Marital status and risk of physical frailty: A systematic review and meta-analysis

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ABSTRACT

Objectives: Evidence on associations between marital status and frailty is limited. The objective of this study was to perform a systematic review for associations between marital status and physical frailty and to perform a meta-analysis to combine findings.

Design: Systematic review and meta-analysis.

Setting and participants: Community-dwelling older people with mean age≥60.

Methods: Systematic literature search using five databases in February 2019 to identify longitudinal and cross-sectional studies examining associations between marital status and Fried's phenotype-based frailty status. Additional studies were searched for by reviewing the reference lists of relevant articles and conducting forward citation tracking of included articles. Odds ratio (OR) of marital status and frailty was pooled using a random-effects meta-analysis. Subgroup analysis and analyses stratified by gender and marital status (married, widowed, divorced/separated, never married) were completed.

Results:
A total of 1565 studies were found, from which 3 studies with longitudinal data and 35 studies with cross-sectional data were included. Although longitudinal studies suggested that married men had lower frailty risks than unmarried men while married women had higher frailty risks than widowed women, meta-analysis was not possible due to different methodologies. Meta-analyses of cross-sectional data from 35 studies including 80,754 individuals showed that unmarried individuals were almost twice more likely to be frail than married individuals (pooled OR=1.88, 95%CI=1.70-2.07). A high degree of heterogeneity was observed (I^2=69%) and was partially explained by reasons for not being married and study location. The higher frailty risks in unmarried compared with married individuals were not statistically different (p for difference=0.62).

Conclusions and Implications: The three and 35 studies were found providing longitudinal and cross-sectional data respectively regarding associations between marital status and frailty among community-dwelling older people. A meta-analysis of cross-sectional data showed almost twice higher frailty risk in unmarried individuals compared with married individuals. Marital status should be recognized as an important factor, and more longitudinal studies controlling for potential confounding factors are needed.

INTRODUCTION

Age-related vulnerability, resulting from a gradual decline in physiological reserve in multiple systems and weakened resilience for maintaining homeostasis against stressors, can be conceptualized as frailty.[1] Although a number of operational definitions of frailty have been proposed, to date no international consensus about how best to define frailty has been reached.[1] Among existing definitions, the most commonly used one is the 'frailty phenotype' advocated by Fried and colleagues and derived from using the Cardiovascular Health Study.[2] They defined frailty as a biological syndrome and considered individuals as frail when they meet three or more of five specific physical components: unintentional weight loss, self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity.[2]

Frailty is associated with negative health outcomes, such as falls, healthcare resource use, disability, and death,[3-12] and can have a devastating impact on older people. Evidence shows that frailty is also associated with increased healthcare costs.[13, 14] Given that the number of older people worldwide is expected to increase due to ongoing population aging, frailty is considered a public health priority.[15, 16] Over the last two decades, the number of studies on frailty has exponentially increased and contributed to the field. Although frailty is more common among people of more advanced age,[17] frailty is neither an inevitable part of aging nor an irreversible decline in health toward death. Multiple studies have demonstrated that frailty is a dynamic state which can be reversed.[18, 19] Therefore, examining risk factors of frailty will further enhance our understanding of the pathophysiology of frailty.

Social factors, such as living alone or social isolation, appear to have significant associations with risk of frailty.[20, 21] We also know that marital status has an impact on a number of health outcomes, including cardiovascular diseases or mortality.[22, 23] There seem to be gender effects on relationship between marital status and health, with men having greater health benefits than women.[24] However, evidence on associations between marital status and frailty is scarce and limited.[5] Therefore, the objectives of this review is thus to conduct a systematic review of the literature for the currently available evidence on marital status and frailty and to perform a meta-analysis to combine the findings and synthesize the first pooled evidence.

METHODS

PICO for the systematic review

Population: community-dwelling older people
Intervention/Exposure: being unmarried (widowed, divorced/separated, or never married in stratified analysis)
Comparison: being married
Outcome: frailty risks

Search Strategy

A systematic review of the literature was carried out by one investigator (**) in February 2019 in five electronic databases (Embase, Medline, PsycINFO, AMED, and CINAHL) within a time frame from January 2000 to February 2019. A protocol was developed a priori in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statements[25] and was registered at PROSPERO (http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019124882). The Medical Subject Heading (MeSH) and free text terms used were as follows: [Marital status (MeSH) OR Marriage (MeSH) OR Widow(s) (MeSH) OR Widowhood (MeSH) OR Widows and widowers (MeSH) OR Divorce (MeSH) OR Single (marital status) (MeSH) OR Single person(s) (MeSH) OR Single women (MeSH) OR Single men (MeSH) OR "marri*" OR "unmarried" OR "widow*" OR "divorc*" OR "separate*"] AND [Frail elderly (MeSH) OR Frailty (MeSH) OR Frailty syndrome (MeSH) OR "frailty"]. The search was conducted using an explosion function when available and without language restriction. Titles, abstracts, and full-texts were screened and evaluated for eligibility by one investigator (GK). In order to identify additional studies, reference lists of included studies and relevant reviews were scrutinized and forward citation tracking of included and relevant studies was conducted.

Study Selection

Studies were included if they provided observational data of cross-sectional or prospective associations between marital status and frailty status among community-dwelling older people with a mean age of 60 years or older. Frailty had to be defined as a two-group categorical variable (frailty vs. non-frailty or frailty vs. prefrailty/robustness) by the frailty phenotype criteria or its modified versions.[2] Randomized controlled trials, editorials, reviews, conference abstracts, book chapters, and dissertations were excluded. Studies that used specific populations, such as a sample of disease-specific patients, were excluded. On the occasion that two or more studies used the same cohort, the study with the largest sample size was included. Corresponding authors were contacted for additional information if necessary.

Data Extraction

Data were collected regarding study design (prospective or cross-sectional), first author, cohort name, publication year, location, sample size, proportion of female participants, mean age, age range, frailty definition, proportion of married participants, marital status category (married, divorced, separated, widowed, unmarried, never married), and effect size of frailty risk.

Methodological Quality Assessment

Prospective studies were assessed using the Newcastle-Ottawa scale for cohort studies (nine items)[26] and cross-sectional studies were assessed using the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies (eight items).[27] Studies were considered to have adequate methodological quality and low risk of bias when their scores were five or higher.

Statistical Analysis

When two or more studies provided the same effect sizes of frailty risk, such as odds ratio (OR) or risk ratio, according to marital status, a meta-analysis was attempted to synthesize pooled risk estimates. Heterogeneity across the studies was assessed using a chi-square test and degree of heterogeneity was evaluated using the I^2 statistic. A random-effects meta-analysis was used given the expected high degree of heterogeneity due to differences in methodologies and cultural backgrounds regarding marriage across the included studies. Three sets of supplementary analyses were conducted in order to explore potential causes of heterogeneity. First, gender-stratified meta-analyses were conducted, where effect sizes were combined among men and women separately. Second, subgroup meta-analyses based on location, sample size, and mean age were conducted. Third, effect sizes for each marital status (never married, divorced/separated, or widowed) compared with being married, were combined. Publication bias was examined using Egger's and Begg's tests. All statistical analyses were performed using the Review Manager 5 (Version 5.2, The Cochrane Collaboration, Copenhagen, Denmark). Two-sided p value of <0.05 was considered statistically significant.

RESULTS

Selection Processes

The search of five databases yielded 1536 studies and an additional 29 studies were found from other sources. After duplicates, randomized controlled trials, conference abstracts, and dissertations were removed, 956 studies were screened. The title and abstract screening excluded 549 studies and the full-texts of 60 studies were reviewed. A further 22 studies were removed due to using non-CHS criteria (n=11), using the same cohort (n=8), not providing relevant data (n=2), and using a selected sample (n=1). Thirty-eight studies (3 studies with prospective data and 35 studies with cross-sectional data) were included in this review. The cross-sectional data from 35 studies were used for meta-analysis. The flow chart of the literature search is summarized in **Figure 1**.

Study Characteristics

Table 1 summarizes three studies with longitudinal data[28-30] and 35 studies with cross-sectional data[31-65] on associations between marital status and frailty.

Methodological quality assessment

Three longitudinal studies were considered to have adequate methodological quality according to the Newcastle-Ottawa scale for cohort studies (range=6-8, mean=7). The 8-item Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies was used for cross-sectional studies. Most of included cross-sectional studies (34/35) did not specifically focus on marital status and frailty but just provided the crude numbers of participants by marital status and frailty categories, from which unadjusted ORs were calculated. Therefore three criteria (confounders, strategies for confounders, and statistical analysis) were not applicable to these studies, and the remaining five criteria were used for evaluation. The 34 studies scored 4-5 out of 5 (mean=4.4) and the other study scored 5 out of 8, so all of the studies were considered to have adequate methodological quality.

Studies with longitudinal data

Three longitudinal studies examined baseline marital status and subsequent frailty risks. Two of them used data regarding older people aged $\geq$65 from the Progetto Veneto Anziani cohort.[29, 30] The first study investigated risk of incident frailty, defined by the frailty phenotype, over 4.4 years according to marital status at baseline, and showed different effects of marital status on incident frailty risks by gender.[29] While men who were widowed were significantly more likely to develop frailty than married men (OR=1.43, 95%CI=1.06-1.95), women who were widowed were significantly less likely to develop frailty than married women (OR=0.77, 95%CI=0.66-0.91).[29] Men who had never married had a significantly higher incident frailty risk (OR=3.84, 95%CI=2.76-5.35), however there was no significant association between never having been married and incident frailty risk among women.[29] The focus of the other study was frailty transition patterns according to a variety of sociodemographic and health-related factors, including marital status.[30] In this study, no clear explanation was provided regarding how marital status was categorized and what the reference group was and, in addition, the effect sizes regarding marital status and frailty transitions were only shown in graphs without an actual value and 95%CI.[30] A US study including only older men showed that married men were significantly more likely to improve frailty status compared with unmarried men (fully adjusted OR=1.5, 95%CI=1.02-2.2 for changing from prefrail to robust; fully adjusted OR=3.6, 95%CI=1.1-11.7 for changing from frail to prefrail or robust) while marital status did not have any significant effects on worsening frailty (age- and site-adjusted OR=0.7-0.9).[28] A meta-analysis was not possible for longitudinal studies due to different methodologies across the three studies (incident frailty[29] or frailty status transitions[28]).

Studies with cross-sectional data
Cross-sectional data on the association between marital status and frailty were obtained from 35 studies,[31-65] incorporating a total of 80,754 community-dwelling older people. It is of note that none of the studies focused specifically on marital status but most of them examined a variety of factors, including marital status, or showed the number of participants stratified by marital status and frailty status in a table of baseline characteristics. Ten studies were from Europe, nine were from Asia, six were from Brazil, four were from USA/Canada, and six from other countries. The size of the cohort ranged from 151[34] to 8,744.[58] One study consisted only of male participants[35] and the rest used mixed-gender cohorts with 43.7% - 70.7% female participants. The mean age of the cohorts ranged from 65.6 years[34] to 84.4 years.[40] The proportion of those who were married ranged from 30.0%[40] to 84.1%.[34] The types of marital status categories used were combinations of married, divorced, separated, widowed, single, never married, and unmarried.

Meta-analysis of cross-sectional associations between marital status and frailty
Unadjusted ORs of associations between marital status and frailty were calculated based on the numbers of participants stratified by marital and frailty status for all studies except for one which showed an unadjusted OR in the text.[32] In the main analysis marital status was dichotomized into “not married” (including never married, divorced, separated, widowed, single, or unmarried) and “married”. Significant heterogeneity was observed (I^2=69%, p<0.001). A random-effects meta-analysis was used showing that those who were not married had an almost doubled odds of frailty compared with those who were married (35 studies: pooled OR=1.88, 95%CI=1.70-2.07, p<0.001). **Figure 2** shows a forest plot. No evidence of publication bias was observed based on Egger’s and Begg’s tests (P=0.52 and 0.95, respectively).

Gender-stratified meta-analysis
One study used a male-only cohort[35] and another study showed data for men and women separately.[58] However, the remaining 33 studies presented data of mixed gender populations. Upon request, additional data were provided from 15 studies and used for gender-stratified meta-analysis. For both men (16 studies: pooled OR=1.86, 95%CI=1.55-2.24, p<0.001, I^2=49%) and women (15 studies: pooled OR=1.74, 95%CI=1.42-2.13, p<0.001, I^2=81%), the unmarried participants had significantly higher risks of being frail compared with the married participants. No significant difference was observed in results between men and women (p for group difference=0.62). The significant heterogeneity persisted in both gender groups.

Subgroup meta-analysis
Factors considered in the subgroup meta-analysis were location (Europe, Asia, Brazil, USA/Canada, and others), sample size (<2000 vs. $\geq$2000), and mean age (<75 vs. $\geq$75). While there was a high degree of heterogeneity across the 35 included studies (I^2=69%), heterogeneity among studies from Europe (I^2=0%), Asia (I^2=0%), and Brazil (I^2=0%) was lower and not statistically significant. Frailty risks for being unmarried in USA/Canada (OR=1.81), Brazil (OR=1.39), and others (OR=1.49) were significantly lower than that in

Europe (OR=2.33). In subgroups stratified by sample size and mean age, a high degree of heterogeneity remained (I^2=42-85%) and there was no significant difference between the two stratified groups (n<2000 vs. n≥2000, mean age <75 vs. ≥75).

Marital status-stratified meta-analysis
Instead of calculating frailty risk for "not married" compared with "married", frailty risks of "widowed", "divorced/separated", or "never married", respectively, compared with "married" were separately calculated and pooled.

Widowed vs. Married
Widows/widowers were significantly more likely to be frail compared with those who were married (12 studies: pooled OR=2.17, 95%CI=1.89-2.50, I^2=35%).

Divorced/Separated vs. Married
Those who were divorced or separated were significantly more likely to be frail compared with those who were married (10 studies: pooled OR=1.86, 95%CI=1.47-2.35, I^2=29%). The risk of frailty was not significantly different from that of widows/widowers.

Never married vs. Married
Those who never married were significantly more likely to be frail compared with those who were married (7 studies: pooled OR=1.37, 95%CI=1.06-1.79, I^2=0%), but the risk of frailty was significantly lower than that of widows/widowers (p for difference<0.01).

The high heterogeneity among the 35 included studies (I^2=69%) fell and became non-significant in all three meta-analyses stratified by reasons for marital status (I^2=0-35%).

Results of the gender-stratified meta-analysis, subgroup meta-analysis, and meta-analysis stratified by marital status are summarized in **Table 2**.

DISCUSSION
Our systematic review identified a total of three studies with prospective data and 35 studies with cross-sectional data on associations between marital status and frailty. Unadjusted ORs of cross-sectional associations between marital status and frailty were combined, which showed pooled evidence that older people who were not married were significantly more likely to be physically frail than their married counterparts. The robustness of the association was shown in subgroup and stratified analyses. As expected, a high degree of heterogeneity was observed and was partially explained by the reasons for not being married (widowed, divorced/separated, or never married) and study location. Only few longitudinal studies were found, one of which suggested that older men may benefit from marriage than older women.[29]

It is not known why those who are not married are more likely to be frail compared with those who are married. Given that widows/widowers (pooled OR=2.11) and the divorced/separated (pooled OR=1.73) have higher odds of frailty risks than those who never married (pooled OR=1.37), the stress of widowhood, divorce, or separation may increase the risk of frailty. Those who lose their partners may experience psychological and emotional stress and may suffer from loss of social support and social networks. These changes may have pervasive and perpetuating effects on health, increasing social vulnerability, depression, loneliness, and social isolation.[66-68] It may also decrease positive health behaviors, such as exercise.[69] All of these consequences will increase risk of frailty. It is also of note that those who never married carry a significantly higher risk of frailty compared with those who are married, although the odds of the risk are lower than that of those who are widowed, divorced, or separated. Some studies have shown that single older people have worse health profiles than those who are married. For example, smoking and alcohol use are more common in those who are single.[69] These factors may also contribute to the higher risk of frailty. Reverse causality may be possible. Those who are frail may be associated with ill-health in themselves and their spouse, sharing the risk factors,[70] and therefore are more likely to lose the spouses.

The degree of the association between marital status and frailty varied across locations. The highest risks were observed in Europe and Asia (OR=2.33 and 2.25, respectively) and risks were lowest in Brazil (OR=1.39). It can be speculated that definitions of marriage and social norm of marriage may differ geographically.

One of the main strengths of this review was its robust methodology, with reproducible search strategy and comprehensive search words, using multiple databases. A total of 35 ORs, although unadjusted, were combined using a meta-analysis. Three series of supplementary analyses were conducted to explore the potential cause of high heterogeneity and found that reasons for not being married and study location may partially explain the heterogeneity.

There are potential limitations. First, only cross-sectional data were able to be pooled, therefore causal relationships could not be inferred. Second, regardless of the large number of cross-sectional studies included, very few of them specifically focused on the association between marital status and frailty, while many used marital status as one of the covariates for adjustment. Therefore, only unadjusted ORs were available for meta-analysis. It should be noted that the longitudinal study showed, controlling for various confounders including age, disabilities, cognition, depression, physical and social factors, that married men had lower risks of frailty while widowed women had a lower risk of frailty compared with married women.[29] Third, the current review only considered the frailty phenotype criteria, which focused mainly on physical factors, and the findings may not be generalizable to data based on other frailty criteria. Some of the frailty phenotype criteria are self-reported (physical activity, exhaustion, and weight loss), which could be influenced by cognitive and social factors that are related to the different categories of unmarried status. Although the frailty phenotype has been mostly widely used,[71] this operational definition of frailty focuses only on the physical components of frailty and does not include other components, such as cognition. Some experts consider that frailty is as a multidimensional construct and should include physical, cognitive, psychological, and social factors.[72] It should be noted that frailty phenotype is merely one of the many definitions of frailty and has not yet been recognized as the gold standard. In addition, it is unknown if the findings of this meta-analysis are a real association between marital status and frailty, or are just results related to specific components of the physical frailty phenotype or other non-physical factors. However, the frailty phenotype defines frailty operationally as a syndrome and may make frailty more tractable than other frailty models, such as the Frailty Index. Lastly, the screening processes of the systematic review were conducted by one investigator only and important studies may have been missed.

Conclusion and implications

This systematic review and meta-analysis showed pooled cross-sectional evidence that community-dwelling older people who are not married are significantly more likely to be frail than those who are married. The association between marital status and frailty was higher for those who were widowed or divorced than those who had never married and varied by location. For future research in this field, marital status should be recognized as an important factor, and more longitudinal studies examining marital status and frailty risk, especially each of frailty components, and controlling for potential confounding factors are needed.

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CONFLICTS OF INTEREST
None.

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Table 1. Summary of cross-sectional studies on frailty and marital status among community-dwelling older people.

Author/Year/Study	Location	Sample size	Female (%)	Age (range)	Frailty criteria	Married	Associations between marital status and frailty risk
Longitudinal							
Pollack 2017 MrOS study	USA	4518	0%	73.4 (≥65)	mCHS	82.9%	Frailty transition patterns for being married compared with being unmarried: Age- and site-aOR=1.6 (95%CI=1.1-2.2) for changing from prefrail to robust. Fully aOR=1.5 (95%CI=1.02-2.2) for changing from prefrail to robust. Age- and site-aOR=4.3 (95%CI=1.8-10.5) for changing from frail to prefrail or robust Fully aOR=2.6 (95%CI=1.1-11.7) for changing from frail to prefrail or robust. Age- and site-aOR=0.9 (95%CI=0.7-1.2) for changing from robust to prefrail, frail, or death Age- and site-aOR=0.9 (95%CI=0.7-1.1) for changing from prefrail to frail or death Age- and site-aOR=0.7 (95%CI=0.5-1.0) for changing from frail to death
Trevisan 2017 Pro.V.A.	Italy	2925	63.3%	74.4 (≥65)	mCHS	-	Unable to described because age- and gender-adjusted ORs for frailty transitions were only shown in graphs, and marital status categorization and reference group were not explained in the text.
Trevisan 2016 Pro.V.A.	Italy	1887	61.2%	74.2 (≥65)	mCHS	77.5%	Incident frailty, being married as reference Women: aOR=1.19 (0.96-1.49) for never married aOR=0.77 (0.66-0.91) for widows Men: aOR=3.84 (2.76-5.35) for never married aOR=1.43 (1.06-1.95) for widowers
Cross-sectional							
Siriwardhana 2019	Sri Lanka	746	56.7%	68 (≥60)	mCHS	61.3%	Divorced, widowed, separated, and never married: cOR=2.00 (95%CI=1.33-2.99)
Ahmad 2018	Malaysia	2310	59.6%	- (≥65)	mCHS	62.9%	Divorce, widowed, and single: cOR=2.37 (95%CI=1.79-3.14)
Aliberti 2018 HRS	USA	7338	54.9%	74.4 (≥50)	mCHS	62.4%	Divorce, widowed, and single: cOR=2.22 (95%CI=1.95-2.53)
Gijon-Conde 2018 Seniors-ENRICA	Spain	1047	49.2%	71.1 (≥60)	mCHS	71.3%	Separated, widowed, and single: cOR=1.95 (95%CI=1.16-3.28)
Gross 2018	Brazil	555	60.9%	71.1 (≥60)	mCHS	64.0%	Divorce, widowed, and single: cOR=1.35 (95%CI=0.94-1.95)
Lewis 2018	Tanzania	196	57.9%	74.8 (≥60)	mCHS	49.5%	Divorce, widowed, separated, and single: cOR=2.78 (95%CI=1.25-6.19)
Mohd Hamidin 2018	Malaysia	279	57.7%	73.3 (63-99)	mCHS	48.7%	Divorced, widowed, and single: cOR=3.88 (95%CI=1.93-7.78)

Author/Year/Study	Location	Sample size	Female (%)	Age (range)	Frailty criteria	Married	Associations between marital status and frailty risk
Nascimento 2018	Brazil	347	56.2%	70.1 (≥60)	mCHS	57.9%	Without marital partner: cOR=1.38 (95%CI=0.88-2.18)
Ntanasi 2018 HELIAD	Greece	1867	58.6%	73.5 (≥65)	mCHS	74.4%	Not married: cOR=2.19 (95%CI=1.37-3.50)
Rahi 2018 Three-City Study	France	560	63.2%	81.7 (≥75)	mCHS	49.6%	Divorce, widowed, separated, and single: cOR=1.54 (95%CI=0.95-2.49)
Thompson 2018 DYNOPTA & NWAHS	Australia	8744	86%	80 (≥65)	mCHS	46.2%	Divorce, widowed, and never married: cOR=1.41 (95%CI=1.27-1.56)
Ferriolli 2017 FIBRA	Brazil	5626	66.2%	73.1 (≥65)	mCHS	49.9%	Divorced, widowed, and single: cOR=1.53 (95%CI=1.26-1.86)
Flippin 2017	Brazil	322	60.6%	67.8 (≥60)	mCHS	57.8%	Divorced, widowed, and single: cOR=1.31 (95%CI=0.76-2.28)
Grden 2017	Brazil	243	66.3%	84.4 (≥80)	mCHS	30.0%	Widowed and single: cOR=1.94 (95%CI=0.81-4.66)
Herr 2017 SIPAF	France	1926	59.4%	83.3 (≥70)	mCHS	45.0%	Not married: cOR=2.57 (95%CI=2.01-3.28)
Moreno-Tamayo 2017 Rural Frailty Study	Mexico	591	52.%	76.3 (≥70)	mCHS	48.6%	Not married: cOR=1.39 (95%CI=0.82-2.36)
Sánchez-García 2017 COSFOMA	Mexico	1252	59.9%	- (≥60)	mCHS	59.4%	Widowed and single: cOR=1.86 (95%CI=1.41-2.46)
Tavares 2017	Brazil	1608	64.4%	- (≥60)	mCHS	42.7%	Without marital companion: cOR=1.13 (95%CI=0.84-1.51)
Vaingankar 2017 Well-being of the Singapore Elderly Study	Singapore	2101	53.9%	69 (≥60)	mCHS	63.2%	Divorce, widowed, separated, and single: cOR=1.86 (95%CI=1.36-2.53)
Veronese 2017 ELSA	UK	4077	53.0%	70.9 (≥60)	mCHS	64.8%	Divorced, single, and not married: cOR=2.02 (95%CI=1.57-2.60)
Wei 2017 SLAS-1 & 2	Singapore	5685	62.8%	66.6 (≥55)	mCHS	69.4%	Divorced, widowed, and single: cOR=2.57 (95%CI=2.00-3.31)
Wu 2017 CHARLS	China	5301	49.4%	- (≥60)	mCHS	77.2%	Widowed or other: cOR=2.70 (95%CI=2.17-3.35)
Al-Kuwaiti 2016	UAE	151	43.7%	65.6 (≥55)	mCHS	84.1%	Divorce, widowed, and unmarried: cOR=2.89 (95%CI=1.12-7.45)
Yamanashi 2016	Japan	1811	63.7%	72.2 (≥60)	mCHS	68.7%	Divorce, widowed, and unmarried: cOR=2.24 (95%CI=1.23-4.08)

Author/Year/Study	Location	Sample size	Female (%)	Age (range)	Frailty criteria	Married	Associations between marital status and frailty risk
Op het Veld 2015	Netherlands	8489	46.8%	74.2 (≥65)	mCHS	68.8%	Divorce, widowed, and unmarried: cOR=2.51 (95%CI=2.16-2.93)
Peklar 2015 TILDA	Ireland	1718	52.4%	73.0 (≥65)	mCHS	69.6%	Not married: cOR=2.00 (95%CI=1.24-3.22)
Llibre Jde 2014 The 10/66 Study	Cuba	2339	64.7%	- (≥65)	mCHS	44.6%	Divorce, widowed, separated, and single: cOR=1.45 (95%CI=1.18-1.78)
Sánchez-García 2014 SADEM	Mexico	1933	58.0%	71.1 (≥60)	mCHS	66.4%	Not married: cOR=1.40 (95%CI=0.87-2.25)
Jürschik 2012 FRALLE	Spain	523	60.3%	81.3 (≥75)	mCHS	50.7%	Widowed, separated, and single: cOR=2.91 (95%CI=1.53-5.53)
Ní Mhaoláin 2012	Ireland	544	70.7%	73 (≥60)	mCHS	50.6%	Divorce, widowed, separated, and never married: cOR=2.09 (95%CI=0.77-5.66)
Lin 2011	Taiwan	929	47.6%	- (≥65)	mCHS	71.0%	Not married: cOR=1.98 (95%CI=1.27-3.09)
Masel 2011 HEPESE	USA	2049	58.6%	74.4 (67-108)	mCHS	54.2%	Not married: cOR=1.50 (95%CI=1.08-2.08)
Alcalá 2010 Cohort of Peñagrande	Spain	814	51.4%	76 (≥65)	mCHS	64.3%	Not married: uOR=2.39 (95%CI=1.59-3.61)
Wong 2010 MUNS	Canada	740	67.8%	79.6 (75-96)	mCHS	30.1%	Widowed and unmarried: cOR=1.60 (95%CI=0.82-3.09)
Cawthon 2007 MrOS	USA	5993	0%	73.7 (≥65)	mCHS	82.3%	Not married: cOR=1.66 (95%CI=1.23-2.23)

aOR: Adjusted odds ratio
CHARLS: China Health and Retirement longitudinal Study
cOR: Calculated odds ratio
COSFOMA: Cohort of Obesity, Sarcopenia and Frailty of Older Mexican Adults
CSHA CFS: Canadian Study of Health and Aging Clinical Frailty Scale
DYNOPTA: Dynamic Analysis to Optimise Ageing Project
EFS: Edmonton Frail Scale
ELSA: English Longitudinal Study of Ageing
FI: Frailty Index
FRALLE: Assessing frailty in elderly people in Lleida
HELIAD: Hellenic Longitudinal Investigation of Aging and Diet
HEPESE: Hispanic Established Populations for Epidemiologic Studies of the Elderly

HRS: Health and Retirement Study
mCHS: Modified Cardiovascular Health Study criteria
MrOS: Osteoporotic Fractures in Men Study
MUNS: Montreal Unmet Needs Study
NWAHS: North West Adelaide Health Study
Pro.V.A.: Progetto Veneto Anziani
SADEM: Study on Aging and Dementia in Mexico
SIPAF: Système d'Information sur la Perte d'Autonomie Fonctionnelle de la personne âgée
SLAS: Singapore Longitudinal Ageing Study
SOF: Study of Osteoporotic Fractures
TFI: Tilburg frailty indicator
TILDA: The Irish Longitudinal Study of Ageing

Table 2. Meta-analysis of cross-sectional associations between marital status and frailty and gender-stratified, marital status-stratified, and subgroup analyses (married participants as reference group)

	Number of studies	Pooled odds ratio (95%CI)	p	P for heterogeneity	I^2	p for subgroup differences
Total	35	1.88 (1.70-2.07)	<0.001	<0.001	69%	-
Gender-stratified						
Female only	15	1.74 (1.42-2.13)	<0.001	<0.001	81%	0.62
Male only	16	1.86 (1.55-2.24)	<0.001	0.01	49%	
Subgroup						
Location						
Europe	10	2.33 (2.11-2.57)	<0.001	0.64	0%	ref
Asia	9	2.25 (2.01-2.53)	<0.001	0.64	0%	0.67
USA/Canada	4	1.81 (1.43-2.29)	<0.001	0.06	59%	0.05
Brazil	6	1.39 (1.22-1.59)	<0.001	0.62	0%	<0.001
Others	6	1.49 (1.33-1.68)	<0.001	0.30	17%	<0.001
Sample size						
n<2000	23	1.86 (1.63-2.12)	<0.001	0.02	42%	ref
n>=2000	12	1.90 (1.63-2.20)	<0.001	<0.001	85%	0.84
Mean age*						
<75	21	1.93 (1.73-2.16)	<0.001	<0.01	54%	ref
>=75	8	1.88 (1.44-2.45)	<0.001	<0.001	75%	0.85
Marital status-stratified (vs. married)						
Widowed	12	2.11 (1.86-2.39)	<0.001	0.11	35%	ref
Divorced/separated	10	1.73 (1.42-2.11)	<0.001	0.19	29%	0.10
Never married	7	1.37 (1.06-1.79)	0.02	0.74	0%	<0.01

CI: Confidence interval

* 6 studies did no provide mean age.

Figure 1. Flow chart of systematic literature review.

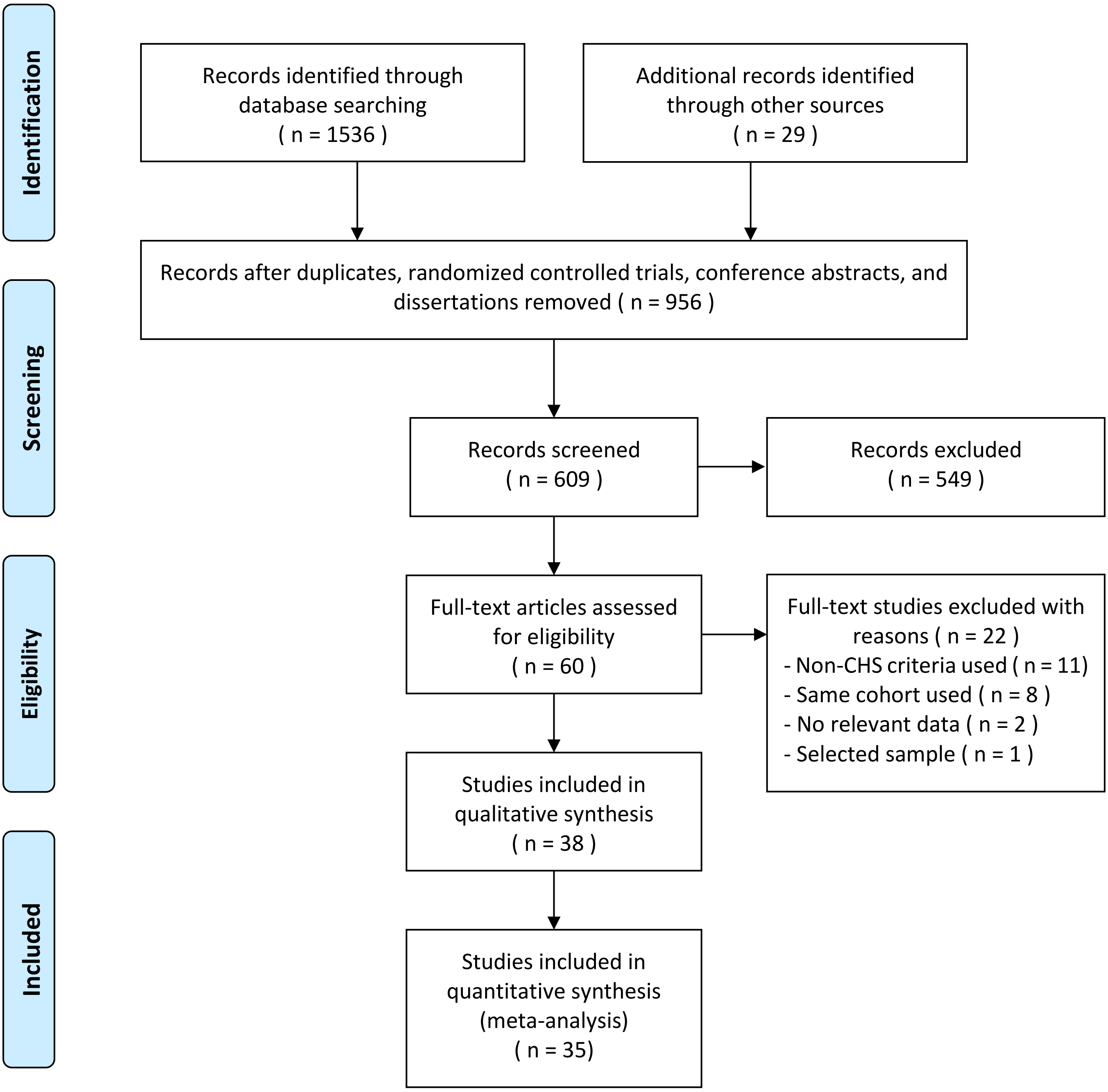

Figure 2. Forest plot of association between marital status and frailty.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Siriwardhana 2019	0.691746	0.205856	2.8%	2.00 [1.33, 2.99]
Ahmad 2018	0.862822	0.143097	3.7%	2.37 [1.79, 3.14]
Aliberti 2018	0.798023	0.066771	4.8%	2.22 [1.95, 2.53]
Gijon-Conde 2018	0.669519	0.264356	2.1%	1.95 [1.16, 3.28]
Gross 2018	0.301892	0.185973	3.1%	1.35 [0.94, 1.95]
Lewis 2018	1.023889	0.408037	1.2%	2.78 [1.25, 6.19]
Mohd Hamidin 2018	1.354546	0.355885	1.4%	3.88 [1.93, 7.78]
Nascimento 2018	0.327242	0.22958	2.5%	1.39 [0.88, 2.18]
Ntanasi 2018	0.813795	0.239025	2.4%	2.26 [1.41, 3.60]
Rahi 2018	0.430158	0.246672	2.3%	1.54 [0.95, 2.49]
Thompson 2018	0.341488	0.053889	5.0%	1.41 [1.27, 1.56]
Ferriolli 2017	0.425583	0.100076	4.4%	1.53 [1.26, 1.86]
Flippin 2017	0.271689	0.282146	2.0%	1.31 [0.75, 2.28]
Grden 2017	0.662281	0.446748	1.0%	1.94 [0.81, 4.65]
Herr 2017	0.942118	0.124522	4.0%	2.57 [2.01, 3.27]
Moreno-Tamayo 2017	0.330093	0.270306	2.1%	1.39 [0.82, 2.36]
Sanchez-Garcia 2017	0.62268	0.140874	3.7%	1.86 [1.41, 2.46]
Tavares 2017	0.121089	0.148096	3.6%	1.13 [0.84, 1.51]
Vaingankar 2017	0.618443	0.158108	3.5%	1.86 [1.36, 2.53]
Veronese 2017	0.702187	0.129603	3.9%	2.02 [1.57, 2.60]
Wei 2017	0.944324	0.128108	3.9%	2.57 [2.00, 3.30]
Wu 2017	0.771824	0.119183	4.1%	2.16 [1.71, 2.73]
Al-Kuwaiti 2016	1.060967	0.48313	0.9%	2.89 [1.12, 7.45]
Yamanashi 2016	0.807458	0.30588	1.8%	2.24 [1.23, 4.08]
Op het Veld 2015	0.921485	0.077935	4.7%	2.51 [2.16, 2.93]
Peklar 2015	0.694169	0.242597	2.4%	2.00 [1.24, 3.22]
Llibre Jde 2014	0.370533	0.105992	4.3%	1.45 [1.18, 1.78]
Sanchez-Garcia 2014	0.333144	0.242917	2.4%	1.40 [0.87, 2.25]
Jurschik 2012	1.067237	0.328169	1.6%	2.91 [1.53, 5.53]
Ni Mhaolain 2012	0.738782	0.507551	0.8%	2.09 [0.77, 5.66]
Lin 2011	0.684414	0.225531	2.6%	1.98 [1.27, 3.08]
Masel 2011	0.406203	0.167475	3.3%	1.50 [1.08, 2.08]
Alcala 2010	0.871293	0.209177	2.8%	2.39 [1.59, 3.60]
Wong 2010	0.466944	0.336806	1.6%	1.60 [0.82, 3.09]
Cawthon 2007	0.504127	0.151517	3.6%	1.66 [1.23, 2.23]
Total (95% CI)			**100.0%**	**1.88 [1.70, 2.07]**

Heterogeneity: Tau² = 0.05; Chi² = 109.73, df = 34 (P < 0.00001); I² = 69%
Test for overall effect: Z = 12.53 (P < 0.00001)