Archives of Gerontology and Geriatrics 84 (2019) 103898

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

Review

Increased healthcare costs associated with frailty among community-dwelling older people: A systematic review and meta-analysis

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ARTICLE INFO

Keywords:
Frailty
Frail elderly
Costs and cost analysis
Health care costs
Health expenditures
Systematic review

ABSTRACT

Background: Although frailty of older people has been shown to be associated with numerous adverse health outcomes, evidence on healthcare costs associated with frailty is scarce.
Methods: Medline, Embase, PsycINFO, and AMED were electronically searched in January 2019 based on a protocol in accordance with the PRISMA statement using Medical Subjective Heading and free text terms, with explosion functions. Language restriction was not applied. Studies were considered if they were published between 2000 to January 2019 and provided healthcare costs stratified by the frailty status categories among community-dwelling older people with a mean age of 60 years or higher. Reference lists of the included studies were reviewed for additional studies. Healthcare costs according to frailty status were compared using standardized mean difference random-effects meta-analysis.
Results: The systematic review found 3116 citations. After screening for title, abstract, and full-text for eligibility, 5 studies involving 3742362 participants were included. Healthcare costs were compared across three frailty status, robust, prefrailty, and frailty. Both prefrailty (5 studies, Hedges' g = 0.24, 95% confidence interval (CI) = 0.15-0.33, p < 0.001) and frailty (5 studies, Hedges' g = 0.62, 95%CI = 0.61-0.62, p < 0.001) were associated with significantly higher healthcare costs when compared with robustness. There was a high degree of heterogeneity. The risk of publication bias was considered to be low in funnel plots.
Conclusions: This systematic review and meta-analysis found a dose-response increase in the healthcare costs associated with frailty among community-dwelling older adults. Future research should recognize frailty as an important factor associated with increased healthcare costs.

1. Introduction

Over the last century, life expectancy has steadily improved worldwide and the number and proportion of older people have markedly increased. (World Health Organization, 2012) This trend is expected to continue in the next few decades and there will be an unprecedentedly large number of older people. (World Health Organization, 2012)

Older adults are the main users of healthcare services and account for the majority of the healthcare costs. (Rockwood & Hubbard, 2004) As people age, they generally tend to develop more health problems, such as chronic diseases, physical and cognitive functional declines, and disabilities, and therefore, require various healthcare resources. In the US, Medicare spending per capita by age steadily increased from 65 years old (mean 5,562 USD) and almost tripled by the age of 96 (mean 15,732 USD). (The Rising Cost of Living Longer, 2015)

A few recent studies have suggested that frailty is associated with increased use of healthcare resources and higher healthcare costs among older adults. (Kojima, Liljas, & Iliffe, 2019) Frailty is conceptually defined as a clinically recognizable state characterized by a compromised ability of older people to tolerate stressors and increased vulnerability due to age-related accumulated health deficits in multiple physiological systems. (Clegg, Young, & Iliffe, 2013; Morley, Vellas, & van Kan, 2013) Frail older adults are at an increased risk of various negative health outcomes, including falls, (Kojima, 2015a) disabilities, (Kojima, 2017, 2018a) dementia, (Kojima, Taniguchi, & Iliffe, 2016) and mortality. (Kojima, 2018b; Kojima, Iliffe, & Walters, 2018; Kojima, Taniguchi, & Kitamura, 2018) Frailty is also associated with increased use of healthcare resources, such as emergency department visits, (Kojima, 2018c) hospitalization, (Kojima, 2016) and institutionalization. (Kojima, 2015b, 2018d) In light of these significant negative impacts on older adults as well as burdens on healthcare systems and the

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https://doi.org/10.1016/j.archger.2019.06.003
Received 19 February 2019; Received in revised form 2 June 2019; Accepted 5 June 2019
Available online 05 June 2019

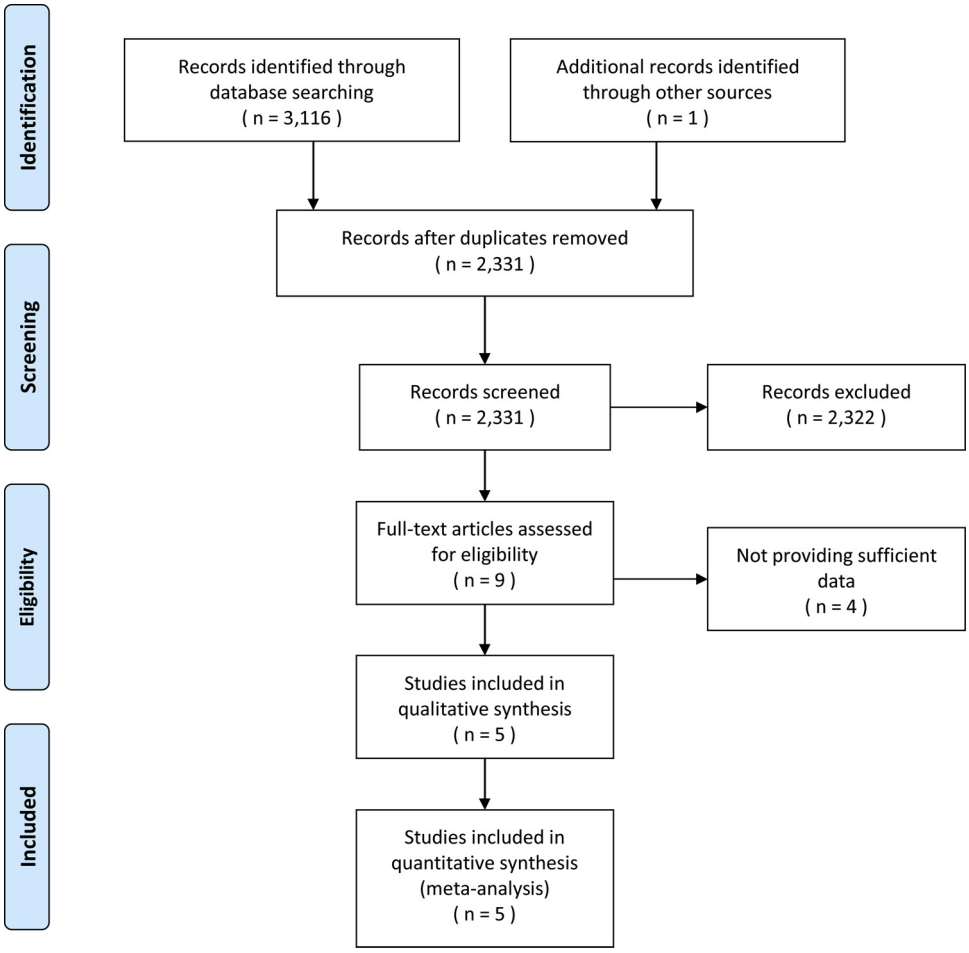


Fig. 1. Flow chart of systematic literature review.

growing number of older adults in an aging population, frailty has been recognized as a public health priority (Cesari, Prince, & Thiyagarajan, 2016; Kojima, Liljas et al., 2019. However there are only a limited amount of evidence found in the literature regarding the healthcare costs associated with frailty.

The objectives of this study are to conduct a systematic review of the literature for the available evidence on the association between frailty and healthcare costs among community-dwelling older adults and to synthesize pooled estimates of excess healthcare costs due to frailty by meta-analysis.

2. Method

2.1. Data source and search strategy

A systematic review of the literature was performed by one investigator (GK) on January 20th 2019 for studies that were published between January 2000 and January 2019 in four electronic databases (Embase, Medline, PsycINFO, and AMED). A protocol was developed a priori according to the PRISMA statements (Moher, Liberati, & Tetzlaff, 2009) and registered at PROSPERO (http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID = CRD42019123101). A combination of Medical Subjective Heading (MeSH) and free text terms was used for the search with explosion functions and without language restriction. The search terms used were: [Frailty (MeSH) OR Frail elderly (MeSH) OR "frailty"] AND [Costs and cost analysis (MeSH) OR Health care cost(s) (MeSH) OR Health expenditures (MeSH) OR Cost (MeSH) OR "cost*" OR "economic*" OR "expenditure*" OR "expense*" OR "finance*" OR "monetary" OR "payment*" OR "reimburs*"]. Additionally, the reference lists of the included studies were hand-searched. Corresponding authors were contacted for the data necessary for the meta-analysis if needed.

2.2. Study selection

Studies were considered to be eligible and were included if (1) they used community-dwelling older people with a mean age of 60 years or higher, (2) divided the cohort into two (non-frail, frail) or three (robust, prefrail, frail) groups based on a validated frailty definition or modified versions of it, and (3) provided healthcare costs before or after the baseline (including prevalent costs or incidental costs) stratified by the frailty status categories. Studies were excluded if they (1) used a selected sample, such as patients with a specific medical condition, (2) used a continuous score to define frailty, such as the Frailty Index, or (3) were reviews, randomized controlled trials, editorials, letters to the editor, comments, or dissertations. Titles, abstracts, and full-texts of the studies found through the review of the literature were screened for eligibility by one investigator (GK) according to the inclusion and exclusion criteria. When two or more studies used the same cohort, the one with the largest sample size was chosen for meta-analysis.

2.3. Data extraction

Data extracted from each of the studies were: first author, study or cohort name, publication year, location, sample size, proportion of female participants, age, frailty definition, and healthcare costs by frailty status.

Table 1
Summary of included studies on frailty and healthcare costs among community-dwelling older people.

First author/ Year/ Study	Location	Sample size	Female (%)	Age (range)	Frailty definition	Healthcare costs (currency)	Mean (SD) n Robust	Prefrail	Frail
Salinas-Rodriguez 2019	Mexico	265	72%	80.5	mCHS	Annual total of direct costs (health resources and services) and indirect costs (loss of labor productivity). (Mexican pesos)	32,401.21 (34,286.51) n = 89	45,825.04 (48,655.34) n = 132	64,951.17 (68,835.21) n = 44
Simpson 2019	US	3,736,540	58.9%	79.9 (≥65)	Faurot frailty index	9-month total of inpatient hospital payments, outpatient services, and prescription medications. (US dollar)	8,100 (25,082) n = 2,795,550	16,305 (38,058) n = 738,462	25,320 (53,066) n = 202,528
Ensrud 2018 SOF	US	2,150	100%	80.2 (≥65)	mCHS	12-month total of acute hospital stays, skilled nursing facility stay paid under Medicare Part A, inpatient rehabilitation facility stays, outpatient care, and home health care. (US dollar)	3,781 (6,920) n = 554	6,632 (12,452) n = 1,188	10,755 (16,589) n = 408
Garcia-Nogueras 2017 FRADEA	Spain	818	37.1%	75.8 (≥70)	mCHS	Annual total of costs for hospital admissions, specialist visits, and emergency visit. (Euro)	1,217 (2,170) n = 213	2,056 (3,496) n = 457	2,476 (3,433) n = 160
Bock 216 ESTHER	Germany	2,589	51.5%	69.6 (57-84)	mCHS	3-month total of inpatient treatment, outpatient treatment, medical supplies, dental protheses, pharmaceuticals, and formal and informal nursing care. (Euro)	642 (1,546) n = 876	821 (1,846)* n = 1,506	2,258 (4,604)* n = 207

GFI: Groningen Frailty Indicator.
mCHS: modified Cardiovascular Health Study criteria.
SD: Standard deviation.
SOF: Study of Osteoporotic Fractures.
* Calculated from available data.

2.4. Methodological quality assessment

Methodological quality of the studies was appraised by one investigator (GK) using the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies, (Critical Appraisal Tools, 2019) which consists of 8 items to be answered either “Yes”, “No”, “Unclear”, or “Not applicable”. The number of “Yes” responses was summed to make a score, ranging from 0 to 8, with a higher score indicative of better methodological quality. A score of 4 or more was considered to be adequate methodological quality.

2.5. Statistical analysis

2.5.1. Standardized mean difference

The healthcare costs of prefrail and frail groups were separately compared with that of robust group by calculating a standardized mean difference (SMD) of the healthcare costs as Hedges’ g, weighted according to the sample size of the studies. Hedges’ g was calculated from the mean, standard deviation, and sample size from each study, and the positive effect size is suggestive of higher healthcare costs in prefrail or frail groups than in the robust group. The magnitude of Hedges’ g was interpreted as small (0.2), medium (0.5), and large (0.8) by Cohen’s convention. (Cohen, 1988) Heterogeneity across the studies was examined using a chi-square test and its degree was assessed using I^2 statistic. If there was a significant heterogeneity, a random-effect meta-analysis was used, and a fixed-effect meta-analysis was used if not. If a high degree of heterogeneity was identified, a subgroup analysis, a sensitivity analysis, and a meta-regression analysis were used to explore the reasons for the high heterogeneity. Publication bias was assessed by visually inspecting a funnel plot.

Statistical analyses were conducted using the Review Manager 5 (Version 5.2, The Cochrane Collaboration, Copenhagen, Denmark). All analyses were two-sided and $p < 0.05$ was considered as statistically significant.

3. Results

3.1. Selection processes

The systematic review identified a total of 3116 studies (2,248 from Embase, 654 from Medline, 184 from PsycINFO, and 30 from AMED), one study was found from other source. After 786 duplicate studies were removed, 2,331 studies were left for title, abstract, and full-text for eligibility. Finally, 5 studies involving a total of 3,742,362 participants were included in this review. (Bock, Konig, & Brenner, 2016; Ensrud, Kats, & Schousboe, 2018; Garcia-Nogueras, Aranda-Reneo, & Pena-Longobardo, 2017; Simpson, Seamon, & Hand, 2018) A flow chart of the systematic review was shown in Fig. 1. Characteristics of the included studies are presented in Table 1.

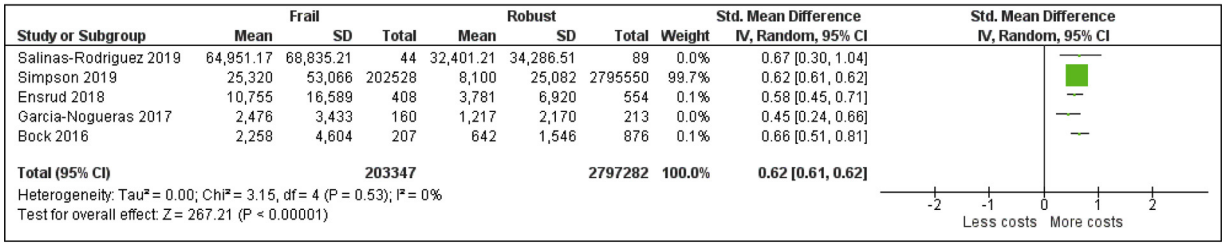
3.2. Methodological quality assessment and publication bias

All included studies were assessed for their methodological quality. The scores ranged from 5 to 8, with a mean of 6.8, and all studies were considered to have adequate methodological quality. Although it was difficult to visually assess forest plots as only five studies were included, there seemed to be no apparent asymmetry in the two forest plots for prefrailty and frailty, respectively compared with the robustness, therefore the risk of publication bias was considered to be low.

3.3. Meta-analysis of healthcare costs by frailty status

Healthcare costs according to the three frailty status groups (robust, prefrail, frail) were available from five studies, (Bock et al., 2016; Ensrud et al., 2018; Garcia-Nogueras et al., 2017; Simpson et al., 2018; Salinas-Rodriguez, Manrique-Espinoza, & Heredia-Pi, 2019) and were

A. Frail vs. Robust



(The pooled standardized mean difference is not shown due to technical reason)

B. Prefrail vs. Robust

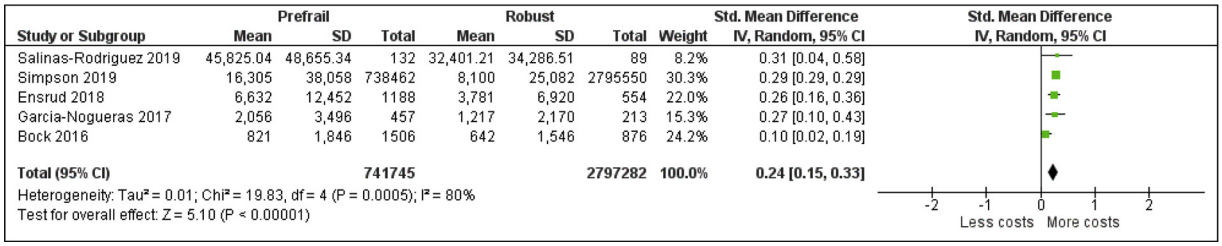


Fig. 2. Standardized mean difference of healthcare costs of frail (A) and prefrail (B), compared with robust.
A. Frail vs. Robust.
B. Prefrail vs. Robust.

pooled using a random-effect meta-analysis based on a high degree of heterogeneity (I^2 = 80%, p < 0.001 for prefrail). Both frailty (5 studies, Hedges' g = 0.62, 95% confidence interval (CI) = 0.61-0.62, p < 0.001) and prefrailty (5 studies, Hedges' g = 0.24, 95%CI = 0.15-0.33, p < 0.001) were associated with significantly higher healthcare costs when compared with robustness (Fig. 2). The higher the degree of frailty was, the more healthcare costs were spent (p for differences between frailty and prefrailty groups < 0.001). Subgroup analysis, sensitivity analysis, and meta-regression analysis were not considered due to the small number of studies included.

4. Discussion

This is the first attempt to describe the association between frailty and healthcare costs among community-dwelling older adults by conducting a systematic review and meta-analysis. The systematic review identified five studies encompassing a total of 3,742,362 participants and the meta-analysis showed a positive association between frailty and healthcare costs in a dose-response manner, regardless of lower power due to the small number of included studies. It should also be noted that, although the included studies examined various types of healthcare costs over difference time ranges, higher degree of frailty was consistently shown to be associated with higher healthcare costs.

One of the five included studies used a cohort of more than 3.6 million Medicare beneficiaries. (Simpson et al., 2018) Because the number of participants was substantially larger than those of the other studies (n = 265-2,589), the findings of this study were heavily weighted in the random-effects meta-analyses especially for the frail vs. robust analysis (99.7% in frail vs. robust, 30.3% for prefrail vs. robust). However, the standardized mean difference did not change significantly when this study was removed; frail vs. robust Hedges' g = 0.62 (95%CI = 0.61-0.62)- > 0.59 (95%CI = 0.50-0.68), prefrail vs. robust Hedges' g = 0.24 (95%CI = 0.15-0.33)- > 0.21 (95%CI = 0.11-0.32).

While four studies were from high income countries, only one study was from low-/middle-income country. (Salinas-Rodriguez et al., 2019) There was no significant subgroup difference between the four studies from high-income countries and the one study from Mexico; frail vs. robust p for difference p = 0.78, prefrail vs. robust p for difference = 0.59.

It seems that frailty plays an important role in terms of healthcare costs possibly through increasing risks of use of healthcare resources. (Kojima, 2016; Kojima, 2018c, 2018d) In a study by Bock et al., frailty was significantly associated with total healthcare costs even after controlling for comorbidity in a multivariate regression model, where age was not associated with healthcare costs when frailty was in the model. (Bock et al., 2016) Ensrud et al. showed that prefrailty and frailty were both significantly associated with higher healthcare costs than robustness, controlling for confounders including age, comorbidity, and functional limitations. (Ensrud et al., 2018) Another study of 1284 French older adults showed that frail and prefrail participants had a significantly higher ambulatory healthcare expenditures when compared with the robust participants in a multivariate generalized linear model controlling for age, the number of chronic diseases and activities of daily living (ADL) limitations, and other factors, where age was not significantly associated with healthcare costs. (Sirven & Rapp, 2017) As shown in these studies, significant associations between frailty and increased healthcare costs seems independent of age, comorbidity, or disability.

One of the main strengths was that the current study was being conducted based on a priori protocol in accordance with the PRISMA statements. The other strengths include the reproducible search strategy of the systematic review using comprehensive search terms including MeSH terms and that methodological quality and publication bias were examined. Additional data were obtained from authors of the original study and were included in the meta-analysis. Lastly, all the included studies are peer-reviewed original contributions.

There are some limitations that should be taken into account. First, there was significant heterogeneity across the included studies, which used different frailty definitions and methodologies to quantify healthcare costs. Therefore, a standardized mean difference was calculated using a random-effect meta-analysis. Regardless of the heterogeneity, the studies showed consistently higher healthcare costs among frailer participants and the meta-analysis found a significant positive association between frailty and healthcare costs. Second, only one investigator was involved in all the processes, therefore some important studies may have been missed. Third, due to the limited number of studies included, subgroup analysis, sensitivity analysis, and meta-regression analysis were not conducted. Forth, gray literature was not considered in the current review.

5. Conclusion

In conclusion, this systematic review and meta-analysis found a dose-response increase in the healthcare costs associated with frailty among community-dwelling older adults. The association between frailty and healthcare costs has significant implications given its spontaneous reversibility (Kojima, Taniguchi, & Iliffe, 2019; Kojima, Taniguchi, & Iliffe, 2019) and improvement by exercise and/or nutritional supplementation. (Lozano-Montoya, Correa-Perez, & Abraha, 2017) In future research, frailty should be recognized an important factor associated with increased healthcare costs.

Funding

None.

Conflicts of interest statement

Author does not have conflict of interest to report.

Acknowledgements

Author appreciate additional data shared by an author of original article. (Salinas-Rodriguez et al., 2019)

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