

BMJ Open Prevalence of frailty and prefrailty among community-dwelling older adults in low-income and middle-income countries: a systematic review and meta-analysis

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ABSTRACT

Objective To systematically review the research conducted on prevalence of frailty and prefrailty among community-dwelling older adults in low-income and middle-income countries (LMICs) and to estimate the pooled prevalence of frailty and prefrailty in community-dwelling older adults in LMICs.

Design Systematic review and meta-analysis. PROSPERO registration number is CRD42016036083.

Data sources MEDLINE, EMBASE, AMED, Web of Science, CINAHL and WHO Global Health Library were searched from their inception to 12 September 2017.

Setting Low-income and middle-income countries.

Participants Community-dwelling older adults aged ≥ 60 years.

Results We screened 7057 citations and 56 studies were included. Forty-seven and 42 studies were included in the frailty and prefrailty meta-analysis, respectively. The majority of studies were from upper middle-income countries. One study was available from low-income countries. The prevalence of frailty varied from 3.9% (China) to 51.4% (Cuba) and prevalence of prefrailty ranged from 13.4% (Tanzania) to 71.6% (Brazil). The pooled prevalence of frailty was 17.4% (95% CI 14.4% to 20.7%, $I^2=99.2\%$) and prefrailty was 49.3% (95% CI 46.4% to 52.2%, $I^2=97.5\%$). The wide variation in prevalence rates across studies was largely explained by differences in frailty assessment method and the geographic region. These findings are for the studies with a minimum recruitment age 60, 65 and 70 years.

Conclusion The prevalence of frailty and prefrailty appears higher in community-dwelling older adults in upper middle-income countries compared with high-income countries, which has important implications for healthcare planning. There is limited evidence on frailty prevalence in lower middle-income and low-income countries.

PROSPERO registration number CRD42016036083.

INTRODUCTION

Population ageing is not confined to high-income countries (HICs). People in

Strengths and limitations of this study

- This is the first systematic review and meta-analysis of the prevalence of frailty and prefrailty among community-dwelling older adults in low-income and middle-income countries.
- We conducted a comprehensive literature search in six electronic databases with a comprehensive search strategy, including WHO Global Health Library to capture studies published regionally.
- No language restriction was imposed.
- Subgroup analysis of prevalence of frailty and prefrailty was performed with substantial number of studies, and meta-regression technique was used to identify the sources of heterogeneity between the studies.
- We did not include grey literature in this review.

low-income and middle-income countries (LMICs) have increasing life expectancy with the advancement of healthcare services.¹ The pace of population ageing is faster in LMICs compared with HICs.² This creates an additional burden for these countries with growing economies as they have to tackle health, social and welfare issues associated with ageing populations.

Frailty is a health problem of older age with no universally agreed conceptual or operational definition. However, there is a common agreement that frailty is an important clinically identifiable state that increases the vulnerability to adverse outcomes due to the decline in reserve and functions in multiple physiological systems.³ The Fried phenotype of frailty, comprising five phenotypic criteria (unintentional weight loss, self-reported exhaustion, weakness, slowness and low physical activity),⁴ and the frailty index (comprising a list of deficits)⁵ are the most

frequently used frailty assessment methods in the literature.⁶ Longitudinal studies have identified several negative outcomes associated with frailty which can have a huge impact on individual lives and society as a whole. These include falls, worsening mobility, disability, hospitalisation and increased risk of mortality.^{4 5 7 8}

Prefrailty is an intermediate state between frailty and non-frailty/robust that has higher risk of progressing to frailty.⁹ Since frailty status is assessed using different assessment methods, most of the assessment methods have its own cut-off for prefrailty status. For instance, having one to two criteria of five is considered as prefrail for the Fried's phenotype.⁴ Like frailty, prefrailty is also associated with adverse health outcomes. Findings from a recent meta-analysis based on six prospective cohort studies suggested increased risk for faster onset of any type of cardiovascular diseases in prefrail versus robust.¹⁰ Another longitudinal study also showed that prefrail individuals are more likely to show persistent and new depressive symptoms.¹¹ Evidence is emerging that frailty as a dynamic state with transitions between frailty statuses; frailty, prefrailty and non-frailty;¹²⁻¹⁴ and there is potential for interventions to improve the health and well-being of both frail and prefrail older adults.

A substantial amount of research on frailty has been conducted in HICs. According to a systematic review conducted in 2012, the weighted prevalence of frailty in HICs is 10.7% and prefrailty is 41.6%.¹⁵ There is some suggestion of a socioeconomic gradient in frailty between HICs; one study from 15 European countries reported a lower mean frailty index in North and Western Europe compared with lower income countries in South and Eastern Europe.¹⁶ In addition, the survival of frail older people was higher in countries with a higher relative income within Europe.¹⁶ It is possible that the prevalence of frailty in LMICs is higher than HICs, given a steeper gradient in income. Alternatively, the prevalence may be lower with a reduced life expectancy of older people in LMICs. A narrative review published in 2015 on frailty in developing countries found limited availability of studies and suggested that frailty occurs more frequently in developing countries.¹⁷ However, no studies are available up-to-date collating all the epidemiological findings available from LMICs to examine the burden of frailty in these countries. This is important to inform healthcare planning in these countries in the context of world-wide population ageing. The aim of this study was to conduct a systematic review and meta-analysis on prevalence of frailty and prefrailty among community-dwelling older adults in LMICs.

METHODS

Search strategy and selection criteria

We performed a comprehensive structured search in six electronic bibliographic databases. MEDLINE, EMBASE and AMED databases using OvidSP interface, Web of Science Core Collection, CINAHL Plus databases

and WHO Global Health Library were searched from their inception to 12 September 2017. Two concepts 'frailty' and 'LMICs' were used to develop the electronic search strategy. The example LMIC filters developed by the Cochrane organisation in 2012 was used with slight modifications.¹⁸ The World Bank country classification issued on 1 July 2017,¹⁹ based on 2016 economic data was used to identify the countries that switched from LMICs to HICs in 2017 or vice versa. Studies in these countries were included only if the country belongs to low-income and middle-income category during the time of data collection. The electronic search strategy was first developed for MEDLINE (online supplementary appendix A) and then adapted accordingly to other databases. The electronic search strategy was developed with the support of specialist librarian (SP). Additionally reference lists of the selected articles were scanned and citation searches were performed in the Web of Science. The search was limited to full-text articles as study quality assessment requires a detailed description on the methodology. No language restriction was imposed on the search.

The condition studied was frailty measured by any assessment method. The review was restricted to studies with community-dwelling older adults aged ≥ 60 years living in the LMICs. This age cut-off is in line with the United Nations's definition of older populations.²⁰ Studies with institutionalised or hospitalised adults, nursing home residents, outpatients of primary or secondary care clinics, or older adults belonging to specific disease groups were excluded. Cross-sectional studies conducted to assess the prevalence and associated factors of frailty, prospective follow-up studies that have baseline prevalence of frailty, cross-sectional studies conducted to explore the association of frailty with some other health variable or disease (eg, haemoglobin level and cardiovascular risk factors) were included in this review.

Identified citations were exported into EndNote X8 and duplicates were removed. In the first stage, the title and abstracts of the citations were screened against inclusion and exclusion criteria to identify potentially eligible citations. In the second stage, full texts of potentially eligible articles were retrieved. Two reviewers (DDS and SH) independently reviewed the full-text articles to identify the articles meeting eligibility criteria. If multiple studies were available from the same cohort, the study with the largest sample and most information was included in the review. The agreement between the two raters was high with a kappa value of 0.84 (95% CI 0.72 to 0.90). Disagreement between the reviewers was resolved through discussions and consulting senior researchers in the research team (KRW, GR and MCW).

Study quality assessment and data extraction

Selected articles were subjected to a quality assessment. Methodological rigour of the articles was assessed using eight criteria proposed by Loney *et al*²¹ for the critical appraisal of the prevalence literature. If a study achieved three criteria or less, it was excluded from the review.

Study quality of all selected articles (61) was assessed by the first reviewer (DDS). The second reviewer (SH) assessed the study quality of a random 10% of articles to check for discrepancies.

Data extraction included information on study background (authors and year of publication, data source, study setting and study period), characteristics of the population (percentage of women in the study population, mean age, age range, number of frail and prefrail participants in the total sample, and by sex and age), study methodology (study design, effective sample, sampling technique and frailty assessment method) and study strengths and limitations. Authors were contacted requesting additional data required for subgroup analysis.

Data analysis

The results of the systematic review are presented in tabular format and narratively synthesised. All statistical analyses were performed in Stata V.14 (StataCorp, College Station, Texas, USA). A random-effects meta-analysis with 95% CI was performed to calculate the pooled prevalence of frailty and prefrailty. A random-effects model was chosen as there is a variation in the true effect from one study to another. And also, there was considerable heterogeneity of the study characteristics including geography, frailty assessment method, frailty cut-offs and recruitment age. When a study has used multiple assessment methods of frailty, the prevalence presented using Fried phenotype was used for the meta-analysis as it was the most commonly used assessment method in the literature.²² The analysis was performed on Freeman-Tukey double arcsine transformed proportions to stabilise the variance. We used *metaprop random fit* command.²³ Results were presented using forest plots. The main meta-analysis and subgroup analysis excluded three studies, two studies with minimum recruitment age of ≥ 80 years and another study with minimum recruitment age of ≥ 90 years as those based on much older populations with expected higher prevalence rates for frailty. The findings from these studies were reported separately.

Cochran's Q statistic was used to assess heterogeneity between the studies. $P < 0.05$ was considered as evidence of heterogeneity. The I^2 statistic was further used to quantify the magnitude of the heterogeneity. I^2 values of 25%, 50% and 75% were considered as low, moderate and high heterogeneity, respectively.²⁴ Funnel plots generated by *metafunnel* command was used to visually inspect the existence of reporting biases and/or between study heterogeneity. In the absence of biases and/or between study heterogeneity, funnel plot will be a symmetrical inverted funnel in shape.²⁵ However, this eye ball test is subjective. Hence, we used Egger's weighted regression test to measure the degree of funnel plot asymmetry. The null hypothesis of Egger's test is that symmetry exists in the funnel plot.^{26 27} Stata *metabias* command was used.

Subgroup analysis of frailty and prefrailty prevalence was performed according to the frailty assessment method (Fried phenotype with five criteria where

weakness and slowness assessed objectively using grip strength and gait speed, Fried phenotype with five criteria where weakness and slowness assessed using self-reported questions (subjective), Fried phenotype with four criteria, Edmonton Frail Scale (EFS), frailty index and FRAIL scale). If the same cohort of participants had been assessed using different frailty assessment methods, we used that information in the subgroup analysis. However, studies that have used different frailty assessment methods to that mentioned above were excluded from the frailty and prefrailty subgroup analysis as they cannot be grouped into a particular category that is Study of Osteoporotic Fractures (SOF) index and Cuban frailty criteria, Brief Frailty Instrument for Tanzania (B-FIT). Further subgroup analyses by sex, age group (60–64, 65–69, 70–74, 75–79, 80–84, 85+ years), age and sex were performed with studies which had employed the Fried phenotype with five criteria where weakness and slowness assessed using objective tests. A two-sample proportion test was used to compare the prevalence of frailty and prefrailty by sex.

We performed a supplementary analysis to compare our findings with HICs. We used published data from a systematic review on prevalence of frailty which includes HICs only.¹⁵ This review included 14 studies which had used Fried's phenotype of frailty assessment method. We estimated the random-effects pooled prevalence of frailty and prefrailty only with the studies that have used the Fried phenotype with five criteria where weakness and slowness assessed using objective tests (10 studies). Minimum recruitment age of the participants included in this review was 65 years. For a fair comparison we calculated the random-effects pooled prevalence of frailty and prefrailty only with the studies of minimum recruitment age 65 years that have used same assessment method included in our review.

Random-effects univariable and multivariable meta-regression were performed using *metareg* command to identify the potential sources of heterogeneity between the studies (demographic, geographical and methodological).²⁸ Three studies which used SOF index, Cuban frailty criteria and Brief Frailty Instrument for Tanzania (B-FIT) were excluded from the analysis. The following explanatory variables were included in the models; mean age, percentage of women in the study sample, study quality assessment score, World Bank region classification (Latin America and the Caribbean, East Asia and Pacific, Europe and Central Asia, and South Asia) and frailty assessment method. All the variables were included in the multivariable model irrespective of their significance (P value) in univariable analysis. Variables with $P < 0.05$ were considered as significant. The systematic review protocol of this study is registered in PROSPERO and the number is CRD42016036083. This systematic review and meta-analysis have been reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2009 checklist is attached separately).²⁹

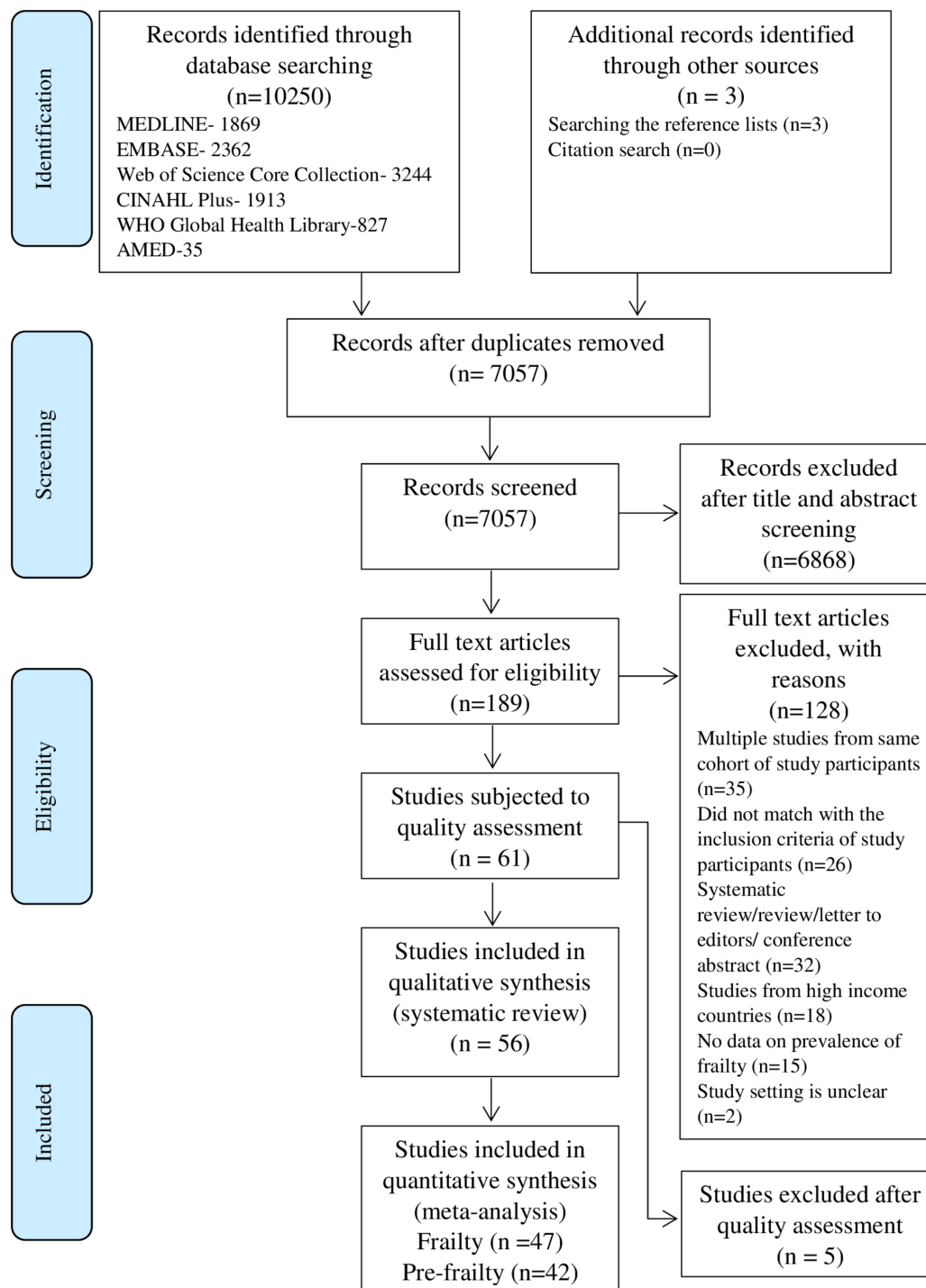


Figure 1 Study selection.

RESULTS

Study characteristics

The search yielded 10 253 records, with 7057 records left after removing duplicates. Fifty-six studies meeting all eligibility criteria were included in the systematic review (figure 1). Forty-seven and 42 studies were included in the meta-analysis of frailty and prefrailty, respectively.

The study quality assessment score of the studies included ranged from 3.5 to 7.5, with a mean score of (SD) 6.0 (1.07). Quality assessment results of the studies are presented in the online supplementary appendix B.

The characteristics of included studies are described in the online supplementary appendix C. Fifty studies have been published between 2012 and 2017. The majority of the studies were from the Latin America and the Caribbean region, predominantly from Brazil (n=24). Most of the studies had used data from large population-based cross-sectional or longitudinal studies on ageing.

The sample size of the studies varied (range 54–12 373) and the minimum recruitment age of the study participants varied from 60 to 90 years. The minimum age at recruitment of the study participants was 60 years in 30

studies, 65 years in 19 studies, 70 years in 4 studies, 80 years in 2 studies and 90 years in 1 study. Fifty-two studies had reported the percentage of women in the study samples and it varied from 48.1% to 100.0%, with more than half of participants being women in all except three studies. Forty-two studies reported the mean age (42/56) of the participants, which ranged from 68.2 to 77.2 years after excluding three studies with minimum recruitment age ≥ 80 years (two studies) and ≥ 90 years (one study).

Studies used various frailty assessment methods. The Fried phenotype was the most extensively used method. Researchers had operationalised the Fried phenotype differently. We identified three broad categories based on the number of phenotypic criteria used and measures used to operationalise those criteria. Those are Fried phenotype with five criteria—weakness and slowness assessed using objective tests, Fried phenotype with five criteria—weakness and slowness assessed using self-reported questions (subjective) and Fried phenotype with only four criteria.

Prevalence of frailty and prefrailty

Irrespective of the frailty assessment method, the prevalence of frailty varied from 3.9% in China (Fried phenotype with five criteria—weakness and slowness assessed using objective tests) to 51.4% in Cuba (Cuban frailty criteria) and prevalence of prefrailty ranged from 13.4% in Tanzania (Brief Frailty Instrument for Tanzania, B-FIT) to 71.6% in Brazil (Fried phenotype with five criteria—weakness and slowness measured objectively) for the studies with minimum recruitment age 60, 65 and 70 years. There was one study in those aged ≥ 90 years, reporting 61.8% participants as frail using the frailty index (not reported prefrailty). Another study with aged ≥ 80 years had not reported a cut-off value for the frailty index to define frail participants. Instead, authors had reported six levels based on the value of the frailty index and the percentage of participants belongs to each level. The other study with aged ≥ 80 years reported 14.8% and 63.8% participants as frail and prefrail, respectively, using Fried phenotype with five criteria—weakness and slowness assessed using objective tests. When restricting to the studies that used Fried phenotype with five criteria and assessed the weakness and slowness objectively, the prevalence of frailty varied from 3.9% (China) to 26.0% in India. The prevalence of prefrailty varied from 40.7% to 71.6% in Brazil.

Pooled prevalence of frailty and prefrailty

Descriptions of included studies in the meta-analysis are presented in [table 1](#). Sixty-nine prevalence estimates (47 studies), corresponding to a total of 75 133 community-dwelling older adults, were included in the frailty meta-analysis. The random-effects pooled prevalence of frailty in community-dwelling older adults was 17.4% (95% CI 14.4% to 20.7%). Cochran's Q and I^2 indicated a high heterogeneity between included studies ($Q=8756.8$, $df=68$, $P<0.001$; $I^2=99.2\%$) ([figure 2](#)). Funnel

plot asymmetry ([figure 3](#)) revealed evidence of reporting biases and/or between study heterogeneity. Results of Egger's weighted regression test further confirmed the funnel plot asymmetry ($P=0.042$).

Fifty four prevalence estimates (42 studies) corresponding to 47 302 participants were included in the prefrailty meta-analysis. The random-effects pooled prevalence of prefrailty in community-dwelling older adults was 49.3% (95% CI 46.4% to 52.2%). High heterogeneity was observed between included studies ($Q=2082.6$, $df=53$, $P<0.001$; $I^2=97.5\%$) ([figure 4](#)). Asymmetric funnel plot ([figure 5](#)) suggested the existence of reporting biases and/or between study heterogeneity. However, results of Egger's weighted regression test was insignificant indicating no funnel plot asymmetry ($P=0.817$).

Subgroup analyses

The pooled prevalence varied by the assessment method and the highest prevalence of frailty was reported for the EFS, 35.9% (95% CI 31.7% to 40.2%, $I^2=61.9\%$, $P=0.022$). The lowest prevalence of frailty was reported for the FRAIL scale, 12.4% (95% CI 8.4% to 17.1%). The pooled prevalence of frailty for the Fried phenotype with five criteria—weakness and slowness assessed using objective tests was 12.7% (95% CI 10.9% to 14.5%, $I^2=94.8\%$, $P<0.001$) (online supplementary appendix D). Results for pooled prevalence of prefrailty stratified by the frailty assessment method is presented in the online supplementary appendix D.

Twenty-four prevalence estimates were available from 24 studies using the same assessment method (Fried Phenotype with objective tests) for sex-stratified analysis of prevalence of frailty and prefrailty. In total, there were 10 507 and 15 458 male and female participants, respectively. The pooled prevalence of frailty in men was 11.1% (95% CI 8.9% to 13.4%, $I^2=91.4\%$, $P<0.001$) compared with 15.2% (95% CI 12.5% to 18.1%, $I^2=95.2\%$, $P<0.001$) in women. Frailty prevalence was significantly higher in women compared with men ($Z=-7.38$, $P<0.001$). The pooled prevalence of prefrailty in men was 53.8% (95% CI 51.3% to 56.3%, $I^2=80.9\%$, $P<0.001$) and women was 56.3% (95% CI 54.0% to 58.7%, $I^2=86.2\%$, $P<0.001$). Similar to frailty, there was a statistically significant sex difference in prefrailty ($Z=-3.51$, $P<0.001$).

The prevalence of frailty increased gradually with advancing age (online supplementary appendix E). The prevalence considerably increased after age of 75 years. The prevalence of prefrailty also slightly increased with advancing age and was $>50\%$ in all age groups. An age-related incremental rise in frailty was evident even after stratification by sex (online supplementary appendix F). Prevalence of frailty was higher in women in all 5-year age bands. There was no age-related trend for prefrailty after stratification by sex (online supplementary appendix G).

Supplementary analysis

Ten prevalence estimates (10 studies), corresponding to a total of 27 660 community-dwelling older adults from

Table 1 Descriptions of the studies included in the meta-analysis of prevalence of frailty and prefrailty

Authors and year of publication	Country	World Bank region classification	World Bank income classification	Age (years)	Frailty assessment method	Effective sample	Prevalence (%)	
							Frailty	Prefrailty
Tribess <i>et al</i> , 2012 ⁴⁵	Brazil	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	622	19.9	49.8
Reis Júnior <i>et al</i> , 2014 ⁴⁶	Brazil	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	286	23.8	58.7
Pegorari and Tavares, 2014 ⁴⁷	Brazil	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	958	12.8	54.5
Santos <i>et al</i> , 2015 ⁴⁸	Brazil	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	136	16.9	61.8
Closs <i>et al</i> , 2016 ⁴⁹	Brazil	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	521	21.5	51.1
Mello <i>et al</i> , 2017 ⁵⁰	Brazil	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	137	12.4	61.3
Sousa <i>et al</i> , 2012 ⁵¹	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	391	17.1	60.1
Amaral <i>et al</i> , 2013 ⁵²	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	295	18.6	55.3
Moreira and Lourenço, 2013 ⁵³	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	754	9.5	47.5
Neri <i>et al</i> , 2013 ⁵⁴ (Belem)	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	720	10.8	48.2
Neri <i>et al</i> , 2013 ⁵⁴ (Parnaíba)	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	431	9.7	55.5
Neri <i>et al</i> , 2013 ⁵⁴ (Campina Grande)	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	395	8.9	51.4
Neri <i>et al</i> , 2013 ⁵⁴ (Pocos de Caldas)	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	388	9.3	53.4
Neri <i>et al</i> , 2013 ⁵⁴ (Ermelino Matrazzo)	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	384	8.1	54.9
Neri <i>et al</i> , 2013 ⁵⁴ (Campinas)	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	898	7.7	52.2
Neri <i>et al</i> , 2013 ⁵⁴ (Ivoti)	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	197	8.6	47.7
Vieira <i>et al</i> , 2013 ⁵⁵	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	601	8.7	46.3
Ricci <i>et al</i> , 2014 ⁵⁶	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	761	9.7	48.0

Continued

Table 1 Continued

Authors and year of publication	Country	World Bank region classification	World Bank income classification	Age (years)	Frailty assessment method	Effective sample	Prevalence (%)	
							Frailty	Prefrailty
Silveira <i>et al</i> , 2015 ⁵⁷	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	54	11.1	46.2
Calado <i>et al</i> , 2016 ⁵⁸	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	385	9.1	49.6
Augusti <i>et al</i> , 2017 ⁵⁹	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	306	21.5	71.6
Ferrioli <i>et al</i> , 2017 ⁶⁰ (Recife)	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	556	12.1	66.9
Ferrioli <i>et al</i> , 2017 ⁶⁰ (Juiz de Fora)	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	412	15.5	63.1
Ferrioli <i>et al</i> , 2017 ⁶⁰ (Fortaleza)	Brazil	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotype*	481	10.4	63.6
Ocampo-Chaparro <i>et al</i> , 2013 ⁶¹	Colombia	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	314	12.7	71.3
Curcio <i>et al</i> , 2014 ⁶²	Colombia	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	1878	12.2	53.0
Samper-Terrent <i>et al</i> , 2016 ⁶³	Colombia	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	1442	9.4	52.4
Sánchez-García <i>et al</i> , 2017 ⁶⁴	Mexico	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	1252	11.2	50.3
Moreno-Tamayo <i>et al</i> , 2017 ⁶⁵	Mexico	Latin America and the Caribbean	Upper middle income	≥70	Fried phenotype*	657	11.9	51.9
Chen <i>et al</i> , 2015 ⁶⁶	China	East Asia and Pacific	Upper middle income	≥60	Fried phenotype*	604	12.7	56.5
Wu <i>et al</i> , 2017 ⁶⁷	China	East Asia and Pacific	Upper middle income	≥60	Fried phenotype*	5290	6.3	51.3
Dong <i>et al</i> , 2017 ⁶⁸	China	East Asia and Pacific	Upper middle income	≥60	Fried phenotype*	1188	3.9	45.9
Wang <i>et al</i> , 2015 ⁶⁹	China	East Asia and Pacific	Upper middle income	≥65	Fried phenotype*	316	14.2	49.1
Badrasawi <i>et al</i> , 2017 ⁷⁰	Malaysia	East Asia and Pacific	Upper middle income	≥60	Fried phenotype*	473	8.9	61.7
Kashikar and Nagarkar, 2016 ³²	India	South Asia	Lower middle income	≥65	Fried phenotype*	250	26.0	63.6
Gurina <i>et al</i> , 2011 ⁷¹	Russia	Europe and Central Asia	Upper middle income	≥65	Fried phenotype*	611	21.1	63.0
Alvarado <i>et al</i> , 2008 ³³ (SABE wave 1)	Barbados	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotype*	1446	26.7	54.4

Continued

Table 1 Continued									
Authors and year of publication	Country	World Bank region classification	World Bank income classification	Age (years)	Frailty assessment method	Effective sample	Prevalence (%)		
							Frailty	Prefrailty	
Alvarado <i>et al.</i> , 2008 ³³ (SABE wave 1)	Brazil	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotypet	1879	40.6	48.8	
Alvarado <i>et al.</i> , 2008 ³³ (SABE wave 1)	Chile	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotypet	1220	42.6	51.4	
Alvarado <i>et al.</i> , 2008 ³³ (SABE wave 1)	Cuba	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotypet	1726	39.0	51.6	
Alvarado <i>et al.</i> , 2008 ³³ (SABE wave 1)	Mexico	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotypet	1063	39.5	49.0	
Aguilar-Navarro <i>et al.</i> , 2015 ⁷² (MHAS wave 1)	Mexico	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotypet	5644	37.2	51.3	
Avila-Funes <i>et al.</i> , 2016 ⁷³	Mexico	Latin America and the Caribbean	Upper middle income	≥70	Fried phenotypet	927	14.1	37.3	
Sánchez-García <i>et al.</i> , 2014 ⁷⁴	Mexico	Latin America and the Caribbean	Upper middle income	≥60	Fried phenotypet	1933	15.7	33.3	
Akin <i>et al.</i> , 2015 ⁷⁵ (KEHES)	Turkey	Europe and Central Asia	Upper middle income	≥60	Fried phenotypet	848	27.8	34.8	
Zhu <i>et al.</i> , 2016 ⁷⁶	China	East Asia and Pacific	Upper middle income	≥70	Fried phenotypet	1478	12.0	42.9	
Jotheeswaran <i>et al.</i> , 2015 ³¹	China (urban)	East Asia and Pacific	Upper middle income	≥65	Fried phenotypet	989	7.8	–	
Jotheeswaran <i>et al.</i> , 2015 ³¹	China (rural)	East Asia and Pacific	Upper middle income	≥65	Fried phenotypet	1002	8.7	–	
Jotheeswaran <i>et al.</i> , 2015 ³¹	Cuba (urban)	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotypet	2637	21.0	–	
Jotheeswaran <i>et al.</i> , 2015 ³¹	Dominican Republic (urban)	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotypet	1706	34.6	–	
Jotheeswaran <i>et al.</i> , 2015 ³¹	India (urban)	South Asia	Lower middle income	≥65	Fried phenotypet	748	11.4	–	
Jotheeswaran <i>et al.</i> , 2015 ³¹	Mexico (urban)	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotypet	909	10.1	–	
Jotheeswaran <i>et al.</i> , 2015 ³¹	Mexico (rural)	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotypet	933	8.5	–	
Jotheeswaran <i>et al.</i> , 2015 ³¹	Peru (urban)	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotypet	1245	25.9	–	
Jotheeswaran <i>et al.</i> , 2015 ³¹	Peru (rural)	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotypet	507	17.2	–	
Jotheeswaran <i>et al.</i> , 2015 ³¹	Venezuela (urban)	Latin America and the Caribbean	Upper middle income	≥65	Fried phenotypet	1697	11.0	–	

Continued

Table 1 Continued

Authors and year of publication	Country	World Bank region classification	World Bank income classification	Age (years)	Frailty assessment method	Prevalence (%)		
						Effective sample	Frailty	
Fhon <i>et al</i> , 2012 ⁷⁷	Brazil	Latin America and the Caribbean	Upper middle income	≥60	EFS	240	39.2	24.6
Agrelli <i>et al</i> , 2013 ⁷⁸	Brazil	Latin America and the Caribbean	Upper middle income	≥60	EFS	103	30.1	22.3
Duarte <i>et al</i> , 2013 ⁷⁹	Brazil	Latin America and the Caribbean	Upper middle income	≥60	EFS	166	39.2	21.7
Del Brutto <i>et al</i> , 2016 ⁸⁰	Ecuador	Latin America and the Caribbean	Upper middle income	≥60	EFS	298	31.2	22.0
Fabricao-Wehbe <i>et al</i> , 2009 ⁸¹	Brazil	Latin America and the Caribbean	Upper middle income	≥65	EFS	137	31.4	20.4
Carneiro <i>et al</i> , 2016 ⁸²	Brazil	Latin America and the Caribbean	Upper middle income	≥65	EFS	511	41.3	–
Woo <i>et al</i> , 2015 ⁴²	China	East Asia and Pacific	Upper middle income	≥65	Frailty index	6320 (urban) 978 (rural)	17.0 5.2	–
Sathasivam <i>et al</i> , 2015 ⁴³	Malaysia	East Asia and Pacific	Upper middle income	≥60	Frailty index	789	5.7	67.7
Pérez-Zepeda <i>et al</i> , 2016 ⁴⁴	Mexico	Latin America and the Caribbean	Upper middle income	≥60	Frailty index	7108	45.2	–
Galbán <i>et al</i> , 2009 ⁸³	Cuba	Latin America and the Caribbean	Upper middle income	≥60	Cuban frailty criteria	541	51.4	–
Boulos <i>et al</i> , 2016 ⁸⁴	Lebanon	Middle East and North Africa	Upper middle income	≥65	SOF frailty index	1120	36.4	30.4
Gray <i>et al</i> , 2017 ³⁰	Tanzania	Sub-Saharan Africa	Low income	≥70	B-FIT	941	4.6	13.4

*Fried Phenotype with five criteria – weakness and slowness assessed using objective tests.

†Fried Phenotype with five criteria – weakness and slowness assessed using self-reported questions (subjective).

‡Fried phenotype with four criteria.

B-FIT, Brief Frailty Instrument for Tanzania; EFS, Edmonton Frail Scale; KEHES, Kayseri Elderly Health Study; MHAS, Mexican Health and Aging Study; SABE-Health, Wellbeing and Ageing Study; SOF, Study of Osteoporotic Fractures frailty index.

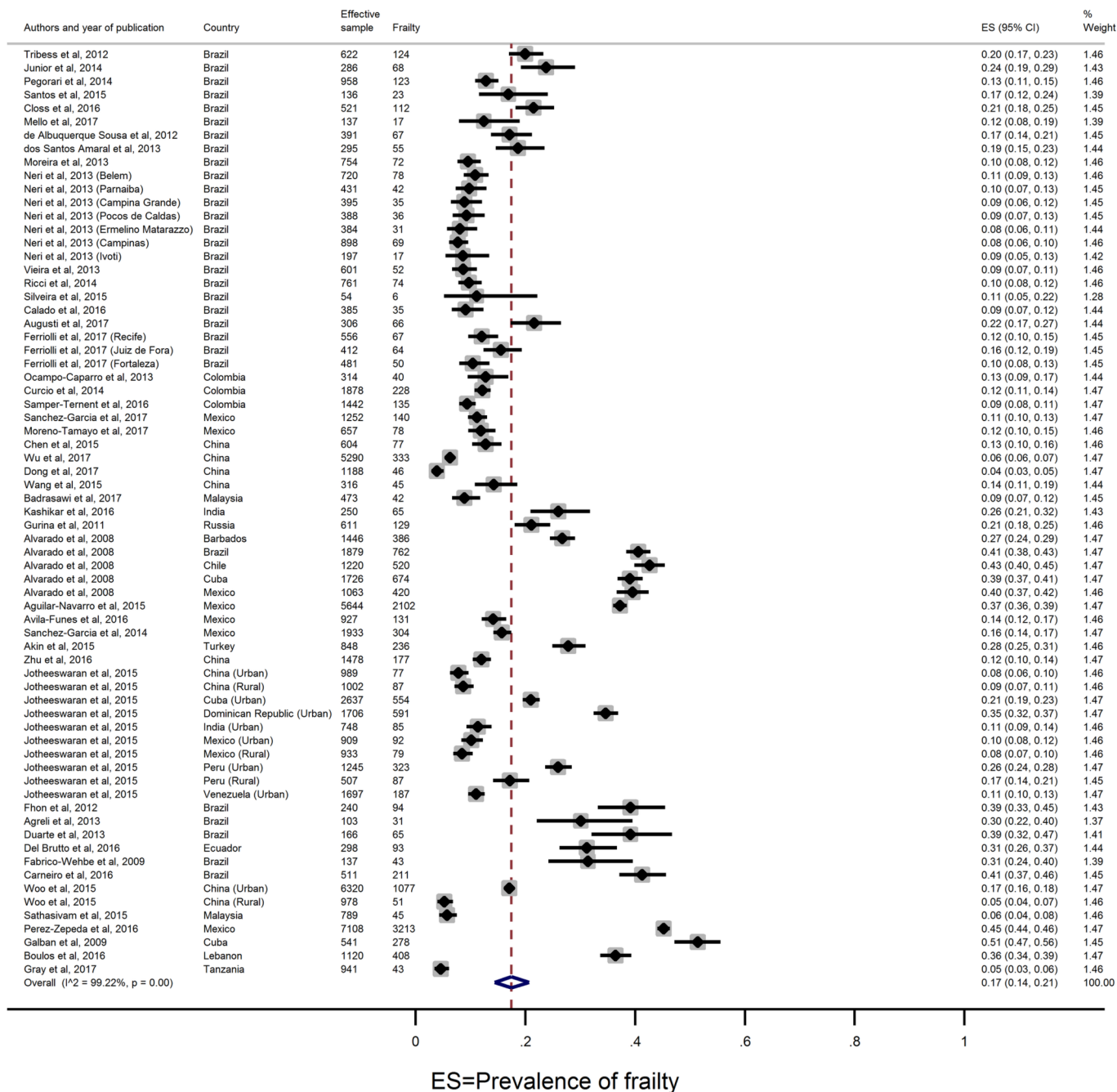


Figure 2 Random-effects pooled prevalence of frailty among community-dwelling older adults in LMICs. ES, effect size; LMICs, low-income and middle-income countries.

HICs and 21 prevalence estimates (13 studies), corresponding to a total of 9586 community-dwelling older adults from middle-income countries, were included in the frailty meta-analysis. The random-effects pooled prevalence of frailty in community-dwelling older adults in HICs and middle-income countries were 8.2% (95% CI 5.7% to 11.2%) (online supplementary appendix H) and 12.3% (95% CI 10.4% to 14.4%) (online supplementary appendix I), respectively. The prevalence of frailty in older adults from middle-income countries was significantly higher compared with the older adults residing in HICs, ($Z=-8.86$, $P<0.001$). However, it is also of note that studies included in the meta-analysis of HICs were

predominantly from the USA whereas studies included in the middle-income countries meta-analysis were predominantly from Brazil and all the countries belong to upper middle-income category except one study from India. The pooled prevalence of frailty except the study from India was 11.8% (95% CI 10.0% to 13.6%) and still significantly higher compared with HICs.

The random-effects pooled prevalence of prefrailty in community-dwelling older adults in HICs and middle-income countries were correspondingly 43.9% (95% CI 40.9% to 46.9%) (online supplementary appendix J) and 55.3% (95% CI 52.0% to 58.6%) (online supplementary appendix K). Like frailty, prevalence of prefrailty also

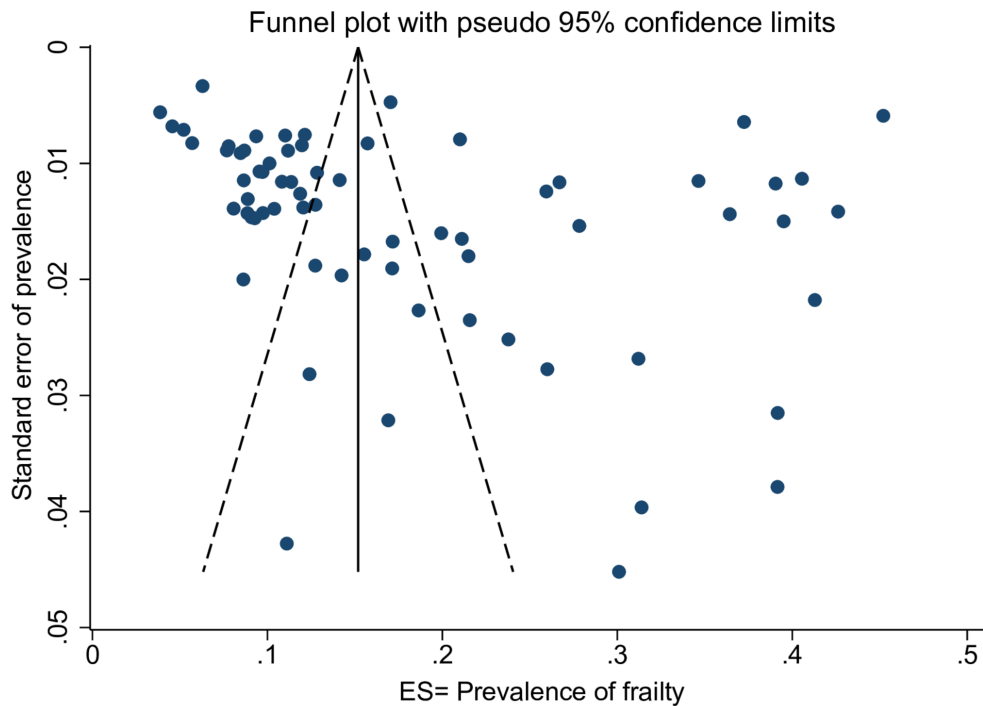


Figure 3 Funnel plot for assessing publication or other types of biases in meta-analysis of prevalence of frailty. ES, effect size.

significantly higher among the older adults in middle-income countries compared with the higher income countries ($Z=-17.14$, $P<0.001$).

Meta-regression

After adjusting for all the other study characteristics in a multivariable meta-regression model, there remained statistically significant differences in frailty prevalence between different assessment methods. Use of EFS, frailty index and Fried phenotype (five criteria, weakness and slowness assessed using self-reported questions (subjective)) was associated with a frailty prevalence approximately 20% higher than the reference method (Fried phenotype five criteria with objective tests). Geographic region was also a statistically significant predictor of frailty. The variables included in the multivariable model (mean age, % of women in the sample, study quality assessment score, geographic region and frailty assessment method) explained 58.4% of variability between the studies included in the analysis (table 2).

DISCUSSION

Summary of main findings

Only one epidemiological study on frailty was found from countries with low-income economies³⁰ (\leq US\$1005) according to World Bank Classification, 2017.¹⁹ Of countries with lower middle-income economies (US\$1006–US\$3955) we only found two studies both from India. One was a study site of a multicountry study³¹ and the other one was a small community-based cross-sectional study.³² All the other studies have been conducted in countries with

upper middle-income economies (US\$3956–US\$12 235) indicating income inequality in frailty research.

The random-effects pooled prevalence of frailty and prefrailty in community-dwelling older adults were 17.4% (95% CI 14.4% to 20.7%) and 49.3% (95% CI 46.4% to 52.2%), respectively. Frailty was significantly higher in women compared with men and as expected increased with age. This finding is consistent with previous research.^{15 33–36} Interestingly, the prevalence of prefrailty was also slightly increasing across all age groups at around half the participants. Both the prevalence of frailty and prefrailty appeared significantly higher in community-dwelling older adults in upper middle-income countries compared with HICs.

Comparison with the existing literature

The pooled prevalence of frailty and prefrailty in LMICs in this review appeared to be higher than the weighted prevalence in HICs reported previously (10.7%, (95% CI 10.5% to 10.9%) and 41.6% (95% CI 41.2% to 42.0%), respectively).¹⁵ However, it is also of note that the participants in HICs included people aged ≥ 65 years, whereas 50% of studies in our meta-analysis included participants aged ≥ 60 years. Given that prevalence of frailty increases with age, when participants of a higher age group are selected, a higher prevalence would be expected. Our meta-analysis included 18 studies (36 estimates) with a population aged ≥ 65 years. The prevalence of frailty of this subsample was 14.6% (95% CI 11.9% to 17.4%) and still higher compared with HICs. In the review of frailty in HICs, most studies were from Europe and North America.

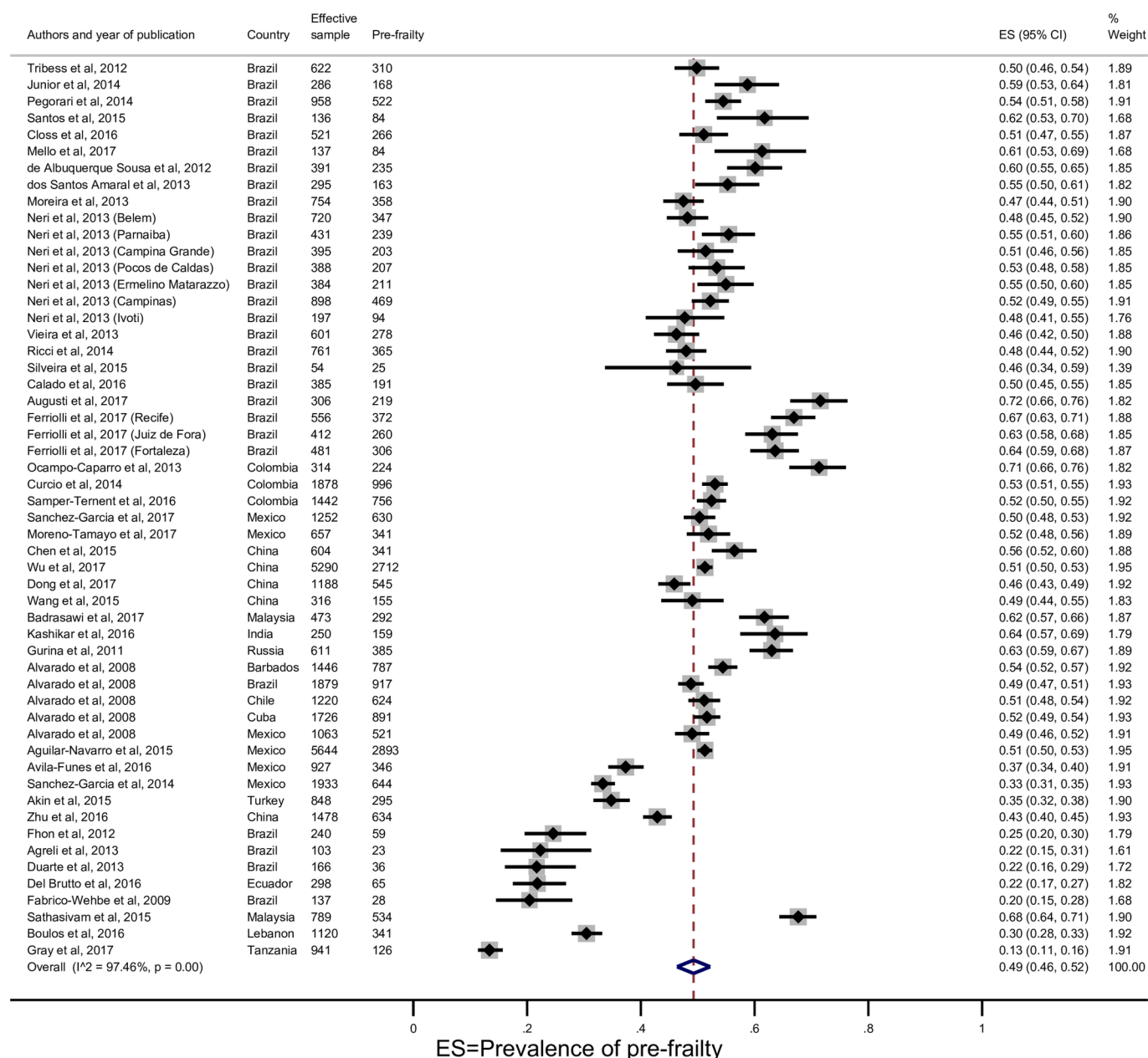


Figure 4 Random-effects pooled prevalence of prefrailty among community-dwelling older adults in LMICs. ES, effect size; LMICs, low-income and middle-income countries.

Studies included in our review were predominantly from Latin America and the Caribbean and belong to the countries with upper middle-income economies, with little representation of lower middle-income and low-income countries. A recent meta-analysis in Latin America and Caribbean showed consistent findings to our study, with nearly one out of five older adult defined as frail.³⁷

We found lower prevalence rates when we restricted the meta-analysis only to the Fried phenotype with five criteria, including objective measures of weakness and slowness. This found a pooled prevalence of frailty of 12.7% and prefrailty of 55.2%. The review on frailty and prefrailty which included only HICs has simply reported the weighted prevalence of frailty and prefrailty.¹⁵ Given the heterogeneity of the studies along with the actual differences of

frailty estimates in different populations, we performed a supplementary analysis for a fair comparison of frailty estimates between HICs and middle-income countries (no studies were available from low-income countries using the same frailty assessment method). Results indicated significantly higher prevalence of frailty and prefrailty among community-dwelling older adults in middle-income countries compared with the HICs. Another review of the prevalence of frailty measured by the Fried phenotype based on community-dwelling older adults ≥ 65 years in nationally representative samples reported lower prevalence to our estimate except in the countries of Southern Europe (France, Italy, Greece and Spain).³⁸ Lower prevalence of frailty is also observed in high-income Asian countries (Japan, Singapore and Taiwan).^{36 39–41}

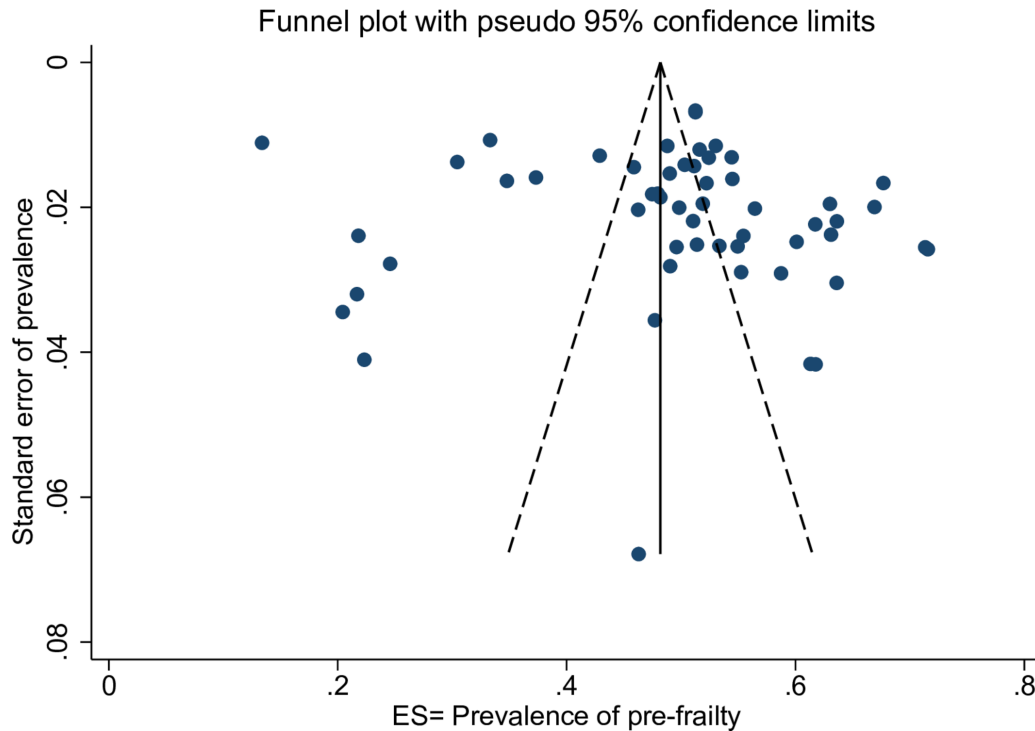


Figure 5 Funnel plot for assessing publication or other types of biases in meta-analysis of prevalence of prefrailty. ES, effect size.

In contrast to these findings, a single multicountry study conducted with data from 14 HICs in Europe and six LMICs (China, Ghana, India, Mexico, Russian Federation and South Africa) reported higher frailty level (high mean frailty index) in HICs compared with the low-income countries.³⁴ This study included nationally representative samples of adults aged ≥ 50 years. They also found an inverse association between level of frailty and income and education in both HICs and low-income countries. Individuals with poor education and low income were more likely to be frail. Higher levels of frailty in HICs could be due to the higher survival rate of participants with advanced healthcare and social protection. On the other hand, as the frailty index is based on a list of deficits including diagnosed diseases, many medical conditions could be under reported/diagnosed in the participants in LMICs. Similarly, in most LMICs where access to continued care is lacking, maintenance of medical records are poor making it difficult to use cumulative deficit models.

In our study, even among the studies using Fried phenotype with objective criteria, there was considerable variation in operationalising the five phenotypic criteria. Furthermore, the approach to deriving frail cut-offs for weakness, slowness and physical activity criteria were varied. Of thirty studies, 17 have calculated their population specific cut-offs based on the anthropometry of their own study populations. Eight studies have used the cut-offs developed by Fried *et al* in the Cardiovascular Health Study (CHS).⁴ The pooled prevalence of frailty is higher with the studies that used CHS cut-offs compared with the studies that used own population specific

cut-offs. However, the pooled prevalence of prefrailty was similar in both groups. Similarly, the number of deficits used in frailty index and cut-off points for defining frailty and prefrailty status were inconsistent.^{42–44} A further meta-analysis with all available studies including both higher and the lower and middle-income countries would be valuable, controlling for frailty assessment method, sex and age composition of the sample. In addition, methodologically comparable studies across countries are required to study the true population difference of frailty.

Strengths and weaknesses

This is the first systematic review and meta-analysis on prevalence of frailty and prefrailty among community-dwelling older adults in LMICs. The strengths of our study include we conducted a comprehensive literature search in six electronic databases with a comprehensive search strategy, including WHO Global Health library to capture studies published regionally. No language restriction, subgroup analysis of prevalence of frailty and prefrailty with substantial number of studies, and using a meta-regression technique to identify the sources of heterogeneity between the studies, contacting authors to get the additional information of the studies required for subgroup analyses were also strengths.

Both funnel plot asymmetry and the results of the Egger's weighted regression test indicated the presence of reporting biases and/or between study heterogeneity in the random-effects meta-analysis of frailty. The nature of our study effect (prevalence) is unlikely to be affected by publication bias. However, publication bias could also be affected by study size, funding source or research

Table 2 Univariable and multivariable meta-regression results

Characteristic	Univariable analysis				Multivariable analysis				Adjusted R ² (%)
	No of estimates	β (95% CI)	P value	Adjusted R ² (%)	No of estimates	β (95% CI)	P value	Adjusted R ² (%)	
Mean age, years (per unit increase)	41	0.003 (-0.012 to 0.018)	0.665	-2.48	41	0.003 (-0.009 to 0.017)	0.570	58.41	
Percentage of women in the sample (per unit increase)	53	0.002 (-0.001 to 0.007)	0.190	0.96	41	-0.000 (-0.004 to 0.004)	0.962		
Study quality assessment score (per unit increase)	53	-0.007 (-0.046 to 0.031)	0.697	-1.77	41	0.015 (-0.020 to 0.051)	0.379		
World Bank region classification (Reference: <i>Latin America and the Caribbean</i>)	38			19.96	29				
East Asia and Pacific	11	-0.138 (-0.212 to -0.063)	0.001		8	-0.105 (-0.177 to -0.033)	0.005		
Europe and Central Asia	2	0.014 (-0.144 to 0.173)	0.856		2	0.068 (-0.051 to 0.189)	0.252		
South Asia	2	-0.051 (-0.217 to -0.114)	0.535		2	0.001 (-0.129 to 0.132)	0.982		
Frailty assessment method (Reference: frailty phenotype with five criteria, weakness and slowness assessed using objective tests)	23			47.11	20				
EFS	6	0.222 (0.124 to 0.319)	0.000		6	0.215 (0.120 to 0.309)	0.000		
Frailty index	4	0.053 (-0.041 to 0.149)	0.264		2	0.171 (0.056 to 0.286)	0.005		
Fried phenotype with four criteria	13	0.026 (-0.037, to 0.089)	0.410		12	0.032 (-0.035 to 0.100)	0.342		
Fried phenotype with five criteria, weakness and slowness assessed using self-reported questions (subjective)	7	0.206 (0.129 to 0.283)	0.000		1	0.223 (0.065 to 0.382)	0.007		
EFS, Edmonton Frail Scale.									

group.²⁷ We noted that majority of the studies included in our meta-analysis have large samples. Multiple sources have been identified that could affect funnel plot asymmetry including reporting biases (publication bias, selective outcome reporting and selective analysis reporting), poor methodological quality, true heterogeneity, artefactual and chance.^{25 26} In our case, we believe that the funnel plot asymmetry is mainly due to the true heterogeneity between the studies mainly because of the use of different frailty assessment methods. And also, it is possible to have a true underlying difference of frailty prevalence in different populations. Another limitation of this study was non-inclusion of grey literature.

Implications for practice

The findings of the study suggest that the prevalence of frailty appears higher among community-dwelling older adults in upper middle-income countries compared with HICs. One study was identified from low-income countries and two studies from a lower middle-income country. Despite evidence that populations are rapidly ageing in many of these countries, we do not currently know the prevalence of frailty in these populations to inform health and social care planning. Research is required from low-income and lower middle-income countries with rapidly ageing populations to estimate burden of frailty and to understand how frailty affects the day-to-day lives of older people. Furthermore, a consensus is required on methods of assessing frailty to allow for more robust comparisons across populations.

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