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Integrated Study Master's thesis

Muscle Mass and Function in Older Adults with Polypharmacy

Raumenų masė ir funkcija vyresnio amžiaus suaugusiesiems, sergantiems polifarmacija

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ABSTRACT

Objective: Both polypharmacy and sarcopenia are common in the elderly population and are linked to poor health outcomes such as frailty, increased morbidity and functional decline. Despite the fact that these conditions often coexist, their relationship is not fully clear.

Aim: This literature review aims to examine the association between polypharmacy and sarcopenia in older adults by reviewing findings from current studies published.

Design: Literature Review

Methods: Searches were conducted in PubMed using database specific search terms including “sarcopenia”, “polypharmacy”, “older adults,” “muscle strength,” “muscle mass,” “multimorbidity,” and related keywords. Results were filtered to only include human studies, English-language publications and studies published between 2015 and 2025. To find additional studies, manual searches of guideline websites were also done.

Results: The review includes thirteen observational studies. The findings reveal higher medication burden was linked to worse muscle-related outcomes and a higher prevalence of sarcopenia in many cross-sectional studies, especially in hospitalized or disease specific groups. This correlation was not found in every study when factors such as multimorbidity, nutrition and functional impairment were taken into consideration. Sarcopenia was not reliably predicted by polypharmacy alone but higher correlations were found when medication quality, including possibly inappropriate pharmaceuticals and anticholinergic drugs, were taken into account. Because of variations in diagnostic criteria, the reported prevalence of sarcopenia differed between studies.

Conclusion: The results suggest that while the association seems to be complicated and influenced by medication quality, underlying illness and diagnostic variation, polypharmacy is often associated with sarcopenia and worsening muscle-related outcomes in older people. When identifying older adults at risk for sarcopenia, assessment of medication type and burden may be crucial. To better understand the mechanisms that cause this and support clinical decision making, more prospective studies using consistent definitions are needed.

Keywords: sarcopenia, polypharmacy, medication burden, muscle mass, geriatrics

ABBREVIATIONS

Table 1. Abbreviations [source: Auste Treska]

EWGSOP	European Working Group on Sarcopenia in Older People
EWGSOP2	European Working Group on Sarcopenia in Older People (revised criteria)
AWGS	Asian Working Group for Sarcopenia
FNIH	Foundation for the National Institutes of Health
SDOC	Sarcopenia Definition and Outcomes Consortium
PIMs	Potentially Inappropriate Medications
ADR(s)	Adverse Drug Reaction(s)
PPIs	Proton Pump Inhibitors
DXA	Dual-energy X-ray Absorptiometry
BIA	Bioelectrical Impedance Analysis
AGS	American Geriatrics Society
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses

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1. INTRODUCTION

1.1 BACKGROUND/SIGNIFICANCE OF SARCOPENIA AND POLYPHARMACY

The aging population has become a significant change in our modern healthcare system as life expectancy increases (1). The population over the age of 65 is increasing faster than the population under that age (1). This causes an increase of age-associated medical conditions that impair quality of life and independence. Sarcopenia and polypharmacy are the two common and clinically significant conditions. These two conditions impact hospitalization, disability, frailty and mortality (2). While sarcopenia is an ongoing loss of skeletal muscle mass, strength and function, polypharmacy is the repeated use of several drugs, frequently as a result of multimorbidity (3, 4). While both sarcopenia and polypharmacy independently can predict poor health outcomes, they often coexist in the aging population and worsen each other's impacts (5). Understanding and addressing polypharmacy and sarcopenia is important since they can be prevented and have an impact on public health (6). Both are somewhat controllable and can be identified early. Healthcare professionals can prioritize interventions like medication evaluation, deprescribing and resistance training to help maintain functional ability and lower the risk of frailty by determining how they interact (5) . Therefore, recognizing this link is critical to enhancing pharmacological care in geriatric medicine and developing healthy aging strategies. Population-based research supports the prevalence of sarcopenia and polypharmacy. Sarcopenia affects approximately 10–20% of people over 65 who live in the community, with prevalence rising to over 30% in hospitalized or institutionalized groups, according to multinational European data cited by the European Working Group on Sarcopenia in Older People (1). Over 40% of older persons regularly take five or more prescriptions and rates in long-term care facilities surpass 60% (4). This indicates that polypharmacy poses a similarly major challenge. These numbers highlight the extent of the issue and emphasize how crucial it is to prevent and treat these conditions in older populations.

1.2 DEFINITION OF SARCOPENIA

Irwin Rosenberg defined the term "sarcopenia" in 1989 to characterize the age-related loss of muscle mass (8). The word comes from the Greek words sarx, which means flesh and penia, which means loss. It has since developed into a clinical diagnosis. Sarcopenia was

classified according to the International Classification of Diseases (ICD-10-CM, M62.84) by the World Health Organization in 2016 as an independent disease entity (3). The European Working Group on Sarcopenia in Older People (EWGSOP2, 2018) is the most extensively used tool for diagnosing sarcopenia (3). It defines sarcopenia as, “a skeletal muscle disease characterized by low muscle strength and low muscle mass, which can be confirmed by documenting both low muscle strength and low muscle mass” (3). Severity is also now measured (3). Other diagnostic guidelines that are used are the Asian Working Group for Sarcopenia (AWGS) and the Foundation for the National Institutes of Health (FNIH) but all of these guidelines highlight the three essential elements. These elements are muscle strength (usually measured by handgrip strength), muscle quantity or quality (assessed by DXA or BIA) and physical performance (usually measured by chair stand tests or gait speed) (3). Depending on demographic factors and criteria, the prevalence of sarcopenia estimates range greatly, from 10–20% for persons 60–70 years old to over 40% for those over the age of 80 (9). Frailty, fractures, falls, poor rehabilitation and greater mortality are all consequences of sarcopenia (10). In addition to its physical effects, higher healthcare usage and long-term care dependency results in significant socioeconomic burden (11).

1.3 DEFINITION OF POLYPHARMACY

Although the word "polypharmacy" is frequently used in geriatric care, different studies and medical guidelines define it differently. The concurrent use of five or more drugs is the most widely recognized definition (12). However, a systematic study from Masnoon found over 100 distinct definitions, ranging from the use of two or more drugs to ten or more drugs, indicating significant variability in the literature (12). There are two classifications of polypharmacy: appropriate and inappropriate. The term "appropriate polypharmacy" describes instances where a number of drugs are clinically demonstrated to be effective, usually for patients with significant multimorbidity (13). Inappropriate polypharmacy is when drugs have no benefit, replicate therapeutic effects, provide additional adverse effects or contain potentially inappropriate pharmaceuticals (PIMs) as determined by methods like the Beers Criteria or STOPP/START (14,15). As age increases, polypharmacy becomes much more frequent. Up to 20% of people 65 years of age or older consistently take ten or

more prescriptions, with 30–60% using at least five (16,17). Multimorbidity, cognitive decline, frailty and chronic diseases like neurological, endocrine and cardiovascular disorders are all closely linked to polypharmacy (18). Polypharmacy is a significant risk factor for adverse drug reactions (ADRs), drug-drug interactions, falls, hospitalization and mortality, even if multiple use of drugs are necessary for treating and managing health conditions (18). The necessity of cautious prescription writing, drug evaluation and deprescribing techniques in elderly patients is highlighted by these dangers. Polypharmacy is acknowledged as a significant geriatric issue and an important factor to take into account in aging research and clinical care because of its high frequency, inconsistent identification and substantial health consequences (7).

1.4 PREVIOUS RESEARCH ON THE RELATIONSHIP BETWEEN SARCOPENIA AND POLYPHARMACY

Although polypharmacy and sarcopenia frequently occur together, the extent of their association is still being studied. Risk factors for both are similar and include advanced age, chronic diseases, sedentary lifestyles, inflammation and malnutrition (18). Over the last ten years, studies have investigated whether polypharmacy is a direct cause of sarcopenia or if it is only an outcome of underlying multimorbidity. Polypharmacy and sarcopenia have been strongly associated in a number of cross-sectional and cohort studies. Hirani et al., Jang et al. and Mastavičiūtė et al. found a correlation between the usage of five or more drugs and decreased grip strength and muscle mass (5, 19, 20). The beginning or advancement of sarcopenia over time may be predicted by baseline polypharmacy, according to two longitudinal analyses conducted by Dodds et al., 2020 and Wu et al., 2016 (21, 22). Nutritional deficiencies caused by drugs, hormone disturbance, mitochondrial toxicity and decreased physical activity are some of the hypotheses suggested to explain this association. Proton pump inhibitors, statins, benzodiazepines, diuretics, antidepressants and antidiabetic medications are among the drug types that are commonly involved (23, 24, 25).

1.5 PURPOSE AND OBJECTIVES OF THE THESIS

Sarcopenia and polypharmacy are both frequent complications in the elderly and they typically appear together. Because each condition has an association to worse medical

outcomes such as frailty, falls, hospitalization and loss of independence, understanding how they are related is important for patients. There is not much research that has looked at the direct association between sarcopenia and polypharmacy, despite the fact that several studies have looked at each condition independently. The research that currently exists is inconsistent because different studies include different definitions, measuring techniques and cut-off levels. This makes it challenging to apply the results to routine clinical practice or draw definitive conclusions. Therefore, it is crucial to examine the available data about whether polypharmacy is primarily a sign of multimorbidity or if it has a role in the onset or progression of sarcopenia. Clinical decisions, particularly in areas like medication evaluation, deprescribing and early muscular weakness screening should be based upon understanding this relationship. This thesis aims to assess the available data about the relationship between sarcopenia in older adults and polypharmacy. In order to accomplish this goal, the objectives include summarizing the definitions of sarcopenia and polypharmacy from various studies, assessing whether polypharmacy is linked to decreased muscle mass, decreased muscle strength or poorer physical performance, identifying the drug classes most frequently associated with detrimental effects on muscle health, examining variations in study design and definitions that may cause different results, identifying gaps in current research and discussing how these findings could be applied in clinical practice. This thesis aims to give a better understanding of the potential effects medications have on elderly muscle health to encourage better decision making in geriatric care.

2. METHODOLOGY

2.1 DATA COLLECTION METHODS

To find research on the connection between polypharmacy and sarcopenia in elderly patients, a systematic search of the literature was conducted. PubMed was chosen for the search because of their wide range of clinical studies. The search strategy combined the following keywords using “sarcopenia,” “muscle strength,” “handgrip strength,” “muscle mass,” and “lean mass,” in combination with “polypharmacy.” The search string was structured as: (“sarcopenia” OR “muscle strength” OR “handgrip strength” OR “muscle

mass" OR "lean mass") AND "polypharmacy,". To limit the results to human studies, English language publications and articles published between 2015 and 2025, filters were used.

To find additional studies that fit the requirements, reference lists of relevant papers were manually searched. Zotero was used to organize and filter all retrieved publications, making it easier to handle sources and eliminate duplicates. The PRISMA framework was followed during the evaluation process. Following a relevant screening of titles and abstracts, entire texts were assessed using inclusion and exclusion criteria. Data, such as author, year, country, sample size, mean age, study design, diagnostic criteria for sarcopenia (ex: EWGSOP2, AWGS), definition of polypharmacy, medication classes evaluated and the primary findings were extracted into a standardized table for each study that met the requirements. Apart from the published results, no further statistical analysis was carried out.

The results could not be statistically analyzed because of significant variations in study design, definitions and measuring techniques. In order to compare and summarize the results, a descriptive and thematic synthesis was carried out.

2.2 INCLUSION AND EXCLUSION CRITERIA

To guarantee that only studies relevant to the association between polypharmacy and sarcopenia were chosen, the inclusion and exclusion criteria were set before analysis. Studies that examined persons 60 years of age and older and evaluated polypharmacy and sarcopenia in the same cohort were included. Only observational study designs were taken into account, including cross-sectional, cohort and longitudinal studies. In order to ensure accuracy, the review was focused on articles published in English between 2015 and 2025 that provided a clear description of the diagnostic criteria for sarcopenia and the definition of polypharmacy, regardless of whether it was based on the number of medications or medication classes.

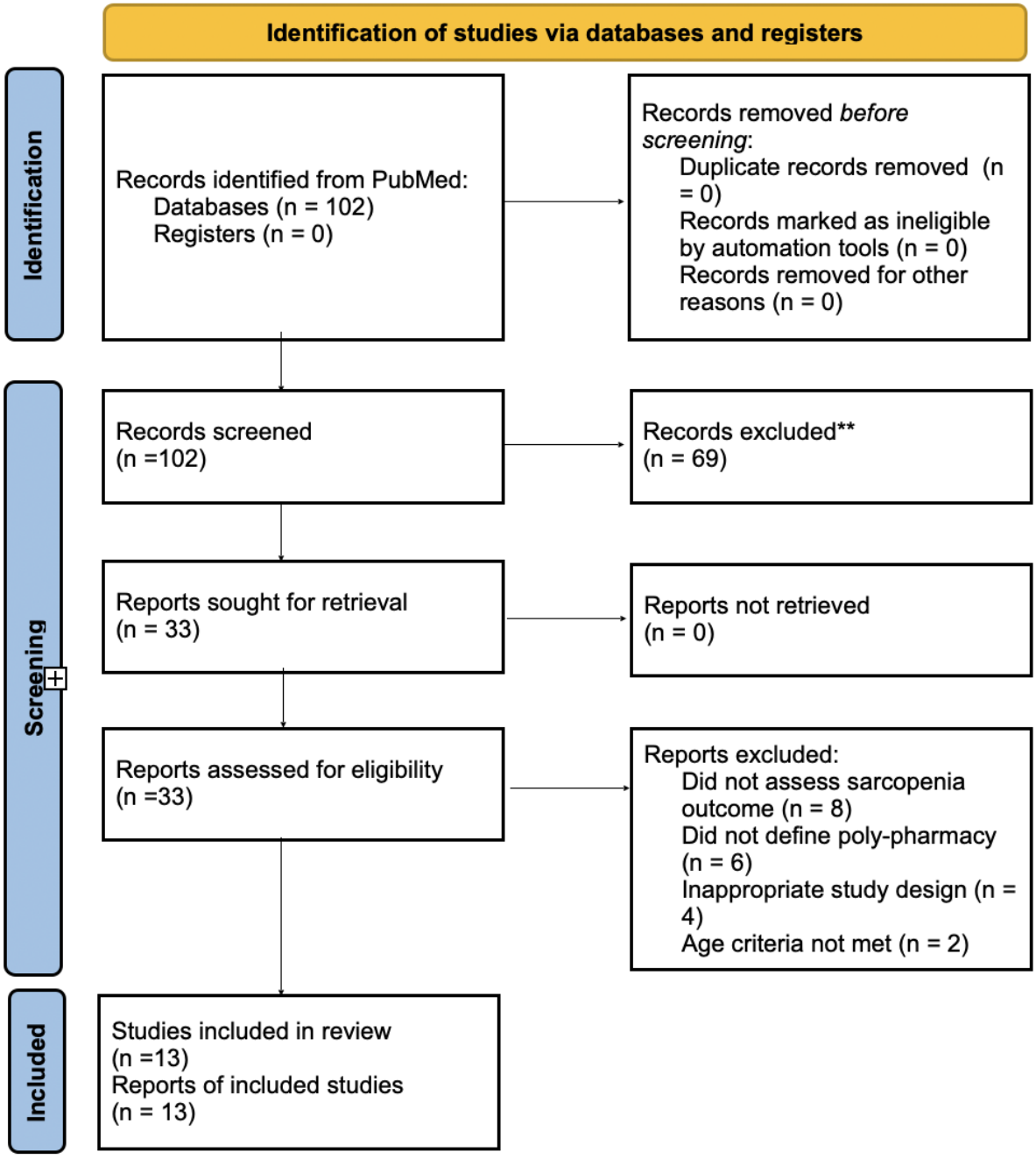
3. RESULTS

3.1 STUDY SELECTION

Studies focused on sarcopenia, polypharmacy and related effects in older adult populations were found through PubMed literature search. Articles that did not evaluate both polypharmacy and sarcopenia (or muscular mass, strength or function) or that did not fit the inclusion criteria were eliminated after title and abstract screening. The relevant studies were then evaluated.

Thirteen studies were included in the final analysis after this screening procedure because they fit all inclusion requirements. The prevalence of polypharmacy and sarcopenia and their correlation in the elderly were reported in these studies, which used a mix of cross-sectional, retrospective and longitudinal cohort designs. The selection process provided a structured and clear approach to research identification and inclusion by following the principles of the PRISMA framework. The study selection process is shown in Figure 1.

Figure 1. PRISMA flow diagram [source: Auste Treska]



3.2 STUDY CHARACTERISTICS

The thirteen research articles that made up this review were published between 2019 and 2025 and covered a variety of observational study designs, such as longitudinal, cross-sectional and retrospective cohort studies. While some used retrospective or prospective cohort designs to look at effects across time, most research was cross-sectional. A broad

range of sample sizes (from 70 to 8,713 participants) showed differences in the populations and study environments.

The mean age of participants in all of the included studies ranged between the late 60s and early 80s suggesting that the populations that were researched were mostly older adults. Although women were somewhat overrepresented in a number of cohorts, especially in community-based and hospital-based samples, the majority of research included both men and women. Depending on the research population, the percentage of female participants varied from about 33% to 66%.

The majority of research was carried out in Japan. Other studies were from China, multicenter international cohorts, and Europe (Italy, Portugal and Spain). Seniors in the community, acute hospital wards, rehabilitation facilities and disease specific populations such as patients with liver cirrhosis, heart failure or stroke were among the several study samples. This variety made it possible to investigate the relationship between polypharmacy and sarcopenia in a variety of clinical settings.

The diagnostic criteria for sarcopenia had significant variation. Many studies used globally recognized definitions, mainly the Asian Working Group for Sarcopenia (AWGS 2019) or the European Working Group on Sarcopenia in Older People (EWGSOP or EWGSOP2). Other studies used different definitions, such as the Sarcopenia Definition and Outcomes Consortium (SDOC) definitions or the Foundation for the National Institutes of Health (FNIH) criteria, or they were focused on specific factors of muscle function rather than a sarcopenia diagnosis.

Additionally, many studies used different definitions of polypharmacy. Although some studies used criteria such as six or seven or more medications, the most common definition of polypharmacy was the daily use of five or more medications. Instead of depending only on numerical medication counts, some research reviewed pharmaceutical effects by looking at hyper-polypharmacy, potentially unsuitable medications or anticholinergic burden. These differences were taken into account when summarizing and comparing the findings. The main characteristics of the thirteen included studies are summarized in Table 2.

Table 2. Characteristics of studies included in the review. [source: Auste Treska]

Study	Methodology	Population and Setting	Criteria for Sarcopenia Diagnosis	Polypharmacy Definition	Medication Classes Mentioned	Results
Hanai et al., 2023	Retrospective cohort	239 patients with liver cirrhosis	Revised JSH criteria (grip strength + muscle mass)	≥6 medications	Loop diuretics PPIs, statins, glucocorticoids	Polypharmacy significantly associated with sarcopenia; both predicted mortality
Agosta et al., 2019	Cross-sectional multicenter	655 hospitalized older adults	EWGSOP	≥5 medications	Not specified	No significant association between polypharmacy and sarcopenia
Sousa et al., 2023	Cross-sectional	384 community dwelling older adults	EWGSOP2	≥5 medications	Not specified	Polypharmacy associated with probable sarcopenia
Liu et al., 2024	Prospective cohort	8713 older adults	Handgrip strength / FRAIL Scale	≥5 medications	Not specified	Polypharmacy associated with frail worsening and mortality
Matsumoto et al., 2022	Cross-sectional	361 hospitalized older adults	AWGS 2019	≥6 medications	PIMs, anticholinergics	Polypharmacy associated with lowe grip strength and nutritional intake
Ruiz-Cárdenas et al., 2024	Cross-sectional	686 older adults	EWGSOP2, AWGS, FNIH, SDOC	≥5 medications	Not specified	Association varied depending on sarcopenia definition
Tanaka et al., 2023	Longitudinal cohort	1549 community-dwelling older adults	AWGS 2019	≥5 medications	PIMs, statins, benzodiazepines	Polypharmacy + PIMs associated with new-onset sarcopenia

Veddeng et al., 2022	Cross-sectional	174 hospitalized older adults	EWGSOP	≥7 medications	Statins	Mixed findings; statin exposure associated with better performance
Matsumoto et al., 2022	Retrospective cohort	91 stroke rehabilitation patients	AWGS 2019	≥6 medications	PPIs, statins, antihypertensives	Deprescribing associated with improved nutritional intake
Valdiviesso et al., 2022	Cross-sectional	136 heart failure patients	EWGSOP	≥5 medications	Statins, cardiovascular drugs	Polypharmacy positively associated with sarcopenia
Moriyama et al. 2024	Retrospective cross-sectiona	517 hospitalized older adults	AWGS 2019	≥5 medications	PPIs, benzodiazepines, NSAIDs	Medication count negatively correlated with phase angle
Tanaka et al., 2025	Longitudinal cohort	2044 community-dwelling older adults	AWGS 2019	≥5 medications	Anticholinergics, PIMs	Polypharmacy + anticholinergic burden increased sarcopenia risk
Morimoto et al. 2020	Retrospective cross-sectiona	70 heart failure patients	Functional and strength measures	Not defined	Cardiovascular drugs, diuretics	Higher medication count associated with worse physical function

3.3 DEFINITIONS AND PREVALENCE OF SARCOPENIA ACROSS STUDIES

Definitions of sarcopenia in the studies differed which resulted in a wide range of reported prevalence. Most of the research used accepted standard definitions, most often those from the Asian Working Group for Sarcopenia (AWGS 2019) or the European Working Group on Sarcopenia in Older People (EWGSOP or EWGSOP2). Although exact evaluation

techniques and cut-off values differed throughout the research, these definitions frequently include measurements of muscle strength, muscle mass and physical performance (26).

The prevalence of sarcopenia ranged from 12% to 35% among studies that used EWGSOP-based criteria. In a multicenter cohort of older persons evaluated utilizing bioimpedance analysis and handgrip strength, Agosta et al. reported a prevalence of 34.7% (27). Sousa et al., observed a lower prevalence of verified sarcopenia (11.98%) using EWGSOP2 criteria, whereas a higher percentage of participants met the criteria for uncertain or severe sarcopenia (28). Higher prevalence estimates were typically found in studies using the AWGS 2019 criteria, especially in older or hospitalized populations. Sarcopenia was found in 54.3% of hospitalized older persons, according to Matsumoto et al., and 34.4% in a Japanese hospital-based cohort, according to Moriyama et al. (30, 31).

When different diagnostic criteria were used within the same study group, significant differences in prevalence were also found. Sarcopenia prevalence ranged from 3.4% using SDOC criteria to 21.3% using AWGS criteria, according to Ruiz-Cárdenas et al.'s comparison of EWGSOP2, AWGS, FNIH and SDOC criteria, suggesting the important effect of diagnostic definitions on prevalence estimates (32).

Some research focused on specific measures of muscle function rather than using an accepted definition of sarcopenia. In addition to evaluating frailty, Liu et al. measured handgrip strength as a measure of muscle function (33). Using functional and strength-based measurements such as handgrip force, quadriceps force, muscle thickness and sit-to-stand performance, Morimoto et al. assessed sarcopenia and found that 18.6% of patients with chronic heart failure had sarcopenia (38).

Overall, there were significant differences in the reported prevalence of sarcopenia among the included studies. When comparing results across studies, this variation was taken into consideration because it represented variations in diagnostic criteria, evaluation techniques and research populations.

3.4 DEFINITIONS AND PREVALENCE OF POLYPHARMACY ACROSS STUDIES

Polypharmacy was defined based on the number of medications used daily, although the specific number varied across studies. The most common definition was the daily use of five

or more drugs (27–29,31,32,35–37). Higher criteria was chosen in other research, which defined polypharmacy as taking six or more drugs (26,30,34) or seven or more medications (33). Despite not using an exact numerical definition, one study found that the study population had a significant pharmaceutical burden with a median medication count of nine medications (38).

The reported prevalence of polypharmacy varied between studies and seemed to be depending on the definition, research population and the location of the study. Polypharmacy prevalence varied from about 23% to 25% in community-based samples (28, 29, 37). Studies carried out in hospital-based populations showed higher polypharmacy estimates. Matsumoto et al. found polypharmacy in 62.9% of hospitalized older individuals (30), while Agosta et al. found polypharmacy in 70.2% of participants in a multicenter geriatric cohort (27). In a Japanese hospital-based population, Moriyama et al. similarly reported a 66% prevalence of polypharmacy (36).

Some studies looked at pharmaceutical burden instead of just focusing on the amount of medications taken. Although this was less frequently reported, some evaluated hyper-polypharmacy, which is defined as taking ten or more drugs per day (27). Others examined anticholinergic load or potentially inappropriate drugs (PIMs) to evaluate medication quality. For instance, Matsumoto et al. found that patients on polypharmacy had higher PIM counts when evaluating PIMs using the 2019 AGS Beers Criteria (30). Tanaka et al.'s longitudinal study looked at PIM use, anticholinergic burden and medication count, emphasizing that medication type and burden were often evaluated together rather than separately (32, 37).

Depending on the population examined and the criteria used, the prevalence of polypharmacy varied greatly among the included studies, ranging from roughly 23% to over 70%. These differences were considered when summarizing and comparing results across the included studies.

3.5 ASSOCIATION BETWEEN POLYPHARMACY AND SARCOPENIA

Depending on the population studied, study design and definition, the relationship between polypharmacy and sarcopenia varied but was usually constant across the studies. Higher

medication burden was found to be positively correlated with decreased muscle mass, muscle strength or physical performance in the majority of cross-sectional investigations, but not all correlations were significant when irrelevant factors were taken into account. Polypharmacy and sarcopenia were found to be strongly associated in a number of cross-sectional studies. According to Hanai et al., sarcopenia in patients with liver cirrhosis was significantly associated with polypharmacy, which is defined as using six or more medications; the combined prevalence of polypharmacy and sarcopenia was 29% (26). Sarcopenia and polypharmacy both independently predicted mortality in this research. Additionally, Sousa et al. reported that polypharmacy (use of 5 or more drugs) was strongly associated with sarcopenia, with a prevalence ratio of 1.57. However, the association decreased for severe and confirmed sarcopenia (28). Valdiviesso et al. found a positive correlation between polypharmacy and sarcopenia in heart failure patients, with polypharmacy significantly increasing the odds of sarcopenia after adjusting for body mass index and age (35).

Some studies did not find polypharmacy to be independently associated with sarcopenia. Agosta et al., in a multicenter geriatric cohort, found no significant association even after accounting for hyper-polypharmacy (27). Moriyama et al. also observed that phase angle decreased as medication count increased, but the polypharmacy cutoff itself was not independently linked to muscle-related outcomes after adjustment (36). This suggests the association may be influenced more by underlying health factors than by the number of medications alone.

Over a nine year period, Tanaka et al. found that polypharmacy by itself was not linked to new onset sarcopenia. Instead, the chance of developing sarcopenia increased significantly when polypharmacy combined with the use of potentially inappropriate medications (32). Tanaka et al. further found that polypharmacy and a high anticholinergic burden were linked to a higher risk of frailty and sarcopenia during follow-up in a later population-based cohort (37). These results suggest that both the quantity and quality of medications may have an impact on long-term results.

Instead of just focusing on the diagnosis of sarcopenia, several studies examined functional outcomes associated with muscular performance. Even after controlling for muscular strength and nutritional state, Morimoto et al. found that a greater number of medications was independently linked to poorer lower extremity function as assessed by sit-to-stand performance (38). According to Liu et al., polypharmacy was associated with increased mortality and increasing frailty over a two year period, but its association with falls was no longer significant if multimorbidity was taken into account (29). Reduced handgrip strength was used as a measure of muscular function even though sarcopenia was not specifically diagnosed in this study.

Deprescribing was associated with increased energy and protein intake in older sarcopenic patients receiving stroke rehabilitation according to a retrospective cohort study by Matsumoto et al. (34). However, there were no significant changes in handgrip strength or muscle mass during the study period. This suggests that even if reducing medication burden doesn't lead to immediate improvements in muscle strength or mass, it may still help by improving nutrition related factors such as appetite and dietary intake.

Overall, the research suggested that polypharmacy is frequently associated with worse muscle related outcomes, particularly in cross-sectional studies and when the drugs involved were anticholinergic or inappropriate. The association was not as strong in every study which probably has to do with variations in populations, study designs and definitions of sarcopenia and polypharmacy (26–38). An overview of the reported associations between polypharmacy and sarcopenia across studies is presented in Table 3.

Table 3. Summary of associations between polypharmacy and sarcopenia outcomes. [source: Auste Treska]

Study	Methodology	Polypharmacy Definition	Outcome	Direction of Association
Hanai et al., 2023	Retrospective cohort	≥6 medications	Sarcopenia	Positive association
Agosta et al., 2019	Cross-sectional	≥5 medications	Sarcopenia	No significant association

Sousa et al., 2023	Cross-sectional	≥5 medications	Probable sarcopenia	Positive association
Liu et al., 2024	Prospective cohort	≥5 medications	Muscle strength / frailty	Positive association (frailty, mortality)
Matsumoto et al., 2022	Cross-sectional	≥6 medications	Muscle strength	Negative muscle-related outcomes
Ruiz-Cárdenas et al., 2024	Cross-sectional	≥5 medications	Sarcopenia	Association varied by definition
Tanaka et al., 2023	Longitudinal cohort	≥5 medications	Incident sarcopenia	Conditional (polypharmacy + PIMs)
Veddeng et al., 2022	Cross-sectional	≥7 medications	Muscle function	Mixed findings
Matsumoto et al., 2022	Retrospective cohort	≥6 medications	Nutritional intake	Deprescribing improved intake
Valdiviesso et al., 2022	Cross-sectional	≥5 medications	Sarcopenia	Positive association
Moriyama et al., 2024	Retrospective cross-sectional	≥5 medications	Phase angle / muscle quality	Negative association with muscle quality
Tanaka et al., 2025	Longitudinal cohort	≥5 medications	Incident sarcopenia	Conditional (anticholinergic burden)
Morimoto et al., 2020	Retrospective cross-sectional	Not defined	Physical function	Higher medication count associated with worse function

3.6 MEDICATION CLASSES ASSOCIATED WITH SARCOPENIA

Other studies evaluated particular drug classes in connection to sarcopenia or outcomes connected to muscles instead of medication count. Certain drug classes were more often linked to decreased muscle mass, muscle strength or physical performance.

Diuretics were frequently mentioned, especially in studies involving patients who had liver cirrhosis or cardiovascular disease. According to Hanai et al., patients with both polypharmacy and sarcopenia typically take loop diuretics (26). Morimoto et al. found that a greater number of medications was associated with worse lower extremities function and documented a high prevalence of loop diuretic use in patients with chronic heart failure (38). This pattern was also seen across studies involving more clinically complex patient populations.

Proton pump inhibitors (PPIs) were also mentioned frequently. Because PPIs are widely used in older adults, they have been discussed as potential contributors to muscle related outcomes. Hanai et al. and Moriyama et al. observed frequent PPI use among patients with polypharmacy and sarcopenia (26,36). Matsumoto et al. found that elderly hospitalized patients with polypharmacy had a significant rate of PPI usage (30).

Studies looking at statins have shown mixed results. Hanai et al. and Valdiviesso et al. reported statins as one of the most commonly prescribed drug classes in populations with polypharmacy and sarcopenia (26,35). Veddeng et al. analyzed statin intake and found that in older patients with complicated medical histories, statin use was linked to improved grip strength and physical performance. The association became weaker after full adjustment, which suggests the effect may be explained by other health related factors (33). Statins were among the potential muscle wasting medications studied by Tanaka et al. (32).

Central nervous system acting medications such as benzodiazepines, antidepressants, antipsychotics and other sedative or anticholinergic drugs were mentioned in multiple studies. Tanaka et al. found that potentially inappropriate medications, particularly benzodiazepines and anticholinergic drugs, were associated with an increased risk of sarcopenia when combined with polypharmacy (32,37). Moriyama et al. also identified benzodiazepines among commonly prescribed medications in older adults with high medication burden (36).

Antidiabetic medications and cardiovascular drugs, such as beta-blockers and antihypertensives, were reported in several studies especially in populations with chronic illnesses such as heart failure or liver disease (26,35,38). While these medications were

frequently present in patients with polypharmacy, many studies did not evaluate whether they were independently linked to sarcopenia.

The research showed that patients with sarcopenia and polypharmacy usually had prescription classes commonly prescribed to older people such as diuretics, PPIs, statins and central nervous system acting medications. Results differed between research and when medication classes were taken into account with overall medication burden or possibly improper medication use rather than alone, they seemed to be more significantly connected with muscle associated outcomes. The medication classes most frequently reported in relation to sarcopenia across studies are summarized in Table 4.

Table 4. Medication classes mentioned in included studies. [source: Auste Treska]

Medication Class	Studies Reporting	Summary of Findings
Proton Pump Inhibitors (PPIs)	Hanai 2023; Matsumoto 2022; Moriyama 2024	Frequently reported in polypharmacy populations
Statins	Hanai 2023; Tanaka 2023; Valdiviesso 2022; Veddeng 2022	Mixed findings across studies
Diuretics	Hanai 2023; Morimoto 2020	Common in disease-specific populations
Benzodiazepines	Tanaka 2023; Moriyama 2024	Associated with sarcopenia when combined with polypharmacy
Anticholinergic medications	Tanaka 2023; Tanaka 2025	Higher burden associated with worse outcomes
Cardiovascular medications	Valdiviesso 2022; Morimoto 2020	Common but not always independently evaluated
NSAIDs	Moriyama 2024; Tanaka 2023	Potential functional impact

3.7 SUMMARY OF KEY FINDINGS

Sarcopenia and polypharmacy were common in older adult populations throughout the thirteen included studies, while reported prevalence varied significantly based on study setting, demographics and definitions used. While polypharmacy prevalence ranged from about 23% in community based samples to over 70% in hospitalized groups, sarcopenia prevalence ranged from 3.4% to over 50% depending on the diagnostic criteria used (26–38).

Higher medication burden has been linked in the majority of studies to negative muscle related outcomes such as decreased muscular strength, decreased physical performance or a higher incidence of sarcopenia. Cross-sectional studies that analyzed drug quality, medication count and anticholinergic medications showed this association more consistently (26,28,32,35,37). A number of studies did not find an independent link between polypharmacy and sarcopenia which emphasizes the inconsistent results in the literature (27,36).

A combination of drug dosage and exposure to potentially inappropriate medications was linked to an elevated risk of sarcopenia and functional deterioration over time, according to longitudinal data, while polypharmacy alone showed less consistent associations with sarcopenia over time (32,37). Diuretics, proton pump inhibitors, statins and medication that affects the central nervous system were among the groups of medications that were commonly reported in populations with sarcopenia. The specific effects of these medications differed between research (26,30,33,36,38). Since the included studies used different study designs and different criteria for diagnosing sarcopenia and defining polypharmacy, the results were compared and summarized into key themes.

4. DISCUSSION

4.1 MAIN FINDINGS

The findings of this review of the literature indicated that polypharmacy seems to be frequently linked to sarcopenia and other poor muscle related outcomes in older adults. Many of the reviewed studies reported that individuals taking a higher number of medications tended to have lower muscle strength, poorer physical performance or a higher prevalence of sarcopenia. Not every study produced the same results. After taking into

consideration variables including multimorbidity, nutritional status and functional decline, the correlation between polypharmacy and sarcopenia decreased in a number of studies. This suggests that polypharmacy may not always be a direct cause of sarcopenia, but may instead show a more complex clinical problem in older patients. Studies that investigated medication quality and count, particularly those concentrating on possibly inappropriate prescriptions or anticholinergic load, tended to reveal more consistent associations with sarcopenia related outcomes.

4.2 COMPARISON WITH PREVIOUS RESEARCH

The review's findings are consistent with a significant amount of research that indicates polypharmacy is linked to sarcopenia and other negative muscle related outcomes in elderly people (5, 6, 39). Higher medication burden is associated with decreased physical performance, weakness, frailty and functional decline, all of which are closely related to the clinical implications of sarcopenia, according to numerous prior research (5). This reinforces the idea that polypharmacy is not only frequent in aging populations, but may also be an indicator of higher vulnerability and reduced physical capacity (39).

Polypharmacy, which is typically defined as taking five or more drugs, has been linked to sarcopenia in a number of prior cross-sectional studies (6). Similar trends were seen in the current study review, where several studies discovered that people with higher medication counts had a higher prevalence of sarcopenia, reduced muscle strength or worse physical performance (40). Patients with liver cirrhosis or heart failure are examples of hospital-based or disease-specific groups where these associations were the most noticeable. Previous studies have suggested that this may be related to the increased burden of multimorbidity in these groups, since both polypharmacy and sarcopenia become more widespread as the number and severity of chronic diseases grow (40, 41).

After controlling for variables including comorbidity burden, nutritional condition or functional impairment, a number of studies in this review did not find an independent link between polypharmacy and sarcopenia. Similar results have been reported in other reviews, which show that the connection between polypharmacy and sarcopenia may decrease once

these factors are taken into consideration (6). This suggests that rather than directly causing muscle atrophy, polypharmacy may occasionally represent overall clinical complexity.

The range of results between studies also seems to be significantly influenced by variations in diagnostic criteria. Sarcopenia prevalence can differ significantly based on the application of EWGSOP, EWGSOP2, AWGS, FNIH or SDOC criteria. The current review also showed this issue, as the prevalence of sarcopenia varied greatly based on the criteria that was used (5,6). Because of this, it is difficult to compare studies and the lack of universal diagnostic definitions may be the cause for some of the discrepancies in reported relationships.

Medication quality may be more significant than medication count alone is another issue identified in earlier studies (6). Multiple studies have highlighted the stronger correlation between inappropriate polypharmacy and adverse outcomes in elderly people, especially when it involves potentially unsuitable or anticholinergic drugs (39, 42, 43). This was supported by the review's longitudinal studies, which discovered that while polypharmacy by itself was not always predictive of the development of sarcopenia, exposure to polypharmacy with potentially inappropriate medications or a high anticholinergic burden was linked to an increased risk of sarcopenia and functional decline (32). Overall, these results are in line with a wider range of studies and indicate that when assessing the risk of sarcopenia in elderly people, both the amount and type of medications should be taken into account.

4.3 BIOLOGICAL AND CLINICAL MECHANISMS LINKING POLYPHARMACY AND SARCOPENIA

The association between polypharmacy and sarcopenia in elderly people may be explained by a number of biological and clinical processes. The association seems to be complex and impacted by medication effects, underlying diseases, diet and decreased physical activity rather than a single cause.

Drug induced nutritional impairment is one suggested explanation. Reduced appetite, impaired taste, gastrointestinal side effects and poor nutrient absorption are more common in people who use several medications. Deficits in protein intake, vitamin B12, magnesium and other micronutrients necessary for muscle metabolism and maintenance have been

linked to medications such as proton pump inhibitors, metformin and certain diuretics (5, 6). Reduced calorie and protein consumption has been proven to lead to muscle loss and decreased muscle strength, particularly in fragile or hospitalized elderly people.

Medication related hormonal and metabolic changes are another significant pathway. Glucocorticoids, statins and antidiabetic drugs are among the frequently prescribed medications that may disrupt anabolic signaling pathways or accelerate the breakdown of muscle proteins. For instance, long term exposure to glucocorticoids is known to increase muscle catabolism. Altered glucose metabolism and insulin resistance might further slow the synthesis of muscle proteins (3). These consequences can lead to decreases in muscle mass and function, especially those with multimorbidity.

Antidepressants, benzodiazepines, antipsychotics and other sedative or anticholinergic medications can impair alertness, balance and mobility which can result in less physical activity. A well known risk factor for sarcopenia is decreased physical activity and drug related drowsiness or lightheadedness may increase muscle deterioration by restricting daily exercise and movement (32, 44). High anticholinergic burden was linked to worse muscle related outcomes and the advancement of frailty, according to some studies included in this review (32, 37). In the study by Tanaka et al., anticholinergic burden was associated with incident sarcopenia which supports a potential neuromuscular mechanism.

Polypharmacy may raise oxidative stress and systemic inflammation through drug to drug interactions. Chronic low grade inflammation, which contributes to sarcopenia, has been connected to decreased muscle regeneration and decreased mitochondrial activity (3). In older adults with chronic disease, the combined effects of several drugs can worsen inflammatory pathways that are already present.

Many of these mechanisms are directly associated with the quality of medications, not just the number taken. According to longitudinal studies, polypharmacy alone is not as strongly linked to sarcopenia as polypharmacy in combination with possibly inappropriate medications or a significant anticholinergic burden (32, 37). This shows that polypharmacy may not give the same risk as inappropriately prescribing medications since inappropriately prescribing can lead to muscle loss.

Polypharmacy and sarcopenia seem to have a complex association that includes both direct drug effects and indirect effects including decreased mobility, inadequate nutrition and underlying illnesses. The inconsistent results reported across studies are likely a result of this.

4.4 STRENGTHS AND LIMITATIONS OF THE REVIEW

In comparison to other geriatric diseases, the connection between polypharmacy and sarcopenia is an issue that is clinically significant but has received little attention. This review was able to collect evidence of both the progression of sarcopenia and functional decline and also associations seen by including both cross-sectional and longitudinal studies. Organizing the data made it possible to compare study designs, demographics, diagnostic standards and definitions between investigations.

Including studies from a variety of settings such as hospitalized patients, rehabilitation groups, community-dwelling older adults and disease-specific populations like those with liver cirrhosis or heart failure is a strength of this review. This strengthens the data and emphasizes how the association between polypharmacy and sarcopenia might vary based on the patient group and clinical setting. A number of included studies looked at drug quality in addition to medication count such as anticholinergic burden or potentially inappropriate medications which allowed for more aspects to look at than just quantity of medications.

The main limitation in this review is the large variability among the selected studies. Variability in reported prevalence and relationships may have been caused by differences in study design, demographics, definitions of polypharmacy and diagnostic criteria for sarcopenia. These differences also made it difficult to compare the studies directly.

Conclusions on causality cannot be made because most of the included studies were observational, specifically cross-sectional. It is difficult to completely rule out variables such as multimorbidity, nutritional status, physical activity and illness severity. In some studies, the association decreased after these variables were taken into account. Medication exposure was usually measured at a single point in time without providing details on dosage, duration or changes over time which does not allow for studies to look at the effects on muscles over a long period of time.

5. CONCLUSION

5.1 RECAP OF KEY FINDINGS

This literature review looked at data from thirteen studies carried out in a variety of clinical settings to investigate the relationship between polypharmacy and sarcopenia in the elderly. The results show that polypharmacy is often linked to sarcopenia and worse outcomes related to muscles such as reduced muscle strength, reduced physical performance and increased frailty. However, depending on the study design, demographics, diagnostic criteria and other factors, the strength and consistency of this association differed between studies. A higher number of medications was associated with a higher prevalence of sarcopenia or worse outcomes related to muscles in a number of studies that were part of this review. Hospitalized patients or patients with specific diseases such as liver cirrhosis or heart failure, showed the strongest correlation with this. After accounting for factors like multimorbidity, nutritional status or functional disability, the association in many studies failed to be statistically significant. This suggests that polypharmacy may represent the overall clinical complexity of elderly individuals rather than serving as a single risk factor for sarcopenia.

Longitudinal studies provided additional information to the relationship between sarcopenia and polypharmacy. The onset of sarcopenia over time was not reliably predicted by polypharmacy alone. More significant associations were found in studies that also looked at the quality of medications. A high anticholinergic dosage or polypharmacy combined with potentially inappropriate medication was associated with a higher risk of sarcopenia and functional impairment. This suggests that when determining someone's likelihood of developing sarcopenia, both the amount and type of medication taken are significant factors. The significant differences in the reported prevalence of sarcopenia between studies was another significant finding from this review. The use of various diagnostic criteria such as EWGSOP, EWGSOP2, AWGS, FNIH and SDOC was primarily the cause for this. These variations made it frequently challenging to compare research directly, which likely contributed to the inconsistent findings that were found. These results emphasize the need for future studies to use more standardized and reliable diagnostic techniques.

Although the relationship is complex, the evidence currently available suggests a correlation between polypharmacy and sarcopenia in older individuals. Muscle health in aging populations appears to be influenced by a number of factors such as diet, physical activity, underlying diseases, medication quantity and medication quality.

5.2 PRACTICAL RECOMMENDATIONS

Several recommendations for clinical treatment and further study can be made because of the review's findings. Regular medication reviews should be done in clinical settings for elderly patients, especially those who have developed sarcopenia, decreased muscle strength or functional impairment. Medication appropriateness should be considered in addition to the quantity of prescription drugs. Minimizing anticholinergic burden and identifying and reducing possibly inappropriate medications are important strategies to lower the risk of muscle related impairment.

For older patients with polypharmacy, routine monitoring for sarcopenia or early signs of muscle weakness may be helpful especially for high risk or hospital-based populations. Simple tests during clinical evaluation such as chair stand tests, handgrip strength or gait speed can help identify patients.

The most effective techniques are generally multidisciplinary. Doctors, pharmacists, nutritionists and physiotherapists working together as a team can treat contributing factors at once such as the amount of medication taken, dietary intake and physical activity. Comprehensive geriatric care should include interventions including nutritional adjustment, exercise and deprescribing unnecessary medications.

Future research should concentrate on prospective studies that use specific requirements for polypharmacy and standardized definitions of sarcopenia. Rather than depending just on the number of medications, more consideration should be given to the quality of the medications, the duration of use and the particular drug classes prescribed. To assess if specific drug management techniques may help lower the risk or progression of sarcopenia in older persons and to gain a better understanding of probable causative mechanisms, additional investigation is required.

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