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Review Paper

Association between frailty and incident risk of disability in community-dwelling elder people: evidence from a meta-analysis

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ABSTRACT

Objective: Frailty is considered to be one of the risk factors of disability. However, the results of original reported studies are not consistent with respect to the frailty and incidence of disability, and previously published meta-analyses have also shown inconsistent results. This meta-analysis was conducted to investigate the relationship between the different stages of frailty and the incidence of disability by examining updated overall trends in community-dwelling elders.

Study design: Cohort studies in English or Chinese based on associations between frailty and incident disability risks that were published from 2000 until the current date were researched using PubMed, Embase, Web of Science, and CENTRAL databases.

Methods: The Q test and I^2 statistic were used to examine between-study heterogeneity. Random-effect models were adopted to synthesize the results based on the study heterogeneity. Subgroup analyses were also conducted to explore the possible sources of between-study heterogeneity based on the characteristics of participants.

Results: Eighteen cohort studies with 88,906 participants were included in our meta-analyses. Compared with the non-frailty category, the combined relative risks (RRs) (95% confidence interval [CI]) of the disability were 1.66 (1.49–1.85) and 2.53 (2.01–3.14) for the category of prefrailty and frailty, respectively. Results suggested that the incident risk of disability at follow-up times <5 (RR = 3.19, 95% CI = 2.25–4.53) was significantly higher than for follow-up times ≥5 in the frailty category (RR = 2.00, 95% CI = 1.55–2.56). The risk in a sample size of ≥1000 (RR = 2.78, 95% CI = 2.04–3.14) was significantly higher than that when the sample size was <1000 (RR = 1.91, 95% CI = 1.53–2.37) in the frailty group. Compared with a value adjusted

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for comorbidity, the unadjusted comorbidity was significantly higher in the prefrailty category (1.90 *vs.* 1.52). Compared with a value adjusted for education, the unadjusted education was significantly higher in the prefrailty category (1.81 *vs.* 1.46). No publication bias was observed. *Conclusion:* The overall meta-analysis confirms that frailty has significantly increased the incident risk of disability. Frail, elderly people are at the highest risk of future disability and may be adequate candidates for taking part in prevention and intervention programs.

Introduction

Today, for the first time in history, most people worldwide have longer life spans and are expected to live into their sixties and beyond.[1] By 2050, the number of people aged 60 years and older worldwide is estimated to reach two billion, an increase from the figure of 900 million in 2015.[1] As a result, the problems of aging in the society have become severe, one of which is the high rate of disability.

A disability may be described as the loss of functional ability, loss of capacity to carry out tasks as an individual, and inability to participate in society.[2] For the elderly and their families, the level of dependence in their daily life is crucial to assessing health outcomes. These outcomes are strongly related to their quality of life, increase in the demand for nursing care, and increase in the possibility of transfer to a nursing home and are also associated with future hospitalizations and rate of mortality.[3–5] Because of the high prevalence and heavy burden of disability on the social, medical, and economic systems, timely prevention of disability in the elderly is a great matter of concern. Therefore, identifying and characterizing modifiable risk factors of disability in the elderly are important for general public health and clinical medicine.

Frailty and disability frequently coexist in older adults but are not synonymous.[6] One study showed that frailty may be a physiological precursor and etiologic factor in disability.[7] Frailty refers to the biological syndrome that is caused by a decline in the physiological reserves of multiple organ systems and leads to increased vulnerability to adverse health outcomes because of age-related cumulative deficits.[8] In general, people are more likely to develop frailty as they get older. Prevalence of frailty among community-dwelling people and the older population is widely variable depending on the setting, ranging from 4.0% to 59.1%.[9] Frailty has been shown to be associated with multiple adverse health outcomes, such as disability, falls, hospitalization, institutionalization, and death.[10] Frailty-associated disability severely affects individuals and their families. The early assessment and prevention of frailty have the potential to reduce the incidence of disability.

Although several definitions and criteria for frailty have been proposed, an international consensus has yet to be reached, partially because of the multidimensional and heterogeneous nature of the concept. The most common operational definitions of frailty are the physical frailty phenotype (FP) described by Fried et al. in the cardiovascular health study (CHS).[7] They defined frailty as a clinical syndrome, using a combination of five physical components: unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity.[7,11] They defined prefrailty as having one or two of the five components. The presence of three or more of the physical components was considered as frailty.[7,11] The study of osteoporotic fractures (SOF) criteria were proposed as a simpler version of the CHS criteria, including three physical components: unintentional or intentional weight loss >5% in the past year, inability to rise from a chair five times without using the arms, and self-reported low energy level.[12] The frailty index (FI) is another popular conceptualization of frailty, proposed by Jones et al.[13] The FI is based on a significant volume of information retrieved from the results of a comprehensive geriatric assessment (CGA).[13] It characterizes frailty across multiple dimensions, providing a quantitative and objective estimate of the accumulation of deficits experienced by the person with increasing age.[14]

Multiple studies have examined the association between frailty and disability and have found that compared with non-frail individuals, frail or prefrail individuals are more likely to develop or worsen disability.[15,16] Numerous investigations and research have shown that frail individuals are significantly more likely to develop disability than non-frail individuals; however, several studies have yielded mixed results on the effects of frailty on developing disability.[17,18] Only one systematic review was found in the literature examining frailty and disability risks.[19] This article reviewed studies from 2000 to 2016 including 20 studies. The author explained how consistently and the degree to which frailty is actually associated with future disability.[19] It should be noted that some important studies published since 2016 were not reported. As new original studies were published since 2016, we aimed to conduct an updated systematic review to identify studies investigating prospective associations between frailty and the incident disability risks and perform a meta-analysis to analyze pooled evidence of the incident disability risks due to physical frailty among community-dwelling elders. Given the inconsistent findings from the previous studies,[17,18] the current systematic review and meta-analysis study providing pooled risk estimates will further promote our understanding of frailty as well as identification of those elders who are at most risk of future disability and who may be adequate candidates for participation in prevention and intervention programs.

Methods

Data sources and search strategy

A systematic literature search was conducted in December 2018 based on a protocol developed in accordance with

Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) using four electronic databases (PubMed, Embase, Web of Science, and CENTRAL). Any prospective studies in English or Chinese published from 2000 until the current date which were based on associations between frailty and incident disability risks were searched because the reviewers are fluent in both of these languages. The following search strategy was used: (disability OR disabled OR physical disability OR disabilit* OR disable* OR ADL OR activities of daily living OR IADL OR instrumental activities of daily living) AND (frailty OR frail OR frailty syndrome OR frail elderly) AND (cohort study OR prospective study OR longitudinal study OR follow-up study). In addition, all references published in the retrieved articles and meta-analyses were manually searched.

Study selection

Studies were included if they met the following criteria: (1) if the study had a prospective study design; (2) if the study involved community-dwelling elders with a mean age of 60 years or older; (3) if the study focused on frailty defined by original or modified versions of valid frailty criteria based on physical components; and (4) if the study provided hazard ratio (HR) or odds ratio (OR) or relative risk (RR) as a risk measure or the above were computable from available data. The exclusion criteria were as follows: (1) frailty was defined by surrogate measures rather than categorizing subjects as frail or prefrail; (2) frailty status was defined by multidimensional criteria including cognitive, psychological, and social factors; (3) poster presentations, review articles, dissertations, or randomized controlled trials; and (4) the scores of methodological quality according to Newcastle-Ottawa Scale (NOS) were <7.

When plenty of eligible studies used data from the same cohort, the study defining three categories (robustness, prefrailty, and frailty) rather than two categories (frailty and non-frailty) and the study with the largest number of individuals were included. When diverse physical frailty criteria were used in one study, the data according to CHS criteria, which are the most frequently used guideline, were included.

Detail extraction and quality assessment

Data were extracted from the eligible studies using a standard data collection sheet which included the name of the first author, year of publication, location, sample size, age (mean or range), duration of follow-up, method used to measure disability, adjustment for potential confounding, and estimate of associations. All eligible studies were assessed for their methodological quality based on the Newcastle-Ottawa scale for cohort studies (range: 0–9 stars).[21] In the current research, a study was considered to be of good quality if seven or more stars were met[20] because standard validated criteria for important endpoints were not established. Data extraction and quality assessment were performed by two independent investigators. Any disagreement was settled by discussion.

Statistical analysis

All analyses were performed using Stata 12.0 software (Stata Corporation, College Station, TX, USA), and two-sided *P* values of less than 0.05 were considered statistically significant. We assumed that hazard ratio (HR) and odds ratio (OR) were valid estimates of relative risk (RR); therefore, we reported all results as RR simplicity. The pooled RR with its corresponding 95% confidence interval (CI) was calculated to assess the association of frailty with the incident risk of disability. Heterogeneity was detected using Cochran's Q test and I^2 statistic, where I^2 values of 25%, 50%, and 75% were considered as low, moderate, and high degrees of heterogeneity, respectively. In the presence of substantial heterogeneity ($I^2 > 50\%$), the Dersimonian and Laird random-effects model was adopted as the pooling method.

Subgroup analysis using the parameters of location, duration of follow-up, frailty criteria, education, comorbidity, and sample size was performed. Sensitivity analysis was performed by excluding one study at a time and analyzing the remaining studies to assess whether the outcomes were markedly affected by a single study or not. We conducted a publication bias using Egger's tests and by performing visual inspection of funnel plots.

Results

Selection processes

Fig. 1 is a flow diagram presenting the literature search and study selection. The systematic review using three electronic databases identified 4711 studies. A total of 1509 duplicate studies were excluded, and 3172 studies were excluded by title and abstract review, leaving 30 studies for the full-text review. An additional 10 studies were excluded for the following reasons: the study used the cross-sectional method (n = 3), no effective measures for defining the frailty category were shown (n = 3), the study did not classify frailty into three or two categories (n = 2), and the study lacked data (n = 1), and same cohort was used (n = 1). The manual search found two relevant studies; 22 studies remained and were examined for methodological quality using the Newcastle-Ottawa quality assessment scale for cohort studies. Four studies were excluded if NOS recorded <7. All remaining 18 studies were scored as seven or greater and were considered as having adequate quality of methodology to be included in the meta-analysis.

Study characteristics

Table 1 shows the characteristics of the 18 included studies involving 88,906 community-dwelling older people who were examined for the incident disability risks according to frailty status.[7,15,16,18,22–35] Eight studies were from the USA,[7,26–30,32,33] three from Spain,[23,24,35] two from Italy,[18,34] and one each from Brazil,[25] the UK,[22] Japan,[15] Mexico,[16] and France.[31] Disability outcomes were classified either as incident activities of daily living (ADLs) or instrumental activities of daily living (IADLs). As many as 66.7% (12/18) of the studies examined ADL disability risks,[7,16,18,22–25,27–29,33,34] while IADL was examined in six studies.[15,26,30–32,35] Methods used to assess frailty were FP, SOF scale, and FRAIL scale. Fifteen studies used FP,[7,15,16,22–24,26–29,31–35] two studies used SOF,[18,30]

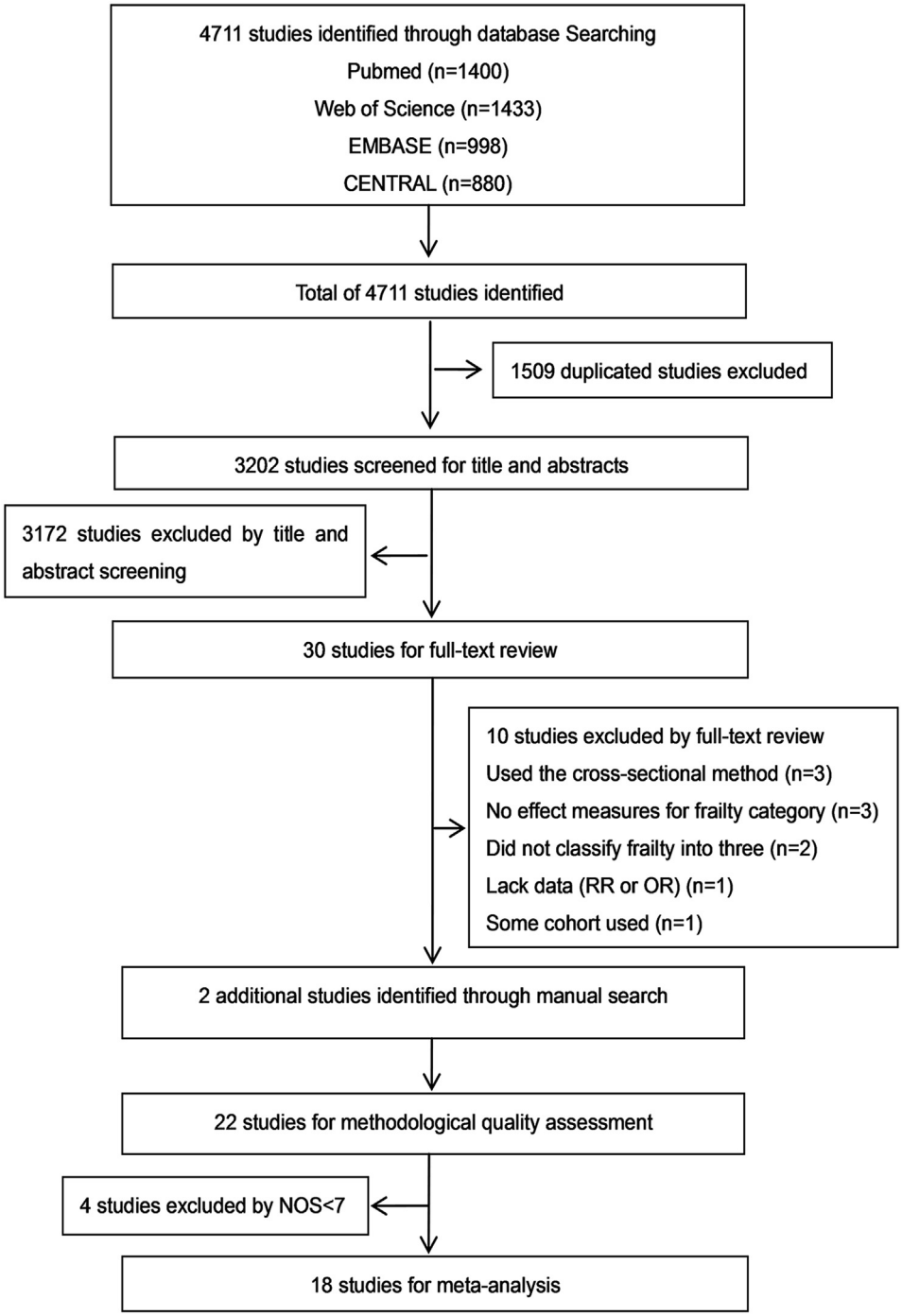

Fig. 1 – Flowchart of the selection of studies for inclusion in this meta-analysis.

and one study used the FRAIL scale.[25] Nine studies[16,18,22,24,27,29–32] reported OR, and another nine studies reported HR.[15,23,25,26,28,33–35] The scores of methodological quality according to the NOS is seven stars in 10 studies,[18,22,25,27–30,32,34,35] eight stars in seven studies,[7,16,23,25,26,31,33] and nine stars in one study.[24] The total population assessed in the included studies varied from 604 to 40657. Three studies involved only women,[27,28,30] two involved only men,[22,32] and the rest involved both men and women. The follow-up periods ranged from one year to 11 years.

Frailty and the incident risk of disability

Compared with the non-frailty category, the pooled RRs (95% CI) of the category of disability were 1.66 (1.49–1.85) and 2.53 (2.01–3.14) for the category of prefrailty and frailty, respectively, (Figs. 2 and 3). No evidence for high heterogeneity was found in the literature for the prefrailty group (I^2 = 55.5%). For the frailty and the incident disability risk, the heterogeneity test showed high heterogeneity in the frailty group (I^2 = 83.7%). Therefore, we undertook the

Table 1 – Characteristics of included cohort studies on frailty and disability.

Author, year, country	Age range (years)	Duration of follow-up (years)	Study size no.	Assessment method of disability	Measure of frailty	Effect measure	HR/OR (95% CIs)	Adjustment factors
Ivan et al., 2018 (Brazil)	≥60	1	785 M + W	ADL	FRAIL scale	HR	1 2.56 (1.41–4.65) 3.80 (2.07–6.97)	Age, sex, race, income
Bonaga et al., 2018 (Spain)	≥70	5.5	993 M + W	ADL	FP	OR	1 1.8 (0.7–4.8) 2.1 (0.5–8.5)	Age, sex, comorbidity
Cristina et al., 2017 (Spain)	≥65	5.5	1645 M + W	ADL	FP	HR	1 1.96 (1.30–2.97) 5.30 (2.82–9.93)	Age, sex, comorbidity
Efstathios et al., 2017 (UK)	71–92	3	1622 M	ADL	FP	OR	1 1.85 (1.19–2.89) 6.19 (3.29–11.65)	Age
Makizako et al., 2015 (Japan)	≥65	2	4341 M + W	IADL	FP	HR	1 2.52 (1.56–4.07) 4.65 (2.63–8.22)	Age, sex, BMI, MMSE
Navarro et al., 2015 (Mexican)	>60	11	5644 M + W	ADL	FP	OR	1 1.36 (0.97–1.90) 1.69 (1.16–2.47)	Age, sex, education, smoking, alcohol, chronic disease, self-reported health, depression, cognitive function
Paola et al., 2014 (Italy)	65–97	3	604 M + W	ADL	SOF	OR	1 1.61 (1.06–2.42) 1.99 (0.92–4.29)	Age, gender, education, smoking, alcohol, BMI, depression
Abizanda et al., 2013 (Spain)	≥70	1.5	993 M + W	IADL	FP	HR	1 1.1 (0.8–1.7) 1.9 (1.1–3.3)	Age, sex, Barthel Index, Charlson Index
Solfrizzi et al., 2012 (Italy)	65–84	7	2851 M + W	ADL	FP	HR	1.16 (0.88–1.56)	Age, sex, education, comorbidity, serum albumin levels
Al snih et al., 2009 (USA)	≥65	10	1645 M + W	ADL	FP	HR	1 1.26 (1.05–1.52) 2.03 (1.40–2.94)	Age, gender, marital status, education, medical conditions, MMSE, BMI
Buchman et al., 2009 (USA)	80.4 mean	8	832 M + W	ADL	FP	HR	1.69 (1.26–2.26)	Age, gender, education
Buchman et al., 2009 (USA)	80.4 mean	8	832 M + W	IADL	FP	HR	1.76 (1.30–2.40)	Age, gender, education
Ensrud et al., 2009 (USA)	≥65	1.2	3132 M	IADL	FP	OR	1 2.61 (1.89–3.62) 7.52 (5.41–11.02)	Age
Avila-Funes et al. 2008 (France)	74.1 mean	4	6078 M + W	IADL	FP	OR	1 1.43 (1.15–1.78) 2.10 (1.41–3.11)	Age, sex, education, income, smoking, alcohol, chronic disease, self-reported health
Ensrud et al., 2008 (USA)	≥65	4.5年	9704 W	IADL	SOF	OR	1 1.84 (1.63–2.09) 2.17 (1.82–2.58)	Age
Sarkisian et al., 2008 (USA)	70–79	4年	1189 M + W	ADL	FP	OR	1 1.8 (1.2–2.7) 4.4 (2.1–9.4)	Age, sex, ethnicity, education, comorbidity

Boyd et al., 2005 (USA)	≥65	3年	1002 W	ADL	FP	HR	1 1.5 (0.9–2.3) 2.2 (1.4–3.6)	Age, race, chronic medical conditions, self-reported health, depression, cognitive function
Woods et al., 2005 (USA)	65-79岁	5.9年	40657 W	ADL	FP	OR	1 1.64 (1.31–2.04) 3.15 (2.47–4.02)	Ethnicity, age, income, education, comorbidity
Fried et al., 2001 (USA)	≥65岁	7年	5201 M + W	ADL	FP	HR	1 1.55 (1.38–1.75) 1.79 (1.47–2.17)	Age, gender, income, smoking

Note: OR: odds ratio; HR: hazard ratio; MMSE: Mini-mental State Examination; (I)ADL: (instrumental) activities of daily living; (m)FP: (modified) frailty phenotype; SOF: Study of Osteoporotic Fractures; NOS: Newcastle-Ottawa Scale; W: women; M: men; BMI: body mass index; CI: confidence interval.

subgroup analysis to identify potential confounding factors.

Subgroup analysis

For the categories of frailty and prefrailty, the subgroup analysis showed results that were consistent with the overall analysis (Table 2). The studies were divided into subgroups based on several study characteristics including location, follow-up period, frailty criteria, education, comorbidity, and sample size.

It was noted that the incident risk of disability at a follow-up period of <5 years (RR = 3.19, 95% CI: 2.25–4.53) was significantly higher than the risk at a follow-up period of ≥5 years (RR = 2.00, 95% CI: 1.55–2.56) in the frailty category. The risk observed in studies with a sample size ≥1000 (RR = 2.78, 95% CI: 2.04–3.14) was significantly higher than what was observed when the sample size was <1000 (RR = 1.91, 95% CI: 1.53–2.37) in the frailty group. Compared with a value adjusted for comorbidity, the unadjusted comorbidity was significantly higher in the prefrailty category (1.90 *vs.* 1.52). Compared with a value adjusted for education, the unadjusted education was significantly higher in the prefrailty category (1.81 *vs.* 1.46).

Sensitivity analysis

In the sensitivity analysis, one study was removed at a time and the rest were analyzed. The results showed that the pooled RRs ranged from 1.45 to 1.91 for prefrailty and from 1.93 to 3.29 for frailty, respectively, which indicated that the pooled estimates were stable and not influenced by any individual study (Fig. 4A and B).

Publication bias

The shape of funnel plots to assess publication bias was roughly symmetrical (Fig. 5A and B). No evidence for publication bias was indicated by Egger's regression test in the literature on prefrailty and the incident disability risk ($P = 0.79$) or on that of frailty and the incident disability risk ($P = 0.53$).

Discussion

This meta-analysis indicates that community-dwelling older people who were classified as frail (RR = 2.53, 95% CI = 2.01–3.14) or prefrail (RR = 1.66, 95% CI = 1.49–1.85) had significantly higher risks of the incident disability than those classified as robust. We discovered an increase in the risk by a factor of 2.53 in frail participants as compared with normal participants. When the analysis was stratified by the follow-up period and sample size, it was observed that the risk of incident disability at a follow-up period of <5 years (RR = 3.19, 95% CI: 2.25–4.53) was significantly higher than what was observed at a follow-up period of ≥5 years (RR = 2.00, 95% CI: 1.55–2.56) in the frailty category. The risk observed in studies having a sample size ≥1000 (RR = 2.78, 95% CI: 2.04–3.14) was significantly higher than when the sample size was <1000

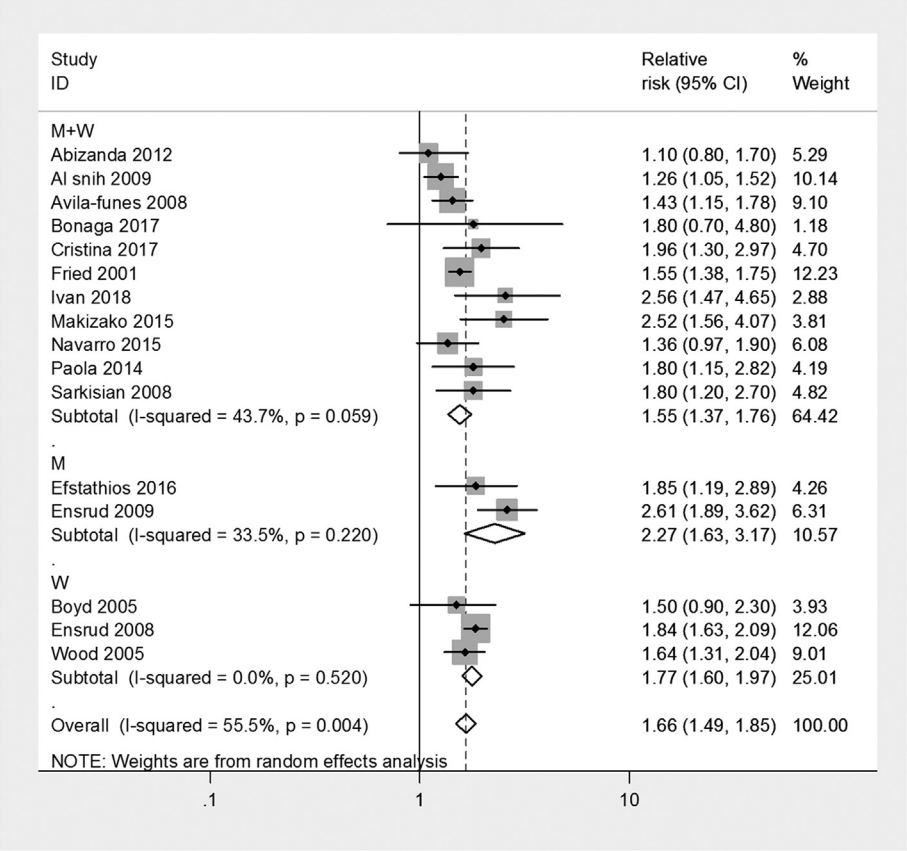

Fig. 2 – Forest plot of RRs of prefrailty *vs.* non-frailty for the incident disability risk. RR: relative risk; CI: confidence interval.

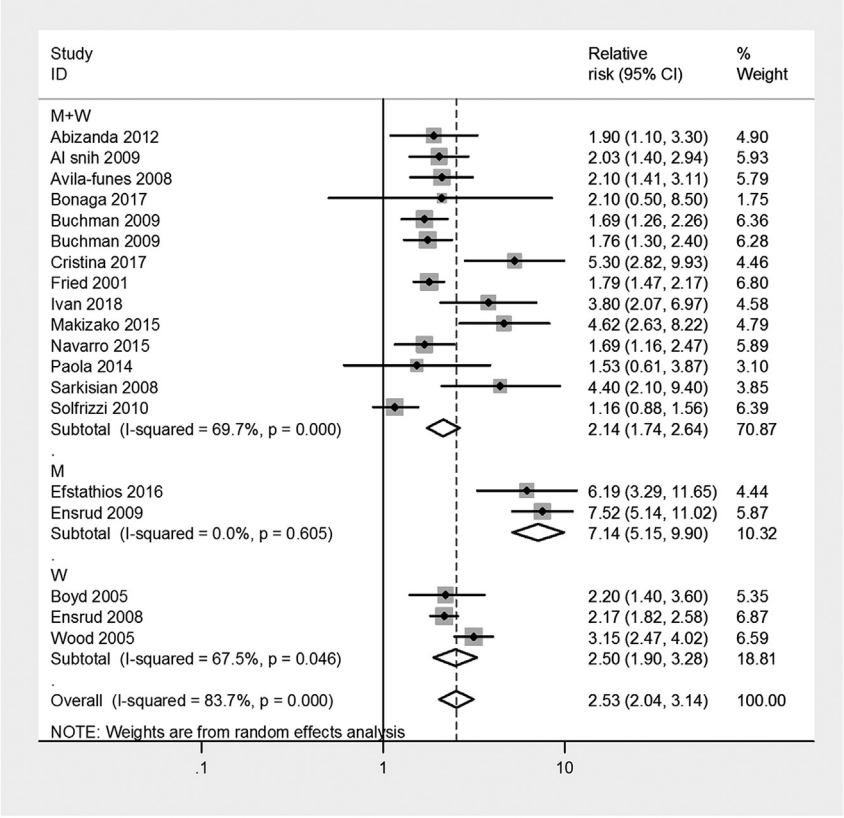

Fig. 3 – Forest plot of RRs of frailty *vs.* non-frailty for the incident disability risk. RR: relative risk; CI: confidence interval.

Table 2 – The subgroup analyses of the association between frailty and risk of disability.

Study	Prefrailty				Frailty			
	No. of studies	RR (95% CI)	I^2 (%)	P	No. of studies	RR (95% CI)	I^2 (%)	P
All studies	16	1.66 (1.49–1.85)	55.5		18	2.53 (2.01–3.14)	83.7	
Study location				0.58				1
Europe	6	1.54 (1.29–1.83)	16.7		7	2.41 (1.44–4.04)	83.1	
North America	8	1.64 (1.43–1.88)	67.2		10	2.41 (1.87–3.10)	85.7	
Measure effect				0.40				0.16
HR	7	1.58 (1.31–1.91)	61.8		10	2.16 (1.70–2.76)	76.1	
OR	9	1.74 (1.54–1.96)	35.0		9	3.00 (2.11–4.27)	84.8	
Duration of follow-up				0.07				0.03
<5 years	10	1.79 (1.53–2.10)	54.6		10	3.19 (2.25–4.53)	72.6	
≥5 years	3	1.50 (1.34–1.67)	21.9		9	2.00 (1.55–2.56)	79.9	
Frailty criteria				0.13				0.25
(m)FP	13	1.61 (1.42–1.82)	53.2		16	2.57 (1.99–3.33)	86	
SOF	2	1.84 (1.63–2.07)	0.00		2	2.14 (1.81–2.55)	84	
Disability criteria				0.61				0.78
ADL	11	1.56 (1.42–1.71)	12.8%		13	2.39 (1.85–3.09)	80.2	
IADL	4	1.68 (1.28–2.20)	80.7%		5	2.58 (1.62–4.12)	90.2	
Education				0.03				0.12
Unadjusted	10	1.81 (1.56–2.11)	56.9		11	2.94 (2.07–4.17)	89	
Adjusted	6	1.46 (1.30–1.63)	9.8		8	2.11 (1.69–2.65)	63.9	
Comorbidity				0.04				0.66
Unadjusted	5	1.90 (1.58–2.28)	67.2		7	2.81 (1.95–4.06)	80.4	
Adjusted	11	1.52 (1.34–1.72)	32.2		12	2.53 (1.78–3.13)	75	
Samples				0.98				0.02
<1000	4	1.66 (1.11–2.48)	54.7		6	1.91 (1.53–2.37)	17.5	
≥1000	12	1.67 (1.49–1.87)	59.2		13	2.78 (2.04–3.14)	88	

Note: RR: relative risks; OR: odds risks; CI: confidence interval; HR: hazard ratio; (m)FP: (modified) frailty phenotype; SOF: Study of Osteoporotic Fractures.

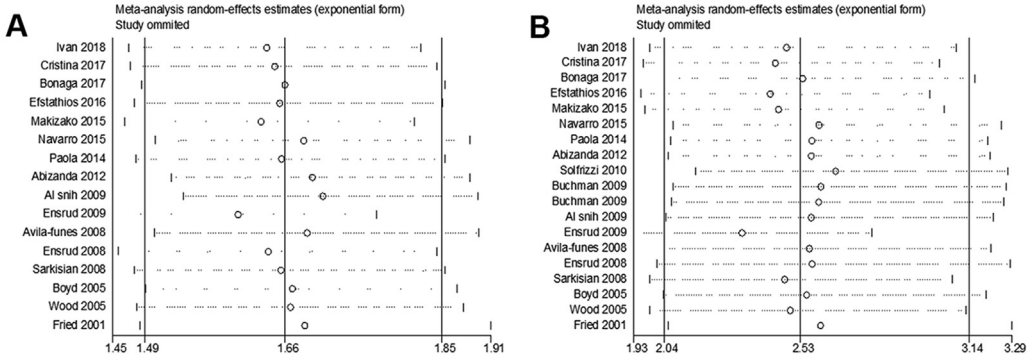

Fig. 4 – (A) Sensitivity analysis of the association between prefrailty and the incident risk of disability. (B) Sensitivity analysis of the association between frailty and the risk of incident disability.

(RR = 1.91, 95% CI: 1.53–2.37) in the frailty group. These differences were not statistically significant in the prefrailty group. This study demonstrates that frailty and disability are not synonymous and that frailty assessment measures may help in identifying those elders who are at the highest risk of future disability and who may be the adequate candidates for participation in prevention and intervention programs.

The meta-analysis by Kojina et al. examined the association between frailty and disability.[19] They reported that frailty is a significant predictor of incident and worsening ADL and IADL disabilities, which is similar to the findings of our study.[19] However, they did not exclude the poorer methodological quality studies that were potentially one of the causes of heterogeneity. Besides, the literature they selected was published before 2016. Their meta-analysis examined only ADL and IADL disability risks and did not conduct synthesized pooled risk estimates on frailty and disability. Our study included four high-quality cohort studies published after 2017,[22–25] and we did conduct synthesized pooled risk estimates on frailty and disability. The subgroup analysis was performed to achieve a risk estimate on unadjusted education and comorbidity. Therefore, it was necessary to collect the results of previous studies and use this meta-analysis to quantitatively evaluate and update the relationship between frailty and incident disability risks.

Subgroup analysis suggested that high incident disability risks according to frailty were associated with two study characteristics: a follow-up period of <5 years and a sample

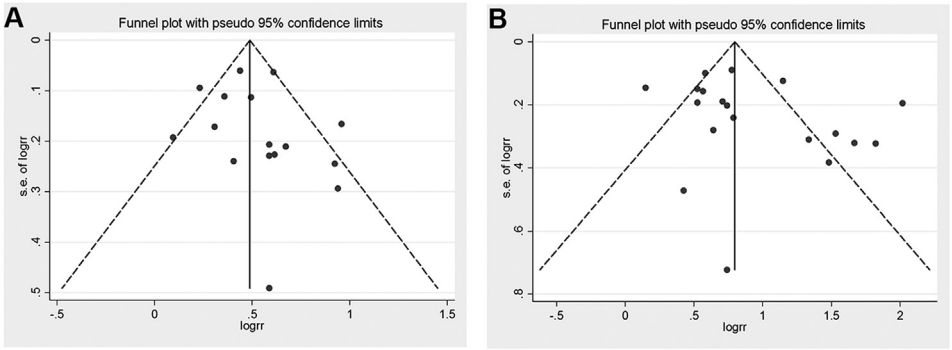

Fig. 5 – (A) Funnel plot corresponding to the random-effects meta-analysis of the relationship between prefrailty and the incident disability ($P = 0.79$ by Egger's test). (B) Funnel plot corresponding to the random-effects meta-analysis of the relationship between frailty and the incident disability ($P = 0.53$ by Egger's test).

size ≥1000. By properly adjusting for comorbidity and education, the pooled risk estimate was smaller among the studies in the prefrailty category. Comorbidity, i.e., the coexistence of multiple chronic conditions in the same individual, is observed at an extremely high frequency in old age.[36,37] Griffith et al. demonstrated that comorbidity not only often leads to functional decline but also it adversely affects the basic ADLs by causing related disabilities that account for 66% of the total disabilities, and the related disabilities related to IADLs, account for nearly 50% of the total disabilities.[38] Generally, individuals whose educational attainment was low were more likely to be frail and were more likely to have low income and less access to health services and insurance, which leads to poorer health.[39] It may be natural that education has an impact on different health-related outcomes also. Therefore, it is important to take comorbidity and education into consideration by adjusting this factor in statistical models to examine independent associations between frailty and incident disability risks. Another subgroup with 13 studies having a bigger sample size (n ≥ 1000) showed higher disability risks (pooled RR = 2.78, 95% CI = 2.11–3.65 *vs.* pooled RR = 1.91, 95% CI = 1.53–2.37). This indicates that the sample size may have an impact on the evaluation of this effect. Too few samples were reported in the research of Jenny et al.,[40] and the power of their test was low in efficiency and lacked a basis for the conclusion. To obtain more reliable and stable results, we should combine the sample size of the same research problem and increase the efficiency of the test.

The mechanisms of frailty and disability remain unclear. Frailty might be associated with increased risk of incident disability through several mechanisms.[41,42] Normally, through the coordination of the brain, immune system, and endocrine system, the body achieves a balance between muscle cell formation, hypertrophy, and protein loss. However, in elderly frail people, the hyperactivity of inflammatory factors, such as interleukin (IL)-6 and tumor necrosis factor (TNF)-α, increases the catabolism of muscles, resulting in the reduction of muscle mass and strength and a decline in related functions, which leads to sarcopenia and further accelerates the progress of chronic disease and disability.[43]

The strengths of the present study were its prospective design, the large number of subjects living in the same community, the ability to examine diverse medical conditions and factors previously reported as being associated with disability, and the completion of the follow-up appointments. Nonetheless, some limitations of this study must be considered. First, high heterogeneity was observed. This may be attributed to the presence of confounders. In the subgroup analyses, comorbidity and the period of follow-up may explain the heterogeneity. By adjusting those confounders, the studies showed low heterogeneity, which may suggest that those were potential causes of heterogeneity. Second, two researcher conducted the systemic review and data extraction; it would have been more appropriate if the same was conducted by more researchers independently.

Conclusion

The overall meta-analysis confirms that frailty has significantly increased the risk of incident disability. However, the included studies suffer from high heterogeneity. It is suggested that a high-quality, prospective cohort study with a large sample size should be carried out in the future. A higher number of representative cases should be selected, the mixed factors in the course of the study should be controlled, the follow-up time should be increased, the number of lost visits should be controlled, and the researchers should be actively concerned about the relationship between frailty and other adverse outcomes, such as falls, deaths, etc.

Author statements

Ethical approval

The present study was reviewed by the research institutional review board of Shandong First Medical University, Shandong, China and found that the utilization of literature data did not require oversight by an ethics committee.

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Aihua Zhang contributed to conceptualization. Huaxue Liu, Wenjing Yu, contributed to data curation, methodology, and use of software. Huaxue Liu performed formal analysis. Taifang Liu and Wenjing Yu contributed to investigation and resources. Aihua Zhang, Aiying Yan, and Haiyan Chen contributed to supervision. Aihua Zhang, Huaxue Liu, and Wenjing Yu validated the study. Huaxue Liu and Guoyong Ding wrote the original draft. Aihua Zhang and Guoyong Ding wrote, reviewed, and edited the original manuscript.

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