74</td>
<td>48.1</td>
<td>Population based, 2 clinical centers</td>
<td>Self-reported early and late onset of mobility limitation</td>
<td>BMI</td>
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<td>Lang, 2008 (33)</td>
<td>5 years</td>
<td>United Kingdom</td>
<td>ELSA</td>
<td>3,793</td>
<td>73</td>
<td>44.9</td>
<td>Population based</td>
<td>Self-reported physical function, performance tests (balance, gait, chair stands)</td>
<td>BMI</td>
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<td>Launer, 1994 (34)</td>
<td>4 years</td>
<td>United States</td>
<td>NHANES</td>
<td>426</td>
<td>66</td>
<td>0</td>
<td>Population-based survey</td>
<td>Self-reported mobility disability</td>
<td>BMI</td>
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<td>Lee, 2005 (35)</td>
<td>30 months</td>
<td>United States</td>
<td>Health ABC</td>
<td>2,932</td>
<td>74</td>
<td>46.7</td>
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<td>Self-reported mobility limitation</td>
<td>BMI</td>
<td>7</td>
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<td>Rantanen, 2001 (57)</td>
<td>3 years</td>
<td>United States</td>
<td>WHAS</td>
<td>758</td>
<td>78</td>
<td>0</td>
<td>Cohort study on women with moderate to severe disability</td>
<td>Walking speed</td>
<td>Knee extensor strength</td>
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<td>Riddle, 2008 (58)</td>
<td>1 year</td>
<td>United States</td>
<td>WHAS</td>
<td>474</td>
<td>78</td>
<td>0</td>
<td>Cohort study on women with moderate to severe disability</td>
<td>Objective measure of gait speed and self-reported walking difficulty</td>
<td>Low grip strength (&lt;11 kg)</td>
<td>6</td>
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<td>Sakari, 2010 (59)</td>
<td>5 years</td>
<td>Finland</td>
<td>Evergreen Project</td>
<td>184</td>
<td>75</td>
<td>34.2</td>
<td>Population based</td>
<td>Objective measures of mobility performance</td>
<td>Knee extensor strength</td>
<td>7</td>
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Table 1. Continued

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<tr>
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<th>Male, %</th>
<th>Setting</th>
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<th>Body Composition Measure</th>
<th>Strength Measure</th>
<th>Quality Score</th>
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<tr>
<td>Seeman, 1994 (39)</td>
<td>3 years</td>
<td>United States</td>
<td>MacArthur Research Network on Successful Aging Community Study</td>
<td>843</td>
<td>74</td>
<td>44.5</td>
<td>Population based</td>
<td>Objective measures of performance</td>
<td>BMI</td>
<td>8</td>
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<tr>
<td>Sharkey, 2006 (18)</td>
<td>1 year</td>
<td>United States</td>
<td>NAFS</td>
<td>282</td>
<td>?</td>
<td>19.2</td>
<td>Population based, home-bound persons</td>
<td>Objective measures of lower extremity performance</td>
<td>BMI</td>
<td>8</td>
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<td>Shinkai, 2000 (60)</td>
<td>6 years</td>
<td>Japan</td>
<td>LISA</td>
<td>736</td>
<td>?</td>
<td>37.7</td>
<td>Population based, ambulatory persons</td>
<td>Self-reported ADL dependence</td>
<td>Grip strength</td>
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<td>Stenholm, 2010 (40)</td>
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<td>United States</td>
<td>Health ABC</td>
<td>2,984</td>
<td>74</td>
<td>49.0</td>
<td>Population based, 2 clinical centers</td>
<td>Self-reported mobility limitations</td>
<td>Weight, BMI, WC</td>
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<td>Stenholm, 2009 (61)</td>
<td>6 years</td>
<td>Italy</td>
<td>InCHIANTI</td>
<td>930</td>
<td>74</td>
<td>44.8</td>
<td>Population based</td>
<td>Self-reported mobility disability and walking speed</td>
<td>BMI, WC</td>
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<tr>
<td>Taekema, 2010 (62)</td>
<td>4 years</td>
<td>Netherlands</td>
<td>Leiden 85+ Study</td>
<td>555</td>
<td>85</td>
<td>35.0</td>
<td>Population based</td>
<td>Self-reported ADL limitations and walking speed</td>
<td>Handgrip strength at baseline and 4 years later</td>
<td>7</td>
<td></td>
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<tr>
<td>Tager, 2004 (21)</td>
<td>6.5 years</td>
<td>United States</td>
<td>1,655</td>
<td>69</td>
<td>42.7</td>
<td>Population based</td>
<td>Self-reported functional limitation</td>
<td>Fat mass and fat-free mass (BIA)</td>
<td>8</td>
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<tr>
<td>Tas, 2007 (17)</td>
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<td>Netherlands</td>
<td>Rotterdam Study</td>
<td>4,258</td>
<td>69</td>
<td>41.4</td>
<td>Population based</td>
<td>Self-reported disability</td>
<td>Weight, BMI</td>
<td>8</td>
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<tr>
<td>Tinetti, 1995 (63)</td>
<td>1 year</td>
<td>United States</td>
<td>927</td>
<td>80</td>
<td>27.0</td>
<td>Population based</td>
<td>Self-reported functional dependence</td>
<td>Grip strength</td>
<td>8</td>
<td></td>
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<tr>
<td>Visser, 1998 (45)</td>
<td>3 years</td>
<td>United States</td>
<td>CHS</td>
<td>3,274</td>
<td>73</td>
<td>43.6</td>
<td>Population based, 15.7% black</td>
<td>Self-reported disability</td>
<td>Fat mass, fat-free mass (BIA)</td>
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<td>United States</td>
<td>Health ABC</td>
<td>2,631</td>
<td>74</td>
<td>48.9</td>
<td>Population based, 2 clinical centers</td>
<td>Self-reported disability</td>
<td>Muscle cross-sectional area, muscle fat infiltration (CT)</td>
<td>Isokinetic knee extensor strength</td>
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<td>Walter, 2009 (19)</td>
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<td>Netherlands</td>
<td>Rotterdam Study</td>
<td>5,980</td>
<td>69</td>
<td>41.4</td>
<td>Population based</td>
<td>Self-reported incident disability</td>
<td>BMI, WC</td>
<td>8</td>
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<tr>
<td>Wee, 2011 (41)</td>
<td>2 years</td>
<td>United States</td>
<td>20,975</td>
<td>75</td>
<td>43</td>
<td>Survey among Medicare beneficiaries</td>
<td>Self-reported new (I)ADL disability or progression of (I)ADL disability</td>
<td>Self-reported weight and height, BMI</td>
<td>8</td>
<td></td>
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<tr>
<td>Wennie Huang, 2010 (64)</td>
<td>1.5 years</td>
<td>United States</td>
<td>110</td>
<td>80</td>
<td>29.1</td>
<td>Population based</td>
<td>Self-reported ADL and IADL difficulty</td>
<td>Handgrip strength</td>
<td>7</td>
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</table>
## Table 1. Body Composition Measures and Outcome Measures

<table>
<thead>
<tr>
<th>First Author</th>
<th>Year</th>
<th>Setting</th>
<th>Male, Female</th>
<th>Sample Size</th>
<th>Strength Measure</th>
<th>Country</th>
<th>Study</th>
<th>Mean Age, Years</th>
<th>Mean % Body Fat</th>
<th>Mean % Fat Mass</th>
<th>BMI</th>
<th>WC, Hip Circumference</th>
<th>WHR</th>
<th>Quality Score</th>
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<tr>
<td>Zoico</td>
<td>2007</td>
<td>Italy</td>
<td>145</td>
<td>71.4</td>
<td>Self-reported ADL disability, lower body performance and healthy at baseline</td>
<td></td>
<td></td>
<td>2 years</td>
<td>41.4</td>
<td>41.4</td>
<td></td>
<td></td>
<td></td>
<td>6</td>
</tr>
</tbody>
</table>

### Body mass index in association with functional decline

There were 26 studies (15–19, 23–43) that reported associations between BMI and functional decline in older persons. One study also examined worsening of ADL limitations (41).

In the meta-analysis, the results of the associations between obesity (BMI ≥30) and functional decline are used (17–19, 23, 24, 26, 27, 30–34, 40, 41, 43). The meta-analysis supported an overall association between obesity (BMI ≥30) and functional decline (pooled OR = 1.60, 95% confidence interval (CI): 1.43, 1.80; $I^2 = 67\%$) (Figure 2) compared with normal weight. Some studies also reported significant associations between severe obesity (BMI >35) and functional decline (18, 19, 26, 33). Because Ho et al. (27) did not use the BMI category of 30 or higher, the category of 25 and higher was included in the meta-analysis. In this study, it was also shown that a low BMI of <20 was associated with a significantly increased risk of mobility decline (OR = 1.7, 95% CI: 1.1, 2.6) compared with BMI between 20 and 24. Sharkey et al. (18) found no significant association between obesity and 1-year decline in physical performance but did find a strong association for severe obesity (BMI ≥35) in this study (OR = 7.00, 95% CI: 2.55, 19.23). The results may have been affected by the short follow-up time and the small sample size. Jensen and Friedmann (30) also reported no associations for obesity but found a strong association between severe obesity and functional decline in men (OR = 3.32, 95% CI: 1.29, 8.46) and in women (OR = 2.61, 95% CI: 1.39, 4.95).

Several studies were not included in the meta-analyses because of differences in the reporting of results (19, 38, 39) or missing data (36, 37). Some studies (29, 36, 38) reported no association between BMI levels and functional decline, while other studies (37, 39), found a positive effect of obesity with functional decline.

There were 2 studies that used data from the Health, Aging, and Body Composition (Health ABC) Study (31, 32) and 2 studies that used data from the Rotterdam Study (17, 19). A sensitivity analysis, excluding the studies by Koster et al. (32) and Tas et al. (17), revealed a small decline in the pooled odds ratio (OR = 1.55, 95% CI: 1.37, 1.75).
In conclusion, there is strong evidence for an association between obesity, as indicated by BMI ≥ 30, and functional decline in older men and women. Furthermore, there seems to be an association between underweight and functional decline as well, although more prospective research in this area is necessary.

Waist circumference in association with functional decline

There were 4 studies that reported associations between a large waist circumference and functional decline, which all showed statistically significant results. In a Spanish study (15), higher waist circumference was associated with disability after 2 years of follow up. Men in the highest waist circumference quintile (≥111.0 cm) had 4.84 (95% CI: 1.81, 12.93) times more risk to develop agility disability (self-reported difficulty bending and kneeling) compared with men in the lowest waist circumference quintile (<93.8 cm), but there were no associations between waist circumference and mobility disability, instrumental activities of daily living (IADL), bathing, or dressing. Similar results were found for women. Bannerman et al. (24) found that persons with a waist circumference greater than 102 cm (men) or greater than 88 cm (women) had an increased risk of developing physical function limitations (OR = 1.86, 95% CI: 1.30, 2.65) and mobility limitation (OR = 1.43, 95% CI: 0.99, 2.08) after 2 years. Koster et al. (31) found similar results using data of the Health ABC Study with 6.5 years of follow-up (white men: OR = 1.36, 95% CI: 1.09, 1.69; black men: OR = 1.43, 95% CI: 1.11, 1.83; white women: OR = 1.53, 95% CI: 1.17, 1.99; black women: OR = 1.66, 95% CI: 1.26, 2.20). Walter et al. (19) found that a large waist circumference (≥102 cm for men and ≥88 cm for women) was associated with disability (hazard ratio = 1.5, 95% CI: 1.2, 1.9, for men and hazard ratio = 1.8, 95% CI: 1.5, 2.3, for women) after 6 years of follow-up. Meta-analysis was not performed for these studies on functional decline.

Waist/hip ratio in association with functional decline

There were 3 studies that examined the association between waist/hip ratio and functional decline. In a study among older Chinese persons from Hong Kong (27), waist/hip ratio was not significantly related to mobility decline after 1.5 years of follow-up. A waist/hip ratio between 0.85 and 0.94 corresponded with an odds ratio of 1.2 (95% CI: 0.8, 1.9) compared with a waist/hip ratio of <0.85. Persons with a waist/hip ratio of 0.95 or greater (this cutoff was used for men as well as women) had an odds ratio of 1.4 (95% CI: 0.9, 2.3) of experiencing mobility decline when adjustment was made for age and sex. Bannerman et al. (24) showed that a waist/hip ratio of 1.0 or greater in men and 0.85 or greater in women was not associated with mobility limitation after 2 years (OR = 0.77, 95% CI: 0.49, 0.97).
2.21) nor with limitation in physical function (OR = 1.47, 95% CI: 0.93, 2.34). In a study with 10 years’ follow-up (44), the waist/hip ratio was associated with decline in performance as tested by the ability to complete 5 chair stands (age-adjusted OR = 1.33, 95% CI: 1.26, 1.42), but this association was no longer significant after additional adjustment for other variables.

Midarm circumference in association with functional decline

A study among older Japanese persons (29) showed that midarm circumference was not associated with loss of ADL function after 2 years (OR = 0.96, 95% CI: 0.90, 1.04). However, a decline in midarm circumference (≥1.6 cm) was associated with loss of ADL function (OR = 3.18, 95% CI: 1.40, 7.20).

Fat mass in association with functional decline

Few studies (20, 31, 45) examined the association between fat mass and functional decline, and all found positive associations. Using data from the Cardiovascular Health Study, Visser et al. (45) found that men and women in the highest quintile of fat mass (>37.5 kg for men and 41.4 kg for women; measured by BIA) were at increased risk of disability after 3 years (OR = 1.72, 95% CI: 1.03, 2.85, and OR = 2.83, 95% CI: 1.80, 4.46, respectively). Broadwin et al. (20) showed that women in the highest quintile of fat mass (33.1%–55.0%; measured by BIA) were more likely to develop overall and lower body functional disability compared with women in the lowest quintile (12.1%–24.7%; OR = 3.8, 95% CI: 1.5, 9.8, and OR = 3.9, 95% CI: 1.9, 8.1, respectively). Men in the highest quintile of fat mass (23.8%–46.0%) were also more likely to develop lower body functional disability (OR = 4.0, 95% CI: 1.5, 10.3) compared with men in the lowest quintile (3.7%–16.5%). Koster et al. (31) found that white men and black women and white women in the highest tertile of percent fat mass (as assessed by DXA) were at increased risk of incident mobility limitation after 6.5 years of follow-up (white men: OR = 1.46, 95% CI: 1.05, 2.04; black men: OR = 1.15, 95% CI: 0.81, 1.64; white women: OR = 1.88, 95% CI: 1.39, 2.53; black women: OR = 2.18, 95% CI: 1.63, 2.91). No meta-analysis was performed on the studies that investigated the association between fat mass and functional decline.

Muscle mass in association with functional decline

The 8 studies included in this review show inconsistent results with regard to the association between a muscle mass indicator and functional decline (25, 42, 46, (DXA); 20, 21, 45, 47 (BIA); 48 (computed tomography)). The meta-analysis included 6 studies (20, 42, 45–48) that all reported the association between low muscle mass and functional decline stratified for men and women. The pooled odds ratio was 1.19 (95% CI: 0.98, 1.45), and I² was 65% (Figure 3). The pooled odds ratio did not change when we stratified by sex (OR for men = 1.12, 95% CI: 0.92, 1.36; OR for women = 1.22, 95% CI: 0.89, 1.67) (data not shown). The Health ABC Study and Cardiovascular Health

![Figure 3. Forest plot of poor muscle mass and functional decline (date range: 1998–2007). The following definitions of low muscle mass were used: Broadwin (20) (bioelectrical impedance analysis): percent fat-free mass, <35.5 for men and <45.6 for women; Delmonico (46) (dual-energy x-ray absorptiometry): use of linear regression to model appendicular lean mass on height and fat mass (the 20th percentile of the distribution of the residuals was used as the cutoff value for sarcopenia); Janssen (47) (bioelectrical impedance analysis): skeletal muscle index (muscle mass/height²), <8.50 kg/m² for men and <5.75 kg/m² for women; Visser (48) (computed tomography): mid thigh muscle cross-sectional area, <230 cm² for white men, <245 cm² for black men, <152 cm² for white women, and <181 cm² for black women; and Zoico (42) (dual-energy x-ray absorptiometry): appendicular skeletal muscle mass/height², <7.6 kg/m² for men and <5.4 kg/m² for women. Heterogeneity: τ² = 0.10, χ² = 22.56, df = 5 (P < 0.0004); F = 78%. Test for overall effect: Z = 1.22 (P = 0.22).]
Study were represented by multiple papers (45–48). The sensitivity analysis, excluding one Health ABC paper and one Cardiovascular Health Study paper, revealed only little change in the pooled odds ratio when different combinations of papers were excluded, except for the exclusion of the papers by Visser et al. (45, 48), which resulted in an odds ratio of 1.28 (95% CI: 1.03, 1.60). Two studies were not included in the meta-analysis. An Italian study (25) investigated worsening of disability as the study outcome and showed that simultaneous loss of appendicular fat-free mass was associated with worsening disability (OR = 2.15, 95% CI: 1.10, 4.20). Tager et al. (21) used the lean/fat ratio (total body lean and fat mass measured by BIA) and found that a 0.5-unit increase in this measure was associated with a reduced risk of self-reported functional limitation in women (OR = 0.56, 95% CI: 0.46, 0.67) and in men (OR = 0.77, 95% CI: 0.65, 0.92) during 6.5 years of follow-up.

**Sarcopenic obesity in association with functional decline**

The combination of low muscle mass with high body fatness has been termed “sarcopenic obesity.” Baumgartner et al. (49) examined the association between sarcopenic obesity and IADL disability after 7 years of follow-up. Sarcopenic obesity was defined as a combination of low appendicular skeletal muscle mass measured by DXA (relative skeletal muscle mass <2 standard deviations below the mean of a sample of healthy young adults) and obesity (percent body fat >60th percentile of the study sample). Sarcopenic obese persons (n = 26) were more than 2.5 times more likely to develop IADL disability compared with persons without sarcopenic obesity (n = 197). Sarcopenia (without obesity) and obesity (without sarcopenia) were not associated with the onset of IADL disability.

**Muscle fat infiltration in association with functional decline**

In a study of Visser et al. (48), the mean attenuation of mid thigh muscle tissue by computed tomography was used as an indicator of fat infiltration of the muscle. In both men and women, greater muscle fat infiltration was associated with an increased risk of mobility limitation after 2.5 years of follow-up (hazard ratio = 1.92, 95% CI: 1.31, 2.83, for men and hazard ratio = 1.68, 95% CI: 1.20, 2.35, for women) in the lowest quartile compared with the highest quartile. Even after adjustment for total body fat, muscle mass, and knee extensor strength, greater fat infiltration remained an independent risk factor for incident mobility limitations. To date, this is the only prospective study examining the effect of muscle fat infiltration on changes in physical functioning with aging. More longitudinal studies are needed to confirm the observed findings in this study.

**Muscle strength in association with functional decline**

Overall, 20 prospective studies conducted in older persons reported associations between measures of muscle strength and physical decline (16, 22, 23, 28, 48, 50–64). A large part of these studies (16, 22, 23, 28, 50, 52–54, 58, 60, 62–64) used hand grip strength as a measure of muscle strength, while 8 studies (48, 51, 52, 55–57, 59, 61) used knee extensor strength and 1 study used plantar flexion strength (16). The meta-analysis (7 studies of which 4 studies including grip strength (23, 54, 60, 64) and 3 studies including knee extensor strength (48, 56, 57)) revealed an overall association between low muscle strength and functional decline (pooled OR = 1.86, 95% CI: 1.32, 2.64; I² = 91%) (Figure 4). Studies examining continuous levels of muscle strength in association with functional decline found significant associations between low muscle strength and increased risk of functional decline (50, 53, 55, 59). In a study among 474 older women (58), it was found that grip strength below 11 kg was not associated with development of severe mobility difficulty (usual gait speed <0.5 m/second, any reported difficulty walking across a small room or dependence on a walking aid during a 4-m walking test) after 1 year (exact data were not reported). In 1997, Hughes et al. (22) examined objectively measured manual performance change among persons aged 60 years or more as an indicator of future independence and found that a low grip strength (<50 mm Hg), among other risk factors, was an important determinant of increased risk of a low manual performance (exact data not shown). In a sample of persons aged 85 years that were followed for 4 years (62), lower grip strength predicted an accelerated decline in ADL disability, but no predictive association was found for IADL disability or accelerated decline in walking speed. In a study among older women with a 3-year follow-up, Ferrucci et al. (52) showed that change over time in muscle strength was a significant, independent predictor of new disability with a hazard ratio of 0.97 (95% CI: 0.94, 0.99) per 1-kg increase per year for mobility disability; a hazard ratio of 0.96 (95% CI: 0.93, 0.99) for ADL disability; and a hazard ratio of 0.79 (95% CI: 0.75, 0.82) for severe limitation in walking, after adjustment for inflammation levels, age, chronic diseases, and BMI. Cawthon et al. (51) used factor analyses to identify a strength and lean body size component with strong loading by lean mass (by computed tomography), weight, and strength (knee extensor strength and grip strength). Other factors in the analyses were an adiposity component (percent body fat, total body fat, arm fat, leg fat, thigh muscle density) and a physical function component (walking speed and chair stands). The strength and lean body size component were not associated with an increased risk of major disability (hazard ratio = 0.98, 95% CI: 0.87, 1.10, for men and hazard ratio = 1.05, 95% CI: 0.94, 1.17, for women). However, there was an association between the physical function component and increased risk of major disability. Because measures of strength also weakly loaded on the physical performance component as well, it was suggested that the association between physical performance and disability may be partly due to strength, possibly as a mediator in the association. Paterson et al. (16) showed that lower plantar flexion strength, but not grip strength, was borderline significantly associated with an increased risk for future dependence (residing in a chronic care facility, nursing home, or senior home with care,
requiring equipment for ambulation or requiring home-care services more than once a week) with an odds ratio of 1.00 (95% CI: 0.97, 1.00). Overall, the above-mentioned studies demonstrate evidence of muscle strength as a predictor of future disability or mobility limitation in older persons.

**Dynapenic obesity**

Stenholm et al. (61) examined the effect of obesity (BMI ≥30) combined with low muscle strength (lowest sex-specific tertile of knee extensor strength) on decline in mobility in 930 persons within the Invecchiare in Chianti (InCHIANTI) study. After 6 years of follow-up, obese persons with low strength had significantly higher rates of new mobility disability compared with those without obesity or low muscle strength. Obese persons with low muscle strength had 17% decline in walking speed compared with 2% in those without obesity or low strength.

**DISCUSSION**

This systematic review aimed to systematically search and summarize the literature regarding measures of adiposity, muscle mass, and muscle strength in association with prospectively assessed functional decline in older men and women, taking into account the methodological quality of these studies. Most of the potentially suitable studies were of moderate to good quality and are included in this review. The meta-analyses revealed that obesity, as indicated by a high BMI of ≥30, a large waist circumference, or a relatively high percentage of body fat were all associated with functional decline. In addition, poor muscle strength in old age was associated with functional decline. The meta-analysis on low muscle mass showed no significant association with functional decline.

A large BMI and waist circumference are associated with functional decline. Waist circumference has been found to be more strongly associated with mobility disability and ADL disability than has BMI (65). This suggests a detrimental role of not only excess body fat but also fat distribution in functional change in old age. Reviews on risk factors of functional decline have been performed in the past (66–68). Stuck et al. (66) and Tas et al. (67) identified BMI, among other risk factors, as a determinant of a low functional status and disability. Vincent et al. (68) focused on obesity in association with mobility and concluded that a high BMI and a large waist circumference are good determinants of mobility decline. A limitation of that review was the inclusion of cross-sectional as well as longitudinal studies. The results of our study, focusing on longitudinal studies only, confirm and extend these results. Accurate measurements of body composition, such as fat mass, support the findings of BMI and waist circumference. Several other measures of body composition, such as waist/hip ratio and midarm circumference, were also reviewed in this article but could not be included in a meta-analysis because of the small number of studies. More research on these determinants is needed to confirm their association with functional decline.

Low muscle mass was not significantly associated with greater functional decline in the meta-analysis. Several articles that examined low lean body mass and functional decline showed that adjustment for fat mass or obesity markedly reduced the association between lean body mass and functional decline (20, 45, 47, 48). Baumgartner et al. (49) also found that sarcopenia, in the absence of obesity, was not a significant risk factor for IADL disability.
Low muscle strength (either measured as grip strength or knee extensor strength), however, was strongly associated with functional decline. One study found significant associations even after adjustment for muscle mass and fat mass (48). These data combined with other cross-sectional data (69, 70) suggest that low muscle strength is a more important risk factor of functional decline than muscle mass.

Overall, it can be concluded that obesity and low muscle strength are both associated with functional decline with aging. These factors are interrelated and need to be taken into account when examining associations of a specific measure with functional decline.

It is still unclear how current knowledge of muscle mass, fat mass, and strength changes with aging should be applied in relation to functional decline. Several studies included in this review attempted to find a working definition of low muscle mass (sarcopenia) that identifies persons at risk of functional decline, taking into account other aspects of body composition such as the amount of fat mass or body size. As shown by Visser et al (48), muscle fat infiltration may be an important risk factor for functional decline. In a study by Delmonico et al. (8), it was shown that intermuscular fat increases with aging, even in weight-stable persons and those who lose body weight. It is unclear whether intermuscular fat is simply a marker of metabolic dysfunction of skeletal muscle or whether it plays a more central role in sarcopenia. Once consensus on a definition of sarcopenia is reached, it will become less complicated to interpret the results of this review. Future research should focus on examining specific locations of fat mass in relation to negative outcomes. Moreover, future studies should focus on the assessment of body composition changes over time, by using precise measurements such as DXA, computed tomography, or magnetic resonance imaging, and investigate how these changes relate to (un)healthy aging.

The strength of this study is the systematical literature search that resulted in a thorough overview of existing evidence in the literature. We focused on prospective studies only, thereby limiting the presence of reverse causation in interpreting the associations. Furthermore, only studies of moderate to good quality were included, and meta-analyses were performed. There are some limitations in this current study. First, because of possible publication bias (71), the reported findings should be interpreted with caution. Second, the meta-analyses revealed large heterogeneity across studies. This was to be expected, as there are differences in study samples, differences in outcomes, and differences in measurement of determinants, and therefore random effects models were used. Furthermore, there was a considerable difference in follow-up time between studies. This review includes several studies that made use of data from the same cohort studies such as the Health ABC Study and the Cardiovascular Health Study. This means that the contribution of these studies to the overall pooled odds ratios was larger compared with other studies. Even though data from the same cohort studies were used, there were considerable differences between findings. For example, Janssen (47) and Visser et al. (45) both investigated fat-free mass in association with disability in the Cardiovascular Health Study. Visser et al. showed an odds ratio of 0.57 (95% CI: 0.37, 0.88) for disability in women in the lowest quintile of fat-free mass, while Janssen showed an odds ratio of 1.37 (95% CI: 1.10, 1.72) for disability in women with severe sarcopenia. These differences in results were probably partly due to differences in follow-up time and differences in expressing muscle mass. We performed meta-analyses to be able to present the results of all studies (including studies that used the same cohort data) in a clear manner and used a random effects model, which takes important study differences into account (72). We additionally performed sensitivity analyses including only one study from each cohort in a single meta-analysis, which did not result in large changes in pooled odds ratios for the association between obesity and functional decline. The association between muscle mass and functional decline also remained similar, although the association became significant after excluding the studies by Visser et al. (45, 48).

As an inevitable consequence of longitudinal studies on aging, there will be selective nonresponse and loss to follow-up. Although the quality of the included articles was moderate to high, many studies scored poorly on the criteria for study participation, sampling, and attrition. This makes it difficult to assess possible selection bias in these studies.

Current research has shown that obesity rates among older persons are increasing and that obesity-related disability trends are worsening (73). There is a great need for effective interventions for older persons that focus on the loss of fat mass and preservation of muscle mass and strength to prevent functional decline. Based on the hypothetical model proposed by Vincent et al. (68), this type of intervention should include specific exercise, pain management, nutritional interventions, and psychosocial support. Future research should focus on the development, validation, and implementation of such interventions.

In conclusion, this study provides a systematic review and summary of the current literature on adiposity, muscle mass, and strength in association with functional decline. Obesity, a large waist circumference, and low muscle strength were all associated with functional decline. The role of muscle mass in the development of functional decline remains unclear but seems much smaller than the role of fat mass and muscle strength. Future intervention research should focus on positive changes in body composition to prevent onset or worsening of functional decline in old age.

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