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REVIEW

Association between frailty and chronic pain among older adults: a systematic review and meta-analysis

Taiping Lin[1,2] · Yanli Zhao[1,2] · Xin Xia[1,2] · Ning Ge[1,2] · Jirong Yue[1,2]

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Key summary points

Aim To estimate the prevalence of frailty and prefrailty among older adults with chronic pain and review the longitudinal association between frailty status and chronic pain.

Finds Frailty and prefrailty are common in persons with chronic pain. Chronic pain is a risk factor for developing frailty among older persons.

Message Non-frail older persons with chronic pain are more likely to experience physical frailty after an average follow-up of 5.8 years.

Abstract

Purpose Frailty and chronic pain are prevalent among older adults. However, no study has systematically reviewed the association between frailty and chronic pain in older adults. Therefore, we aimed to estimate the prevalence of frailty and prefrailty among older adults with chronic pain and review the longitudinal association between frailty status and chronic pain.

Methods Embase, Medline, Pubmed, and Cochrane library were searched from inception to March 2020. The methodological quality of the studies was assessed using the Newcastle Ottawa Scale. Random effect models and Mantel–Haenszel weighting were adopted to synthesize the estimates.

Results Among the initial 846 articles retrieved, 24 were included in the review (12 cross-sectional, and 12 longitudinal). The pooled prevalence in persons with chronic pain was 18% (95% CI 14–23%; $I^2=98.7\%$) for frailty and 43% (95% CI 36–51%; $I^2=98.2\%$) for prefrailty. The pooled prevalence of chronic pain was 50% (95% CI 45–55%; $I^2=88.3\%$) for individuals with frailty and 37% (95% CI 31–42%; $I^2=97.1\%$) for individuals with prefrailty. Persons with chronic pain were 1.85 (95% CI 1.49–2.28; $I^2=93.2\%$) times more likely to develop frailty after an average follow-up of 5.8 years compared to those without.

Conclusion Frailty and prefrailty are common in persons with chronic pain. Chronic pain among non-frail older persons significantly predicts the incidence of frailty after an average follow-up of 5.8 years. Future studies should explore the efficacy of different pain management strategies in reducing physical frailty and clarify the association of other types of frailty (cognitive, social and psychological) with chronic pain.

Keywords Frailty · Chronic pain · Older adults · Systematic review · Meta-analysis

Introduction

Frailty is a common clinical syndrome characterized by an underlying state of decline in reserve and function due to multisystem dysfunction [1, 2]. Frailty mainly manifests as the vulnerability to internal and external stress and the subsequent inability to restore to previous functional state. This means that even a small disturbance can render the older persons at risk of multiple adverse health outcomes, such as faster functional decline, prolonged hospitalizations, disability, higher health care-related expenses, and higher

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✉ Jirong Yue
yuejirong11@hotmail.com

1 Department of Geriatrics, West China Hospital, Sichuan University, Chengdu, Sichuan, China

2 Department of National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, Chengdu 610041, Sichuan Province, China

mortality rates [2–5]. Currently, there is no existing consensus regarding a standard definition of frailty. However, the frailty phenotype and deficits accumulation model has been extensively validated and widely used to conceptualize frailty. Fried et al. [5] characterized frailty as a purely physical condition of multisystem physiological dysregulation consisting of the presence of three or more of the following five components: weight loss, exhaustion, weakness, slow walking speed, and low physical activity. However, Rockwood et al. [6] defined frailty as predominantly an accumulation of deficits in various areas (symptoms, signs, functional impairment, and laboratory abnormalities). Beyond these two common definitions of frailty, several variations on the diagnostic criteria for frailty have also been developed [7]. Considering the dynamic nature of frailty and its development over time, many definitions also point out an identifiable intermediate stage between frail and non-frail known as prefrailty [8].

Studies have shown that the prevalence of pain in older adults increases with age [9]. Many older adults may have to spend most of their older age tackling the consequences of multiple chronic conditions. Among them, chronic pain is one of the most prevalent and burdensome in later life and it frequently leads to deleterious outcomes, including serious disability from reduced mobility, fall, depression, anxiety, sleep interference, isolation and sarcopenia [9–11]. Growing evidence suggests pain-related health consequences is linked to frailty onset and progression [12–23]. Chronic pain can be addressed through appropriate approaches, which represents one of the modifiable factors in improving frailty situation or reversing frailty status [9, 11, 24, 25]. The association between pain and frailty was not straightforward: some studies demonstrated that pain could act as a risk factor in increased frailty incidences [12–23], while other studies showed that pain is a consequence of frailty [24, 26, 27]. Since pain is a treatable condition, elucidating the association between pain and frailty can pave the way for the prevention, deceleration of progression, or even reversing the course of frailty among older people.

Therefore, the aims of our study were: (1) to perform a systematic review and meta-analysis of all studies regarding the prevalence of chronic pain and frailty and; (2) to perform a systematic review and meta-analysis of prospective studies regarding the longitudinal association between chronic pain and frailty among older persons.

Methods

The systematic review was reported following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Table S1) [28].

Data sources and search strategy

We first conducted a systematic literature search in Embase, Medline, Pubmed and Cochrane library via Ovid SP for observational studies from inception through the end of March 2020 without language restrictions. The keywords were chosen by examining other reviews on similar topics. The detailed search strategies are reported in Table S2. Moreover, references from the selected studies and other relevant reviews were also manually checked to determine their fit for potential candidates as selected studies.

Selection criteria

The titles and abstracts of all the selected articles in the initial search were screened independently by two reviewers (T. Lin and Y. Zhao). If either reviewer thought further evaluation was needed after the abstract screening, a full-text review was carried out against our selection criteria. Any discrepancy regarding the screening and selection of studies or the following extraction of data was resolved through consensus with a third independent reviewer (J. Yue).

Selection criteria were presented as follows: (1) cross-sectional and longitudinal studies that reported information on any of the above-mentioned aims were included; (2) studies reported the association between frailty and chronic pain in individuals aged 60 or older were included. Studies were excluded if: (1) individuals suffering from oncological, acute, or postoperative pain; (2) frailty was defined only with an indicator measurement (timed up-and-go test or gait speed); (3) they were case reports, letters, comments or editorials. When multiple studies used the same cohort, the study on the largest number of participants was selected.

Many cohort studies investigated the longitudinal relationship between frailty and chronic pain. And if the studies also reported frailty/pre-frailty prevalence in chronic pain or chronic pain prevalence in those with frailty/pre-frailty, they were also reported as cross-sectional and their relevant data were extracted.

Data extraction

The following items were extracted independently by two reviewers (T. Lin and X. Xia) from the eligible studies. A third reviewer (N. Ge) reviewed the data extraction, and any disagreement was resolved through consensus. The items included in the data extraction were as follows: the basic information of articles (the first author name, publication year, and cohort name), study design, location, cohort size, female proportion, mean age, follow-up period, the prevalence of frailty/prefrailty in chronic pain and pain prevalence in frailty/prefrailty older adults, effect measures of interest, pain assessment method and frailty definition. Effect measures adjusted for confounders, such as age and gender, would be included with priority. When an article provided several adjusted models, the model that adjusted for the largest number of confounders was extracted. If the estimates of ORs concerning the association between frailty and chronic pain was not reported in the original study, the relevant data included in the article were used to calculate an unadjusted effect measure.

Quality assessment

The methodological quality of the studies was evaluated independently by the two authors (T. Lin and Y. Zhao) using the Newcastle–Ottawa Scale (NOS) [29]. For observational studies, this validated assessment tool utilizes nine multiple-choice items covering three main domains: the selection of the cohort, comparability of the groups, and quality of the outcomes. The scale scores ranged from 0 to 9 points. Score ≥7 was classified as high quality, 5–7 point as moderate quality, and 4 or less indicated low quality.

Statistical analysis

All statistical analyses were performed using the *metan* and *metainf* packages in the STATA/SE (version15.1, Stata Corp, College Station, TX, USA). Two-tailed P value < 0.05 was considered statistically significant. Considering the observational design of the included studies, and the methodological differences that might have contributed to a significant share of the variance within the measures of interest, we obtained the pooled estimates through random effect models and Mantel–Haenszel weighting. Heterogeneity across the studies was assessed using the I^2 statistics (significant if $I^2 \geq 50\%$) [30]. Subgroup analysis based on different population was conducted to explore the stratified prevalence of frailty and chronic pain. Sensitivity analysis was performed by omitting each study to check the impact of individual study on the overall results. To limit the impact of extremes or outliers, we also performed sensitivity analyses which excluded studies with small sample sizes (≤ 500 participants, considering that studies with larger sample sizes are more likely to represent the general population. Publication bias was assessed using a funnel plot and Egger's test (linear regression method) [31].

Results

Literature search

Figure 1 shows the PRISMA flow diagram presenting the literature search as well as the number and reason for study exclusion. The initial search identified 844 records, and the manual review of the references yielded 2 eligible studies. 712 studies were retained after duplications were removed. After screening the titles and abstracts, 638 studies failed our selection criteria, leaving 74 studies for full-text review. Among them, 38 studies were excluded for the following reasons: (1). they did not investigate the aims of the review; (2). they did not provide an explicit definition of frailty or evaluated with a single measure; (3). the pain definition was unreported; (4). they were conference abstracts and there were no complete data. Ultimately, 36 articles were selected for the review and 24 studies were eligible to be assessed for methodological quality and perform the meta-analyses.

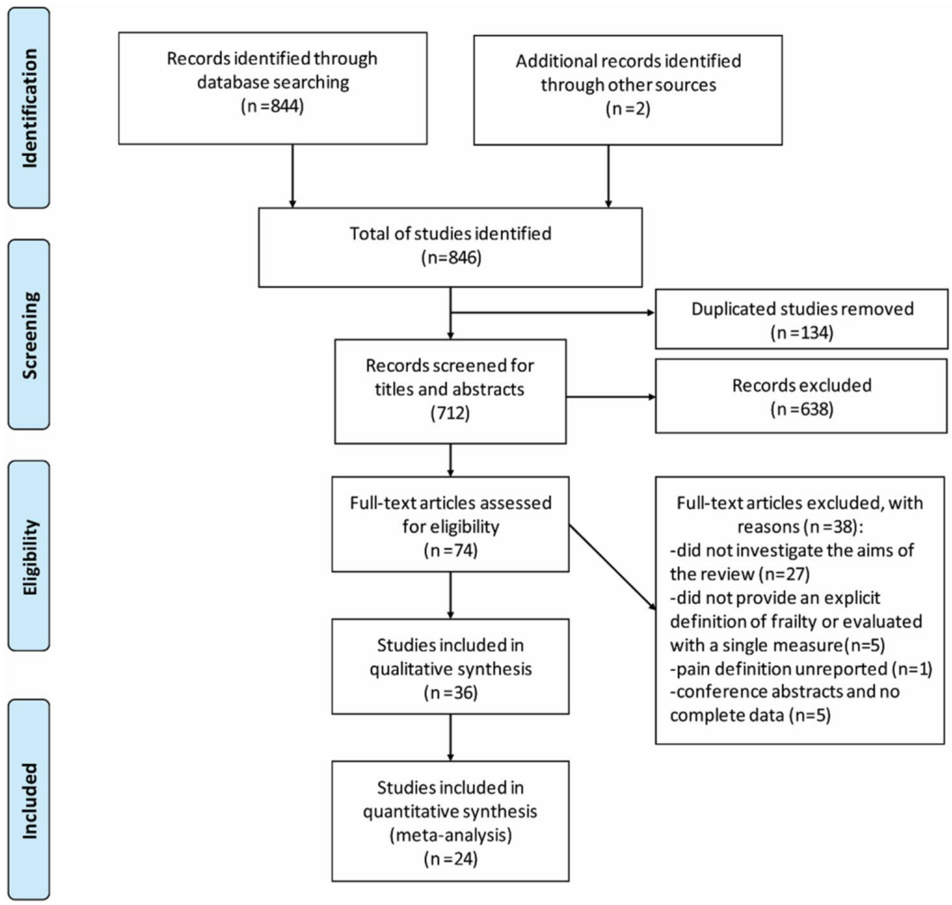
Study characteristics

The characteristics of the 24 included studies [12–24, 26, 32–41] were summarized in Table 1. The studies involved 39,370 older adults from 13 countries with six studies from North America, two from South America, eight from Europe, three from China, two from Australia and Japan. 22 studies involved community-dwelling older adults, one study [35] enrolled in nursing home individuals, and one study [40] included older adults with HIV. Frailty was defined based on the original or modified version of the Fried phenotype in 17 studies [13–16, 19, 21–23, 26, 32, 34–38, 40, 41], three studies [17, 18, 23] used the Frailty Index (the number of deficits used ranged from 33 to 51), and one study [12] used both methods, whereas another 4 studies used FRAIL scale ($n=2$) [23, 39], SOF frailty index ($n=1$) [20] and Kihon Checklist ($n=1$) [33]. Pain was assessed using different methods among the included studies. Most of them applied a simple question for pain evaluation: "Have you experience chronic pain lasting for several months?" Only nine studies defined pain intensity on a scale, and another seven studies defined specific locations of pain (knee, hip or hand pain). The NOS scores were presented in Table S3.

Cross-sectional association between chronic pain and frailty

Table 1 summarized the cross-sectional prevalence data from all 24 studies [12–24, 26, 32–41] on the association between chronic pain and frailty. One study [34] provided specific results concerning the relationship between analgesic use and frailty in community-dwelling older people. For this study, only data on the duration of pain lasting at least 3 months were extracted for our purpose. Another study [40] evaluated frailty and its association with health-related quality of life in older people with HIV. For this study, only data on chronic bodily pain and frailty were extracted. The pooled prevalence in individuals with

Fig. 1 PRISMA flow chart for selection of papers for systematic review



chronic pain was 18% (95% CI 14–23%; $I^2=98.7\%$) for frailty (derived from 23 studies; Fig. 2) and 43% (95% CI 36–51%; $I^2=98.2\%$) for prefrailty (derived from 16 studies; Fig. S1). The pooled prevalence of chronic pain was 50% (derived from 17 studies; Fig. 3) among individuals with frailty (95% CI 45–55%; $I^2=88.3\%$) and 37% (derived from 13 studies; Fig. S2) among those with prefrailty (95% CI 31–42%; $I^2=97.1\%$). As high heterogeneity was observed across the above meta-analyses, we limited the analyses to studies with at least 500 participants and the estimates and heterogeneity only changed minimally (data not shown). Additionally, a sensitivity analysis suggested that no individual study significantly affected the pooled prevalence of frailty in pain. We also conducted subgroup analyses based on different population settings to investigate the stratified prevalence of frailty/prefrailty in older persons with chronic pain and the prevalence of chronic pain among older adults with frailty/prefrailty. Results revealed that older persons from a nursing home or suffering from HIV were more susceptible to frailty or a combination of chronic pain. Results also revealed a lack of statistical significance existing between different subgroups (Supplementary Fig. S3, 4, 5, and 6).

Longitudinal association between chronic pain and frailty

Table 1 summarizes the 12 studies [12–23] (a total sample of 27,004 community-dwelling older persons) that evaluated the longitudinal association between chronic pain and the risks for frailty occurrence during the follow-up period. Ten studies [12–14, 16–18, 20–23] included in this review provided ORs with multiple confounders adjusted of frailty risks for pain. Two studies [15, 19] did not report relevant effect measures and unadjusted ORs were calculated according to study data. As shown in Fig. 4, non-frail participants who reported chronic pain were 1.85 (95% CI 1.49–2.28; $I^2=93.2\%$) times more likely to develop frailty after an average follow-up of 5.8 years compared to those who reported no chronic pain. This finding revealed that chronic pain at baseline is a risk factor for frailty incidence. As higher heterogeneity was observed across these studies, we performed a sensitivity analysis by omitting every single study and no statistical significance changed (Fig. S7). The asymmetric funnel plot (Fig. S8) and Egger's test ($P=0.002$) suggested the existence of publication bias or between-study heterogeneity.

Table 1 Characteristics of the observational studies on frailty and chronic pain among older persons

First author, year	Study characteristics	Pain definition	Frailty assessment method	Prevalence of frailty in pain group (%)/*n*		Prevalence of pain in frailty group (%)/*n*		NOS	Effect Measure	Adjusted confounders
				Frailty	Prefrailty	Frailty	Prefrailty			
Isabel [12] 2019	Prospective cohort; 1505 participants; Female (%): 654 (50); mean age (year): 70.3; Spain	Persistent pain based on the survey on Chronic Pain in Europe; pain intensity was based on its impact on habitual activities; Pain location was reported in six categories: (a) head and neck; (b) back; (c) bones and joints;(d) legs; (e) arms and (f) other sites	Fried phenotype[b] Frailty index	7.1/409 14.1/391	–	43.3/67 41.7/132	–	8/9	aOR	Age, sex, educational level, tobacco smoking, BMI, alcohol intake, time watching TV
Bindawas [13] 2018	Prospective cohort; 3053 participants; Female (%): 1672 (55); mean age (year): 59.9 ± 8.8; US	Questions about whether any pain, aching, or stiffness in or around unilateral or bilateral knee pain during the past 12 months	Fried phenotype[c]	4.3/1453	34.1/1453	–	–	7/9	aOR	Age, sex, race, education, marital status, smoking status, comorbidity, and BMI
Megale [14] 2018	Prospective cohort; 1705 participants; Female (%): 0 (0); mean age (year): 76.9 ± 5.5; Australia	Question for chronic pain: Dose pain last at least 3 months in the past 6 months. Intrusive pain based on the SF-12 questionnaire	Fried phenotype[b]	12.8/484	42.8/484	39.3/158	30.5/679	7/9	aOR	Age, living alone, post-school qualification, BMI, comorbidities, MMSE, depression
Dapp [15] 2014	Prospective cohort; 1679 participants; Female (%):1043 (62.1); mean age (year): 72.3; Germany	Questions about "whether chronic pain never completely goes away"	Fried phenotype[b]	26.3/453	8.6/453	44.9/265	22.7/172	5/9	Unreported	Unreported
Veronese [16] 2017	Prospective cohort study; 1775 participants; Female (%):1168 (65.8); mean age (year): 76.7 ± 7.6; Italy	Pain (hand, hip and knee) was ascertained based on medical records, symptoms, signs, and use of analgesics	Fried phenotype[b]	15.6/1304	–	–	–	7/9	aOR	Age, sex, BMI, GDS score; educational level; smoking habits; cognitive impairment, and so on

Table 1 (continued)

First author, year	Study characteristics	Pain definition	Frailty assessment method	Prevalence of frailty in pain group (%)/n		Prevalence of pain in frailty group (%)/n		NOS	Effect Measure	Adjusted confounders
				Frailty	Prefrailty	Frailty	Prefrailty			
Wade [17] 2016	Prospective cohort; 2736 participants; Female (%):0 (0); mean age (year): 59.3 ±10.6; Multiple[a]	Self-reported questions about whether pain lasting 3 months, and chronic widespread pain was based on the ACR criteria	Frailty index	12.4/218	20.6/218	27.3/99	12.3/366	7/9	aOR	Age, centre, BMI, smoking status, depression and physical activity
Wade [18] 2017	Prospective cohort; 5316 participants; Female (%):2993 (56.3); mean age (year): 64.5 ±8.5; UK	Questions about if they were often troubled by pain, and evaluate the intensity of their pain on a 3-point scale (mild, moderate, severe)	Frailty index	10.6/1890	–	61/328	–	8/9	aOR	Age, gender, BMI, smoking status, depressive symptoms, physical activity, occupation and wealth
Ferrer [19] 2015	Prospective cohort; 290 participants; Female (%):348 (60); mean age (year): ≥85; Spain	EQ-5D questionnaire and a visual analogue self-rating scale (VAS) for pain assessment	Fried phenotype[b]	–	–	–	–	5/9	Unreported	Unreported
Misra [20] 2014	Prospective cohort study; 3707 participants; Female (%): 2261 (61); mean age (year): 68 ±5.4; US	Pain on one knee or both knees resulted from knee osteoarthritis defined radiographically and symptomatically	SOF frailty index	5.9/1225	–	51.1/141	–	7/9	aRR	Age, sex, BMI, education, physical activity, comorbidities, smoking, and study indicator
Wise [21] 2013	Prospective cohort; 4130 participants; Female (%): 0 (0); mean age (year): 71.3 ±5.4; US	Self-reported question: "Have you experienced left or right hip pain within the past 1 month?" Hip pain only: defined as men with hip pain but no radiographic hip osteoarthritis (RHOA) or total hip replacement (THR)	Fried phenotype[b]	11.4/1140	43.4/1140	38.7/336	28.7/1724	7/9	aOR	Age, clinic site, BMI, college education, and comorbidities

Table 1 (continued)

First author, year	Study characteristics	Pain definition	Frailty assessment method	Prevalence of frailty in pain group (%)/*n*		Prevalence of pain in frailty group (%)/*n*		NOS	Effect Measure	Adjusted confounders
				Frailty	Prefrailty	Frailty	Prefrailty			
Sodhi [22] 2019	Prospective cohort; 1545 participants; Female (%): 902 (58.4); mean age (year): 74.3 ± 5.6; US	Self-reported the question: "In the past month, have you experienced pain or discomfort when you stood or walked?"	Fried phenotype[d]	24.4/538	–	–	–	6/9	aOR	Age, sex, marital status, education, comorbid conditions, BMI, MMSE, depressive symptoms, and limitation in activities of daily livings
Yang [23] 2019	Prospective cohort; 653 participants; Female (%): 303 (59.8); mean age (year): 73.0 ± 6.6; China	Comprehensive Geriatric Assessment (CGA) for chronic pain evaluation	FRAIL scale	13.4/291	28.2/291	68.4/57	61.7/133	6/9	aOR	Age, sex, BMI, education, smoking, MMSE, depressive
Shega [24] 2012	Cross-sectional study; 1765 participants; Female (%):1190 (67.4); mean age (year): 79.9 ± 6.1; Canada	5-point verbal descriptor scale for pain assessment (VDS)	Frailty index	49.8/1765	34.1/1765	55.7/1577	34.8/1728	6/9	Unreported	Unreported
Lohman [26] 2017	Cross-sectional study; 3652 participants; Female (%):2065 (56.5); mean age (year): 73.4 ± 6.5; USA	Questions "whether they were often troubled by pain and degree of this pain most of the time, who reported moderate or severe pain most of the time to be experiencing persistent pain"	Fried phenotype[b]	31.7/843	53.3/843	42.2/633	23.4/1921	6/9	Unreported	Unreported
Blyth [32] 2008	Cross-sectional study; 1705 participants female (%): 0 (0); mean age (year): 76.9 ±5.5; Australia	Questions from the SF-12 questionnaire about impact of pain: During the past 4 weeks, how much did pain interfere with your normal work? Intrusive pain was defined with moderate–severe interference with activities	Fried phenotype[b]	17.7/391	45.7/391	43.9/158	26.3/679	5/9	Unreported	Unreported

Table 1 (continued)

First author, year	Study characteristics	Pain definition	Frailty assessment method	Prevalence of frailty in pain group (%)/*n*		Prevalence of pain in frailty group (%)/*n*		NOS	Effect Measure	Adjusted confounders
				Frailty	Prefrailty	Frailty	Prefrailty			
Hirase [33] 2018	Cross-sectional study; 378 participants; Female (%): 329 (86.8); mean age (year): 79.3 ± 5.7; Japan	Chronic pain was defined as related symptoms within the past month that had continued for at least 6 months and corresponded to a numerical rating scale score of ≥ 5 at the site of maximum pain	Kihon Checklist	40.9/198	–	60.4/134	–	6/9	Unreported	Unreported
Marjaana [34] 2013	Cross-sectional study; 605 participants Female (%): 424 (70.1); mean age (year): 81.9 ±4.5; Finland	Chronic pain was defined as presence of pain over 3 months	Fried phenotype[b]	12.2/278	55.8/278	49.3/69	51.8/299	5/9	Unreported	Unreported
Morais [35] 2016	Cross-sectional study; 187 participants; female (%):151 (81.8); mean age (year): 68.95 ±7.1; Brazil	The Multidimensional Pain Assessment Scale was used for pain measurement, as follows: intensity of pain in the last week using a 0–10 scale. Chronic pain was defined as continuous or recurrent pain lasting 6 months or more	Fried phenotype[b]	23.5/182	54.0/187	–	–	4/9	Unreported	Unreported
Tian [36] 2017	Cross-sectional study; 1788 participants; female (%): 1191 (66.9); mean age (year): 69.1 ± 6.9; China	The Faces Pain Scale-revised (FPS-R) was used to measure the presence of pain and pain intensity. Respondents were asked to point to the face that best describes how much he or she hurts right now	Fried phenotype[b]	7.1/708	49.0/708	63.3/79	44.7/777	6/9	Unreported	Unreported

Table 1 (continued)

First author, year	Study characteristics	Pain definition	Frailty assessment method	Prevalence of frailty in pain group (%)/*n*		Prevalence of pain in frailty group (%)/*n*		NOS	Effect Measure	Adjusted confounders
				Frailty	Prefrailty	Frailty	Prefrailty			
Tse [37] 2016	Cross-sectional study; 142 participants; Female (%):74 (52.1); Mean age (year): 76.5 ± 7.7; Hong Kong	The 11-item Numerical Pain Rating Scale was used to measure the pain situations. This is a 0- to 10-point numerical rating scale used to assess the presence and intensity of pain among the participants	FRAIL scale	39.8/98	53.1/98	63.9/61	53.6/97	4/9	Unreported	Unreported
Coyle [38] 2015	Cross-sectional study; 123 participants; Female (%):77 (62.6); mean age (year): 70.1 ± 6.9; USA	The modified Oswestry Disability Questionnaire was used to measure low back pain-related disability. Participants with chronic low back pain were included if they met the following pain criteria: ≥ 3/10 pain intensity rating, ≥ 4 days per week in frequency, and ≥ 3 months duration	Fried phenotype[d]	6.1/66	66.7/66	–	–	4/9	Unreported	Unreported
Nakai [39] 2019	Cross-sectional study; 323 participants; female (%):241 (74.6); mean age (year): 75.2 ± 6.5; Japan	A face-to-face interview using the following questions: “Do you have low back pain or knee pain at the present time? Has that pain endured more than 2 months?”	Fried phenotype[b]	7.2/138	55.1/138	52.6/19	50.0/152	5/9	Unreported	Unreported

Table 1 (continued)

First author, year	Study characteristics	Pain definition	Frailty assessment method	Prevalence of frailty in pain group (%)/*n*		Prevalence of pain in frailty group (%)/*n*		NOS	Effect Measure	Adjusted confounders
				Frailty	Prefrailty	Frailty	Prefrailty			
Zeballos [40] 2019	Cross-sectional study; 201 participants; Female (%):73 (36.3); mean age (year): 60.2 ± 4.5; Brazil	Pain was defined as the presence of symptoms in the past 4 weeks, which compromised daily activities	Fried phenotype[b]	29.9/87	50.6/87	66.7/39	44.4/99	4/9	Unreported	Unreported
Hermsen [41] 2014	Cross-sectional study; 407 participants; Female (%):254 (62.4); mean age (year): 76.8(6.3); Netherlands	Asked participants whether joint pain site was most severe in the past 6 months. The Chronic Pain Grade was used to measure pain intensity of this most severe pain site	Fried phenotype[b]	20.9/358	20.9/358	–	–	5/9	Unreported	Unreported

NOS Newcastle–Ottawa scale for cohort studies, *SOF* study of osteoporotic fracture index, *aOR* adjusted odds ratio, *aRR* adjusted risk ratio, *SF-12* 12-item short-form, *ACR* America college of rheumatology

[a]Multiple: Italy, Belgium, Poland, Sweden, UK, Spain, Hungary, Estonia

[b] Fried phenotype with five criteria-weakness and slowness assessed using objective tests

[c]Fried phenotype with five criteria-weakness and slowness assessed using self-reported questions (subjective)

[d]Fried phenotype with four criteria

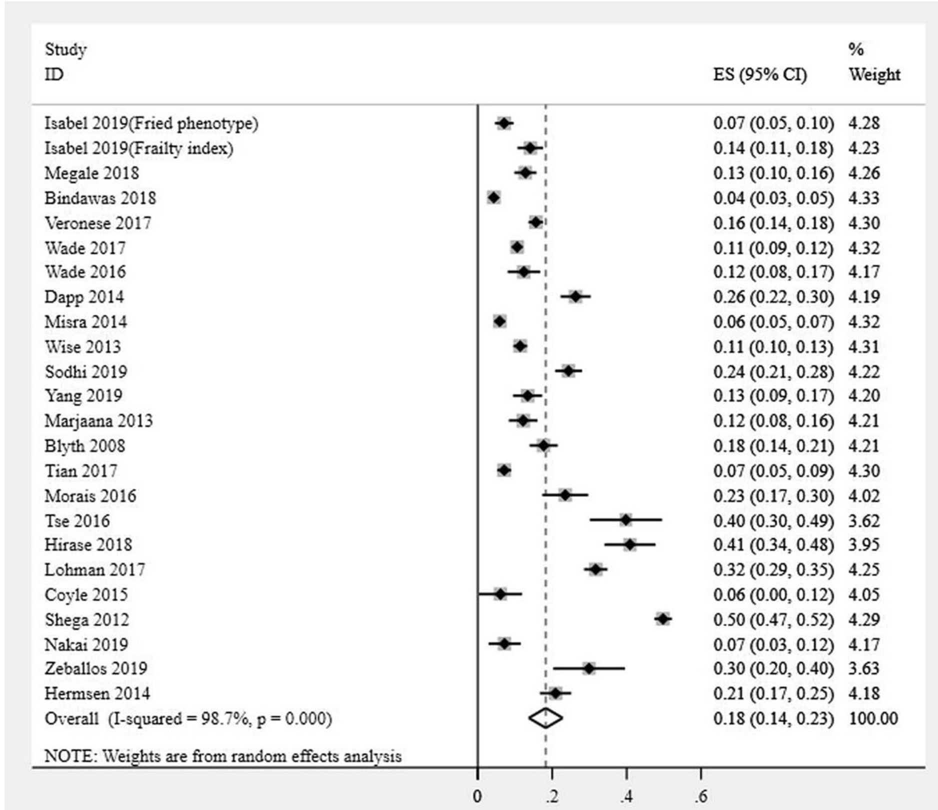


Fig. 2 Prevalence of chronic pain participants with frailty

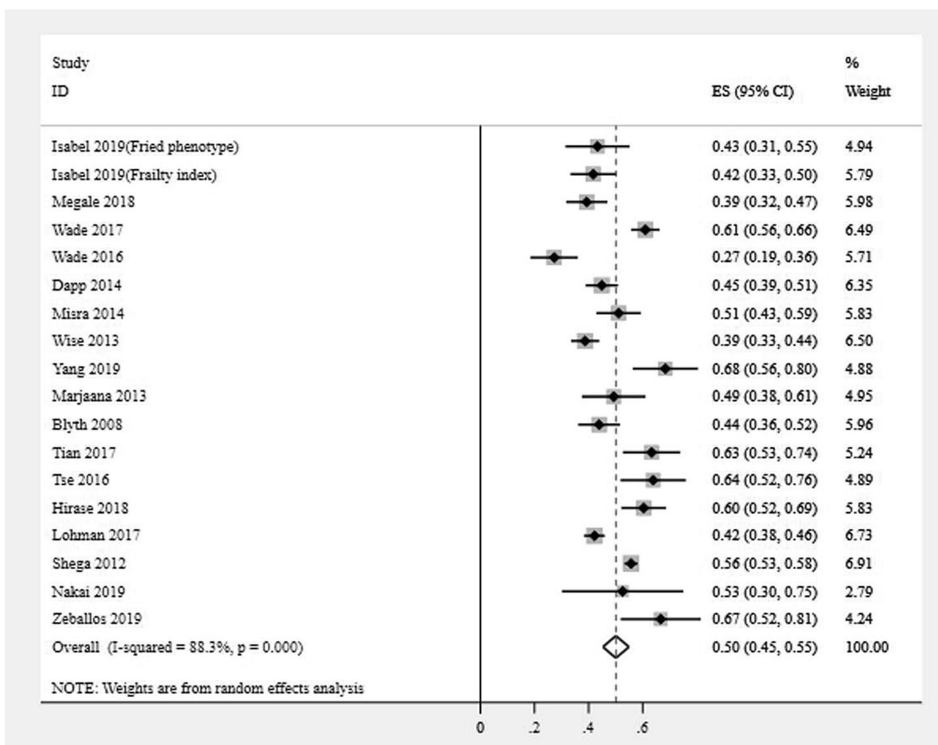


Fig. 3 Prevalence of frail participants with chronic pain

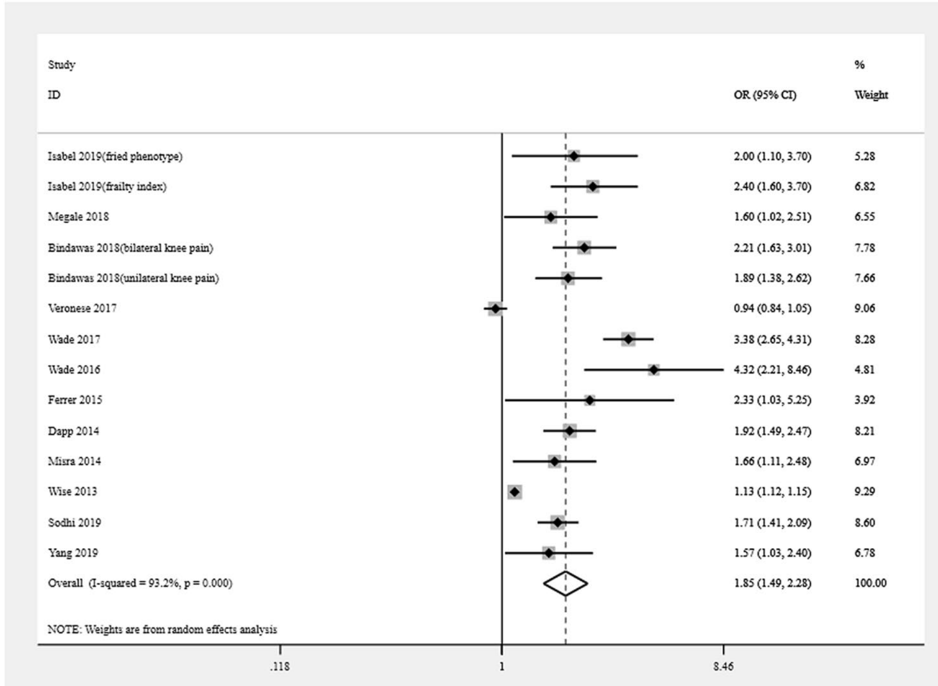


Fig. 4 Meta-analysis for the longitudinal association between baseline chronic pain and the risks for frailty occurrence

One study [14] with all 1705 older men analyzed the longitudinal association between frailty status at baseline and the risk of chronic pain in the future. In multi-adjusted models, those with baseline frailty did not independently increase the risk of developing chronic (OR = 0.82; 95% CI 0.38–1.79) or intrusive pain (OR = 1.38; 95% CI 0.70–2.74). Conversely, this study established that the presence of chronic pain had an increased likelihood of developing frailty among community-dwelling older men (OR = 1.60; 95% CI 1.02–2.51), even after adjusting for potential confounders.

Discussion

This systematic review and meta-analysis revealed that 5 out of 10 frail older adults have chronic pain, while about 2 out of 11 of older persons with chronic pain are frail. 37% of older persons with pre-frailty have chronic pain and 43% of older people with chronic pain present a condition of pre-frailty. The longitudinal studies found that baseline chronic pain increased the likelihood of developing frailty among older adults. Furthermore, only one study has been conducted to determine whether frailty predicts chronic pain incidence while failed to find a significant association between these two conditions.

When older patients suffer from the comorbidity of frailty and chronic pain, the treatment strategies might change. There are two reasons: first, frailty is related to limited life expectancy [42]. The evidence suggested that the expected years of life for frail individuals at age 70 ranged from 0.4 to 5.5 years (female) and 0.1–1.8 years (male) [42]. Treatment plans for those older persons with chronic pain and physical frailty require not only the formulation of tailored therapeutic approaches for chronic pain but also the emphasis of interventions with multidisciplinary physical frailty management [43–46]. Otherwise, the efficacy and process of pain management may be adversely affected by physical frailty [44, 45]. Second, the pain management strategies based on the existing evidence may not be suitable to be generalized for frail older persons with chronic pain, since older people with frailty usually do not participate in the clinical trials. This is extremely important when considering the observation that 50% of frail individuals studied also have chronic pain and 18% of persons with chronic pain are frail. To date, there have been no clinical trials of treatments for chronic pain which also considered the effects of frailty. Additionally, there are no clear guidelines that make any specific recommendations concerning treatments of chronic pain in frail older persons [9, 46].

Chronic pain and frailty share several mechanisms including sedentary behaviors, malnutrition, and sleep impairment [2, 4, 9, 10]. Frailty is positively associated with sedentary behaviors [47]. Similarly, a sedentary lifestyle is a major contributor to muscle weakness, which in turn leads to further declines in activity levels and loss of muscle mass and strength, causing the development of sarcopenia [48]. Nevertheless, the fear-avoidance behavior in physical exercises leads to the formation of a sedentary lifestyle and the misleading common sense for treatment recommendations is to rest as much as possible, which can be a frequent problem among patients with chronic pain, gradually experiencing mobility impairments and slow gait speed [49, 50]. Both weight loss resulted from sarcopenia, and gait speed reductions are essential components for frailty [5]. In addition, it is well-known that unhealthy dietary behaviors can often be observed in patients with chronic pain [51]. In turn, emotional anxiety, depression, and social loneliness caused by chronic pain may lead to anorexia and even malnutrition [52]. These data emphasize the importance of considering frailty when making therapeutic regimens for chronic pain as well as the importance of developing tailored exercise programs and nutrition interventions for frail patients with chronic pain.

The meta-analysis of longitudinal studies showed a nearly two-fold increase in the likelihood of developing frailty in older adults affected by chronic pain compared with persons without after an average follow-up of 5.8 years. This observation is consistent with the results of a previous systematic review [53]. A possible explanation for our findings could be that chronic diseases, including chronic pain, are generally considered to be the determinants of frailty, and the adverse outcomes, such as disability and malnutrition, induced by chronic pain can result in frailty incidence [5]. It is estimated that 66% of older adults have at least two chronic conditions [54]. Thus, effective and tailored prevention strategies for comorbidity are crucial to reduce the overall disease burden.

Nonetheless, only one longitudinal study assessed the impact of frailty on the development of chronic pain, and no statistical significance was found. Lack of evidence does not mean a lack of significant association between these two conditions. Since there was only one cohort study included, we were unable to conduct a meta-analysis. This finding might be explained by the fact that frail individuals are associated with limited life expectancy and persons with frailty could be more likely to be lost in follow-up [42]. As a result, it is difficult to draw any firm conclusions about the causal association between baseline frailty and future chronic pain.

This study had several unique characteristics. It was the first systematic review and meta-analysis on the prevalence of frailty and prefrailty among older patients with chronic pain. Also, we conducted a comprehensive literature search and rigorous literature selection as well as methodological evaluation, providing a reliable review of the evidence concerning the association between frailty and chronic pain.

However, our study has some limitations. First, substantial heterogeneity was detected among the included studies, which could be explained by the lack of standard diagnostic methods for frailty and chronic pain and by the demographic discrepancies across studies. However, in the meta-analyses of observational studies, heterogeneity is often inevitable, and it does not necessarily invalidate the research results [55]. Second, only one longitudinal analyzed the association between frailty and the development of chronic pain, which limited the opportunity to conclude whether a causal association existed between frailty and chronic pain. Third, there are limited original studies examining the impact of chronic pain on cognitive, social, or psychological frailty. Therefore, more studies are needed to better understand the association between pain and types of frailty other than physical frailty.

Conclusion

We have found that non-frail older persons with chronic pain were more likely to experience physical frailty after an average follow-up of 5.8 years. We also found that frailty and prefrailty were common in older persons with chronic pain. Taken together, our findings suggest that early assessment and effective interventions of chronic pain may help reduce physical frailty and improve the quality of life. Future studies should explore the efficacy of different pain management strategies in reducing physical frailty and clarify the association of other types of frailty (cognitive, social and psychological) with chronic pain.

Author contributions TL and JY designed the study, developed the study protocol, and performed all analyses, and oversaw the management of all aspects of the study. All co-author conducted the literature search and participated in screening, full-text review and data extraction. JY and NG advised on analysis and contributed to the interpretation of findings. TL contributed to the writing of the final manuscript and all co-author approved the final version for submission.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent not applicable.

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