Prevalence of sarcopenia as a comorbid disease: A systematic review and meta-analysis

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\textbf{ABSTRACT}

\textbf{Background:} Sarcopenia shares risk factors with various other age-related diseases. This meta-analysis aimed to determine the prevalence of sarcopenia as a comorbid disease.

\textbf{Methods:} Medline, EMBASE and Cochrane databases were searched for articles from inception to 8th June 2018, reporting the prevalence of sarcopenia in individuals with a diagnosis of cardiovascular disease (CVD), dementia, diabetes mellitus or respiratory disease and, if applicable their controls. No exclusion criteria were applied with regards to definition of sarcopenia, individuals' age, study design and setting. Meta-analyses were stratified by disease, definition of sarcopenia and continent.

\textbf{Results:} The 63 included articles described 17,206 diseased individuals (mean age: 65.3 ± 1.6 years, 49.9% females) and 22,375 non-diseased controls (mean age: 54.6 ± 16.2 years, 53.8% females). The prevalence of sarcopenia in individuals with CVD was 31.4% (95% CI: 22.4–42.1%), no controls were available. The prevalence of sarcopenia was 26.4% (95% CI: 13.6–44.8%) in individuals with dementia compared to 8.3% (95% CI: 2.8–21.9%) in their controls; 31.1% (95% CI: 19.8–45.2%) in individuals with diabetes mellitus compared to 16.2% (95% CI: 9.5–26.2%) in controls; and 26.8% (95% CI: 17.8–38.1%) in individuals with respiratory diseases compared to 13.3% (95% CI: 8.3–20.7%) in controls.

\textbf{Conclusions:} Sarcopenia is highly prevalent in individuals with CVD, dementia, diabetes mellitus and respiratory disease.

\section{1. Introduction}

Older adults are at risk of developing age-related diseases resulting in multimorbidity, which is defined as the coexistence of two or more diseases (Violan et al., 2014). Over 50% of older adults are afflicted with 3 or more chronic diseases (Guiding principles for the care of older adults with multimorbidity: an approach for clinicians, 2012). Sarcopenia is an age-related disease characterised by low muscle mass, muscle strength and physical performance (Fielding et al., 2011; Zanker et al., 2019) and is prevalent in up to 15% of healthy older adults (Reijnierse et al., 2015b) up to 76% of acutely hospitalised older patients (Bianchi et al., 2017; Cruz-Jentoft et al., 2014; Reijnierse et al., 2018) and up to 69% of patients admitted to post-acute geriatric rehabilitation (Churilov et al., 2018). Sarcopenia is associated with poor health outcomes such as cognitive impairment (Chang et al., 2016), depression (Chang et al., 2017), functional decline (Beaudart et al., 2017), falls (Yeung et al., 2019), fractures (Yeung et al., 2019) and mortality (Beaudart et al., 2017).

Other diseases such as cardiovascular diseases (CVD), dementia, diabetes mellitus (DM) and respiratory diseases are frequently co-occurring in older individuals and share common risk factors with sarcopenia such as aging, physical inactivity, malnutrition and/or obesity (Baumgart et al., 2015; Cerri et al., 2015; Fletcher et al., 2002; Pierik et al., 2017; Postma et al., 2015; Sabzamakan et al., 2014). Currently, sarcopenia is frequently underdiagnosed in clinical practice (Reijnierse et al., 2017; Yeung et al., 2019) despite effective interventions to increase muscle mass, muscle strength and physical performance (Kamleh et al., 2019; Martin-Cantero et al., 2019) and willingness of older adults

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to undergo treatment to counteract sarcopenia (Van Ancum et al., 2019). To date, treatment protocols do not take comorbid diseases into account (Yoshimura et al., 2017). Therewith it is of utmost importance to determine the prevalence of sarcopenia in cohorts of older adults at risk, to eventually introduce diagnostics and treatment of the disease.

This systematic review and meta-analysis aimed to determine the prevalence of sarcopenia in individuals with CVD, dementia, DM and respiratory disease.

2. Methods

2.1. Search strategy

A systematic search was performed in Medline, EMBASE, and Cochrane for published articles from inception date until 8th June 2018. The protocol was registered at PROSPERO International prospective register of systematic reviews (CRD42019127817). The systematic review was conducted according to the PRISMA standards (Moher et al., 2010). Pre-defined search terms included MeSH terms and keywords for ‘cardiovascular disease’, ‘dementia’, ‘diabetes mellitus’, ‘respiratory disease’ and ‘sarcopenia’. The search was constructed by a senior liaison librarian of the biomedical university library, The University of Melbourne. The complete search strategy can be found in Table A.1. The reference section of each included article was also used to identify additional relevant articles.

2.2. Article selection

All articles were assessed for eligibility via title and abstract screening and subsequently as full-text articles by two independent reviewers (JP and MAJG). A third reviewer (WKL) resolved any discrepancies between the two reviewers. Articles were selected if they included individuals with one of the following diseases: CVD, dementia, DM or respiratory disease. These diseases were chosen as they are highly prevalent at older age and among the top ten leading cause of global deaths (World Health Organisation, 2018). No restrictions were applied in regards to the definition of sarcopenia, age of individuals, study design and study setting. Articles were excluded if: individuals had active cancer as cancer cachexia is difficult to distinguish from sarcopenia (Cruz-Jentoft et al., 2010), the applied sarcopenia definition was not described, animal studies, conference abstracts, case reports (less than five reported cases), reviews, letters to the editor and articles not published in English.

2.3. Data extraction and quality assessment

Two independent reviewers (JP and MG) extracted the data and assessed the quality of included articles. The following data were extracted: study characteristics (first author, publication year), cohort characteristics (continent, study setting, type of disease, age, sample size, sex) stratified for disease groups and controls if applicable, and characteristics of sarcopenia diagnosis (definition of sarcopenia, prevalence for the total cohort and stratified for sex, and assessment method for each parameter included in the sarcopenia diagnosis). Controls were defined as not afflicted with the disease of interest. The weighted mean age of the individuals was calculated if the age was stratified by groups.

A modified Newcastle-Ottawa Scale (NOS) (Table A.2) was used to assess the quality of each article (Lo et al., 2014; Wells et al., 2001). The NOS evaluates the quality of an article through three criteria: 1) Selection, 2) Comparability and 3) Exposure. High-quality articles were defined as ≥ 4 stars (Hermont et al., 2014).

2.4. Statistical analysis

A random-effects model (Fleiss, 1993) was used to pool prevalence rates of sarcopenia separately for disease groups and controls, presented as a percentage and 95% confidence interval (CI). Analyses were stratified for articles with controls and articles without controls. If articles included controls but did not report the prevalence of sarcopenia, these articles were grouped with the articles without controls. If an article included more than one disease group was or stratified sarcopenia prevalence by severity of diseases, groups were included separately in the meta-analyses.

Subgroup-analyses were performed based on the definition of sarcopenia and continent. Sarcopenia definitions vary in their inclusion of muscle parameters (muscle mass, muscle strength and physical performance) and their cut-off values for each parameter (Baumgartner et al., 1998; Chen et al., 2014; Cruz-Jentoft et al., 2010; Fielding et al., 2011; Ishii et al., 2014; Janssen et al., 2004; Janssen et al., 2002; Newman et al., 2003; Studenski et al., 2014). This variance has been shown to impact on the prevalence of sarcopenia in various cohorts (Bijlsma et al., 2014; Reijnierse et al., 2018; Reijnierse et al., 2015b). Current definitions include muscle mass alone (Baumgartner et al., 1998; Delmonico et al., 2007; Janssen et al., 2004; Janssen et al., 2002; Newman et al., 2003); muscle mass and muscle strength (Nishikawa et al., 2016); muscle mass and physical performance (Fielding et al., 2011; Muscaritoli et al., 2010) and muscle mass, muscle strength and physical performance (Chen et al., 2014; Cruz-Jentoft et al., 2010; Studenski et al., 2014). Articles presenting sarcopenia prevalence by use of multiple sarcopenia definitions, the following definitions were selected for the meta-analysis: 1) the definition which applied to the cohort's country of origin was used (e.g. European Working Group for Sarcopenia in Older People (EWGSOP) for European cohorts, Asian Working Group for Sarcopenia (AWGS) for Asian cohorts) or 2) if 1 was not applicable, results were prioritised based on the following order: EWGSOP, AWGS, Foundation for the National Institutes of Health (FNIH), Baumgartner, other definitions.

If a study included both disease groups and controls, odds ratios (OR) for sarcopenia were calculated and a random-effects model was used to pool these OR. If an article included multiple disease groups or disease severities, they were combined into one disease group for the above analyses.

Heterogeneity was assessed using the I²-test, where a value of < 25% was rated low, 25–75% was moderate, and > 75% was high heterogeneity (Higgins and Thompson, 2002). A two-sided p-value of < 0.05 was considered statistically significant. All meta-analyses were performed using Comprehensive Meta-Analysis (version 3.3; Biotstat Inc., Englewood NK).

3. Results

3.1. Search strategy

The search strategy identified 6727 articles (Table A.1) and 38 articles were identified from other sources. A total of 1728 duplicate articles were removed. Following title and abstract screening (4999 articles), 214 articles were included for full-text review, of which 63 articles were included in the systematic review and meta-analysis (Fig. 1).

3.2. Study characteristics

Table 1 shows the characteristics of the included studies. Most articles (40/63) included individuals from Asia, 17/63 from Europe, 5/63 from North and South America and 1/63 from Australia. The mean age of the included 17,206 diseased individuals was 65.3 ± 11.6 years and 49.9% were female and the mean age of the included 22,375 controls was 54.6 ± 16.2 years and 53.8% were female. Thirteen articles included CVD, eleven articles dementia, 21 articles DM and 18 articles respiratory disease. The group of CVD consisted of acute and chronic heart failure, heart failure with preserved ejection fraction and stroke.
Dementia included Alzheimer’s disease (mild and moderate) and cognitive impairment (unspecified and severe). The DM group included type 1 and 2 DM, latent autoimmune diabetes, DM with peripheral neuropathy, diabetic nephropathy and diabetic retinopathy (proliferative and non-proliferative). Respiratory diseases included chronic obstructive pulmonary disease (COPD) and restrictive lung disease.

Table 2 shows the sarcopenia prevalence and the applied definitions, including AWGS (17/63), Baumgartner (19/63), Delmonico (1/63), EWGSOP (2010) (18/63), FNIH (4/63), International Working Group for Sarcopenia (IWGS) (2/63), Janssen (2002 and 2004) (6/63), Japan Society of Hepatology (1/63), Newman (3/63) and Special Interest Group on cachexia-anorexia (SIG) (1/63). The parameters used in each definition of sarcopenia are given in Table A.3.

3.3. Quality assessment

Table A.4 shows the total NOS score and individual question scores for each included article. Eighteen studies were scored as high quality and forty-five studies were scored as low quality. The NOS includes four questions referring to controls. If an article did not include a control group, the ‘selection’, ‘comparability’ and ‘exposure’ criteria were not scored maximally.

3.4. Meta-analysis

Table 3 summarizes the prevalence of sarcopenia in disease groups (Fig. 2) and controls (Fig. 3) and the OR for being sarcopenic in diseased groups compared to controls (Fig. A.1). Nineteen out of 63 articles reported the prevalence of sarcopenia in both diseased cohorts (dementia, DM, respiratory disease) and controls. There were no articles reporting the prevalence of sarcopenia in CVD and controls. All disease groups had a higher prevalence of sarcopenia compared to their controls. Individuals with dementia had a sarcopenia prevalence of 26.4% (95% CI: 13.6–44.8%, I² = 94.6%) compared to a sarcopenia prevalence of 8.3% in controls (95% CI: 2.8–21.9%, I² = 97.0%; OR = 3.14, 95% CI: 1.51–6.55). In individuals with DM, sarcopenia was prevalent in 31.1% (95% CI: 19.8–45.2%, I² = 97.2%) compared to a prevalence of 16.2% in controls (95% CI: 9.5–26.2%, I² = 98.2%; OR = 2.07, 95% CI: 1.62–2.65). In individuals with respiratory disease, 26.8% (95% CI: 17.8–38.1%, I² = 96.8%) were diagnosed with sarcopenia compared 13.3% in controls (95% CI: 8.3–20.7%, I² = 88.4%; OR = 2.71, 95% CI: 2.03–3.62).

In articles without controls, the sarcopenia prevalence was 31.4% (95% CI: 22.4–42.1%, I² = 95.1%) in individuals with CVD, 27.4% (95% CI: 14.4–45.8%, I² = 95.3%) with dementia, 20.7% (95% CI: 14.5–28.7%, I² = 90.1%) with DM and 25.3% (95% CI: 16.8–36.5%, I² = 98.2%) with respiratory disease (Fig. 4, Table 3).

In individuals with CVD, sarcopenia prevalence was the highest when diagnosed with the AWGS definition (40.4%, 95% CI: 27.1–55.3%, I² = 94.6%) compared to the Baumgartner definition (22.3%, 95% CI: 15.4–31.2%, I² = 83.5%) and EWGSOP (20.7%, 95% CI: 9.3–39.8%, I² = 92.5%) (Fig. A.2). Dementia cohorts had the highest prevalence of sarcopenia when diagnosed using the AWGS definition (28.7%, 95% CI: 12.3–53.7%, I² = 96.9%) compared to the Baumgartner (24.1%, 95% CI: 10.5–46.3%, I² = 90.9%) and EWGSOP definitions (22.8%, 95% CI: 12.1–38.7%, I² = 22.8%) (Fig. A.3). In DM, the Janssen (2004) definition (78.6%, 95% CI: 61.3–89.4%, I² = 19.4%) yielded the highest prevalence of sarcopenia compared to the AWGS (16.5%, 95% CI: 14.3–18.9%, I² = 0.0%), Baumgartner (20.1%, 95% CI: 10.5–35.1%, I² = 87.3%), EWGSOP (42.4%, 95% CI: 23.7–63.5%, I² = 93.1%), Janssen (2002) (25.9%, 95% CI: 7.7–59.3%, I² = 98.7%) and other definitions (19.5%, 95% CI: 9.8–35.1%, I² = 71.3%) (Fig. A.4). In respiratory disease cohorts had the highest prevalence of sarcopenia when diagnosed by the AWGS definition (32.3%, 95% CI: 29.4–35.4%, I² = 34.3%) compared to the Baumgartner (32.2%, 95% CI: 14.8–56.6%, I² = 99.1%), EWGSOP (23.7%, 95% CI: 14.4–36.4%, I² = 96.6%) and other definitions (14.4%, 95% CI: 5.7–31.9%, I² = 89.5%) (Fig. A.5).

In individuals with CVD, sarcopenia was more prevalent in Asia (44.7%, 95% CI: 34.2–55.8%, I² = 92.1%) in comparison to Europe (15.5%, 95% CI: 10.8–21.6%, I² = 72.0%). Dementia cohorts also had the highest prevalence of sarcopenia in Asia (33.3%, 95% CI: 21.1–48.4%, I² = 95.0%) compared to Europe (12.6%, 95% CI: 3.5–36.5%, I² = 93.9%). In DM, sarcopenia was most prevalent in Asia...
| First author (year) | Continent | Setting | Disease | Age (y) | Sample size | Type | Age (y) | Sample size |
|---------------------|-----------|---------|---------|---------|-------------|------|---------|-------------|
|                     |           |         |         |         | N Female    |      |         | N Female    |
| **Cardiovascular disease** |           |         |         |         |             |      |         |             |
| Bekfani (2016)      | Europe    | OP      | HFpEF   | 69.8 ± 8.5 | 117 38      |      |         |             |
| dos Santos (2017)   | Europe    | NR      | CHF     | 68.8 ± 9.6 | 228 47      |      |         |             |
| Fulster (2013)      | Europe    | NR      | CHF     | 66.9 ± 10.6 | 200 41      |      |         |             |
| Harada (2017, a)    | Asia      | IP      | CVD     | 73.0 ± 12.0 | 132 52      |      |         |             |
| Harada (2017, b)    | Asia      | IP      | CVD     | 72.0 ± 12.0 | 322 135     |      |         |             |
| Izawa (2016, a)     | Asia      | OP      | CVD     | 70.8 ± 4.5  | 67 NA       |      |         |             |
| Izawa (2016, b)     | Asia      | OP      | CVD     | 70.9 ± 4.5  | 63 NA       |      |         |             |
| Onoue (2016)        | Asia      | IP      | CHF     | 76.1 ± 6.2  | 119 46      |      |         |             |
| Ryan (2017)         | N. America| CD      | Stroke  | 63.0 ± 13.8 | 190 74      |      |         |             |
| Shiraishi (2018)    | Asia      | IP      | Stroke  | 72.2 ± 12.5 | 202 95      |      |         |             |
| Tsuchida (2018)     | Asia      | IP      | CHF     | 75.0 ± 11.4 | 38 13       |      |         |             |
| Vahlberg (2016)     | Europe    | CD      | Stroke  | 74.0 ± 7.0  | 134 41      |      |         |             |
| Yashuda (2017)      | Asia      | IP      | CVD     | 76.2 ± 6.9  | 239 98      |      |         |             |
| **Dementia**        |           |         |         |         |             |      |         |             |
| Abellan van Kan (2013) | Europe      | CD | CI     | NR | 2533 2533  | Cog. healthy | NR | 492 492  |
| Chong (2015)        | Asia      | CD      | AD-Mild | 76.4 ± 6.9 | 68 44       |      |         |             |
| Papachristou (2015) | Europe    | CD      | SCI     | 78.9 ± 4.8 | 133 NA      |      |         |             |
| Sugimoto (2017)     | Asia      | OP      | AD      | 78.0 ± 6.0 | 208 135     |      |         |             |
| Sugimoto (2016)     | Asia      | OP      | AD      | 79.2 ± 5.9 | 343 234     |      |         |             |
| Gillette-Guyonnet (2000) | Europe | RC (DG) | AD | 81.5 ± 4.9 | 32 32       | Healthy | 81.6 ± 2.5 | 32 32       |
| Henwood (2017)      | Australia | RC     | Dementia | 82.4 ± 6.6 | 46 28       |      |         |             |
| Huang (2015)        | Asia      | CD      | Dementia | 73.4 ± 5.4 | 731 345     |      |         |             |
| Papachristou (2015) | Europe    | CD      | SCI     | 78.9 ± 4.8 | 133 NA      |      |         |             |
| Sugimoto (2017)     | Asia      | OP      | AD      | 78.0 ± 6.0 | 208 135     |      |         |             |
| Sugimoto (2016)     | Asia      | OP      | AD      | 79.2 ± 5.9 | 343 234     |      |         |             |
| Tay (2018)          | Asia      | CD      | AD-Mild | NR | 74 NA       |      |         |             |
| Tsugawa (2017)      | Asia      | OP      | AD      | 82.6 ± 5.1 | 106 63      |      |         |             |
| **Diabetes mellitus** |           |         |         |         |             |      |         |             |
| Aghili (2014)       | Asia      | NR      | DM-T2   | 52.7 ± 10.4 | 51 30       |      |         |             |
| Alptncar (2014)     | Asia      | NR      | DM      | 63.4 ± 7.7 | 32 NR       | Non-DM | 48.7 ± 22.1 | 34 NR       |
| Bittel (2017)       | N. America| OP      | DM-T2   | 55.0 ± 11.0 | 12 6        | Non-DM | 67.0 ± 6.0 | 10 5        |
| Bouchi (2017, a)    | Asia      | OP (DG) | DM-T2-PN | 64.0 ± 13.0 | 21 6        | Non-DM | 64.0 ± 8.0 | 41 19       |
| Bouchi (2017, b)    | Asia      | OP      | DM-T2   | 64.0 ± 11.0 | 312 127     |      |         |             |
| Bouchi (2017, c)    | Asia      | OP      | DM-T2-PN | 64.0 ± 11.0 | 238 93      |      |         |             |
| Celiker (2018)      | Asia      | OP (DG) | DM     | 61.7 ± 7.2 | 56 NR       | Healthy | 59.4 ± 6.5 | 53 NR       |
| Fukuda (2017)       | Asia      | OP      | DM-NDR  | 63.0 ± 12.0 | 261 97      |      |         |             |
| Ida (2017)          | Asia      | OP      | DM     | 71.9 ± 5.4 | 207 81      |      |         |             |
| Jansen (2015)       | Europe    | NR      | DM-COA  | 60.3 ± 8.4 | 29 6        |      |         |             |
| Kim (2014)          | Asia      | OP (DG) | DM-T2   | 71.2 ± 4.8 | 144 85      | Non-DM | 70.5 ± 5.0 | 270 140     |
| Kim (2010)          | Asia      | NR (DG) | DM-T2   | 58.9 ± 8.9 | 414 196     | Non-DM | 58.2 ± 10.5 | 396 244     |
| Koo (2016)          | Asia      | CD      | DM     | 57.0 ± 13.4 | 690 278     | Non-DM | 46.1 ± 15.5 | 12,102 6180 |
| Mori (2017)         | Asia      | OP      | DM-T1   | 55.7 ± 10.3 | 36 27       |      |         |             |
| Murata (2018)       | Asia      | OP      | DM-T2   | 73.3 ± 6.1 | 288 137     |      |         |             |
| Osaka (2018)        | Asia      | OP      | DM-T2   | 66.2 ± 11.6 | 285 126     |      |         |             |
| Tanaka (2015)       | Asia      | IP      | DM-T2   | 60.2 ± 12.5 | 191 NA      |      |         |             |
| Trierweiler (2018)  | S. America| OP      | DM-T2   | 65.8 ± 8.8 | 83 59       | Healthy | 65.9 ± 8.8 | 83 59       |
| Ucak (2018)         | Asia      | OP      | DM-T2   | 56.6 ± 11.5 | 98 NA       |      |         |             |
| Wang (2016)         | Asia      | CD (DG) | DM-T2   | 68.6 ± 7.1 | 236 120     | Healthy | 69.4 ± 7.2 | 854 450     |
| Yang (2016)         | Asia      | NR      | DM-T2   | 52.8 ± 10.8 | 762 261     | Non-DM | 51.7 ± 8.1 | 793 243     |
| **Respiratory disease** |           |         |         |         |             |      |         |             |
| Byun (2017)         | Asia      | OP      | COPD    | 68.4 ± 8.9 | 80 13       |      |         |             |
| Chung (2015)        | Asia      | CD      | COPD    | 54.6 ± 10.2 | 1039 279    | Healthy | 64.5 ± 9.6 | 6077 3731   |
| Costa (2018)        | S. America| OP      | COPD    | 67.9 ± 8.6 | 121 65      |      |         |             |
| Costa (2015)        | S. America| OP      | COPD    | 67.4 ± 8.7 | 91 50       |      |         |             |
| di Gregorio (2018)  | Europe    | IP      | COPD    | 69.8 ± 8.0 | 263 NR      |      |         |             |

(continued on next page)
Table 1 (continued)

| First author (year) | Continent | Setting | Disease | Age (y) | Sample size | Control |
|---------------------|-----------|---------|---------|---------|-------------|---------|
|                     |           |         |         | N       | Female      | Type    | Age (y) | Sample size |
| Gologanu (2014)     | Europe    | NR      | COPD    | 65.6 ± 7.5 | 36 3       | NA      |
| Hwang (2016)        | Asia      | CD      | COPD    | 63.9 ± 10.6 | 777 NA     | NA      |
| Jones (2015)        | Europe    | OP      | COPD    | 70.4 ± 9.7  | 622 268    | NA      |
| Joppa (2016)        | Europe    | NR      | COPD    | 63.5 ± 7.1  | 2000 686   | NA      |
| Kneppers (2017)     | Europe    | NR      | COPD    | 62.0 ± 7.6  | 92 31      | NA      |
| Koo (2014)          | Asia      | CD      | COPD    | 64.0 ± 14.4 | 574 NA     | NA      |
| Lee (2017)          | Asia      | CD      | COPD    | 65.8 ± 8.0  | 748 173    | NA      |
| Lee (2016)          | Asia      | CD      | COPD    | 65.9 ± 7.9  | 858 217    | NA      |
| Limpawattana (2017) | Asia      | OP      | COPD    | 70.0 ± 9.0  | 121 9      | NA      |
| Pothirat (2016)     | Asia      | OP      | COPD    | 75.7 ± 5.3  | 40 NA      | Healthy 77.7 ± 7.0 | 46 NA | Non-COPD 52 17 | NA |
| van de Boil (2016)  | Europe    | OP      | COPD    | 64.0 (3.0-87.0) | 505 217   | NA      |
| van de Boil (2015)  | Europe    | NR      | COPD    | 64.0 (3.0-87.0) | 505 217   | NA      |

Age data are presented as: mean ± SD or median (range).

ACOS = asthma-COPD overlap syndrome, AD = Alzheimer’s disease, AD-Mild = mild AD, AD-Mod = moderate AD, CD = community-dwelling, CG = control group, CHF = chronic heart failure, CI = cognitive impairment, Cog. healthy = cognitively healthy, COPD = chronic obstructive pulmonary disease, DM-COA = Charcot osteoarthropathy, DM-COA = Charcot osteoarthropathy, DM-NDR = non-diabetic retinopathy, DM-T1 = type-1 DM, DM-T2 = type-2 DM, DM-T2-PN = DM-T2 with peripheral neuropathy, HFpEF = heart failure with preserved ejection fraction, IP = inpatient, LAD = left autoimmune diabetes, S. America = South America, SCI = severe CI.

4. Discussion

The prevalence of sarcopenia is significantly higher in individuals with dementia, DM and respiratory disease compared to individuals without these diseases, irrespective of the applied definition of sarcopenia. The highest prevalence of sarcopenia was found in individuals with COPD compared to individuals with dementia, DM and respiratory disease.

Sarcopenia shares many risk factors with CVD, dementia, DM and respiratory disease, such as sedentary behaviour, low physical activity, inflammation, malnutrition and various other mechanisms, which might explain the higher prevalence of sarcopenia in individuals with these age-related diseases.

4.1. Sedentary behaviour and physical activity

Sedentary behaviour is a form of physical inactivity defined as performing insufficient amounts of physical activity (Gonzalez et al., 2017) associated with low energy expenditure (Pate et al., 2008). Low physical activity is highly prevalent in older adults (Watson et al., 2016) and older adults may spend an average of 10 h per day in sedentary behaviour (Fitzgerald et al., 2015), which is a known risk factor of sarcopenia (Dennison et al., 2017). With each one hour increment of daily sitting time, community-dwelling older adults are 33% more likely to develop sarcopenia (Gianoudis et al., 2015). A sedentary lifestyle is also a risk factor of sarcopenia and CVD (Bekiani et al., 2016; Lee et al., 2012), dementia (Burns et al., 2019), DM (Lee et al., 2012) and respiratory diseases (Pothisrat et al., 2016), which may partly explain why sarcopenia is more prevalent in individuals with these diseases.

Individuals may also experience a more sedentary lifestyle as a result of CVD, dementia, DM and respiratory diseases. Individuals with CVD, e.g. chronic heart failure, experience a lower level of exercise capacity (Fulster et al., 2013), leading to more physical activity (Brunjes et al., 2017). Individuals with dementia spend up to 72% of their day in sedentary behaviour (van Alphen et al., 2016) and individuals with DM spend an average of 9 h a day in sedentary behaviour (Mathe et al., 2017). Individuals with respiratory disease have increased energy expenditure due to enhanced expiration and also experience physical inactivity caused by exercise intolerance (Pothisrat et al., 2016).

4.2. Inflammation

Systemic inflammation is common at higher age (Franceschi and Campisi, 2014) and especially in individuals with age-related diseases (Guo et al., 2015). Interleukin-6, a widely studied inflammatory marker, is common in the pathogenesis of many age-related diseases, including DM and Alzheimer’s disease (Franceschi and Campisi, 2014; Maggio et al., 2006). Furthermore, systemic inflammation has been associated with lower levels of muscle mass and strength (Londhe and Guttridge, 2015; van Attevelde et al., 2019), particularly in older adults, potentially through oxidative stress increasing the activation of catabolic processes (Dalle et al., 2017). Higher lipid levels lead to cell stress and apoptosis which could lead to inflammation and the inflammation damages blood vessels and may cause atherosclerosis, a precursor to CVD (Golia et al., 2014). Beta-amyloid and tau proteins, thought to be the cause of Alzheimer’s disease, cause glial cells to produce inflammatory mediators which cause synaptic loss (Maggio et al., 2006). Type-2 DM may be caused by inflammation as low-grade inflammation may cause insulin resistance leading to type-2 DM (Lontchi-Yimagou et al., 2013). Smoking is strongly associated with COPD as it triggers an inflammatory immune response due to inhaled toxins, which contributes to the development of COPD (Racanelli et al., 2018). As
Table 2
Sarcopenia prevalence by disease groups.

| First author (year) | Sarcopenia definition | Sarcopenia prevalence | Controls |
|---------------------|-----------------------|-----------------------|----------|
|                     | Disease               | Total n (%) | Female n (%) | Male n (%) | Female n (%) | Male n (%) |
| Cardiovascular disease |                       |              |              |            |              |            |
| Bekfani (2016)      | Baumgartner HFpEF     | 23 (19.7)    | 3 (7.9)      | 20 (25.3)  | NA           |
| dos Santos (2017)   | Baumgartner CHF       | 37 (16.2)    | 1 (2.1)      | 36 (19.9)  | NA           |
| Fulster (2013)      | Baumgartner CHF       | 39 (19.5)    | 2 (4.9)      | 37 (23.3)  | NA           |
| Harada (2017, a)    | AWGS CVD              | 29 (26.0)    | 35 (40.0)    | 13 (16.3)  | NA           |
| Harada (2017, b)    | AWGS CVD              | 28 (28.0)    | 56 (41.5)    | 34 (28.2)  | NA           |
| Izzawa (2016, a)    | EWGSOP CVD            | 25 (37.3)    | NA           | 25 (37.3)  | NA           |
| Izzawa (2016, b)    | EWGSOP CVD            | 24 (38.1)    | NA           | 24 (38.1)  | NA           |
| Onoue (2016)        | NA HF                 | 82 (68.9)    | 29 (62.0)    | 53 (72.6)  | NA           |
| Ryan (2017)         | Baumgartner Stroke    | 32 (16.8)    | 12 (16.2)    | 20 (17.2)  | NA           |
|                     | EWGSOP Stroke         | 27 (14.3)    | 14 (18.9)    | 13 (11.2)  | NA           |
|                     | IWGS Stroke           | 32 (16.7)    | 16 (21.6)    | 16 (13.8)  | NA           |
|                     | FNHI Stroke           | 34 (17.9)    | 7 (9.5)      | 27 (23.3)  | NA           |
| Shiraiishi (2018)   | AWGS Stroke           | 108 (53.5)   | 47 (49.5)    | 61 (57.0)  | NA           |
| Tsuchida (2018)     | 2SD < young ref.      | 20 (52.6)    | 4 (30.8)     | 16 (64.0)  | NA           |
| Vahlberg (2016)     | EWGSOP Stroke         | 9 (7.0)      | NR           | NR         | NA           |
| Yasuda (2017)       | AWGS CVD              | 126 (52.7)   | 59 (60.2)    | 67 (47.5)  | NA           |
| Dementia            |                       |              |              |            |              |            |
| Abellan van Kan (2013)| Baumgartner CI       | 43 (10.3)    | NR           | NR         | 240 (10.4)   | NR         |
|                     | Delmonico CI          | 71 (17.5)    | NR           | NR         | 438 (19.0)   | NR         |
|                     | Newman CI             | 62 (15.1)    | NR           | NR         | 362 (15.7)   | NR         |
|                     | IWGS CI               | 64 (15.3)    | NR           | NR         | 326 (14.0)   | NR         |
|                     | SIG CI                | 22 (5.4)     | NR           | NR         | 67 (2.9)     | NR         |
|                     | EWGSOP CI             | 28 (6.7)     | NR           | NR         | 114 (4.9)    | NR         |
| Chong (2014)        | Baumgartner AD-Mild   | 19 (31.6)    | NR           | NR         | NA           |
|                     | AD-Mod                | 3 (23.1)     | NR           | NR         | NA           |
|                     | EWGSOP AD-Mild        | 21 (35.1)    | NR           | NR         | NA           |
|                     | EWGSOP AD-Mod         | 4 (30.8)     | NR           | NR         | NA           |
| Chong (2015)        | AWGS AD-Mild          | 32 (47.1)    | NR           | NR         | 49 (24.6)    | NR         |
|                     | AD-Mod                | 9 (60.0)     | NR           | NR         | NA           |
| Gillette-Guyonnet (2000) | Baumgartner AD       | 13 (40.6)    | 13 (40.6)    | 7 (21.9)   | 7 (21.9)     | NA         |
| Henwood (2017)      | EWGSOP Dementia       | 5 (11.4)     | NR           | NR         | NA           |
| Huang (2015)        | AWGS Dementia         | 50 (6.8)     | 14 (4.1)     | 36 (9.3)   | NA           |
| Papachristos (2015) | EWGSOP Dementia       | 8 (7.5)      | NA           | 8 (7.5)    | 11 (1.5)     | NA         |
|                     | FNHI Dementia         | 6 (5.7)      | NA           | 6 (5.7)    | 13 (1.8)     | NA         |
| Sugiimoto (2017)    | AWGS AD               | 38 (18.3)    | NR           | NR         | NA           |
| Sugiimoto (2016)    | EWGSOP AD             | 80 (23.3)    | NR           | NR         | 3 (8.6)      | NR         |
| Tay (2018)          | EWGSOP AD-Mild        | 37 (50.0)    | NR           | NR         | NA           |
|                     | AD-Mod                | 10 (71.4)    | NR           | NR         | NA           |
| Tsugawa (2017)      | AWGS AD               | 40 (37.7)    | 24 (38.1)    | 16 (37.2)  | NA           |
| Diabetes mellitus |                       |              |              |            |              |            |
| Aghili (2014)       | Baumgartner DM-T2     | 1 (2.0)      | NR           | NR         | NA           |
|                     | Janssen CI (2002)     | DM-T2        | NR           | NR         | NA           |
|                     | Janssen CI (2002)     | DM-T2        | 0 (0.0)      | 0 (0.0)    | 0 (0.0)      | NA         |
| Alpinar (2014)      | MM 2SD < young ref.   | DM-T2        | 0 (0.0)      | NR         | 2 (5.9)      | NR         |
|                     | MS 2SD < young ref.   | DM-T2        | 4 (12.5)     | NR         | 5 (14.7)     | NR         |
| Bittel (2017)       | Janssen (2004)        | DM-T2        | 10 (83.0)    | NR         | 6 (60.0)     | NR         |
|                     | DM-T2-PN              | 16 (76.0)    | NR           | NR         | NA           |
| Bouchi (2017, a)    | AWGS DM-T2            | 28 (13.3)    | NR           | 4 (9.8)    | NR           |
|                     | LADA                  | 7 (35.0)     | NR           | NR         | NA           |
| Bouchi (2017, b)    | AWGS DM-T2            | 56 (17.0)    | NR           | NR         | NA           |
| Bouchi (2017, c)    | AWGS DM-T2            | 42 (17.7)    | 18 (19.8)    | 24 (16.6)  | NA           |
| Celiker (2018)      | EWGSOP DM             | 12 (21.4)    | NR           | 8 (15.1)   | NR           |
|                     | DM-Nu                 | 17 (34.0)    | NR           | NR         | NA           |
| Fukuda (2017)       | Low MM + low MS       | DM-NDR       | 40 (15.5)    | NR         | NR           |
|                     | DM-NDR                | 8 (20.7)     | NR           | NR         | NA           |
|                     | DM-PDR                | 7 (40.0)     | NR           | NR         | NA           |
| Ida (2017)          | EWGSOP DM             | 41 (19.8)    | 23 (28.4)    | 18 (14.3)  | NA           |
| Jansen (2015)       | Baumgartner DM-COA    | 5 (17.2)     | NR           | NR         | NA           |
|                     | DM-COA                | 5 (17.2)     | NR           | NR         | NA           |
|                     | DM-Nu                 | 1 (11.1)     | NR           | NR         | NA           |
| Kim (2014)          | Baumgartner DM-T2     | 40 (27.8)    | 6 (7.1)      | 34 (57.6)  | 66 (24.4)    | 12 (8.57)  |
|                     | Janssen (2002)        | DM-T2        | 36 (25.0)    | 22 (25.9)  | 14 (23.7)    | 37 (13.7)  |
|                     | Janssen (2002)        | DM-T2        | 57 (39.6)    | 28 (32.9)  | 29 (49.2)    | 54 (20.0)  |
| Kim (2010)          | Janssen (2002)        | DM-T2        | 65 (15.7)    | NR         | 27 (6.9)     | NR         |

(continued on next page)
inflammation plays a role in muscle health (i.e. muscle mass and strength) and the development of age-related diseases, this may explain why sarcopenia is more prevalent as a comorbid disease.

4.3. Malnutrition

Malnutrition is a condition which is common in older adults, particularly protein-energy malnutrition (Agarwal et al., 2013). About 10% of older adults do not have a sufficient protein intake to meet the nutritional recommendations which may lead to a decline in muscle mass (Cruz-Jentoft et al., 2017). As such, malnutrition can lead to sarcopenia, but they also often co-occur in individuals (Reijnierse et al., 2015a; Vandewoude et al., 2012). Cognitivedecline and dementia have been associated with malnutrition (Favaro-Moreira et al., 2016) due to a reduced intake (Volkert et al., 2015). Malnutrition is also very common in individuals with COPD (Raad et al., 2019) mainly due to

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Table 2 (continued)

| First author (year) | Sarcopenia definition | Sarcopenia prevalence |
|---------------------|-----------------------|-----------------------|
| Koo (2016)          | Janssen CI (2002)     | DM 450 (66.0) NR NR   |
| Mor (2017)          | Janssen C2 (2002)     | DM-T1 6 (16.7) 6 (22.2) 0 (0.0) NA |
| Murata (2018)       | AWGS                  | DM-T2 44 (15.3) 21 (15.3) 23 (15.2) NA |
| Osaka (2018)        | Japan Society of Hepatology | DM-T2 25 (8.8) 17 (13.5) 8 (5.0) NA |
| Tanaka (2015)       | EWGSOP                | DM-T2 85 (44.5) NA 85 (44.5) NA |
| Trierweiler (2018)  | FNIH                  | DM-T2 13 (15.7) 9 (15.3) 4 (16.7) 2 (2.4) 0 (0.0) 2 (8.3) |
| Ucak (2018)         | EWGSOP                | DM-T2 99 (78.0) NA 97 (99.0) NA |
| Wang (2016)         | AWGS                  | DM-T2 35 (14.8) 15 (12.5) 20 (17.2) 96 (11.2) 43 (9.6) 53 (13.1) |
| Yang (2016)         | Baumgartner           | DM-T2 342 (44.9) 117 (44.8) 225 (44.9) 208 (26.2) 64 (26.3) 144 (26.2) |

Respiratory diseases

Byun (2017)  | EWGSOP  | COPD  | 20 (25.0) 3 (23.1) 17 (25.4) 566 (9.2) 175 (4.9) 381 (16.2) |
| Chung (2015)  | Baumgartner | COPD  | 283 (27.2) 34 (12.2) 249 (32.8) NA |
| Costa (2015)  | Baumgartner | COPD  | 37 (40.7) NR NR NA |
| Costa (2018)  | FNIH  | COPD  | 15 (12.4) NR NR NA |
| Di Gregorio (2018)  | EWGSOP  | COPD  | 63 (24.2) NR NR NA |
| Gologanu (2014) | Low MM + high BMI | COPD  | 3 (8.3) NR NR NA |
| Hwang (2017)  | Baumgartner | COPD  | 41 (5.3) NA 41 (5.3) NA |
| Jones (2015)  | EWGSOP  | COPD  | 90 (14.5) 33 (12.3) 57 (16.1) NA |
| Joppa (2016)  | NA  | COPD  | 682 (34.1) 173 (25.2) 509 (38.7) 55 (10) NR NR |
| Kneppe (2017)  | BAUMGARTNER | COPD  | 39 (42.4) 10 (32.3) 29 (47.5) NA |
| Koo (2014)  | 1SD < young ref. | COPD  | 155 (27.0) NA 155 (27.0) NA |
| Lee (2016)  | AWGS  | COPD  | 286 (33.3) 60 (27.7) 226 (35.3) NA |
| Lee (2017)  | AWGS  | COPD  | 251 (33.6) 48 (28.7) 203 (35.3) NA |
| Limpawattana (2017)  | AWGS  | COPD  | 35 (31.8) 12 (27.3) 23 (43.8) NA |
| Lipton (2016)  | Low MM + high BMI | COPD  | 12 (9.9) NR NR NA |
| Sergi (2006)  | Baumgartner | COPD  | 15 (38) NA 15 (38) 14 (31) NA 14 (31) |
| van de Boul (2016)  | Baumgartner | COPD  | 14 (31.1) 1 (6.25) 3 (44.8) 3 (5.8) 0 (0.0) 3 (8.6) |
| van de Boul (2015)  | Baumgartner | COPD  | 437 (86.5) 198 (91.2) 239 (83.0) NA |

ACOS: asthma-COPD overlap syndrome, AD: Alzheimer’s disease, AD-Mild: mild AD, AD-Mod: moderate AD, CHF: chronic heart failure, CI: cognitive impairment, COPD: chronic obstructive pulmonary disease, CVD: cardiovascular disease, DM: diabetes mellitus, DM-COA: Charcot osteoarthropathy, DM-NDR: non-diabetic retinopathy, DM-Ne: diabetic nephropathy, DM-NPDR: non-proliferative diabetic retinopathy, DM-Nu: diabetic neuropathy, DMPDR: proliferative diabetic neuropathy, DM-T1: type-1 DM, DM-T2: type-2 DM, DM-T2-PN: DM-T2 with peripheral neuropathy, EWGSOP: European Working Group for Sarcopenia in Older People, FNIH: Foundation for the National Institutes of Health, HFpEF: heart failure with preserved ejection fraction, IWGS: International Working Group for Sarcopenia in Older People, LADA: latent autoimmune diabetes, NA: not applicable, NR: not reported, RLD: restrictive lung disease, SCI: severe CI, SIG: Special Interest Group on cachexia-anorexia.

* There was no stratification for Janssen (2002) classes in this article.

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ACOS = asthma-COPD overlap syndrome, AD = Alzheimer’s disease, AD-Mild = mild AD, AD-Mod = moderate AD, CHF = chronic heart failure, CI = cognitive impairment, COPD = chronic obstructive pulmonary disease, CVD = cardiovascular disease, DM = diabetes mellitus, DM-COA = Charcot osteoarthropathy, DM-NDR = non-diabetic retinopathy, DM-Ne = diabetic nephropathy, DM-NPDR = non-proliferative diabetic retinopathy, DM-Nu = diabetic neuropathy, DM-PDR = proliferative diabetic neuropathy, DM-T1 = type-1 DM, DM-T2 = type-2 DM, DM-T2-PN = DM-T2 with peripheral neuropathy, EWGSOP = European Working Group for Sarcopenia in Older People, FNIH = Foundation for the National Institutes of Health, HFpEF = heart failure with preserved ejection fraction, IWGS = International Working Group for Sarcopenia, LADA = latent autoimmune diabetes, NA = not applicable, OR = odds ratios.
insufficient protein and energy intake due to the higher requirements, putting patients at risk for sarcopenia (Nguyen et al., 2019).

4.4. Relevance of diagnosing sarcopenia

Sarcopenia was only recently given an ICD-10 code (M62.84) and as such is newly recognised as a disease. It is important to diagnose and intervene sarcopenia due to its associations with a plethora of health outcomes such as cognitive impairment (Chang et al., 2016), loss of dependence (Beaudart et al., 2017), fractures (Yeung et al., 2019), fractures (Yeung et al., 2019) and mortality (Beaudart et al., 2017). Typical sarcopenia interventions consist of exercise and nutrition-based interventions.

Resistance exercise training (RET) is a commonly used exercise intervention in treating sarcopenia (Kamleh et al., 2019). Furthermore, nutritional interventions, such as protein, creatine and β-hydroxy-β-methylbutyric acid supplementation, are also effective in increasing muscle mass in older adults (Martin-Cantero et al., 2019) and combined RET and protein supplementation have been shown to enhance the effectiveness in increasing muscle mass and muscle strength (Liao et al., 2017). However, comorbidities such as CVD, dementia, DM and respiratory diseases may interfere with these interventions. Individuals with CVD and respiratory diseases have increased exercise intolerance (Fulster et al., 2013; Pothirat et al., 2016) and would potentially be unable to complete rigorous RET. Individuals with dementia need adapted protocols to comply with the intensity and load of a RET or dietary plan.

A multifaceted intervention, i.e. exercise training and nutritional intervention, can not only treat sarcopenia but potentially also prevent the occurrence of sarcopenia (Cruz-Jentoft et al., 2019). As the present review indicates that sarcopenia is more prevalent when present alongside diseases, there is the need for future research to develop...
tailored interventions when sarcopenia is present as a comorbid disease.

4.5. Sarcopenia prevalence in controls

The sarcopenia prevalence varied between 8.3% and 16.2%, which is comparable to prevalence rates reported in an earlier review including community-dwelling populations (Cruz-Jentoft et al., 2014).

4.6. Strengths and limitations

This is the first review systematically determining the prevalence of sarcopenia in the major age-related diseases CVD, dementia, DM and respiratory disease. In the absence of a worldwide accepted definition of sarcopenia (Suetta and Maier, 2019), all definitions of sarcopenia were included, allowing for the inclusion of all studies. A limitation of this, however, is that the differences between definitions may have contributed to a higher heterogeneity of the meta-analyses results. Stratification for sarcopenia definition reduced the heterogeneity values while maintaining a higher prevalence of sarcopenia in the disease groups than the controls. Articles which studied dynapenia (age-related low muscle strength) (Chang et al., 2018) and muscle failure (Sueta and Maier, 2019) were excluded from the search, as they are different from sarcopenia (age-related low muscle mass and strength).

The heterogeneity could also be influenced by differences in the study setting and disease severity. It can also not be excluded that included participants in specific disease groups suffered from other diseases than the disease of interest, which might have overestimated the sarcopenia prevalence.

5. Conclusion

Sarcopenia is highly prevalent as a comorbid disease in individuals with CVD, dementia, DM and respiratory disease, which highlights the need to screen and diagnose sarcopenia.

Future research should investigate if individuals with sarcopenia as a comorbid disease experience worse health outcomes than their non-sarcopenic counterparts. Furthermore, it should be determined if sarcopenia as a comorbid disease require specific tailored interventions taking the index disease into account.
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Appendix A

Table A.1
Search strategy.

| Number | Search (MEDLINE (Ovid))                                      |
|--------|-------------------------------------------------------------|
| 1      | muscle weakness/ or muscular atrophy/ or sarcopenia/       |
| 2      | (sarcopenia or “muscular atrophy” or “muscle weakness” or “muscular weakness”).ti,ab. |
| 3      | 1 or 2                                                      |
| 4      | (“cardiovascular disease”” or (CVD and cardiovascular) or “myocardial infarction” or (MI and infarction) or (AMI and infarction) or “congestive heart failure” or “congestive cardiac failure” or stroke or “ischaemic heart disease” or (IHD and ischaemic) or “coronary heart disease” or (CHD and coronary) or “hypertensive heart disease”).ti,ab. |
| 5      | exp Cardiovascular Diseases/                               |
| 6      | 4 or 5                                                      |
| 7      | (“respiratory tract disease”” or “lung disease”” or asthma or “chronic obstructive pulmonary disease” or (COPD and pulmonary) or “interstitial lung disease” or (ILD and interstitial) or “chronic bronchitis”).ti,ab. |
| 8      | exp Respiratory Tract Diseases/                            |
| 9      | 7 or 8                                                      |
| 10     | (dementia or “Alzheimer’s disease” or (AD and Alzheimer’s) or “vascular dementia” or (VaD and dementia) or “Lewy Body dementia” or “Lewy Body disease” or “Lewy Body”).ti,ab. |
| 11     | exp DEMENTIA/                                               |
| 12     | 10 or 11                                                    |
| 13     | diabet*.ti,ab.                                             |
| 14     | exp DIABETES MELLITUS/                                     |
| 15     | 13 or 14                                                   |
| 16     | 6 or 9 or 12 or 15                                         |
| 17     | 3 and 16                                                   |
| 18     | (case report” or editorial or letter or review”).pt.       |
| 19     | 17 not 18                                                  |
| 20     | limit 19 to English language                               |

| Number | Search (EMBASE (Ovid))                                      |
|--------|-------------------------------------------------------------|
| 1      | “muscle weakness/ or “muscular atrophy” or sarcopenia/     |
| 2      | (sarcopenia or “muscular atrophy” or “muscle weakness” or “muscular weakness”).ti,ab. |
| 3      | 1 or 2                                                      |
| 4      | (“cardiovascular disease”” or (CVD and cardiovascular) or “myocardial infarction” or (MI and infarction) or (AMI and infarction) or “congestive heart failure” or “congestive cardiac failure” or stroke or “ischaemic heart disease” or (IHD and ischaemic) or “coronary heart disease” or (CHD and coronary) or “hypertensive heart disease”).ti,ab. |
| 5      | exp Cardiovascular Diseases/                               |
| 6      | 4 or 5                                                      |
| 7      | (“respiratory tract disease”” or “lung disease”” or asthma or “chronic obstructive pulmonary disease” or (COPD and pulmonary) or “interstitial lung disease” or (ILD and interstitial) or “chronic bronchitis”).ti,ab. |
| 8      | exp Respiratory Tract Diseases/                            |
| 9      | 7 or 8                                                      |
| 10     | (dementia or “Alzheimer’s disease” or (AD and Alzheimer’s) or “vascular dementia” or (VaD and dementia) or “Lewy Body dementia” or “Lewy Body disease” or “Lewy Body”).ti,ab. |
| 11     | exp DEMENTIA/                                               |
| 12     | 10 or 11                                                    |
| 13     | diabet*.ti,ab.                                             |
| 14     | exp DIABETES MELLITUS/                                     |
| 15     | 13 or 14                                                   |
| 16     | 6 or 9 or 12 or 15                                         |
| 17     | 3 and 16                                                   |
| 18     | (case report” or editorial or letter or review”).pt.       |
| 19     | 17 not 18                                                  |
| 20     | limit 19 to English language                               |
| 21     | limit 20 to conference abstract status                     |
| 22     | 20 not 21                                                  |

| Number | Search (Cochrane (Ovid))                                      |
|--------|-------------------------------------------------------------|
| 1      | muscle weakness/ or muscular atrophy/ or sarcopenia/       |
| 2      | (sarcopenia or “muscular atrophy” or “muscle weakness” or “muscular weakness”).ti,ab. |
| 3      | 1 or 2                                                      |
| 4      | (“cardiovascular disease”” or (CVD and cardiovascular) or “myocardial infarction” or (MI and infarction) or (AMI and infarction) or “congestive heart failure” or “congestive cardiac failure” or stroke or “ischaemic heart disease” or (IHD and ischaemic) or “coronary heart disease” or (CHD and coronary) or “hypertensive heart disease”).ti,ab. |
| 5      | exp Cardiovascular Diseases/                               |
| 6      | 4 or 5                                                      |

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Table A.1 (continued)

| Number | Search (Cochrane (Ovid)) |
|--------|--------------------------|
| 7      | (“respiratory tract disease” or “lung disease” or asthma or “chronic obstructive pulmonary disease” or (COPD and pulmonary) or “interstitial lung disease” or (ILD and interstitial) or “chronic bronchitis”).ti,ab. |
| 8      | exp Respiratory Tract Diseases/ |
| 9      | 7 or 8 |
| 10     | (dementia or “Alzheimer’s disease” or (AD and Alzheimer’s) or “vascular dementia” or (VaD and dementia) or “Lewy Body dementia” or “Lewy Body disease” or “Lewy Body” or (DLB or Lewy)).ti,ab. |
| 11     | exp DEMENTIA/ |
| 12     | 10 or 11 |
| 13     | diabet*.ti,ab. |
| 14     | exp DIABETES MELLITUS/ |
| 15     | 13 or 14 |
| 16     | 6 or 9 or 12 or 15 |
| 17     | 3 and 16 |
| 18     | (case report* or editorial or letter or review*).pt. |
| 19     | 17 not 18 |
| 20     | limit 19 to English language |

Table A.2
Newcastle-Ottawa Scale.

Selection
1. Is the case definition (participant with diabetes, dementia, cardiovascular or respiratory diseases) adequate?
   a. Yes, validated diagnostic criteria or clinical diagnosis
   b. Yes, e.g. record linkage or based on self-reports
   c. No description
2. Representativeness of the cases
   a. Consecutive or obviously representative series of cases
   b. Potential for selection bias or not stated
3. Selection of Controls
   a. Community controls
   b. Hospital controls without disease of cases
   c. No description
   d. No control
4. Definition of Controls
   a. No history of disease of the cases
   b. No description of the source
   c. No control

Comparability
1. Comparability of cases and controls on the basis of the design or analysis
   a. Study controls for age (within 5 years)
   b. Study controls for sex (within 10%)
   c. No control

Exposure
1. Ascertainment of exposure (sarcopenia)
   a. Defined diagnostic criteria (EWGSOP, AWGS, IWGS, Baumgartner, Janssen, etc.)
   b. Non-defined diagnostic criteria
   c. Non-objective measure of sarcopenic parameters
   d. No description
2. Same method of ascertainment for cases and controls
   a. Yes
   b. No
   c. No control

Table A.3
Sarcopenia definitions and their parameters with cut-off values used in included articles.

| First author (year) | Sarcopenia definition | Assessment method/cut-off values |
|---------------------|-----------------------|----------------------------------|
| Baumgartner         |                       | Muscle Mass | Muscle strength | Physical performance |
| Bekfani (2016)      |                       | DXA M ASMI < 7.26 kg/m² | NA | NA | NA |
| dos Santos (2017)   |                       | DXA M ASMI/m² ≤ NR | NA | NA | NA |
| Fulster (2013)      |                       | DXA M SMI < 7.26 kg/m² | NA | NA | NA |
| Harada (2017, a)    | AWGS                  | BIA M SMI < 7.0 kg/m² | HGS < 26.0 kg | 10 m-walk < 0.8 m/s |
| Harada (2017, b)    | AWGS                  | DXA M SMI < 7.0 kg/m² | HGS < 26.0 kg | 10 m-walk < 0.8 m/s |
|                     |                       | F SMI < 5.4 kg/m² | < 18.0 kg | < 0.8 m/s |

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### Table A.3 (continued)

| First author (year) | Sarcopenia definition | Assessment method/cut-off values | Muscle Mass | Muscle strength | Physical performance |
|---------------------|-----------------------|----------------------------------|-------------|-----------------|----------------------|
| Izawa (2016, a)     | EWGSOP                | BIA M                            | HGS < 30 kg | 10 m-walk       | NR                   |
| Izawa (2016, b)     | EWGSOP                | BIA M                            | HGS NR      | 10 m-walk       | NR                   |
| Onoue (2016)        | NA                    | NA                               | NA          | NA              | NA                   |
| Ryan (2017)         | Baumgartner           | DXA M                            | ALM/h² < 7.26 kg/m² | NA                   | NA                   |
|                     |                       | F                                | ALM/h² < 5.45 kg/m² | 6-minute walk < 0.8 m/s | NA                   |
|                     | EWGSOP                | DXA M                            | ALM/h² < 7.23 kg/m² | NA                   | 6-minute walk < 1.0 m/s |
|                     | IWGS                  | DXA M                            | ALM/h² < 5.67 kg/m² | NA                   | NA                   |
|                     | FNIH                  | DXA M                            | ALM/BMI < 0.512 | NA                   | NA                   |
| Shirasaki (2018)    | AWGS                  | BIA M                            | SMI < 7.0 kg/m² | NA                   | NA                   |
|                     |                       | F                                | SMI < 5.7 kg/m² | 6-minute walk < 1.0 m/s |
| Tsuchida (2018)     | Baumgartner           | DXA M                            | SMI < 6.87 kg/m² | NA                   | NA                   |
| Vahlberg (2016)     | EWGSOP                | BIA M                            | ASMI < 7.0 kg/m² | HGS < 26.0 kg      | 4 m-walk < 0.8 m/s   |
|                     |                       | F                                | ASMI < 5.7 kg/m² | 6-minute walk < 0.8 m/s |
| Dementia            | Abellian van Kan (2013)| Baumgartner         | DXA F               | HGS < 26.0 kg      | 4 m-walk < 1.0 m/s   |
|                     |                       | F                                | HGS < 18.0 kg      | 10 m-walk < 1.0 m/s |
|                     | Gillette-Guyonnet (2000)| Baumgartner       | DXA F               | HGS < 26.0 kg      | 4 m-walk < 1.0 m/s   |
|                     |                       | F                                | HGS < 18.0 kg      | 10 m-walk < 1.0 m/s |
|                     | Henwood (2017)        | EWGSOP                          | ASMI ≤ 2SD < control | NA                   | NA                   |
|                     |                       | F                                | ASMI ≤ 2SD < control | NA                   | NA                   |
|                     | Huang (2015)          | AWGS                            | ASMI ≤ 37%         | NA                   | NA                   |
|                     |                       | F                                | ASMI ≤ 28%         | 6 m-walk < 1.0 m/s   |
|                     | Papachristos (2015)   | EWGSOP                          | ASMI < 7.23 kg/m²  | HGS < 26.0 kg      | 4 m-walk < 0.8 m/s   |
|                     |                       | F                                | ASMI < 5.4 kg/m²   | 6 m-walk < 0.8 m/s   |
|                     | Sugimoto (2017)       | AWGS                            | ASMI < 7.0 kg/m²   | HGS < 26.0 kg      | Timed Up and Go > 14 s |
|                     |                       | F                                | ASMI < 5.4 kg/m²   | 6 m-walk < 0.8 m/s   |
|                     | Sugimoto (2016)       | EWGSOP                          | ASMI < 7.0 kg/m²   | HGS < 26.0 kg      | Timed Up and Go < 13.56 s |
|                     |                       | F                                | ASMI < 5.4 kg/m²   | 6 m-walk < 0.8 m/s   |
|                     | Tay (2018)            | EWGSOP                          | ASMI < 7.0 kg/m²   | HGS < 26.0 kg      | NA                   |
|                     |                       | F                                | ASMI < 5.4 kg/m²   | NA                   |
|                     | Tsugawa (2017)        | AWGS                            | ASMI < 7.0 kg/m²   | HGS < 26.0 kg      | 6 m-walk < 0.8 m/s   |
|                     |                       | F                                | ASMI < 5.7 kg/m²   | 6 m-walk < 0.8 m/s   |
| Diabetes mellitus   | Aghili (2014)         | Baumgartner         | DXA M              | ASMI < 7.26 kg/m²  | 10 m-walk < 1.0 m/s  |
|                     |                       | F                                | ASMI < 5.45 kg/m²  | 10 m-walk < 1.0 m/s  |
|                     | Jansen (2002)         | DEXA M                           | SMI 2SD < control | NA                   | NA                   |
|                     | Jansen (2002)         | F                                | SMI 2SD < control | 6 m-walk < 0.8 m/s   |
|                     | Newman (2018)         | DXA M                           | Residuals < 20th percentile | NA               | NA                   |
|                     | Alpinar (2014)        | MM 2SD < young ref.            | BIA FMMI < 16.91 kg/m² | NA               | NA                   |
|                     |                       | NA                              | Isokinetic Knee F/E | 95.56 Nm            | NA                   |
|                     | Bittel (2017)         | Jansen (2004)               | NA               | NA                   | NA                   |
|                     |                       | F                                | 95.56 Nm            | NA                   |
|                     | Bouchi (2017, a)      | AWGS                            | ASMI < 7.0 kg/m²   | HGS < 26.0 kg      | NA                   |
|                     |                       | F                                | ASMI < 5.4 kg/m²   | < 18.0 kg           |
|                     | Bouchi (2017, b)      | AWGS                            | ASMI < 7.0 kg/m²   | HGS < 26.0 kg      | NA                   |
|                     |                       | F                                | ASMI < 5.4 kg/m²   | < 18.0 kg           |
|                     | Bouchi (2017, c)      | AWGS                            | ASMI < 7.0 kg/m²   | HGS < 26.0 kg      | NA                   |
|                     |                       | F                                | ASMI < 5.4 kg/m²   | < 18.0 kg           |
|                     | Celiker (2018)        | BIA M                           | ASMI < 7.0 kg/m²   | HGS < 26.0 kg      | 6 m-walk < 1.0 m/s   |
|                     |                       | F                                | ASMI < 5.4 kg/m²   | 6 m-walk < 1.0 m/s   |
|                     | Fukuda (2017)         | Low MM + low MS                  | DXA M              | ASMI < 7.0 kg/m²   | NA                   |
|                     |                       | F                                | ASMI < 5.4 kg/m²   | < 18.0 kg           |
|                     | Ida (2017)            | EWGSOP                          | BIA M              | ASMI < 6.80 kg/m²   | 5 m-walk < 0.8 m/s   |
|                     |                       | F                                | ASMI < 6.40 kg/m²   | 5 m-walk < 0.8 m/s   |
|                     | Jansen (2015)         | Baumgartner         | DXA M              | ALM/h² < 7.23 kg/m² | NA                   |
|                     |                       | F                                | ALM/h² < 5.67 kg/m² | NA                   |

(continued on next page)
| First author (year) | Sarcopenia definition | Assessment method/cut-off values | Muscle Mass | Muscle strength | Physical performance |
|---------------------|-----------------------|----------------------------------|-------------|----------------|----------------------|
| Kim (2014)          | Baumgartner           | DXA M ASMI < 7.40 kg/m²          | NA          | NA             | NA                   |
|                     |                       | F ASMI < 5.14 kg/m²              | NA          | NA             | NA                   |
| Janssen (2002)      |                       | DXA M ASMI/wt < 29.5%           | NA          | NA             | NA                   |
|                     |                       | F ASMI/wt < 23.2%               | NA          | NA             | NA                   |
| Janssen (2002)      |                       | DXA M SMI < 24.4%               | NA          | NA             | NA                   |
|                     |                       | F SMM/wt < 25.8%                | NA          | NA             | NA                   |
| Kim (2010)          | Janssen Cl (2002)     | DXA M ASMI/wt < 32.3%           | NA          | NA             | NA                   |
|                     |                       | F ASMI/wt < 25.6%               | NA          | NA             | NA                   |
| Janssen Cl (2002)   |                       | DXA M ASMI/wt < 29.1%           | NA          | NA             | NA                   |
|                     |                       | F ASMI/wt < 23.0%               | NA          | NA             | NA                   |
| Mori (2017)         | AWGS                  | BIA M SMI < 7.0 kg/m²            | HGS < 26.0 kg | 5 m-walk    | < 0.8 m/s            |
|                     |                       | F SMI < 5.4 kg/m²               |            | 6 m-walk | < 0.8 m/s            |
| Murata (2018)       | AWGS                  | BIA M SMI < 7.0 kg/m²            | HGS < 26.0 kg |            | NA                   |
|                     |                       | F SMI < 5.4 kg/m²               |            |            | NA                   |
| Osaka (2018)        | Japan Society of Hepatology | BIA M SMI < 7.0 kg/m²          | HGS < 26.0 kg |            | NA                   |
| Tanaka (2015)       | EWGSOP                | DXA M SMI/wt < 8.67 kg/m²        | NA          | NA             | NA                   |
|                     |                       | F SMI/wt < 4.1 kg/m²            | NA          | NA             | NA                   |
| Trierweiler (2018)  | FNHI                  | DXA M ALM/BMI < 0.789           | NA          | 6-minute walk | < 0.8 m/s            |
|                     |                       | F ALM/BMI < 0.512               | NA          |            | NA                   |
| Ucak (2018)         | EWGSOP                | BIA M SMI < 10.75 kg/m²          | NA          | NA             | NA                   |
| Wang (2016)         | AWGS                  | BIA M SMI < 7.0 kg/m²            | HGS < 26.0 kg | 4 m-walk | < 0.8 m/s            |
| Yang (2016)         | Baumgartner           | DXA M ASMI < 7.26 kg/m²          | NA          | NA             | NA                   |
|                     |                       | F ASMI < 5.45 kg/m²             | NA          | NA             | NA                   |
| Respiratory diseases | Byun (2017)           | EWGSOP BIA M SMI 2SD < young ref. | HGS ≤ 30 kg | 4 m-walk | < 0.8 m/s            |
|                     |                       | F SMI 2SD < young ref.           | ≤ 20 kg    |            | NA                   |
| Chung (2015)        | Baumgartner           | DXA M ASMI < 6.95 kg/m²          | NA          | NA             | NA                   |
|                     |                       | F ASMI < 4.94 kg/m²             | NA          | NA             | NA                   |
| Costa (2018)        | FNHI                  | DXA M ALM/BMI < 0.789           | NA          | 6-minute walk | < 0.8 m/s            |
|                     |                       | F ALM/BMI < 0.512               | NA          |            | NA                   |
| Costa (2015)        | Baumgartner           | DXA M ASMI < 7.26 kg/m²          | NA          | NA             | NA                   |
|                     |                       | F ASMI < 5.45 kg/m²             | NA          | NA             | NA                   |
| Di Gregorio (2018)  | EWGSOP                | BIA M SMI < 8.50 kg/m²           | HGS ≤ 30 kg | 4 m-walk | < 0.8 m/s            |
|                     |                       | F SMI ≤ 5.75 kg/m²              | ≤ 20 kg    |            | NA                   |
| Gologanu (2014)     | Low MM + high BMI     | BIA M FMMI ≤ 16 kg/m²            | NA          | NA             | NA                   |
|                     |                       | F FMMI ≤ 15 kg/m²               | NA          | NA             | NA                   |
| Hwang (2017)        | Baumgartner           | DXA M ASMI < 6.94 kg/m²          | NA          | NA             | NA                   |
|                     |                       | F SMI < 5.45 kg/m²              | NA          | NA             | NA                   |
| Jones (2015)        | EWGSOP                | BIA M NR HGS ≤ 30 kg             | F NR       | 4 m-walk | NR                   |
|                     |                       | F NR ≤ 20 kg                    | NA          |            | NA                   |
| Joppa (2016)        | NA                    | BIA M FMI < 10th percentile      | NA          | NA             | NA                   |
| Kneppers (2017)     | Baumgartner           | DXA M ASMI < 7.23 kg/m²          | NA          | NA             | NA                   |
|                     |                       | F ASMI < 5.76 kg/m²             | NA          | NA             | NA                   |
| Koo (2014)          | ISD < young ref.      | DXA M SMI < 29.8%               | NA          | NA             | NA                   |
| Lee (2017)          | AWGS                  | DXA M ASMI < 7.0 kg/m²           | NA          | NA             | NA                   |
|                     |                       | F ASMI < 5.4 kg/m²              | NA          | NA             | NA                   |
| Lee (2016)          | AWGS                  | DXA M ASMI < 7.0 kg/m²           | NA          | NA             | NA                   |
|                     |                       | F ASMI < 5.4 kg/m²              | NA          | NA             | NA                   |
| Limpawattana (2017) | AWGS                  | DXA M ASMI < 7.0 kg/m²           | HGS < 26.0 kg | 6-minute walk | < 0.8 m/s            |
|                     |                       | F ASMI < 5.4 kg/m²              | < 18.0 kg  |            | NA                   |
| Pothirat (2016)     | Low MM + high BMI     | BIA M FMI ≥ 16 kg/m²             | NA          | NA             | NA                   |
|                     |                       | F FMI ≥ 15 kg/m²                | NA          | NA             | NA                   |
| Sergi (2006)        | Baumgartner           | DXA M ASMI < 7.26 kg/m²          | NA          | NA             | NA                   |
| van de Bool (2016)  | Baumgartner           | DXA M ASMI < 7.23 kg/m²          | NA          | NA             | NA                   |
|                     |                       | F ASMI < 5.76 kg/m²             | NA          | NA             | NA                   |
| van de Bool (2015)  | Baumgartner           | DXA M ASMI < 7.23 kg/m²          | NA          | NA             | NA                   |
|                     |                       | F ASMI < 5.76 kg/m²             | NA          | NA             | NA                   |

ALM = appendicular lean mass, ASMI = appendicular skeletal muscle mass index, AWGS = Asian Working Group for Sarcopenia, BIA = bioelectrical impedance analysis, BMI = body mass index, C1 = class 1, C2 = class 2, CC = calf circumference, DXA = dual energy X-ray absorptiometry, EWGSOP = European Working Group for Sarcopenia in Older People, F = female, F/E = flexion/extension, FMFI = fat-free mass index, FNHI = Foundation for the National Institutes of Health, HGS = handgrip strength, IWGS = International Working Group for Sarcopenia, LM = lean muscle mass, M = male, MM = muscle mass, MS = muscle strength, NA = not applicable, NR = not reported, SD = standard deviation, SIG = Special Interest Group on cachexia-anorexia, SMI = skeletal muscle mass index, SPPB = short physical performance battery, young ref. = young reference group.
## Table A.4
Quality assessment of included articles using the Newcastle-Ottawa Scale.

| First author (year) | Selection | Comparability | Exposure | Total |
|---------------------|-----------|---------------|----------|-------|
|                     | Q1 Q2 Q3 Q4 | Q1 Q1 Q2      |          |       |
| Abellan van Kan (2013) | 1 0 0 1 | 0 1 1 | 4 |
| Aghili (2014)       | 1 0 0 0 | 0 1 0 | 2 |
| Alipinar (2014)     | 0 0 0 1 | 0 1 1 | 3 |
| Bekiani (2016)      | 1 0 0 0 | 0 1 0 | 2 |
| Bittel (2017)       | 1 0 0 1 | 1 1 1 | 5 |
| Bouchi (2017, a)    | 1 0 0 1 | 2 1 1 | 6 |
| Bouchi (2017, b)    | 1 0 0 0 | 0 1 0 | 2 |
| Bouchi (2017, c)    | 1 1 0 0 | 0 1 0 | 3 |
| Byun (2017)         | 1 1 0 0 | 0 1 0 | 3 |
| Celiker (2018)      | 1 0 0 1 | 1 1 1 | 5 |
| Chong (2015)        | 1 1 1 1 | 1 1 1 | 7 |
| Chong (2014)        | 1 0 0 0 | 0 1 0 | 2 |
| Chung (2015)        | 1 1 1 1 | 0 1 1 | 6 |
| Costa (2018)        | 1 0 1 0 | 0 1 0 | 3 |
| Costa (2015)        | 1 1 0 0 | 0 1 0 | 3 |
| Di Gregorio (2018)  | 1 1 0 0 | 0 1 0 | 3 |
| dos Santos (2017)   | 1 0 0 0 | 0 1 0 | 3 |
| Fukuda (2017)       | 1 0 0 0 | 0 1 0 | 2 |
| Fulster (2013)      | 1 1 0 0 | 0 1 0 | 3 |
| Gillette-Guyonnet (2000) | 1 0 1 1 | 2 1 1 | 7 |
| Gologanu (2014)     | 1 1 0 0 | 0 1 0 | 2 |
| Harada (2017, a)    | 1 0 0 0 | 0 1 0 | 2 |
| Harada (2017, b)    | 1 1 0 0 | 0 1 0 | 3 |
| Henwood (2017)      | 1 0 0 0 | 0 1 0 | 2 |
| Huang (2015)        | 1 0 0 0 | 0 1 0 | 2 |
| Hwang (2017)        | 1 0 0 0 | 0 1 0 | 2 |
| Iida (2017)         | 1 0 0 0 | 0 1 0 | 2 |
| Izawa (2016, a)     | 1 1 0 0 | 0 1 0 | 3 |
| Izawa (2016, b)     | 1 0 0 0 | 0 1 0 | 2 |
| Jansen (2015)       | 1 1 0 0 | 0 1 0 | 2 |
| Jones (2015)        | 1 1 0 0 | 0 1 0 | 3 |
| Joppa (2016)        | 1 1 0 0 | 0 1 0 | 4 |
| Kim (2014)          | 1 1 1 1 | 2 1 1 | 8 |
| Kim (2010)          | 1 0 1 1 | 1 1 1 | 6 |
| Knepers (2017)      | 1 1 0 0 | 0 1 0 | 3 |
| Koo (2016)          | 1 1 1 0 | 0 1 1 | 5 |
| Koo (2014)          | 1 1 0 0 | 0 1 0 | 2 |
| Lee (2017)          | 1 1 0 0 | 0 1 0 | 3 |
| Lee (2016)          | 1 1 0 0 | 0 1 0 | 3 |
| Limpawattana (2017) | 1 0 0 0 | 0 1 0 | 2 |
| Mori (2017)         | 0 0 0 0 | 0 1 0 | 1 |
| Murata (2018)       | 1 0 0 0 | 0 1 0 | 2 |
| Onoue (2016)        | 1 1 0 0 | 0 1 0 | 2 |
| Osaka (2018)        | 1 1 0 0 | 0 1 0 | 3 |
| Papachristou (2015) | 1 0 1 1 | 2 1 1 | 7 |
| Pothirat (2016)     | 1 0 0 0 | 0 0 0 | 1 |
| Ryan (2017)         | 1 0 0 0 | 0 1 0 | 2 |
| Serji (2006)        | 1 0 1 1 | 2 1 1 | 6 |
| Shiraiishi (2018)   | 1 1 0 0 | 0 1 0 | 3 |
| Sugimoto (2017)     | 1 1 0 0 | 0 1 0 | 3 |
| Sugimoto (2016)     | 1 0 0 1 | 2 1 1 | 6 |
| Tanaka (2015)       | 1 0 0 0 | 0 1 0 | 2 |
| Tay (2018)          | 1 0 0 0 | 0 1 0 | 2 |
| Trierweiler (2018)  | 1 0 0 1 | 2 1 1 | 6 |
| Tsudhida (2018)     | 1 0 0 0 | 0 1 0 | 2 |
| Tsugawa (2017)      | 1 0 0 0 | 0 1 0 | 2 |
| Ucak (2018)         | 1 0 0 0 | 0 1 0 | 2 |
| Vahlberg (2016)     | 1 0 0 0 | 0 1 0 | 2 |
| van de Boel (2016)  | 1 1 1 1 | 2 1 1 | 8 |
| van de Boel (2015)  | 1 0 0 0 | 0 1 0 | 2 |
| Wang (2016)         | 1 0 1 0 | 2 1 1 | 6 |
| Yang (2016)         | 1 0 0 1 | 2 1 1 | 6 |
| Yoneda (2017)       | 1 0 0 0 | 0 1 0 | 2 |
Fig. A.1. Risk of sarcopenia in disease (dementia, DM and respiratory disease) groups compared to controls. Heterogeneity ($I^2$): dementia (80.9%), DM (62.2%), respiratory disease (57.3%).

![Image](image1.png)

Fig. A.2. Sarcopenia prevalence in articles including individuals with CVDs stratified by sarcopenia definitions. Heterogeneity ($I^2$): AWGS (94.6%), Baumgartner (93.5%), EWGSOP (92.5%). AWGS = Asian Working Group for Sarcopenia, EWGSOP = European Working Group for Sarcopenia in Older People.

![Image](image2.png)

Fig. A.3. Sarcopenia prevalence in articles including individuals with dementia stratified by sarcopenia definitions. Heterogeneity ($I^2$): AWGS (96.9%), Baumgartner (90.9%), EWGSOP (94.0%). AWGS = Asian Working Group for Sarcopenia, EWGSOP = European Working Group for Sarcopenia in Older People.
| Group by | Study name | Statistics for each study | Event rate and 95% CI | Relative weight |
|---------|------------|---------------------------|-----------------------|-----------------|
| Definition | Event rate | Lower limit | Upper limit |                 |                 |
| AWGS    | Bouchi (2017, a) (A) | 0.135 | 0.095 | 0.188 | 14.34 |
| AWGS    | Bouchi (2017, a) (B) | 0.390 | 0.177 | 0.574 | 3.19 |
| AWGS    | Bouchi (2017, b) | 0.176 | 0.141 | 0.226 | 19.10 |
| AWGS    | Bouchi (2017, c) | 0.176 | 0.133 | 0.230 | 18.91 |
| AWGS    | Mori (2017) | 0.167 | 0.077 | 0.325 | 3.49 |
| AWGS    | Murata (2018) | 0.153 | 0.116 | 0.199 | 19.90 |
| AWGS    | Wang (2016) | 0.148 | 0.108 | 0.200 | 16.89 |
| AWGS    | 0.165 | 0.143 | 0.189 |                 |                 |
| Baumgartner | Aghili (2014) (1) | 0.020 | 0.003 | 0.126 | 9.64 |
| Baumgartner | Jansen (2015) (A) | 0.172 | 0.074 | 0.353 | 19.10 |
| Baumgartner | Jansen (2015) (B) | 0.091 | 0.013 | 0.439 | 9.17 |
| Baumgartner | Jansen (2015) (C) | 0.111 | 0.015 | 0.500 | 9.03 |
| Baumgartner | Kim (2014) (1) | 0.278 | 0.211 | 0.356 | 25.85 |
| Baumgartner | Yang (2016) | 0.449 | 0.414 | 0.484 | 27.21 |
| Baumgartner | 0.201 | 0.105 | 0.351 |                 |                 |
| EWGSOP | Celiker (2018) (A) | 0.214 | 0.126 | 0.341 | 21.21 |
| EWGSOP | Celiker (2018) (B) | 0.340 | 0.223 | 0.480 | 21.82 |
| EWGSOP | Ida (2017) | 0.198 | 0.149 | 0.258 | 23.14 |
| EWGSOP | Tanaka (2015) | 0.445 | 0.376 | 0.516 | 23.40 |
| EWGSOP | Ucak (2016) | 0.990 | 0.931 | 0.999 | 10.63 |
| EWGSOP | 0.424 | 0.237 | 0.635 |                 |                 |
| Janssen (2002) | Aghili (2014) (2b) | 0.010 | 0.001 | 0.136 | 13.77 |
| Janssen (2002) | Kim (2010) | 0.157 | 0.125 | 0.195 | 28.74 |
| Janssen (2002) | Kim (2014) (3) | 0.396 | 0.319 | 0.478 | 28.57 |
| Janssen (2002) | Koo (2016) | 0.659 | 0.623 | 0.694 | 28.92 |
| Janssen (2002) | 0.269 | 0.077 | 0.503 |                 |                 |
| Janssen (2004) | Bittel (2017) (A) | 0.833 | 0.523 | 0.958 | 30.43 |
| Janssen (2004) | Bittel (2017) (B) | 0.762 | 0.540 | 0.897 | 69.57 |
| Janssen (2004) | 0.766 | 0.613 | 0.894 |                 |                 |
| Other | Alpinar (2014) | 0.015 | 0.001 | 0.201 | 6.91 |
| Other | Fukuda (2017) (A) | 0.153 | 0.114 | 0.202 | 37.98 |
| Other | Fukuda (2017) (B) | 0.211 | 0.109 | 0.308 | 25.60 |
| Other | Fukuda (2017) (C) | 0.412 | 0.210 | 0.648 | 25.67 |
| Other | 0.195 | 0.098 | 0.351 |                 |                 |

Fig. A.4. Sarcopenia prevalence in articles including individuals with DM stratified by sarcopenia definitions. Heterogeneity ($I^2$): AWGS (19.4%), Baumgartner (87.3%), EWGSOP (93.1%), Janssen (2002) (98.7%), Janssen (2004) (0.0%), other (71.3%). AWGS = Asian Working Group for Sarcopenia, EWGSOP = European Working Group for Sarcopenia in Older People.

| Group by | Study name | Statistics for each study | Event rate and 95% CI | Relative weight |
|---------|------------|---------------------------|-----------------------|-----------------|
| Definition | Event rate | Lower limit | Upper limit |                 |                 |
| AWGS    | Lee (2016) | 0.333 | 0.303 | 0.366 | 41.52 |
| AWGS    | Lee (2017) (A) | 0.336 | 0.303 | 0.370 | 39.02 |
| AWGS    | Lee (2017) (B) | 0.318 | 0.238 | 0.411 | 10.07 |
| AWGS    | Limpawattana (2017) | 0.240 | 0.172 | 0.324 | 9.40 |
| Baumgartner | Chung (2015) (A) | 0.272 | 0.246 | 0.300 | 12.73 |
| Baumgartner | Chung (2015) (B) | 0.120 | 0.107 | 0.148 | 12.71 |
| Baumgartner | Costa (2015) (1) | 0.407 | 0.311 | 0.510 | 12.49 |
| Baumgartner | Hwang (2017) | 0.053 | 0.039 | 0.071 | 12.61 |
| Baumgartner | Knoppers (2017) | 0.424 | 0.327 | 0.527 | 12.90 |
| Baumgartner | Sergi (2008) | 0.375 | 0.240 | 0.532 | 12.14 |
| Baumgartner | van de Boot (2015) | 0.805 | 0.633 | 0.902 | 12.06 |
| Baumgartner | van de Boot (2016) | 0.311 | 0.194 | 0.459 | 12.16 |
| Baumgartner | 0.322 | 0.148 | 0.566 |                 |                 |
| EWGSOP | Byon (2017) | 0.250 | 0.167 | 0.356 | 22.55 |
| EWGSOP | Di Gregorio (2018) | 0.240 | 0.192 | 0.285 | 25.22 |
| EWGSOP | Jones (2015) | 0.145 | 0.119 | 0.175 | 25.74 |
| EWGSOP | Joppa (2016) | 0.341 | 0.321 | 0.362 | 26.50 |
| EWGSOP | 0.237 | 0.144 | 0.364 |                 |                 |
| Other | Gologanu (2014) | 0.083 | 0.027 | 0.229 | 25.94 |
| Other | Koo (2014) | 0.270 | 0.235 | 0.308 | 39.12 |
| Other | Pothirat (2016) | 0.099 | 0.057 | 0.167 | 34.04 |
| Other | 0.144 | 0.067 | 0.319 |                 |                 |

Fig. A.5. Sarcopenia prevalence in articles including individuals with respiratory diseases stratified by sarcopenia definitions. Heterogeneity ($I^2$): AWGS (34.3%), Baumgartner (99.1%), EWGSOP (96.6%), other (89.5%). AWGS = Asian Working Group for Sarcopenia, EWGSOP = European Working Group for Sarcopenia in Older People.
Fig. A.6. Sarcopenia in disease groups (CVD, dementia, DM and respiratory disease) of all articles stratified by continent.

Heterogeneity (I²):
- CVD + Asia (92.1%), CVD + Europe (72.0%), dementia + Asia (95.0%), dementia + Europe (93.9%), DM + Asia (97.2%), DM + Europe (0.0%), DM + North America (0.0%), respiratory disease + Asia (96.8%), respiratory disease + Europe (98.6%), respiratory disease + South America (95.1%).

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