#### REVIEW

# Sarcopenia and Chronic Pain in the Elderly: A Systematic Review and Meta-Analysis

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**Objective:** Sarcopenia and chronic pain are prevalent among older adults, and despite numerous studies, the potential epidemiological link between the two conditions remains a topic of controversy. Therefore, we performed a comprehensive systematic review and meta-analysis to assess the relationship between chronic pain and sarcopenia in the elderly.

**Methods:** EMBASE, Web of Science, PubMed, and the Cochrane Library were searched through 22 March 2023 with additional manual searches of reference lists of included studies and relevant reviews. We used a random effects model to conduct the meta-analysis and evaluated heterogeneity across studies with Cochran's Q statistic and I<sup>2</sup>. Subgroup analyses were conducted based on income level, diagnostic criteria for sarcopenia, and pain site.

**Results:** 17 observational studies (33,600 participants, 49% female) were included, of which 6 articles were retrieved for narrative review. The pooled prevalence of sarcopenia and the pooled odds ratios (OR) between chronic pain and sarcopenia were extracted from the remaining 11 studies. The pooled prevalence of sarcopenia among older adults suffering from chronic pain was 0.11 (95% CI, 0.08–0.18). Our analysis revealed a statistically significant positive association between chronic pain and an increased risk of sarcopenia, yielding a pooled OR of 1.52 (95% CI, 1.31–1.76). Furthermore, our subgroup analysis demonstrated that the low-income countries group showed a stronger association (OR, 1.73; 95% CI, 1.54–1.95) between chronic pain and sarcopenia than the high-income countries group (OR, 1.38; 95% CI, 1.20–1.60).

**Conclusion:** Older adults with chronic pain have a significantly higher prevalence of sarcopenia and risk of developing sarcopenia compared to those without pain. These findings highlight the importance of prioritizing the assessment and early detection of chronic pain in older people, as well as implementing proactive intervention measures in clinical practice. In addition, our results suggest that older people with chronic pain should be actively screened for sarcopenia.

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Keywords: the elderly, chronic pain, sarcopenia, meta-analysis

#### Introduction

Sarcopenia is an age-related syndrome characterized by pathological loss of muscle mass and quality, leading to low muscle strength and/or impaired physical performance.<sup>1</sup> It has gradually been found to be associated with a range of negative outcomes such as falls, disability, hospitalization, and death, and is a significant cause of the need for long-term care in older adults.<sup>2,3</sup> As the global population ages, sarcopenia is now a global threat. To date, there is still a lack of effective drugs to treat sarcopenia.<sup>4</sup> Therefore, it is particularly important to identify the risk factors associated with this disease to reduce its onset in older adults.

Chronic pain is defined as pain that persists beyond the normal healing time.<sup>5</sup> Unlike acute pain, chronic pain presents in pathological ways, causing significant distress to the affected individual.<sup>6</sup> It is highly prevalent among the elderly population, affecting approximately 30% to 50% of community-dwelling individuals.<sup>7</sup> Chronic pain has been linked to reduced mobility, immobility, sedentary behavior, falls, chronic stress, depression, anxiety, sleep disturbances, and frailty.<sup>8–10</sup> These chronic pain-related adverse outcomes are considered underlying factors of risk for the advancement

of sarcopenia.<sup>11</sup> Furthermore, there appear to be shared pathophysiological mechanisms between sarcopenia and chronic pain, such as elevated circulating levels of pro-inflammatory factors and oxidative stress.<sup>12,13</sup>

The relationship between sarcopenia and chronic pain has not yet been clearly elucidated. Studies have shown that people with sarcopenia tend to report higher rates of pain compared to non-sarcopenic populations.<sup>14</sup> However, whether chronic pain increases the risk of sarcopenia, sarcopenia exacerbates pain, or there is an interaction between the two remains controversial. A prospective cohort study of the Health, Aging, and Body Composition found pain to be a predictor of transition towards sarcopenia.<sup>15</sup> In contrast, a cross-sectional study from Japan reported that chronic pain in the elderly was not associated with sarcopenia.<sup>16</sup> Similarly, a prospective cohort study conducted in England revealed that only severe pain was linked to sarcopenia, while moderate or mild pain did not show any significant correlation. The researchers suggest that this result could be attributed to the use of medication prescribed for severe pain, which likely has a crucial role in the link between sarcopenia and pain.<sup>17</sup> Furthermore, although the results of a recent systematic review and meta-analysis of 14 observational studies showed a significant correlation between pain and sarcopenia, the majority of the studies included in this analysis were case-control studies, with some studies having a relatively young average age and all studies being from high-income countries. This may lead to heterogeneity in the results, which could affect the reliability and applicability of the meta-analysis.<sup>18</sup> Therefore, we performed a comprehensive systematic review and meta-analysis to assess the relationship between chronic pain and sarcopenia in the elderly. Our primary objective was to determine whether there was significant variation in the occurrence of sarcopenia between older adults with and without chronic pain, and to uncover possible connections between chronic pain and sarcopenia. Our secondary objectives were to evaluate whether the location of pain, the diagnostic criteria for sarcopenia, or the level of income affects the correlation between chronic pain and sarcopenia.

## Methods

#### Protocol Registration

This review had adhered to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines<sup>19</sup> for conducting and reporting systematic reviews and meta-analyses and had a registered protocol with the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42023416618 (Supplementary Table 1).

## Search Strategy and Selection Criteria

We conducted a comprehensive literature search across multiple databases including EMBASE, PubMed, the Cochrane Library, and the Web of Science. Our search utilized Medical Subject Headings (MeSH) terms in combination with relevant free-text terms ("muscle atrophy", "sarcopenia", "chronic pain", "pain", "low back pain", "musculoskeletal pain", "neuralgia", "arthralgia", and "fibromyalgia") to ensure a thorough search from the inception of the databases to March 22, 2023 (Supplementary Table 2). We limited our search to human studies and also manually reviewed the reference lists of included studies and relevant reviews to identify additional articles. To ensure consistency, two independent authors (J.T. Chen and X.Y. Wang) performed the title/abstract eligibility screening using a pre-planned list of inclusion/exclusion criteria. Any discrepancies were resolved through discussion with the corresponding author (Z.R. Xu). In cases where there were overlapping cohorts, we prioritized studies with larger sample sizes or more data available for subgroup analysis.

We included studies meeting these criteria: (1) no language restrictions; (2) cross-sectional, case-control, and cohort studies examining the association between sarcopenia and chronic pain in older adults; (3) application of a validated and approved consensus or scale (eg European Working Group on Sarcopenia in Older People and the Asian Working Group for Sarcopenia, etc.), to distinguish between participants with and without sarcopenia; and (4) reporting of chronic primary pain syndromes, chronic postsurgical or posttraumatic pain, chronic neuropathic pain, chronic secondary head-ache or orofacial pain, chronic secondary visceral pain, or chronic secondary musculoskeletal pain, based on the latest World Health Organization criteria for chronic pain classification.

We excluded studies that met the following criteria: (1) abstracts of meetings, case reports, letters, comments, or editorials; (2) cancer-related pain and rheumatoid arthritis pain, the pain-causing diseases themselves increase the risk of myasthenia; and (3) average age was less than 60 years old.

#### Data Extraction and Study Quality Assessment

Two independent authors (J.T. Chen and X.Y. Wang) utilized a standardized data extraction table to extract data from each included study. The extracted data included various parameters such as the first author's name, publication year, country of study, study design, sample size, mean age, proportion of females, diagnostic criteria for sarcopenia, measurement tool for muscle mass, pain assessment method, number of sarcopenic individuals with chronic pain, number of individuals with chronic pain, number of non-chronic pain sarcopenic individuals, number of individuals with chronic pain, and confounding variables. The primary objective of the study was to determine the prevalence of sarcopenia in older adults with chronic pain, and investigate the relationship between chronic pain and sarcopenia, along with its influencing factors. The results were expressed using odds ratios (OR) and 95% confidence intervals (CI).

The quality of included studies was also assessed by two authors (J.T. Chen and X.Y. Wang) using a scale in accordance with the Newcastle-Ottawa scale (NOS). Assessments were conducted independently, and any disagreements were resolved through discussions with the corresponding author (Z.R. Xu).

#### Statistical Analysis

In this study, the eligible study data was subjected to a meta-analysis using the Cochrane Collaboration Review Manager (RevMan 5.4) software. To avoid overestimation of effect sizes, all analyses were performed using a random effects model and heterogeneity across studies was assessed via Cochran's Q statistic and  $I^2$ . Significant heterogeneity was defined as  $I^2>50\%$  or P value of Q statistic<0.1. Pre-planned subgroup analyses were performed based on income level (According to the country of residence of the study population, the included studies were categorized into a group of lower- and middle-income countries and a group of high-income countries.), diagnostic criteria for sarcopenia, and pain site (Based on whether the studies differentiate specific pain sites, the included studies were categorized into a group that does not differentiate pain locations and a group that focuses on pain in the lower back or limbs.). Sensitivity analyses were carried out by systematically excluding one study at a time and pooling the remaining studies. Additionally, publication bias was evaluated using funnel plots. The significance level for all analyses was set at p<0.05 (two-tailed).

## Results

## Study Selection and Characteristics of Included Studies

Out of 16,006 articles identified through electronic database searches, 2254 duplicates and 13,696 ineligible titles/ abstracts were excluded. In addition, 2 relevant studies were obtained by manually reviewing the reference lists of the included studies and related reviews. Following a full-text review of the remaining 56 articles, 39 were excluded according to the pre-defined criteria. Ultimately, 17 studies were deemed eligible for qualitative review, with 11 articles included in the subsequent meta-analysis (Figure 1).

Table 1 presents a summary of the characteristics of all included studies. Of the 17 studies, 14 were conducted in high-income countries and 3 in low- and middle-income countries. Cross-sectional studies accounted for 11 of the 17 studies, while 6 were prospective cohort studies. The sample size of the included studies ranged from 72 to 14,585, with a total of 33,600 individuals across all 17 studies. The average age of the participants ranged from 63.5 to 81.5 years. The results of the NOS quality assessment for the studies included in the quantitative analysis were rated as moderate to high quality (Supplementary Table 3).

Among the included studies, 5 studies employed muscle mass alone as the diagnostic criterion for sarcopenia, whereas 12 studies used a combination of muscle mass and grip strength as the diagnostic criterion. Regarding the measurement of muscle mass, dual-energy X-ray absorptiometry (DXA) was used in 7 studies, bioelectrical impedance analysis (BIA) in 8 studies, and a validated equation estimation in 2 studies.

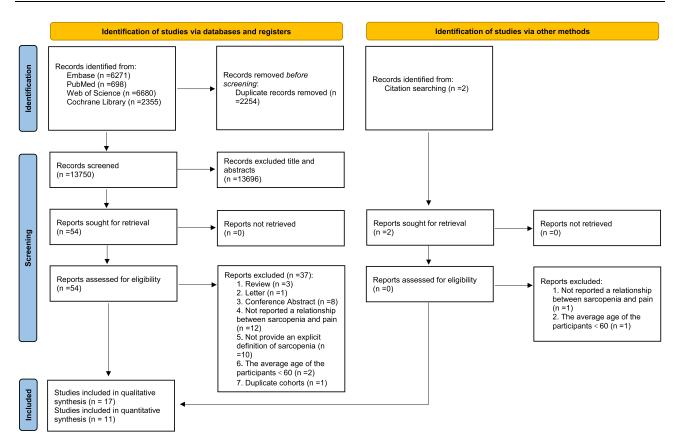


Figure I The PRISMA flow chart for the study selection process.

In the included studies, pain assessment methods have shown considerable diversity. For example, the 25-question Geriatric Locomotive Functional Scale questionnaire, the EuroQol-5 dimension, the painDETECT questionnaire, and the Shoulder Pain and Disability Index (SPADI) tool were used to determine the presence or absence of pain. However, about 8 studies used a similar question, such as "Do you feel pain in your daily life or last for a month or more?" Most of the studies did not provide information about the specific location of pain, while 7 studies explored the specific location of pain, such as low back, hip, or knee pain. In addition, most studies used a visual analog scale or a numerical rating scale as a tool to measure pain severity.

## Sarcopenia and Chronic Pain

In the absence of a dichotomous classification for chronic pain and sarcopenia, we conducted a narrative synthesis of six studies. Among them, three demonstrated that individuals with sarcopenia in chronic pain populations were more prone to experiencing higher levels of pain than those without sarcopenia.<sup>21,31,32</sup> Notably, one study identified pain as a predictive factor for the transition from a normal state to sarcopenia.<sup>15</sup> Furthermore, one study found individuals with sarcopenia are more likely to develop shoulder pain than those without the condition.<sup>28</sup> Similarly, another study revealed an association between sarcopenia and the onset of new neuropathic pain.<sup>27</sup> All the six studies supported a potential link between chronic pain and sarcopenia.

## Prevalence of Sarcopenia Among Older Adults with Chronic Pain

Prevalence data for sarcopenia were extracted from 11 remaining studies (n=29,832),<sup>13,16,17,20,22–26,29,30</sup> yielding a cumulative prevalence of 0.11 (95% CI, 0.08–0.14) (Figure 2). Subgroup analysis revealed a slightly higher prevalence of sarcopenia in low- and middle-income countries (0.12, 95% CI, 0.09–0.16) than in high-income countries (0.11, 95% CI, 0.07–0.15). Moreover, the prevalence of sarcopenia was higher in the group using only muscle mass as the diagnostic criterion (0.14, 95% CI, 0.06–0.22) than in the group using grip strength and/or physical performance as part of the

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Author, Year	Study Design	Country and Population	Sample Size	Female	Mean Age, Years	Definition of Sarcopenia	Pain Assessment	Pain Site
Scott 2021 <sup>20</sup>	Prospective	Australia, community	1304	0	76.5±5.2	EWGSOP2: Low muscle mass (DXA) + low muscle strength (Hand grip strength).	In the last 6 months, have you experienced pain in any part of your body which has lasted for 3 months or more, that is pain experienced every day for at least 3 months? In which part(s) of your body have you experienced this pain?	Pain anywhere
Wada 2019 <sup>21</sup>	Cross- sectional	Japan, outpatients	72	34	70.4±6.9	AWGS: Low muscle mass (BIA).	With both clinically and radiologically defined lumbar spinal stenosis with indications for surgical treatment. The participants were asked to rate their pain on a NRS in which 0 indicates no pain and 10 indicates the worst imaginable pain.	Low back or limb pain
Sakai 2017 <sup>22</sup>	Cross- sectional	Japan, outpatients	660	311	74.4±6.0	Low muscle mass (DXA). A relative SMI that was more than 2 standard deviations below the mean of young adults. (SMI:<6.87 kg/m2 for men and <5.46 kg/m2 for women)	Patients with CLBP who had no symptoms in the lower extremities, exhibit moderate to severe LBP persisting for a minimum of 3 months prior to treatment. All patients completed VAS for LBP.	Low back pain
Tsuji 2020 <sup>16</sup>	Cross- sectional	Japan, community	722	482	74.0±5.9	AWGS 2019: Low muscle mass (BIA) + low muscle strength (Hand grip strength) and/or low physical performance (Normal gait speed).	Do you feel low back pain in your daily life lately? We used the ODI score to assess functional outcomes associated with low back pain.	Low back pain
Tanishima 2017 <sup>23</sup>	Cross- sectional	Japan, community	216	137	73.0±7.8	AWGS: Low muscle mass (BIA) + low muscle strength (Hand grip strength) and/or Low physical performance (Gait speed).	Do you feel low back pain in your daily life lately? Subjects were asked to make a vertical mark through a 100-mm horizontal VAS Scale. We used ODI to assess functional outcomes associated with LBP.	Low back pain
Fransen 2014 <sup>24</sup>	Prospective	Australia, community	1555	0	76.9±5.5	Low muscle mass (DXA). Sarcopenia was defined as having an appendicular lean mass relative to the fat mass in the lowest 20% of the cohort distribution.	Pain in or around either knee on "most days for at least one month in the past 12 months".	Knee pain

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<b>Table I</b> (Continued).
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Author, Year	Study Design	CountrySampleFemaleMeanDefinition of SarcopeniaandSizeAge,PopulationYears		nd Size Age,				Pain Site	
Sun 2017 <sup>25</sup>	Cross- sectional	South Korea, community	4937	2777	70.3±0.2	Low muscle mass (DXA). Sarcopenia was defined as an appendicular skeletal muscle index of two standard deviations or more below the mean for young, healthy reference populations. The cut- off values were 6.03 kg/m2 in men and 4.14 kg/m2 in women.	The EuroQol-5 dimension descriptive system comprises five dimensions: mobility, self-care, usual activities, anxiety/depression, and pain/ discomfort.	Pain anywhere	
Maruya 2019 <sup>26</sup>	Cross- sectional	Japan, community	765	410	69.3±5.2	AWGS: Low muscle mass (BIA) + low muscle strength (Hand grip strength) and/or low physical performance (Gait speed).	The 25-question Geriatric Locomotive Functional Scale questionnaire has 25 questions comprising categories evaluating pain and difficulty in performing daily activities in the past 1-month period. Participants were judged to have pain if they scored more than 1 in the subcategories of lower limb pain of the GLFS-25.	Low limb pain	
Imagama 2020 <sup>27</sup>	Prospective	Japan, community	366	220	63.5±8.9	Low muscle mass (BIA). Sarcopenia was defined as appendicular skeletal muscle indexes of <7.0 kg/m2 and <5.8 kg/m2 in men and women, respectively.	Neuropathic Pain was investigated using the painDETECT questionnaire.	Neuropathic pain	
Han 202 I <sup>28</sup>	Cross- sectional	China, community	112	86	75.1±5.7	EWGSOP: Low muscle mass (DXA) + low muscle strength (Hand grip strength).	All participants were required to complete two copies of the Chinese version of the SPADI tool.	Shoulder pain	
Murphy 2013 <sup>15</sup>	Prospective	North America, community	2928	1502	73.5±2.9	EWGSOP: low muscle mass (DXA) + low muscle strength (Hand grip strength).	Pain and knee pain were self-reported in the previous 30 days.	Knee pain	
Veronese 2023 <sup>17</sup>	Prospective		4102	1821	69.7±7.2	EWGSOP2: Low muscle mass (SMM= 0.244*weight + 7.8*height + 6.6*sex – 0.098*age + race – 3.3 (where female=0 and male=1; race=0 [White and Hispanic], race=1.4 [Black] and race=-1.2 [Asian]).) + low muscle strength (Hand grip strength). Lower skeletal mass index was defined as the lowest quartile of the SMI based on sex- stratified values.	If they were often troubled by pain. The presence of pain was also ascertained in four sites (low back, hip, knee, feet) using VAS pain score.	Low back or limb pain	

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Lin 2022 <sup>29</sup>	Prospective	China, community	873	524	67.1±4.9	AWGS 2019: Low muscle mass (BIA) + low muscle strength (Hand grip strength) and/or low physical performance (Usual gait speed).	Have you experienced any pain persisting at least 1 month in the last 6 months? On a scale of 0 to 10, how would you rate the overall intensity of pain? What locations of the body were often affected by pain?	Pain anywhere
Imai 2022 <sup>13</sup>	Cross- sectional	Japan, community	113	-	76.3±5.6	AWGS2019: Low muscle mass (BIA) + low muscle strength (Hand grip strength) + low physical performance (Gait speed).	Chronic pain was defined by related symptoms within the month prior to the health check that had continued for $\geq 3$ months and corresponded to a numerical rating scale score of $\geq 1$ at the site of maximum pain.	Pain anywhere
Smith 2022 <sup>30</sup>	Cross- sectional	Low- and middle- income countries, community	14,585	8022	72.6±11.5	EWGSOP2: Low muscle mass (SMM= 0.244*weight + 7.8*height + 6.6*sex – 0.098*age + race – 3.3 (where female=0 and male=1; race=0 [White and Hispanic], race=1.4 [Black] and race=–1.2 [Asian]).) +low muscle strength (Hand grip strength). Lower skeletal mass index was defined as the lowest quartile of the SMI based on sex- stratified values.	Pain was assessed with the question "Overall in the last 30 days, how much of bodily aches or pain did you have?"	Pain anywhere
Tsuji 2023 <sup>31</sup>	Retrospective cross- sectional	Japan, outpatients	190	139	67.2±13.5	AWGS2019: Low muscle mass (BIA) + low muscle strength (Hand grip strength) + low physical performance (Gait speed).	The NRS was used for assessment of pain intensity.	Chronic musculoskeletal pain
lwahashi 2022 <sup>32</sup>	Cross- sectional	Japan, Outpatients	100	88	81.5±6.3	AWGS: Low muscle mass (BIA) + low muscle strength (Hand grip strength) + low physical performance (Gait speed).	Low back pain was evaluated using VAS with 100 being an extreme amount of pain and 0 no pain.	Low back pain

Abbreviations: AWGS, Asian Working Group for Sarcopenia; EWGSOP, European Working Group on Sarcopenia in Older People; BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry; SMM, skeletal muscle mass; CLBP, chronic low back pain; VAS, the Visual Analogue Scale; GLFS-25, 25-question Geriatric Locomotive Functional Scale; ODI, the Oswestry Disability Index; SPADI, the Shoulder Pain and Disability Index; NRS, numerical rating scale.

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% Cl	Mean Difference IV, Random, 95% Cl
Fransen 2014	0.0417335	0.008012	10.3%	0.04 [0.03, 0.06]	
Imai 2022		0.0585833	4.7%	0.22 [0.11, 0.33]	
Lin 2022	0.1024096	0.0166395	9.6%	0.10 [0.07, 0.14]	-
Maruya 2019	0.0441176	0.011137	10.1%	0.04 [0.02, 0.07]	-
Sakai 2017	0.4	0.0489898	5.7%	0.40 [0.30, 0.50]	
Scott 2021	0.0569948	0.0118	10.0%	0.06 [0.03, 0.08]	+
Smith 2022	0.1379175	0.0034127	10.5%	0.14 [0.13, 0.14]	•
Sun 2017	0.0751979	0.0095784	10.2%	0.08 [0.06, 0.09]	
Tanishima 2017	0.0714286	0.021766	9.0%	0.07 [0.03, 0.11]	-
Tsuji 2020	0.0767386	0.0130347	9.9%	0.08 [0.05, 0.10]	+
Veronese 2023	0.1618056	0.0097048	10.2%	0.16 [0.14, 0.18]	-
Total (95% CI)			100.0%	0.11 [0.08, 0.14]	•
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:		•	0.00001)	; I <sup>2</sup> = 96%	-0.5 -0.25 0 0.25 0.5 prevalence of sarcopenia

Figure 2 Forest plot of the prevalence of sarcopenia among older adults with chronic pain.

diagnostic criteria (0.10, 95% CI, 0.07–0.14). Additionally, the incidence of sarcopenia was observed to be greater in individuals who reported experiencing low back or limb pain (0.12, 95% CI, 0.06–0.17) as opposed to those who did not distinguish between pain locations (0.10, 95% CI, 0.06–0.15) (Table 2).

#### The Link Between Chronic Pain and Sarcopenia

Data regarding the link between chronic pain and sarcopenia were available from 11 studies.<sup>13,16,17,20,22–26,29,30</sup> These studies revealed a statistically significant positive correlation between chronic pain and an increased risk of sarcopenia, with a pooled OR of 1.52 (95% CI, 1.31-1.76), and relatively low heterogeneity between studies (I<sup>2</sup>=36%, p=0.11) (Figure 3). Subgroup analysis based on income level indicated significant differences between subgroups (p=0.02), with the low- and middle-income countries group showing a stronger association (OR, 1.73; 95% CI, 1.54-1.95) than the high-income countries group (OR, 1.38; 95% CI, 1.20-1.60). In terms of the diagnostic criteria for sarcopenia, the group using only muscle mass tended to have a higher correlation (OR, 1.65; 95% CI, 1.08-2.53) than the group using grip strength and/or physical performance as part of the diagnostic criteria (OR, 1.52; 95% CI, 1.30-1.77). Furthermore, the group reporting lower back pain or low limb pain tended to have a higher correlation (OR, 1.47; 95% CI, 1.16-1.86) (Table 3).

Subgroups	Studies (n)	Sample Size (n)	Heterogeneity P-value I <sup>2</sup> (%)		Prevalence (%) and (95% CI)	Subgroup Differences (P-value)
Income levels						
Low- and middle-income countries	2	15,458	P=0.04	77	12 (9–16)	P=0.53
High-income countries	9	14,374	P<0.001	95	(7–15)	
Diagnostic criteria of sarcopenia						
LMM	3	7152	P<0.001	96	14 (6–22)	P=0.35
LMM+LMS/LPP	8	22,680	P<0.001	95	10 (7–14)	
Pain sites						
No differentiate pain sites	5	21,812	P<0.001	95	10 (6-15)	P=0.73
Low back or limb pain	6	8020	P<0.001	97	12 (6–17)	

 Table 2 Subgroup Analyses of the Prevalence of Sarcopenia in People with Chronic

Abbreviations: LMM, low muscle mass; LMS, low muscle strength; LPP, low physical performance.

	Chronic pain No		Non-chronic pain Odds Ratio			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	I M-H, Random, 95% Cl
Veronese 2023	233	1440	338	2662	21.9%	1.33 [1.11, 1.59]	
Tsuji 2020	32	417	19	305	5.2%	1.25 [0.69, 2.25]	
Tanishima 2017	10	140	2	76	0.9%	2.85 [0.61, 13.34]	
Sun 2017	57	758	267	4179	14.0%	1.19 [0.89, 1.60]	+
Smith 2022	1408	10209	372	4376	27.0%	1.72 [1.53, 1.94]	<b>•</b>
Scott 2021	22	386	49	918	6.4%	1.07 [0.64, 1.80]	
Sakai 2017	40	100	149	560	8.2%	1.84 [1.18, 2.86]	
Maruya 2019	15	340	10	419	2.9%	1.89 [0.84, 4.26]	
Lin 2022	34	332	30	541	6.6%	1.94 [1.17, 3.24]	
lmai 2022	11	50	11	63	2.3%	1.33 [0.52, 3.39]	
Fransen 2014	26	623	16	932	4.6%	2.49 [1.33, 4.69]	
Total (95% CI)		14795		15031	100.0%	1.52 [1.31, 1.76]	•
Total events	1888		1263				
Heterogeneity: Tau <sup>2</sup> =	0.02; Chi <sup>2</sup>	= 15.67	df = 10 (P =	0.11); l <sup>2</sup> :	= 36%		
Test for overall effect:	Z = 5.62 (I	P < 0.00	001)				0.05 0.2 1 5 20 Negative association Positive association

Figure 3 Forest plot of the link between chronic pain and sarcopenia.

#### Sensitivity Analysis

To assess the robustness and credibility of our results, we conducted a leave-one-out sensitivity analysis. By systematically excluding one study at a time and pooling the remaining studies, we obtained adjusted estimates of sarcopenia prevalence ranging from 9% to 12%, and an adjusted OR between chronic pain and sarcopenia ranging from 1.43 to 1.58. Importantly, these adjusted estimates were akin to those derived from the original analysis, bolstering the reliability and stability of our results.

#### **Publication Bias**

In our present systematic review and meta-analysis, we visually inspected the funnel plot and observed a symmetrical distribution of studies, with a roughly even and concentrated distribution on both sides of the pooled effect size (Figure 4). Such a pattern suggests an absence of potential publication bias in our results.

## Discussion

In this systematic review and meta-analysis of 17 studies involving 33,600 older adults with low heterogeneity in the majority of analyses, the analysis revealed that a significant correlation between chronic pain and a higher prevalence of sarcopenia in older adults, with chronic pain being linked to an increased risk of developing sarcopenia. Notably, subgroup analyses showed that these associations were more significant in low- and middle-income countries. Our

Subgroups	Studies (n)	Sample Size (n)	Heterogeneity P-value I <sup>2</sup> (%)		OR (95% CI) M-H Random	Subgroup Differences (P-value)
Income levels						
Low- and middle-income countries	2	15,458	P=0.65	0	1.73 (1.54–1.95)	P=0.02
High-income countries	9	14,374	P=0.38	6	1.38 (1.20-1.60)	
Diagnostic criteria of sarcopenia						
LMM	3	7152	P=0.06	64	1.65 (1.08–2.53)	P=0.72
LMM+LMS/LPP	8	22,680	P=0.20	29	1.52 (1.30–1.77)	
Pain sites						
No differentiate pain sites	5	21,812	P=0.08	51	1.47 (1.16–1.86)	P=0.73
Low back or limb pain	6	8020	P=0.28	20	1.55 (1.25–1.93)	

Table 3 Subgroup Analysis of the Association Between Chronic Pain and Sarcopenia

Abbreviations: LMM, low muscle mass; LMS, low muscle strength; LPP, low physical performance.

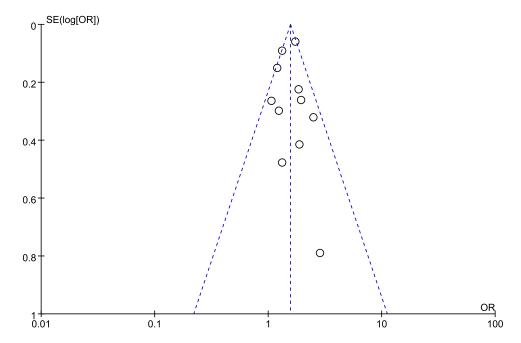


Figure 4 Funnel plot in the meta-analysis.

findings highlight the potential impact of chronic pain on the development of sarcopenia in older adults, particularly in certain global regions.

According to previous epidemiological studies that found significant differences in the prevalence of chronic pain across different socioeconomic conditions,<sup>33</sup> we divided the included studies into two subgroups based on their income levels for analysis. Our findings demonstrated that the correlation between chronic pain and sarcopenia was more pronounced in low-and middle-income countries than in high-income countries. There are two possible reasons for this observation. Firstly, low-and middle-income countries often have inadequate healthcare infrastructure and limited medical resources, which may hinder the provision of effective interventions for elderly individuals suffering from chronic pain.<sup>34,35</sup> Secondly, low- and middle-income countries tend to have lower levels of education, resulting in a general lack of awareness among the population regarding pain management. This often leads to misconceptions that pain is an inevitable part of aging, which can discourage individuals from taking active measures to manage and alleviate their pain. These factors, combined with the higher prevalence of chronic pain and limited access to appropriate medical care in low-income countries, contribute to an increased incidence of pain-related complications. These findings also indirectly suggest that aggressive treatment of chronic pain may significantly reduce the risk of developing sarcopenia. Therefore, we advocate for greater health education initiatives for the elderly in the community, aimed at dispelling traditional beliefs and promoting awareness and consultation rates, leading to a reduction in the incidence and delay of complications related to chronic pain.

We stratified our study into two subgroups based on the diagnostic criteria for sarcopenia, and the results were consistent with our expectations. When diagnosing sarcopenia based on low muscle mass (LMM) alone, the cumulative prevalence increased to 14%, whereas it decreased to 10% when combined with poor physical function and/or low muscle strength (LMS). Furthermore, the meta-analysis revealed that the pooled OR of studies that employed a combination of LMM, LMS, and/or poor physical performance as diagnostic criteria for sarcopenia was lower than that of studies that solely utilized LMM as the diagnostic criterion. This is due to the contradictory relationship between sensitivity and specificity of diagnostic criteria. Generally, using LMM alone may increase sensitivity and decrease specificity, whereas using LMM in combination with LMS and/or physical function may increase specificity and decrease sensitivity. Therefore, when developing diagnostic criteria in clinical studies, a balance must be achieved between sensitivity and specificity, and the most appropriate diagnostic criteria must be selected according to the practical application scenarios. The current international consensus recommends defining sarcopenia as a geriatric syndrome characterized by LMM, LMS, and/or poor physical performance, rather than just LMM. We recommend using international consensus diagnostic criteria as much as possible in such studies to obtain more convincing results.

To investigate the hypothesis that chronic pain may increase the risk of sarcopenia by impairing mobility and promoting a sedentary lifestyle,<sup>30</sup> we conducted analysis on two subgroups based on pain location. Our findings support the proposed hypothesis, as the group reporting low back pain or low limb pain exhibited a higher prevalence of sarcopenia than the control group that did not differentiate by pain site. Moreover, individuals reporting low back pain or low limb pain displayed an increased risk of developing sarcopenia compared to those who did not differentiate between pain sites. Nevertheless, the intergroup analysis did not reveal significant differences, which we suspect may be attributed to the relatively limited number of participants in the group reporting low back pain or low limb pain. Additional research is necessary to validate the results in the future. Nonetheless, our findings indicate that we must prioritize pain areas that hinder mobility in older adults and implement aggressive pain relief interventions.

The findings of this study are in line with those of a recent systematic review and meta-analysis of 14 observational studies.<sup>18</sup> However, this study has three distinct advantages. Firstly, most of the studies included in this meta-analysis are large sample cohort studies, which lend greater reliability and applicability to the results. In contrast, recent meta-analyses have included more case-control studies, which may introduce greater heterogeneity into the findings. Secondly, the population included in this study has an average age of 60 years or older, making the results of the meta-analysis more applicable to the elderly population. By comparison, recent meta-analyses have included younger populations, which may introduce bias and limit the reliability of the results. Thirdly, this study includes research from countries with diverse income levels, increasing the generalizability of the meta-analysis results. Recent meta-analyses have predominantly included research from high-income countries, which may limit the universality of the findings. Of course, our meta-analysis is not immune to limitations. Firstly, most of the included studies were cross-sectional in design, precluding the establishment of causality. Secondly, there were significant variations in the appraisal of chronic pain among the included studies, potentially impacting the accuracy of our outcomes. Lastly, the availability of data in the included studies was constrained, precluding an inquiry into the relationship between pain severity and sarcopenia.

## Conclusion

Our systematic review and meta-analysis provided evidence that the prevalence of sarcopenia is significantly higher in older adults with chronic pain compared to those without pain. There was also a significant positive correlation between chronic pain and an increased risk of sarcopenia. Additionally, pain in the low back or lower limbs, which can affect the mobility of older adults, was found to be associated with a higher likelihood of developing sarcopenia. However, the pathogenesis underlying the relationship between chronic pain and sarcopenia in older adults remains unknown. Several possible mechanisms have been proposed, including reduced activity and chronic inflammation, but these require further investigation through large-scale clinical studies in the future.

## **Data Sharing Statement**

No new data were created or analyzed in this study. Data sharing is not applicable to this article.

## **Consent for Publication**

Approval was obtained from all authors.

# **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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The authors report no conflicts of interest in this work.

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