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Review Article

Frailty, Sarcopenia, and Malnutrition Frequently (Co-)occur in Hospitalized Older Adults: A Systematic Review and Meta-analysis



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A B S T R A C T

Keywords:
Malnutrition
sarcopenia
frail older adults
prevalence
association
patients

Objectives: The purpose of this systematic review and meta-analysis was to summarize the prevalence of, and association between, physical frailty or sarcopenia and malnutrition in older hospitalized adults.

Design: A systematic literature search was performed in 10 databases.

Setting and Participants: Articles were selected that evaluated physical frailty or sarcopenia and malnutrition according to predefined criteria and cutoffs in older hospitalized patients.

Measures: Data were pooled in a meta-analysis to evaluate the prevalence of prefrailty and frailty [together (pre-)frailty], sarcopenia, and risk of malnutrition and malnutrition [together (risk of) malnutrition], and the association between either (pre-)frailty or sarcopenia and (risk of) malnutrition.

Results: Forty-seven articles with 18,039 patients (55% female) were included in the systematic review, and 39 articles (8868 patients, 62% female) were eligible for the meta-analysis. Pooling 11 studies (2725 patients) revealed that 84% [95% confidence interval (CI): 77%, 91%, $I^2 = 98.4%$] of patients were physically (pre-)frail. Pooling 15 studies (4014 patients) revealed that 37% (95% CI: 26%, 48%, $I^2 = 98.6%$) of patients had sarcopenia. Pooling 28 studies (7256 patients) revealed a prevalence of 66% (95% CI: 58%, 73%, $I^2 = 98.6%$) (risk of) malnutrition. Pooling 10 studies (2427 patients) revealed a high association [odds ratio (OR): 5.77 (95% CI: 3.88, 8.58), $P < .0001$, $I^2 = 42.3%$] and considerable overlap (49.7%) between physical (pre-)frailty and (risk of) malnutrition. Pooling 7 studies (2506 patients) revealed a high association [OR: 4.06 (95% CI: 2.43, 6.80), $P < .0001$, $I^2 = 71.4%$] and considerable overlap (41.6%) between sarcopenia and (risk of) malnutrition.

Conclusions and Implications: The association between and prevalence of (pre-)frailty or sarcopenia and (risk of) malnutrition in older hospitalized adults is substantial. About half of the hospitalized older adults suffer from 2 and perhaps 3 of these debilitating conditions. Therefore, standardized screening for these conditions at hospital admission is highly warranted to guide targeted nutritional and physical interventions.

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Conflict of interest statement: Y.C.L. and A.K. are employees, and G.C.L.-M. a contractor, of Danone Nutricia Research Advanced Medical Nutrition. The authors declare no conflicts of interest.

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Older adults are large users of hospital care.^{1–3} Hospitalization in older adults is a risk factor for losing independence and consequent nursing home admittance.^{4–6} Older age is accompanied by multimorbidity and physically debilitating conditions that are predictive of adverse clinical outcomes. These conditions are partly reversible and include frailty, sarcopenia, and/or malnutrition.^{2–4,7–15}

Frailty is a state of vulnerability and nonresilience with limited reserve capacity in major organ systems. It leads to reduced capability to withstand physical stress such as trauma or disease and is, therefore, accompanied by adverse clinical outcomes and increased risk of dependence and disability.^{2,3,9,16,17} Frailty was observed to increase length of hospital stay and risk of mortality in older patients at medical wards,^{18,19} and predicted postoperative complications, length of stay, and discharge to a skilled or assisted-living facility of older surgical patients who previously lived at home.³

Sarcopenia is characterized by progressive and generalized loss of skeletal muscle mass and strength,^{12,20} with a risk of adverse outcomes such as physical disability, poor quality of life, and death.^{12,13,21} Muscle mass and strength were associated with developing geriatric conditions and poorer cognition at hospital admission,^{22,23} and predictive for difficulties in performing activities of daily living,²⁴ falls,^{25,26} and mortality²⁶ 3 months after discharge. Sarcopenia is now recognized by the WHO as a muscle disease with an International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis code M62.84.^{27–29}

Malnutrition or undernutrition is the result of inadequate nutritional intake, often associated with inflammatory catabolism, leading to altered body composition, for example, decreased fat-free mass and body cell mass.¹¹ Under the general diagnosis of malnutrition are the etiology-based types of malnutrition, whereby cachexia represents chronic disease-related malnutrition with inflammation.^{17,30} Malnutrition in older hospitalized patients is associated with increased medical resource use, increased in-hospital length of stay and mortality, impairments in functional ability, low muscle mass, reduced quality of life, and a higher rate of discharge to nursing homes.^{8,31–38} After hip surgery, malnourished patients suffered from loss in activities of daily living more often and regained their prefracture mobility level less often, compared with well-nourished patients.³⁴ Malnutrition is also an important modifiable factor in both sarcopenia and frailty.³⁹

Criteria to determine frailty, sarcopenia, and malnutrition, especially weight loss and loss of muscle mass and muscle strength, overlap.⁴⁰ Therefore, older people may suffer from more of these conditions at the same time. Previously, we observed a strong association between physical prefrailty or frailty and risk of malnutrition or malnutrition in community-dwelling older adults, with an overlapping prevalence of 19%.⁴¹ The association between prevalence of prefrailty or frailty [together (pre-)frailty] and risk of malnutrition or malnutrition [together (risk of) malnutrition] is likely to be higher in the hospital, because community-dwelling older people who are frail and malnourished are likely more prone to hospitalization.

The purpose of this systematic review and meta-analysis was to gain insight into the prevalence and the magnitude of the association between physical (pre-)frailty or sarcopenia and (risk of) malnutrition in older hospitalized adults, because this knowledge can guide the need for standardized screening and targeted interventions, which have a positive impact on the recovery of older hospitalized patients during and after hospitalization and improve their level of independence after discharge from hospital.

Methods

Data Sources and Searches

The systematic review was conducted in line with the PRISMA standards.⁴² A systematic literature search was performed by a

librarian (S.E.) in PubMed and the ProQuest Databases Medline, Embase, SciSearch, EMCare, Current Contents, Gale Group Health Periodicals, Biosis Previews, CAB Abstracts, and FSTA, using the following search terms in title and/or abstract: (frail OR frailty OR prefrail OR prefrailty OR pre-frail OR pre-frailty OR “pre frail” OR “pre frailty” OR sarcopenia OR sarcopenic) AND (cachexia OR cachectic OR wasting OR malnutrition OR malnourish* OR undernutrition OR undernourish* OR nutrition*) AND (hospital* OR clinic OR clinics OR “medical centre” OR “medical center*”) AND (prevalence OR prevalent OR incidence OR incident OR epidemiolog* OR frequency OR frequent OR risk). There were no restrictions regarding language or publication date. The last search was run on May 23, 2018. Duplicate records were removed by the Endnote reference manager program (before screening) and manually before and during screening.

Study Selection

Records were assessed for eligibility independently by 2 researchers (G.C.L-M. and S.E.) by screening of titles and abstracts and subsequent screening of full texts when abstracts were considered relevant. Abstracts were considered relevant when both physical (ie, NOT cognitive) frailty and nutritional status, or sarcopenia and nutritional status, were addressed in hospitalized participants with a mean age of 60 years or older. Full texts were selected when physical (pre-)frailty, sarcopenia, or (risk of) malnutrition were measured according to predefined criteria and cutoffs, prior to or during hospitalization, with no restrictions regarding study design or assessment/screening methods applied. Full texts were excluded when study participants were preselected for any of these 3 conditions. Furthermore, articles were included only when prevalence data were present in the full text or when these were provided by the authors on request. Authors who did not respond to such a request were reminded once. Conference abstracts, reviews, letters to the editor, case reports, and protocol articles without data were also excluded. Disagreements between reviewers were resolved by consulting a third reviewer (Y.C.L.).

Articles presenting results from the same study population were described individually in the qualitative part of the review, but the study population was only used once for the meta-analysis.

Data Extraction

One investigator (G.C.L-M.) extracted data regarding study design, country, study population, sample size, gender, age, tools or methods used to assess physical (pre-)frailty, sarcopenia, and (risk of) malnutrition and the applied cutoffs and prevalence of these conditions. In case of an intervention study, only baseline data were used. This data extraction was checked by a second researcher (J.H.). The quality of the reported prevalence of (pre-)frailty, sarcopenia, and (risk of) malnutrition was not tested for individual studies. However, we tried to ensure the inclusion of high-quality information in the meta-analysis by excluding articles that described study populations that were preselected for frailty, sarcopenia, or nutritional status by including studies in the meta-analysis that applied valid screening/assessment tools and clearly defined (pre-)frailty or sarcopenia and (risk of) malnutrition according to described/referred cutoffs, and by pooling data from studies that applied similar tools.

Data Synthesis and Statistical Analysis

Prevalence data on physical (pre-)frailty or sarcopenia and (risk of) malnutrition were included in the meta-analysis when valid and similar tools were used to assess these conditions. Tools were considered valid when their validity was described in prior studies. Tools were considered similar when they applied comparable definitions to determine (pre-)frailty, sarcopenia, and (risk of) malnutrition. For the

purpose of the meta-analysis, data were dichotomized into “robust” vs “(pre-)frail,” “non-sarcopenic” vs “sarcopenic,” and “normal nutritional status” vs “(risk of) malnutrition.” Studies were also stratified into subgroups titled “medical,” referring to patients admitted for any reason except surgical treatment; “surgical,” referring to patients admitted for acute or elective surgery; and “mixed medical & surgical,” referring to patients hospitalized for medical and surgical purposes.

To assess the association between physical (pre-)frailty and (risk of) malnutrition, and the association between sarcopenia and (risk of) malnutrition, data on the overlap of both conditions were required. When these were not reported in the article, authors were asked to complete cross tables with absolute data on the overlap of (pre-)frailty

and (risk of) malnutrition or sarcopenia and (risk of) malnutrition, according to the predefined cutoffs used in their studies.

A random-effects (RE) model was applied to account for possible heterogeneity between pooled studies. Heterogeneity between pooled studies was assessed using the I^2 statistic; I^2 values closer to 100% indicate high heterogeneity, whereas values near 0% indicate low heterogeneity. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to evaluate the association between (pre-)frailty and (risk of) malnutrition and the association between sarcopenia and (risk of) malnutrition when data on the overlap of both conditions were available.

Forest plots were used to visualize the results of the prevalence of (pre-)frailty, sarcopenia, and (risk of) malnutrition, and the OR of (pre-)frailty in the presence of (risk of) malnutrition relative to

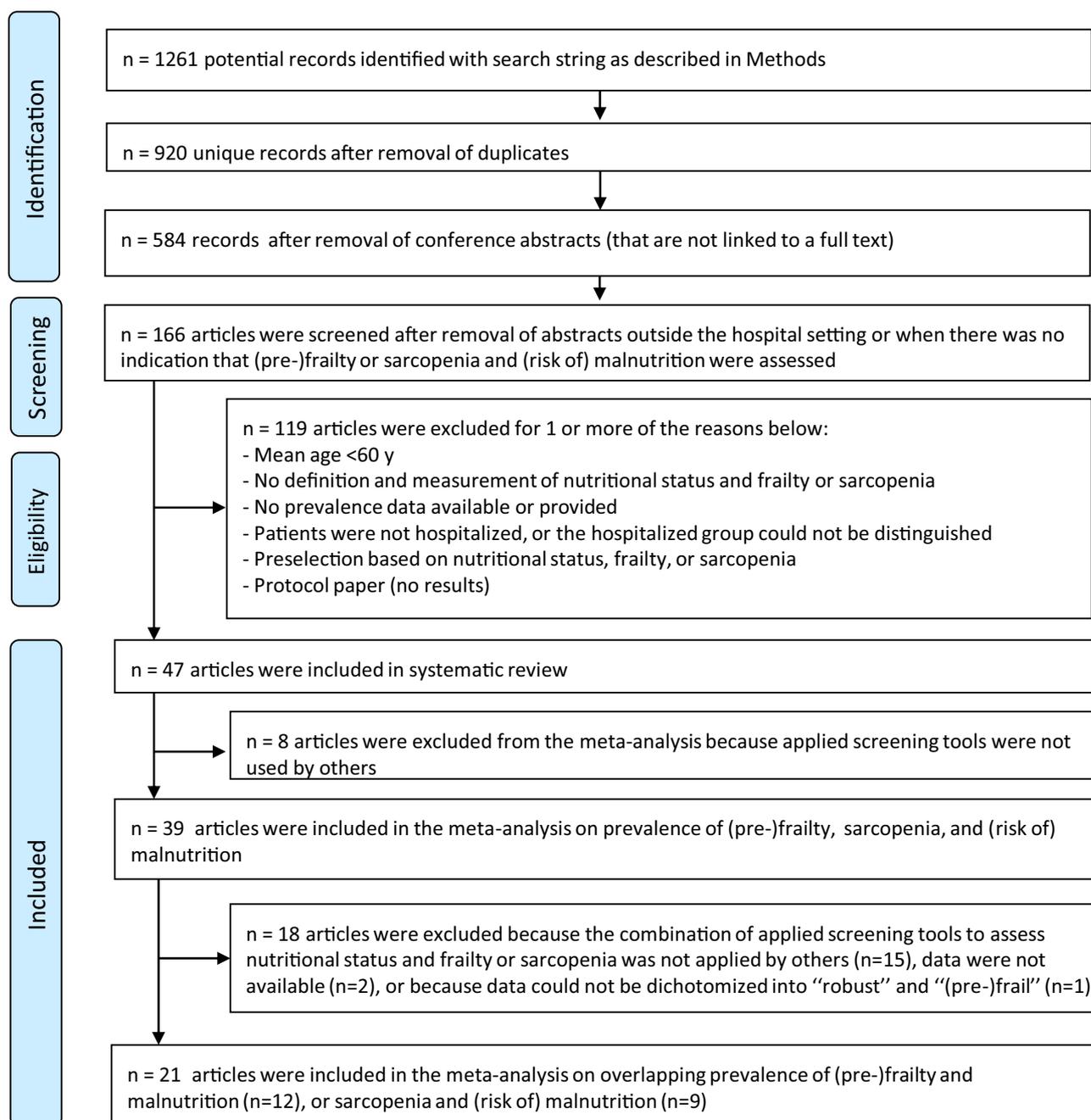


Fig. 1. PRISMA flowchart of study selection for systematic review and meta-analysis of articles on studies that provide information about the prevalence of (pre-)frailty or sarcopenia and (risk of) malnutrition among hospitalized older adults.

absence of (risk of) malnutrition, as well as the OR of sarcopenia in the presence of (risk of) malnutrition relative to absence of (risk of) malnutrition. Funnel plots of either proportion or log OR estimates against their standard errors were plotted to visualize the heterogeneity between studies, whereas the Egger regression test⁴³ and Begg rank correlation test⁴⁴ were used to test funnel plots asymmetry, which may suggest a biased outcome. Bubble plots were used to visualize the overlapping prevalence of (pre-)frailty and (risk of) malnutrition and of sarcopenia and (risk of) malnutrition.

All analyses were performed in the statistical software environment R. The “metafor” R-package was used to produce the pooled estimates and create the forest plots. A *P* value < .05 was considered to indicate significance.

Results

Study Characteristics

From 920 unique records retrieved with the search, 166 articles were screened for eligibility (Figure 1). We contacted 44 authors for prevalence data and received additional data for 33 articles.^{18,33,37,38,45–73} Forty-seven articles were included in the systematic review (Figure 1). Characteristics of these articles concerning 18,039 older hospitalized adults are summarized in Table 1, and provided as online Supplementary Material 1 (Tables S1 and S2).

Table 1 also shows the diversity in applied tools for screening and diagnosis of (pre-)frailty, sarcopenia, and (risk of) malnutrition. We

Table 1
Summary of Characteristics of the 47 Articles Included in the Systematic Review and Meta-analysis

	(Pre-)frailty and (Risk of) Malnutrition (n = 29* Articles) [†]	Sarcopenia and (Risk of) Malnutrition (n = 20* Articles) [‡]
Total patients with data, n	14,372	4604
Mean age range, y	73-85	62-86
% female range	25-76	30-79
Design	Prospective cohort (n = 18) ^{§, ,**} Cross-sectional (n = 5) Retrospective (n = 4) Survey (n = 2)	Prospective cohort (n = 8) ^{**} Cross-sectional (n = 8) ^{††} Retrospective (n = 4)
Study population	Medical (n = 16) ^{§,**} Surgery (n = 9) Mixed Medical & Surgery (n = 4)	Medical (n = 12) ^{**,**††} Surgery (n = 3) Mixed Medical & Surgery (n = 5) ^{††}
Largest subpopulation	Geriatrics (n = 10) ^{§,**}	Geriatrics (n = 10) ^{**,**††}
Screening tool frailty or sarcopenia (>1 in some studies)	Fried (n = 7) [§] Share-Fi (n = 4) Trabucci (n = 3) Adapted Fried (n = 2) VMS (n = 2) EFS (n = 2) ^{**} CDM, CGA, Frail Scale, G8, GFI, GFI Storstecky, ISAR, MFI, CFS, DFI, AFN (n = 1) ^{††}	EWGSOP no. 1 (n = 11) ^{**} AWGS (n = 7) ^{††,‡‡} CT, SMI, MAMA, and HGS (with SNS muscle component ≥ 3 points) (n = 1)
Screening Tool Malnutrition Status (>1 in some studies)	MNA-LF/FF (n = 13) ^{§,***} MNA-SF (n = 8) MUST (n = 3) NGE, GNRI, CONUT, PNI, MST, SNAQ, SNS (n = 1) ^{§§}	MNA-LF (n = 7) ^{**,**§§} MNA-SF (n = 7) ^{††,} PG-SGA (n = 2) BMI (n = 2) CONUT (n = 2) ^{††} MUST, NRS, BMI (with albumin), ESPEN diagnostic criteria malnutrition together with MNA-SF, SNS (n = 1)
Supplemental data provided	n = 23 ^{§, ,**}	n = 12 ^{**,**††,‡‡}
Included in meta-analysis on prevalence of (pre-)frailty, sarcopenia, and (risk of) malnutrition	n = 22 ^{§, ,**}	n = 19 ^{**,**††,‡‡}
Included in meta-analysis on association between either (pre-)frailty or sarcopenia and (risk of) malnutrition	n = 11 [§]	n = 9 ^{**,**††}

Frailty tools: Fried, phenotype according to Fried; Share-Fi, Survey of Health, Ageing and Retirement in Europe Frailty Instrument; VMS, Veiligheids Management Systeem; EFS, Edmonton Frail Scale; CDM, Cumulative Deficit Model; CGA items, items of Comprehensive Geriatric Assessment; G8, geriatric screening scale for frailty; GFI, Groningen Frailty Indicator; GFI Storstecky, Global Frailty Index Storstecky; ISAR, Identification of Seniors At Risk; MFI, Modified Frailty Index according to Robinson; CFS, Clinical Frailty Scale; DFI, Derby Frailty Index; AFN, Acute Frailty Network criteria. *Sarcopenia tools:* EWGSOP no. 1, 2010 definition European Working Group on Sarcopenia in Older People; AWGS, diagnostic algorithm of the Asian Working Group for Sarcopenia; CT, computed tomography; SMI, Skeletal Muscle Index; MAMA, midarm muscle area; HGS, handgrip strength. *Nutritional status tools:* MNA-LF/FF, Mini Nutritional Assessment–Long/Full Form; MNA-SF, MNA–Short Form; MUST, Malnutrition Universal Screening Tool; PG-SGA, Patient-Generated Subjective Global Assessment; BMI, body mass index; NGE, Nutritional Global Evaluation; GNRI, Geriatric Nutritional Risk Index; CONUT, Controlling Nutritional Status score; PNI, Prognostic Nutritional Index; MST, Malnutrition Screening Tool according to Ferguson; SNAQ, Short Nutritional Assessment Questionnaire; SNS, Subjective Nutritional Score; NRS, Nutritional Risk Screening; ESPEN, European Society for Clinical Nutrition and Metabolism. (See Supplementary Material 1 for references with these screening/assessment tools.)

*Articles by Perna et al^{60,73} and Hernández-Luis et al¹⁸ include data on frailty and sarcopenia and are therefore included in both the frailty and the sarcopenia population.

[†]Supplementary Material 1, Table S1.

[‡]Supplementary Material 1, Table S2.

[§]In 2 articles by Dent et al,^{49,50} the study populations overlap.

^{||}Two articles by O’Shea et al. and Timmons et al^{37,71} describe the same study population.

^{**}Two articles by Perna et al. describe the same study population.^{60,73}

^{††}Two articles by Maeda et al^{56,57} describe the same study population.

^{‡‡}Two articles by Harada et al^{63,64} describe the same study population.

^{§§}One article by Sze et al³⁸ applied GNRI, CONUT, and PNI to assess nutritional status and CFS, DFI, and AFN to determine frailty.

^{|||}One article by Yürüyen et al⁷⁰ applied MNA-LF, MNA-SF, MUST, as well as NRS, to assess nutritional status.

decided to pool data from studies that applied similar and valid screening or assessment tools, as explained in Methods.

For frailty, results obtained with the (adapted) Fried frailty phenotype criteria, Share-Fi, or FRAIL scale were pooled in the meta-analysis. Eleven studies, described in 13 articles,^{18,36,37,45–47,49–51,59,71,74,75} applied these tools, which all distinguish 3 categories: “robust,” “pre-frail,” and “frail.” The validated Fried phenotype is perhaps the most established and most frequently applied phenotypic definition of physical frailty,⁷⁶ which is approximated by the validated Share-Fi definition of frailty⁷⁷ and validated FRAIL Scale.^{78,79}

For sarcopenia, results obtained with the 2010 definition according to the European Working Group on Sarcopenia in Older People (EWGSOP no. 1)¹² or the diagnostic algorithm of the Asian Working Group for Sarcopenia (AWGS)⁸⁰ were pooled in the meta-analysis. Fifteen studies, described in 18 articles,^{35,60,62–70,72,73,81–85} applied these definitions, which both distinguish “sarcopenic” from “non-sarcopenic.” The AWGS definition is in agreement with the EWGSOP no. 1 definition but applies different cutoffs in line with differences between muscle mass and strength between Asians and Europeans.

For (risk of) malnutrition, results obtained with the Mini Nutritional Assessment Long Form or Short Form (MNA LF/SF),^{86–89} were pooled in the meta-analysis. Twenty-eight studies, described in 34 articles,^{33,35–37,45–55,59,60,65–68,70,71,73–75,81–83,85,90,91} applied these tools, which are well-established tools for identification of nutritional status in older people. The MNA-SF is validated against the MNA-LF.^{87,88} Both apply the categories “well nourished,” “risk of malnutrition,” and “malnutrition.”

Meta-analysis Results

Prevalence of (Pre-)frailty, Sarcopenia and (Risk of) Malnutrition

Pre frailty and frailty

Eleven studies with data from 2725 patients were pooled for the prevalence of (pre-)frailty (Figure 2), which was 84% (95% CI: 77%, 91%) across all studies. The prevalence of prefrailty and frailty together and apart is described for all subgroups in Table 2. Asymmetry seemed present across the overall population (Supplementary Material 2, Figure S1; Egger test, $P = .03$). This asymmetry would be solved with removal of the study by Guerrero-Garcia,⁷⁵ which included only (pre-)frail patients without preselection; however, removal would not have changed the pooled estimates.

Sarcopenia

Fifteen studies with data from 4014 patients were pooled for the proportion of sarcopenia (Figure 3), which was 37% (95% CI: 26%, 48%) across all studies and is described for all subgroups in Table 2.

Risk of malnutrition and malnutrition

Twenty-eight studies with data from 7256 patients were pooled for the proportion of (risk of) malnutrition (Figure 4), which was 66% (95% CI: 58%, 73%) across all studies. The prevalence of risk of malnutrition and malnutrition together and apart is described for all subgroups in Table 2. We also investigated whether the pooled prevalence estimates were perhaps asymmetrical because of the selection of studies

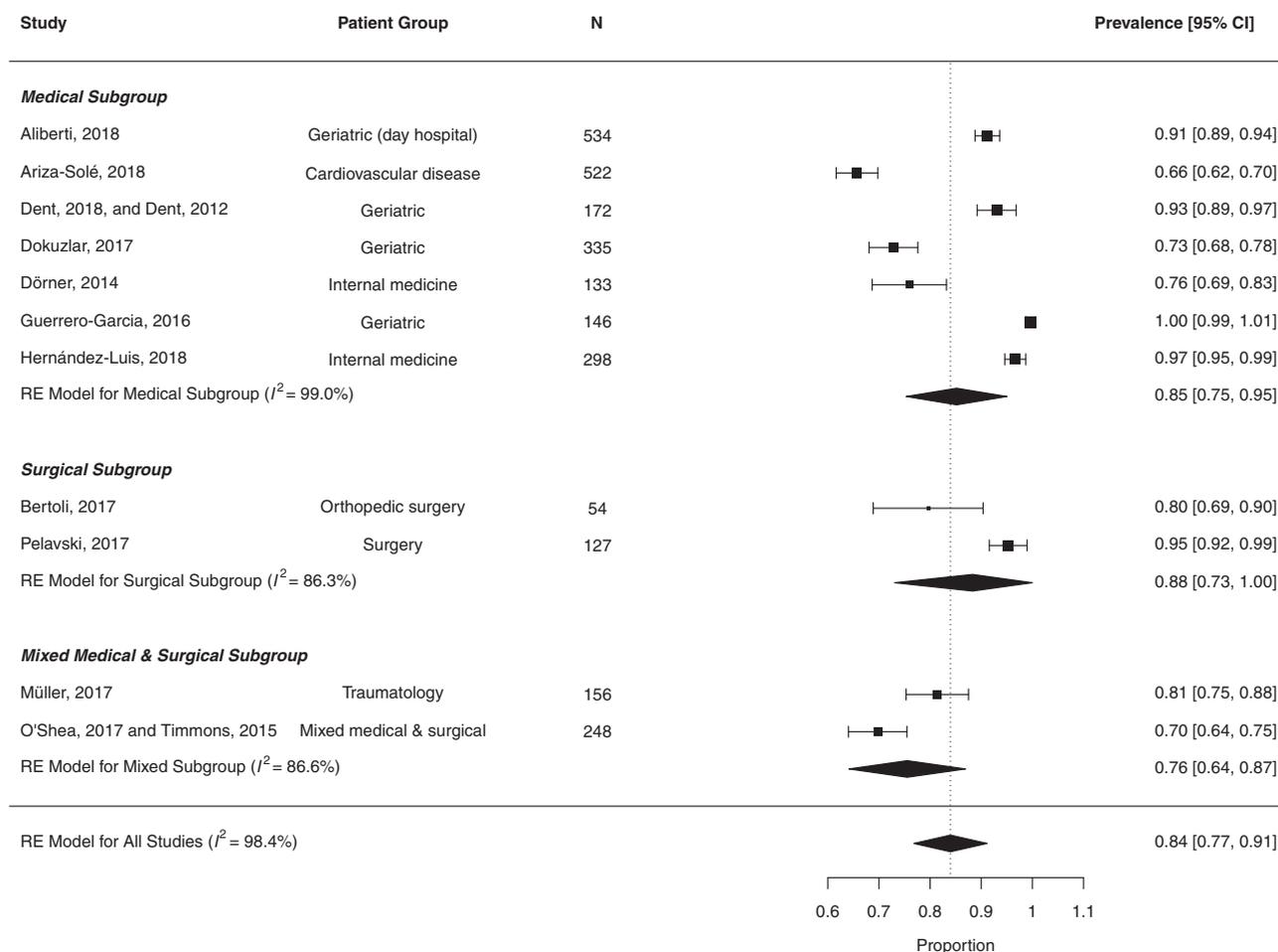


Fig. 2. Forest plot of the prevalence of (pre-)frailty among older hospitalized adults for the total population and for the medical, surgical, and mixed medical & surgical subgroups separately.

Table 2
Prevalence of Prefrailty and Frailty Together and Separately, Sarcopenia, and Risk of Malnutrition and Malnutrition Together and Separately

Condition	All Studies		Medical Subgroup		Surgical Subgroup		Mixed Medical & Surgical Subgroup	
	% (95% CI)	I^2 %	% (95% CI)	I^2 %	% (95% CI)	I^2 %	% (95% CI)	I^2 %
Pooled (pre-)frail	84 (77–91)	98.4	85 (75–95)	99.0	88 (73–100)	86.3	76 (64–87)	86.6
Prefrail	36 (29–44)	93.6	35 (29–41)	89.6	36 (9–63)	93.1	42 (8–76)	98.1
Frail	47 (37–57)	96.7	50 (37–64)	97.7	50 (39–62)	53.0	34 (11–56)	96.2
Sarcopenia	37 (26–48)	98.6	44 (29–58)	98.7	22 (19–25)	0.0	25 (9–40)	96.1
Pooled (Risk of) malnutrition	66 (58–73)	98.6	72 (63–81)	99.0	51 (40–62)	92.1	60 (55–65)	42.2
Risk of malnutrition	45 (41–49)	93.5	44 (38–51)	95.6	44 (36–52)	85.5	48 (41–55)	69.4
Malnutrition	20 (13–27)	99.8	26 (16–36)	99.4	6 (2–10)	88.7	11 (0–23)	96.8

I^2 represents heterogeneity. I^2 values closer to 100% indicate high heterogeneity, whereas values near 0% indicate low heterogeneity.

reporting frailty status or sarcopenia in combination with assessment of malnutrition (Supplementary Material 2, Figures S2 and S3). The pooled prevalence of (risk of) malnutrition for studies reporting sarcopenia (73%, 95% CI: 62%, 84%) was found to be marginally higher than for studies reporting (pre-)frailty (63%, 95% CI: 54%, 72%). This may imply that studies reporting on sarcopenia included an overall more malnourished (or at risk of malnutrition) population or that patients with (risk of) malnutrition are more prone to sarcopenia.

Overlap and Association Between (Pre-)frailty and (Risk of) Malnutrition

Ten studies in 12 articles,^{36,37,45–47,49–51,59,71,74,75} with data from 2427 patients were included in the meta-analysis evaluating the association between (pre-)frailty and (risk of) malnutrition. For the total population, the overlapping prevalence of (pre-)frail with (risk of) malnutrition was 49.7%; 14.6% had neither of the conditions (Figure 5). The OR of (pre-)frailty in the presence of (risk of) malnutrition relative

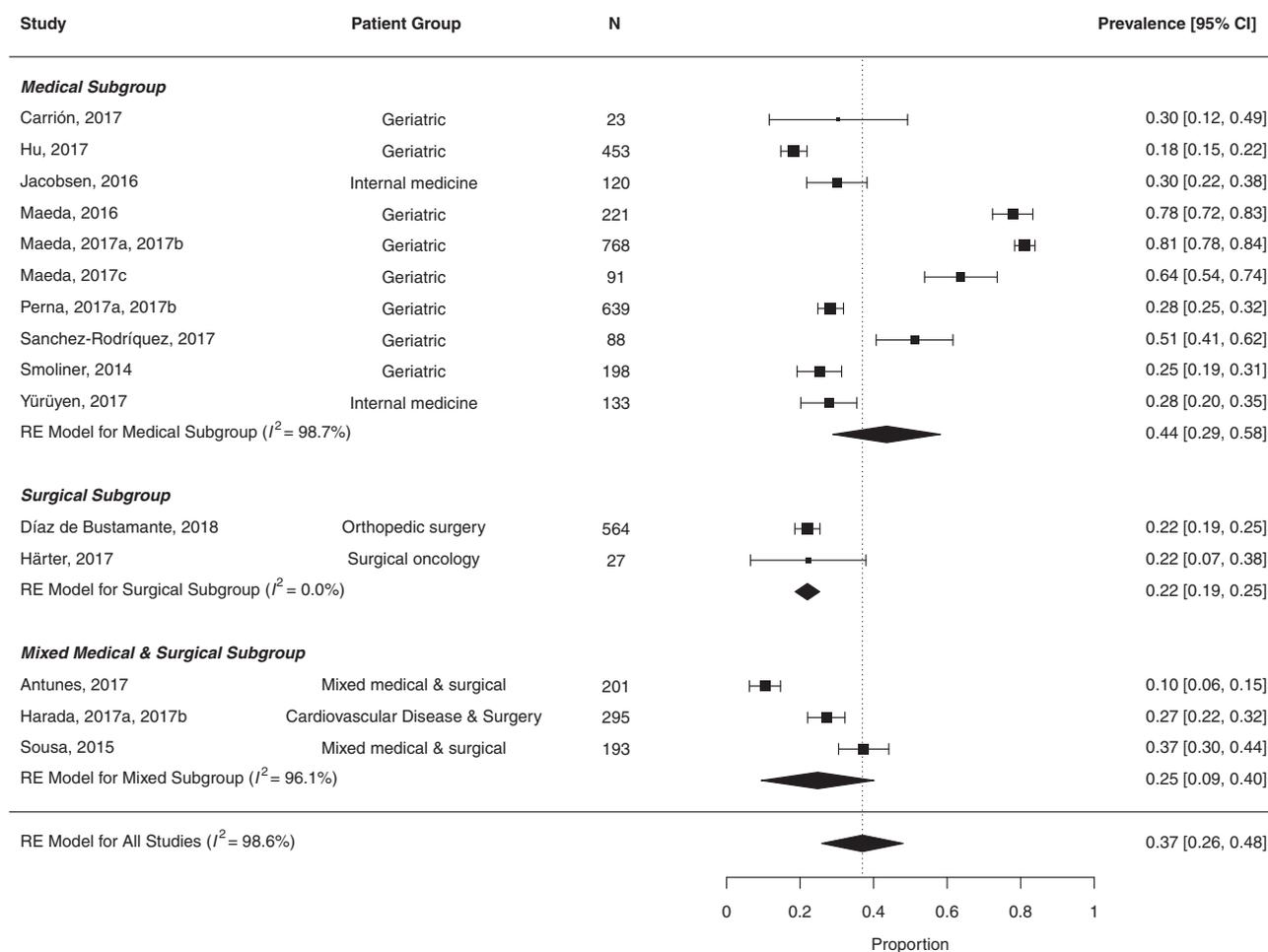


Fig. 3. Forest plot of the prevalence of sarcopenia among older hospitalized adults for the total population and for the medical, surgical, and mixed medical & surgical subgroups separately.

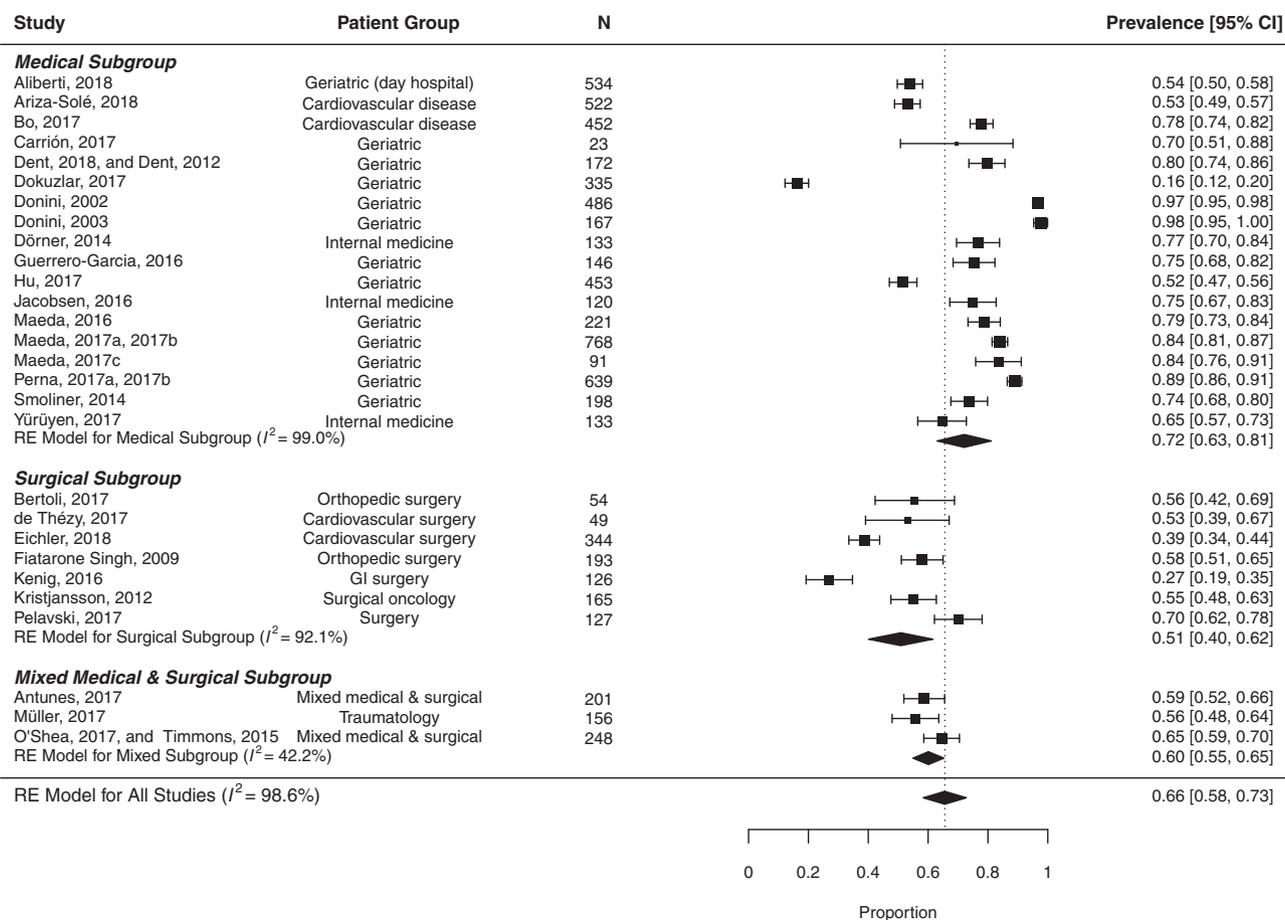


Fig. 4. Forest plot of the prevalence of (risk of) malnutrition among older hospitalized adults for the total population and for the medical, surgical, and mixed medical & surgical subgroups separately.

to absence of (risk of) malnutrition was 5.77 (95% CI: 3.88, 8.58; $P < .001$, $I^2 = 42.3\%$) in the total population, 6.00 (95% CI: 3.50, 10.29; $P < .001$, $I^2 = 51.0\%$) in the medical subgroup, 16.67 (95% CI: 3.60, 77.23; $P < .001$, $I^2 = 0.0\%$) in the surgical subgroup, and 4.31 (95% CI: 2.38, 7.79; $P < .001$, $I^2 = 23.1\%$) in the mixed medical & surgical subgroup (Figure 6). Asymmetry was present across the overall population (Supplemental Material 2, Figure S4; Egger test, $P = .008$) but not in the biggest medical subgroup (Egger test, $P = .26$) that contributed most to the estimation of the overall pooled OR across studies. The asymmetry seemed mostly due to 2 surgical studies with small sample sizes and large standard errors of OR estimates.

Overlap and Association Between Sarcopenia and (Risk of) Malnutrition

Seven studies, described in 9 articles,^{35,60,65–68,70,73,81} with data from 2506 patients were included in the meta-analysis evaluating the association between sarcopenia and (risk of) malnutrition. The overlapping prevalence of sarcopenia with (risk of) malnutrition was 41.6%; 18.9% of the patients had neither of the conditions (Figure 7). The OR of sarcopenia in the presence of (risk of) malnutrition relative to the absence of (risk of) malnutrition was 4.06 (95% CI: 2.43, 6.80; $P < .001$, $I^2 = 71.4\%$) in the total population, 3.99 (95% CI: 2.25, 7.06; $P < .0001$, $I^2 = 76.5\%$) in the medical subgroup, and 4.80 (95% CI: 1.37, 16.87) in the single mixed medical and surgical study (Figure 8).

Heterogeneity of Results

Large heterogeneity was observed for prevalence of (pre-)frailty, sarcopenia, and (risk of) malnutrition at the total population level (Figures 2–4). Because of stratification in medical, surgical, and mixed medical & surgical subgroups, heterogeneity decreased in the surgical and in the mixed medical & surgical subgroup. The heterogeneity of results on the OR between (pre-)frailty and (risk of) malnutrition was moderate for the total group and medical subgroup, low for the mixed medical & surgical subgroup, and absent for the surgical subgroup. Heterogeneity of results on the association between sarcopenia and (risk of) malnutrition were higher than the association between (pre-)frailty and (risk of) malnutrition.

Discussion

In this systematic review and meta-analysis, we summarized the literature on the prevalence of (pre-)frailty or sarcopenia in combination with the prevalence of (risk of) malnutrition in older hospitalized adults. Eight of 10 of the older patients were (pre-)frail (36% prefrail and 47% frail), one-third had sarcopenia, and two-thirds had (risk of) malnutrition (45% risk of malnutrition and 20% malnutrition). The OR between and overlapping prevalence of (pre-)frailty and (risk of) malnutrition were 5.77 and 50%, respectively. The OR between and overlapping prevalence of sarcopenia and (risk of) malnutrition were 4.06 and 42%, respectively.

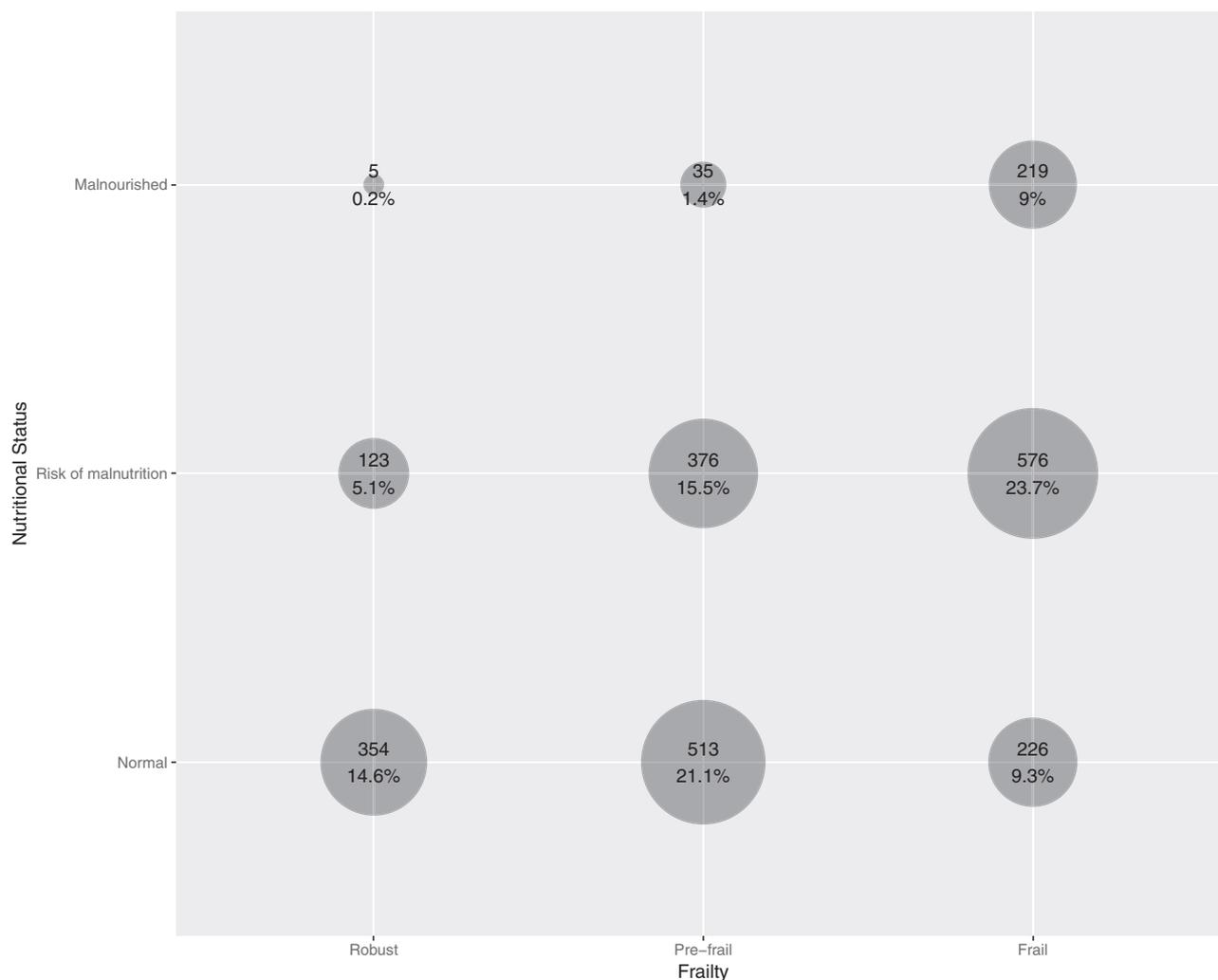


Fig. 5. Bubble plot of the overlapping prevalence of robust, prefrail, and frail and normal nutritional status, risk of malnutrition, or malnourished for the total population.

Prevalence of (Risk of) Malnutrition, (Pre-)frailty, and Sarcopenia

We are not aware of other meta-analyses with respect to the prevalence of frailty in hospitalized older adults, except for 1 in ICU patients.⁹² In our study, the pooled prevalence of (pre-)frailty (84%) among older hospitalized adults was observed to be higher than in community-dwelling older adults (71%).⁴¹ The prevalence of frailty (ie, excluding prefrailty) was twice as high compared with community results (47% vs 19%). The observed prevalence of 37% sarcopenia in our meta-analysis could also not be compared with results of other meta-analyses in hospitalized patients. The sarcopenia prevalence of hospitalized older adults was substantially higher than among community-dwelling as reported in the systematic review by Cruz-Jentoft et al,⁹³ who showed that prevalence of sarcopenia in community-dwelling older adults ranged from 1% to 29%. It is likely that the sarcopenia prevalence in inpatients depends considerably on the applied definition,⁹⁴ and that the prevalence is even higher when measured at hospital discharge, because of a rapid decline of strength and mass during hospitalization.⁹⁵ The observed pooled overall prevalence of 66% for (risk of) malnutrition, with 45% at risk of malnutrition and 20% malnourished, was very much in agreement with previous meta-analyses in hospitalized older patients based on MNA data. Cereda et al⁹⁶ reported a pooled prevalence of 46% at risk of malnutrition and 22% malnutrition, and a recently published meta-analysis by the MaNuEl Consortium⁹⁷ reported a pooled prevalence

of (risk of) malnutrition in European hospitalized older adults of 61% (95% CI: 55%, 67%) using MNA-SF. Our previous meta-analysis in community-dwelling older adults⁴¹ revealed an MNA-assessed prevalence of 21% for (risk of) malnutrition, with 19% at risk of malnutrition and 2.3% malnourished. Altogether, the prevalence of (pre-)frailty, sarcopenia, and (risk of) malnutrition was shown to be substantial, and also much higher among older hospitalized than among community-dwelling older adults. The high prevalence of these conditions likely contributes to the large proportion of hospitalized older adults who are discharged from the hospital to post-acute care services that largely encompass physical and/or occupational therapy services; namely, skilled nursing facility for rehabilitation and home health services.

Association Between Either Frailty or Sarcopenia and (Risk of) Malnutrition

As anticipated beforehand, this meta-analysis revealed a high overlapping prevalence of (pre-)frailty and (risk of) malnutrition (50%) in hospitalized older adults, which was much larger than in the community, with 19% of older people having both (pre-)frailty and (risk of) malnutrition.⁴¹ The current meta-analysis furthermore revealed a high overlapping prevalence of sarcopenia and (risk of) malnutrition (42%). In 1 of 5 patients, none of the conditions was observed. When only 1 condition was present, the highest prevalence

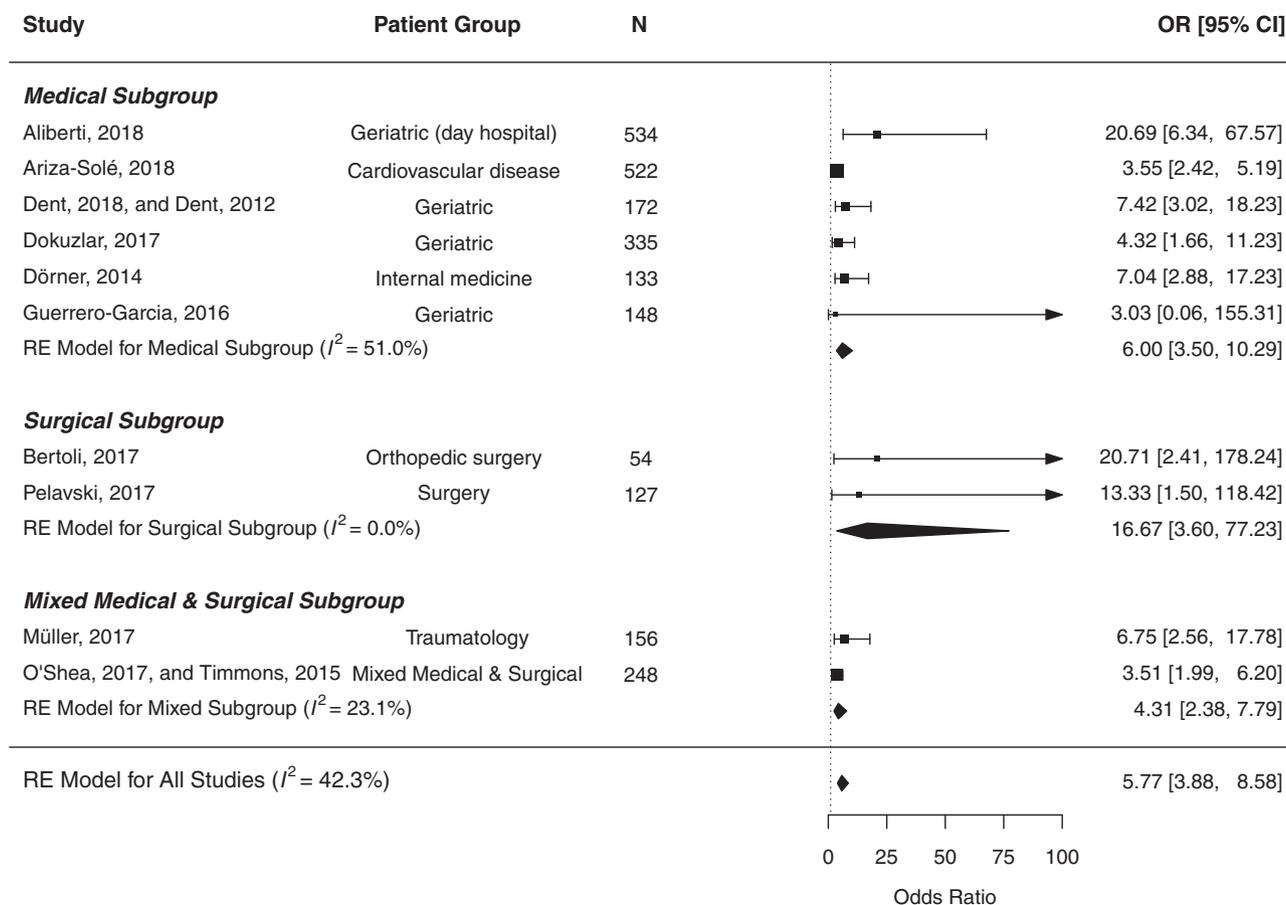


Fig. 6. Forest plot of the OR of (pre-)frailty in the presence of (risk of) malnutrition relative to absence of (risk of) malnutrition for the total population and for the medical, surgical, and mixed medical & surgical subgroups separately.

was observed for (pre-)frailty without (risk of) malnutrition (30%), or (risk of) malnutrition without sarcopenia (34%). The high overlapping prevalence of frailty or sarcopenia with (risk of) malnutrition agrees with the outcome of strong associations between those conditions, as estimated by their ORs. This substantial overlap of conditions furthermore shows that approximately half of the hospitalized older adults suffer from at least 2 of these debilitating conditions. A combination of these conditions likely synergistically impairs outcome. For example, older adults admitted to an acute care unit, who were at risk of malnutrition or malnourished according to the MNA-SF, were significantly more likely to die within 3 months after admission than those without sarcopenia.⁹⁸ Furthermore, the high prevalence, and the overlap in criteria, of conditions makes it plausible that a number of older patients suffer from all 3 conditions.

Clinical Relevance of Findings and Future Research

The high prevalence and overlap between frailty or sarcopenia and malnutrition argues for standardized screening for these conditions at or before hospital admission. The question remains how our findings can guide interventions that will reduce the added risk of impaired clinical outcome because of these conditions. Because of the substantial overlap in the evaluated geriatric conditions, most older patients are likely to benefit from nutritional support with a protein-enriched diet that also provides an adequate amount of energy. This is supported by the observation in Dutch hospitalized undernourished older adults that only 1 in 4 had a protein and energy intake level that met their requirements on the fourth day of hospital admission.⁹⁹ The

effort to reach nutritional requirements is worthwhile, as shown by Schuetz et al.¹⁰⁰ in the recent EFFORT trial. This trial showed that individualized nutritional support, including oral nutritional supplements, in older medical inpatients at nutritional risk (NRS 2002 ≥ 3 points) reduced adverse clinical outcome and mortality within 30 days after admission.¹⁰⁰ Besides nutrition, inclusion of physical exercise in some form is warranted, especially in case of, but also to prevent, sarcopenia and consequent loss of mobility and independence.^{14,101–104} Recently, the quality and performance committee of the American Geriatrics Society advocated for greater focus on mobility as an outcome for hospitalized older adults, and provided recommendations to implement exercise in basic hospital care for older people, preferably by nursing staff, based on already existing successful exercise programs in some hospitals.¹⁰⁴ Also, the maintenance of muscle mass in disease is nowadays considered an important outcome of nutritional intervention.⁷ Future research should focus on implementation of screening for frailty, sarcopenia, and malnutrition as part of comprehensive geriatric assessment, and evidence-based interventions such as nutritional support and an exercise program. This will preserve or restore nutritional status, muscle mass, strength, and function, and hence contribute to improved clinical outcome.

Strengths and Limitations

Strengths of this systematic review and meta-analysis are the systematic approach and the extensive quantitative analysis. Many authors were approached, and they were kind enough to provide requested data. Eight articles were not included in the systematic

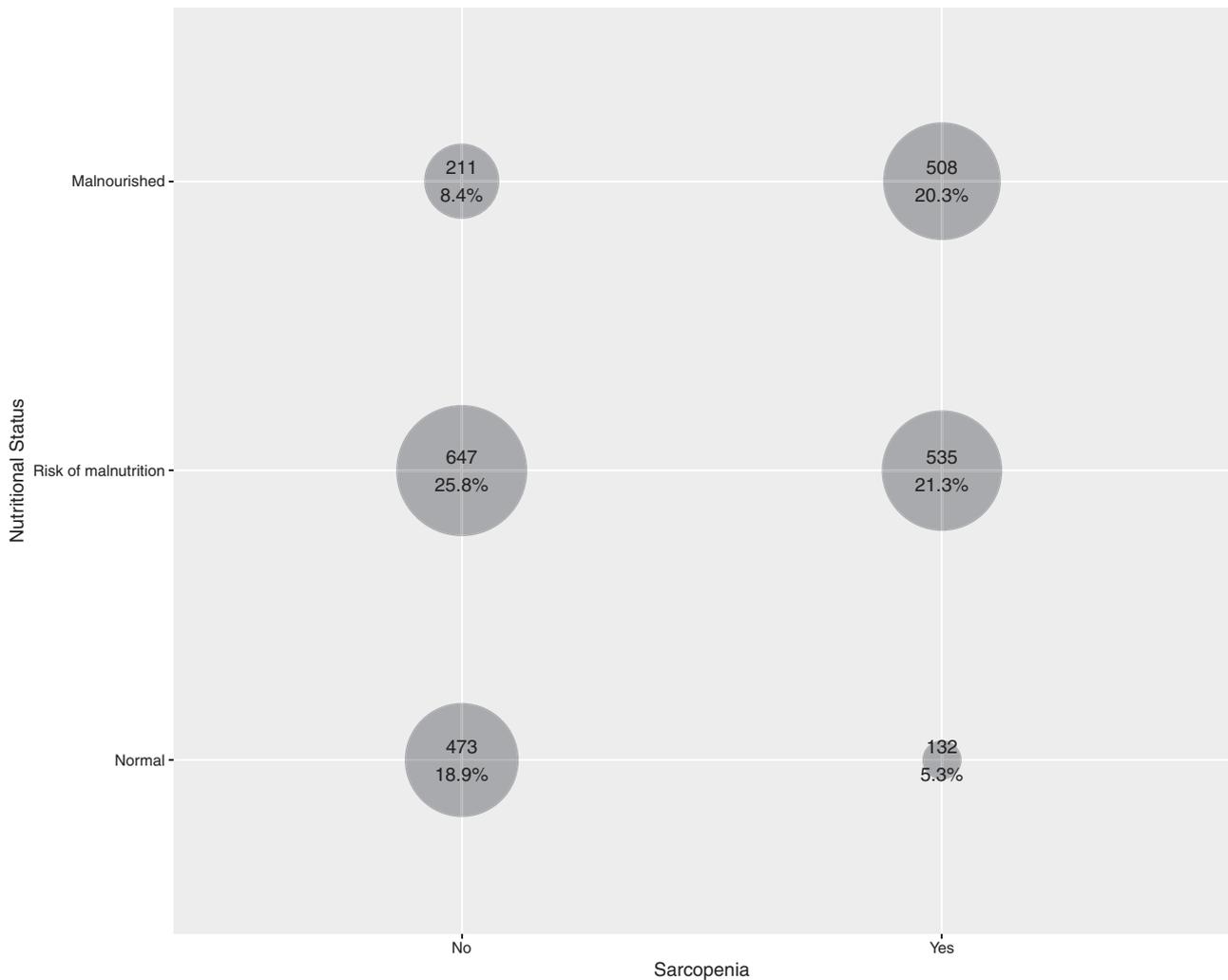


Fig. 7. Bubble plot of the overlapping prevalence of no sarcopenia or sarcopenia and normal nutritional status, risk of malnutrition, or malnourished for the total population.

review, because prevalence data were not provided, and 3 articles could not be included in the meta-analysis because no overlapping data were provided.

It may be considered a limitation that this systematic review and meta-analysis is partly based on the outcome of screening tools and not on assessment. Another limitation is that the MNA does not reveal the etiology of malnutrition. In the future, when studies use the GLIM criteria³⁰ to diagnose malnutrition, a meta-analysis may be able to distinguish the prevalence of cachexia in older hospitalized adults. Such a meta-analysis may also reveal a greater overlap between cachexia and sarcopenia, considering the characteristics of both conditions.⁴⁰ Furthermore, in spite of applied stratification, heterogeneity remained high, possibly because of the difference in type of patients inherent to the variety of reasons for admission. Heterogeneity may also have been enhanced by differences in the timing of assessment, which varied from at admission to 4 days after admission. However, the reduced heterogeneity with pooling of the ORs is encouraging, since this confirms a true overall effect in our meta-analysis and, hence, provides evidence of a strong relationship between (pre-) frailty and (risk of) malnutrition, and between sarcopenia and (risk of) malnutrition. Another limitation of the study is the observed asymmetry for the association between and prevalence of (pre-) frailty and (risk of) malnutrition, although pooled estimates remained valid. Specific inclusion of studies that report on both conditions may have

contributed to observed asymmetry. We did not look at the overlapping prevalence of (pre-)frailty and sarcopenia, but the 2 articles included in the systematic review that reported prevalence of both frailty and sarcopenia together with nutritional status^{60,73} observed that sarcopenia was associated with higher frailty scores. Finally, we did not include a quality assessment of individual articles, but tried to improve the quality of our meta-analysis data by selecting studies that applied similar and valid tools to identify (pre-)frailty or sarcopenia (risk of) malnutrition, and by excluding studies that preselected for any of these conditions. However, information on how screening/assessment was performed in the included studies in the meta-analysis was limited, and we cannot exclude that this may have led to a risk of bias.

Conclusions and Implications

The association between either (pre-)frailty or sarcopenia and (risk of) malnutrition is substantial, indicating that most hospitalized older adults suffer from 2 or perhaps even 3 of these debilitating conditions during their hospital stay. This advocates the inclusion of screening tools to assess nutritional status, frailty, and sarcopenia in comprehensive geriatric assessment before or at hospital admission and during hospital stay. The high overlap in the studied geriatric conditions also justifies treatment with an appropriate combination of

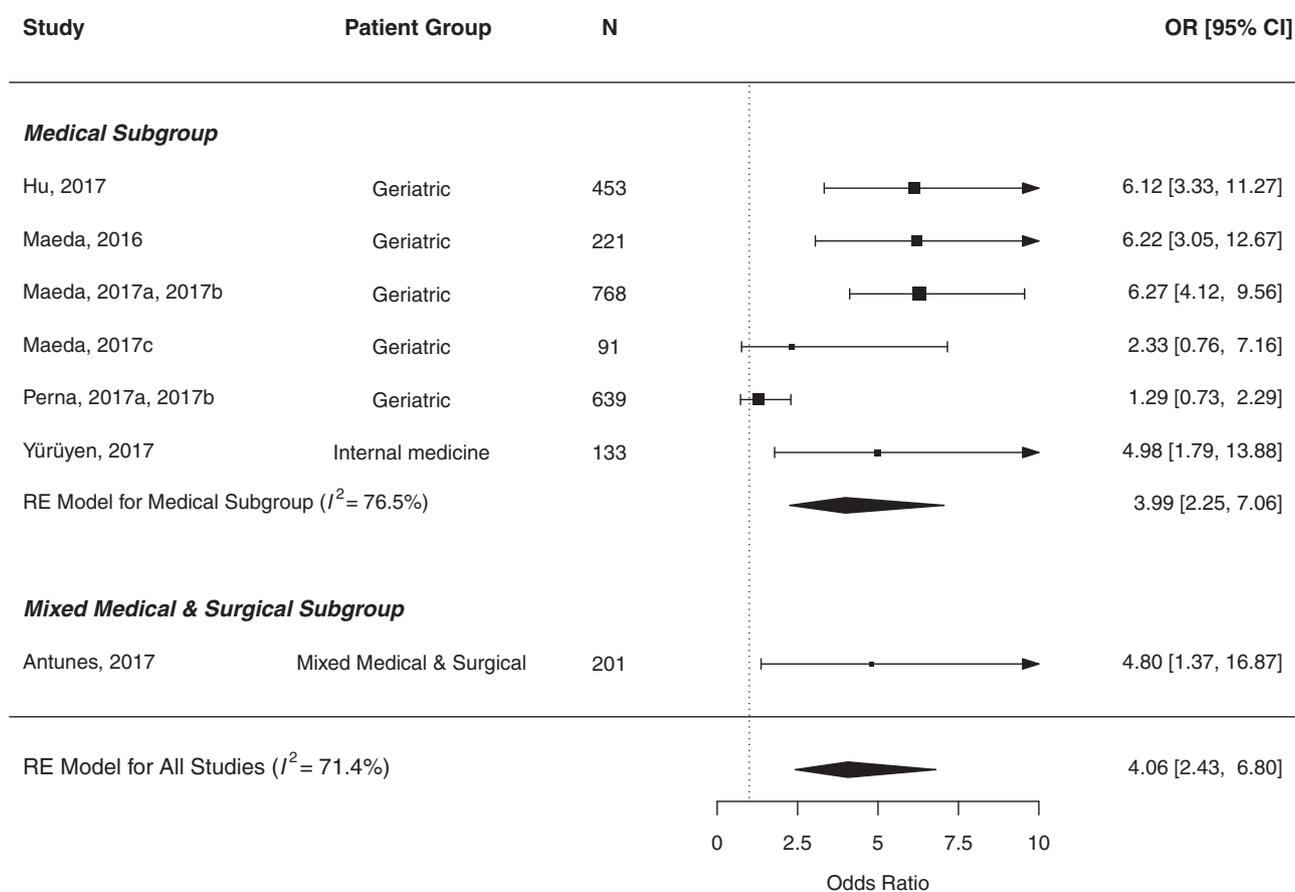


Fig. 8. Forest plot of the OR of sarcopenia in the presence of (risk of) malnutrition relative to absence of (risk of) malnutrition for the total population and for the medical, surgical and mixed medical & surgical subgroups separately.

nutritional support and exercise program in the majority of older hospitalized adults. Further research is needed to evaluate the effect of screening for (pre-)frailty, sarcopenia, and (risk of) malnutrition and subsequent nutritional and exercise intervention during and after hospital stay on clinical outcomes. Ideally, an assessment and treatment plan with regular follow-up is put in place for all hospitalized older patients.

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Supplementary Data

Supplementary data related to this article can be found online at <https://doi.org/10.1016/j.jamda.2020.03.006>.

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