CLINICAL SCHOLARSHIP

The Relationship Between Depression and Frailty in Community-Dwelling Older People: A Systematic Review and Meta-Analysis of 84,351 Older Adults

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Key words
Depression, frailty, meta-analysis, systematic review

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Abstract

Objectives: In this study we investigated the correlation between depression and frailty in older adults. Additionally, correlations among study designs (prospective vs. cross-sectional), regions, depression indices, frailty indices, covariance corrections, and sexes were explored to support the analysis.
Methods: A systematic literature review and meta-analysis were conducted. A total of 84,351 older adults, all 65 years of age or older, were analyzed. Both authors independently extracted and examined retrieved articles. Searched keywords included "depression" or "depressive"; "frailty" or "frail"; and "older people," "elderly," "geriatric," or "senior." Articles published between January 2000 and December 2016 were searched. A literature quality assessment was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic
Reviews and Meta-Analyses: Systematic literature searches were conducted on the Embase, PubMed, MEDLINE, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Library databases, and collected studies were analyzed using a random effects model.
Results: Fourteen studies on people 65 years of age or older were collected, and a correlation analysis was conducted for depression and frailty. According to the meta-analysis, the risk for frailty due to depression was nonsignificant among the subgroups for study design (p for heterogeneity = .149), region (p = .429), depression criteria (p = .934), covariate adjustment (p = .702), and frailty criteria (p = .661). Notably, the risk for frailty due to depression was significantly higher in men than in women (pooled odds ratios for men and women: 4.76 and 2.25, respectively; Qbetween χ^2 = 9.93, p = .002).
Conclusion: Older adults with depression are more prone to frailty than are those without depression. Regardless of study design, region, depression index, frailty index, and covariance corrections, no significant differences were observed in the results of studies on depression and frailty in older adults. The only factor that had a significant influence was sex; older men with depression were at a higher risk for frailty than were older women with depression.
Clinical Relevance: Depression and frailty are pertinent health concerns related to geriatric syndromes. Because older adults with depression have a high risk for frailty, nursing personnel should use a depression index as early as possible to screen for depression and further reduce the occurrence of frailty in older adults. Furthermore, based on the aforementioned differences between the sexes, special attention should be paid to older men with depression to reduce their risk for frailty.

In line with the aging global population, the World Health Organization (WHO) has defined "the elderly population" as those 65 years of age or older. A society is considered an aging society when the proportion of elderly people exceeds 7% of the total population; when this proportion reaches 14%, it is known as an aged society, and a society where 20% of the population is elderly is called a hyperaged society (WHO, 2002). According to estimations from Global Health and Ageing (WHO, 2002), the proportion of people over the age of 60 years is projected to increase from 11% to 22% between 2000 and 2050. In view of this, geriatric syndrome has received global attention.

According to a U.S. epidemiological survey, the prevalence of geriatric depression affects 8% to 15% of elderly people, and the prevalence of older adults receiving long-term care in institutions such as nursing homes is as high as 30% to 45% (Lin, 2017). Vanoh, Shahar, Yahya, and Hamid (2016) revealed that the prevalence of geriatric depression in Asian countries is 12% to 34%; Malaysia had the highest prevalence of geriatric depression in Asia, at 16.5%. A study of elderly people in southern Taiwan between 1997 and 2000 revealed that the prevalence of geriatric depression was 12.9% to 21.7%; in addition, 6.2% had severe depression and 6.8% to 15.5% had mild depression. Geriatric depression increased almost 10-fold between 1997 and 2007 (Lin, 2007). Depression in elderly people is a serious global public health concern that leads to high medical expenses and mortality (Vanoh et al., 2016); therefore, geriatric depression requires an in-depth investigation.

Frailty is a core concept of geriatric health, and the WHO has noted that frailty has become a crucial factor affecting aging in older adults (WHO, 2002). Frailty is seen as a precursor to functional degradation in older adults, and represents an intermediate stage before loss of independence and death (Chang & Lin, 2015). A definition of frailty was first proposed by Fried et al. (2001), the clinical characterization including unintentional weight loss, weakness, poor endurance or exhaustion (low energy), slowness (slow gait), and low physical activity. Those who satisfy three or more of these indicators are classified as frail, those who satisfy one or two are defined as being in the prefrail stage, and those who satisfy none are said to be in robust health. However, because of the large number of indicators and substantial amount of time required for evaluation and measurement, Ensrud et al. (2008) proposed trustworthy and valid frailty indices termed Study of Osteoporotic Fractures (SOF) indicators; these require few questions and little time and are relatively easy to administer compared with the conventional approach. The SOF indicators contain three assessment indicators: unintentional weight loss, inability to rise five times from a chair without using armrests, and conscious inactivity. Those who meet two or more of these indicators are classified as frail, those who meet one are defined as being in the prefrail stage, and those who meet none are defined as being in robust health. Studies have shown that frailty has a profound effect on quality of life, care institution life conditions, and death among older adults (Avila-Funes et al., 2009; Shamliyan et al., 2013).

Relevant studies have revealed prevalences of frailty in older adults of 9.6%, 14%, and 26% in the United States, the United Kingdom, and Europe, respectively. In addition, early stage prevalence of 47% in the United States and 38.8% in Europe have been observed (Buttery, Busch, Gaertner, Scheidt-Nave, & Fuchs, 2015; Gale, Cooper, & Aihie Sayer, 2014; Jürschik et al., 2012). Biritwum et al. (2016) demonstrated that people 50 years of age and older in China, Ghana, India, Mexico, Russia, and South Africa accounted for 43% of the global elderly population. According to a survey conducted among these countries, the prevalence of frailty among older adults was lowest in China (13.1%) and highest in India (55.5%). Yu, Wu, Leung, Hu, and Woo (1982) conducted a survey on the prevalence of frailty in older adults in Hong Kong and urban and rural regions in Taiwan. The results confirmed that the prevalences of frailty among older adults were 38.10%, 33.06%, and 16.57% in rural Taiwan, urban Taiwan, and Hong Kong, respectively. These results indicate that older adults are prone to frailty.

Collard et al. (2014) stated that depression and frailty both have common comorbidities. Brown et al. (2014) also posited that depression and frailty have common risk factors that make distinguishing between them difficult. According to Pegorari and Tavares (2014), older adults with depression are 80% more prone to frailty than are those without depression because depression affects their behaviors and activity levels, resulting in a reduction in social participation, deterioration in their functional status, and an increase in frailty. Thus, having symptoms of depression may increase the risk for frailty. According to the findings of relevant studies, a strong correlation exists between depression and frailty. Most such studies have adopted major depressive disorder as the proxy variable for depression (Almeida et al., 2015; Bilotta et al., 2010; Collard, Comijs, Naarding, & Oude Voshaar, 2014; de Albuquerque Sousa, Dias, Maciel, & Guerra, 2012; Espinoza & Hazuda, 2015; Gurina, Frolova, & Degryse, 2011; Jürschik et al., 2012; Lohman, Dumenci, &

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Mezuk, 2014; Pegorari & Tavares, 2014; Sánchez-García et al., 2013). However, the results of these studies are controversial in terms of the correlation between depression and frailty in older adults of different sex. Some studies have shown that women with depression have a higher risk for frailty than men (Chang, Weiss, Xue, & Fried, 2010; Fugate Woods et al., 2005; Lakey et al., 2012; Lohman, Dumenci, & Mezuk, 2015), whereas some have indicated the opposite (Almeida et al., 2015); therefore, further analysis is required. Additionally, few studies have used alternative study methods, such as analysis according to study design (prospective vs. cross-sectional), region, depression indices, frailty indices, and covariance corrections, to investigate differences related to depression and frailty among older adults. Therefore, the present study analyzed the addressed concerns by conducting a systematic literature review and meta-analysis. Nursing personnel could use the results of this evidence-based study to determine prevention measures or improve care plans for older adults with depression in order to reduce frailty.

Objectives

The main objective of this study was to determine the correlation between depression and frailty in older adults. A differential analysis between depression and frailty in older adults was conducted in relation to study design (prospective vs. cross-sectional), region, depression indices, frailty indices, covariance corrections, and sex.

Methods

Depression Assessment

The assessment tools for major depressive disorder included the Center for Epidemiologic Studies Depression (CESD) scale, Patient Health Questionnaire-9 (PHQ-9), *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV), Diagnostic Interview Schedule (DIS), and Geriatric Depression Scale (GDS). The most commonly used indicator for depression assessment is the CESD scale, which was developed by Radloff in 1977 to measure levels of depression among the general population. It is a self-reported depression scale with 20 questions; its content covers depressed mood, guilt and worthlessness, feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance. Participants are asked about their frequencies of depression in the preceding week, and each question is scored from 0 to 3. Radloff recommended that results be interpreted based on the total score; the higher the total score, the more severe is the participant's depression. Because the scale established by Radloff is time consuming for older adults to complete, Kohout, Berkman, Evans, and Cornoni-Huntley (1993) subsequently developed a simpler version, namely a 10-question scale, and confirmed its reliability and validity. Depression symptoms are suspected if participants score more than 8 points, and the simple version is more suitable for assessing older adults than other individuals. The GDS is a common assessment tool that was first proposed by Yesavage et al. (2011). The purpose of the GDS is to measure the conscious feelings of older adults in the preceding 2 weeks. This assessment tool can usually detect depression among older adults at an early stage. A score of 5 to 9 points indicates that the participant may have depression, and those with 10 points or more are confirmed as having major depressive disorder.

Frailty Assessment

Assessment indicators for frailty include the Cardiovascular Health Study (CHS) indicator, SOF indicators, the International Association of Nutrition and Aging (IANA) Task Force definition of frailty, the Modified CHS (mCHS) frailty index, and the Women's Health Initiative Observational Study (WHI-OS) instrument. Among these, the CHS indicator is the most commonly used. This indicator was proposed by Fried et al. (2001) and covers five aspects, namely grip strength, walking speed, exhaustion, physical activity, and unintentional weight loss. Those who satisfy three or more of these indicators are determined to be in the frail stage, those who meet one or two are in the prefrail stage, and those who meet zero are in the robust stage.

Another common assessment tool is the SOF indicators, proposed by Ensrud et al. (2008). Compared with most related scales, the SOF indicators have fewer questions, are less time consuming, and are easier to administer. Moreover, they have reliability and validity similar to those of the other scales, with items including unintentional weight loss of more than 5% body weight over the preceding year, inability to rise five times from a chair without using armrests, and answering "no" to the question "Do you feel full of energy?" On the SOF indicator scale, frailty is suspected if two or three of the indicators are satisfied, the prefrail stage is suspected if one indicator is satisfied, and the robust stage is suggested if no indicators are satisfied.

Data Sources and Search Strategy

The present study conducted a systematic literature search on Embase, Scopus, PubMed, Ovid MEDLINE, MEDLINE, and the Cumulative Index to Nursing and Allied Health Literature for papers published between January 1990 and December 2016. The key words used were "depression" or "depressive"; "frailty" or "frail"; and "older people," "elderly," "geriatric," or "senior." The exact search strategy was as follows: (depression or depressive) AND (frailty or frail) AND (older people or elderly or geriatric or senior).

Inclusion and Exclusion Criteria

The prerequisites of papers for inclusion were (a) a cross-sectional design or prospective cohort design, (b) a study of participants 65 years of age or older, (c) results presented as adjusted or unadjusted odds ratios (ORs) or hazard ratios (HRs), (d) an assessment of the degrees of depression and frailty in the study sample, (e) inclusion of 95% confidence intervals (CIs), and (f) having been published in English and constituting a full text. Only articles published between 2000 and 2016 were selected for this study.

Literature review articles, letters to editors, book chapters, postgraduate theses, experimental studies, and interventional studies were excluded.

Data Extraction

Both authors independently examined and extracted the searched data and analyzed the study methods, sample numbers, evaluation criteria, and correlations between various stages of depression and frailty. The authors intended to invite a third data reviewer to scrutinize the data if inconsistencies were noted during data extraction.

Quality Assessment

The Newcastle–Ottawa Scale (NOS) was used to evaluate the prospective cohort studies for selection, comparability, and assessment of outcome and exposure (Wells et al., 2014), with a maximum possible score of 9. Scores of ≥7 indicated a low risk of bias, scores of 4 to 6 indicated a moderate risk of bias, and scores of <4 indicated a high risk of bias. Additionally, the quality of cross-sectional studies was assessed using the Agency for Healthcare Research and Quality (AHRQ) scale. The AHRQ scale has 11 items, all of which are rated as "yes" (1 point) or "no" or "unclear" (0 point), and the highest possible total score is 11. The quality of the study is scored as follows: 0 to 3 indicates low quality, 4 to 7 indicates medium quality, and 8 to 11 indicates high quality.

Statistical Analysis

We extracted or calculated ORs of depression comparison groups (depression vs. nondepression) for risk for frailty in individual studies including either prospective or cross-sectional studies. We then pooled these ORs using a random effects model that assumed that the true underlying effect followed a normal distribution. Furthermore, the summary effects of contrasting the depression groups in terms of frailty risk subgrouped by study characteristics (i.e., study design [prospective vs. cross-sectional]) were compared using a mixed effects model. We evaluated the heterogeneity of effect sizes (ORs) across individual studies by using I^2 statistics, with proportions greater than 25%, 50%, and 75% considered to have low, moderate, and high heterogeneity, respectively (Higgins et al., 2003). Finally, we tested for publication bias by using a funnel plot and Egger's intercept test (Egger, Smith, Schneider, & Minder, 1997). Data analyses were performed using Comprehensive Meta-Analysis version 2.2 (BioStat Solutions, Inc., Englewood, NJ, USA).

Results

Study Sample

Figure 1 presents the results of the literature review. Among the studies initially identified, some were excluded for the following reasons: not constituting a full text or not written in English, having duplicate cohorts, being a review article, not satisfying the study criteria, or not having extracted relevant HRs or ORs. After all such studies had been excluded, 14 prospective cohort and cross-sectional studies were agreed upon for inclusion by the two reviewers. Table 1 summarizes the characteristics of the 14 studies included for meta-analysis.

The final 14 studies collectively analyzed 84,351 community-dwelling older adults. As shown in Table 1, 10 studies adopted a cross-sectional design and four were prospective cohort studies (reported ORs or cross-table of depression by frailty). Six studies were from the United States, four were from Europe, and four were conducted in other regions (one in Mexico, two in Brazil, and one in Australia). Most studies (12 of 14) adopted screening measures to

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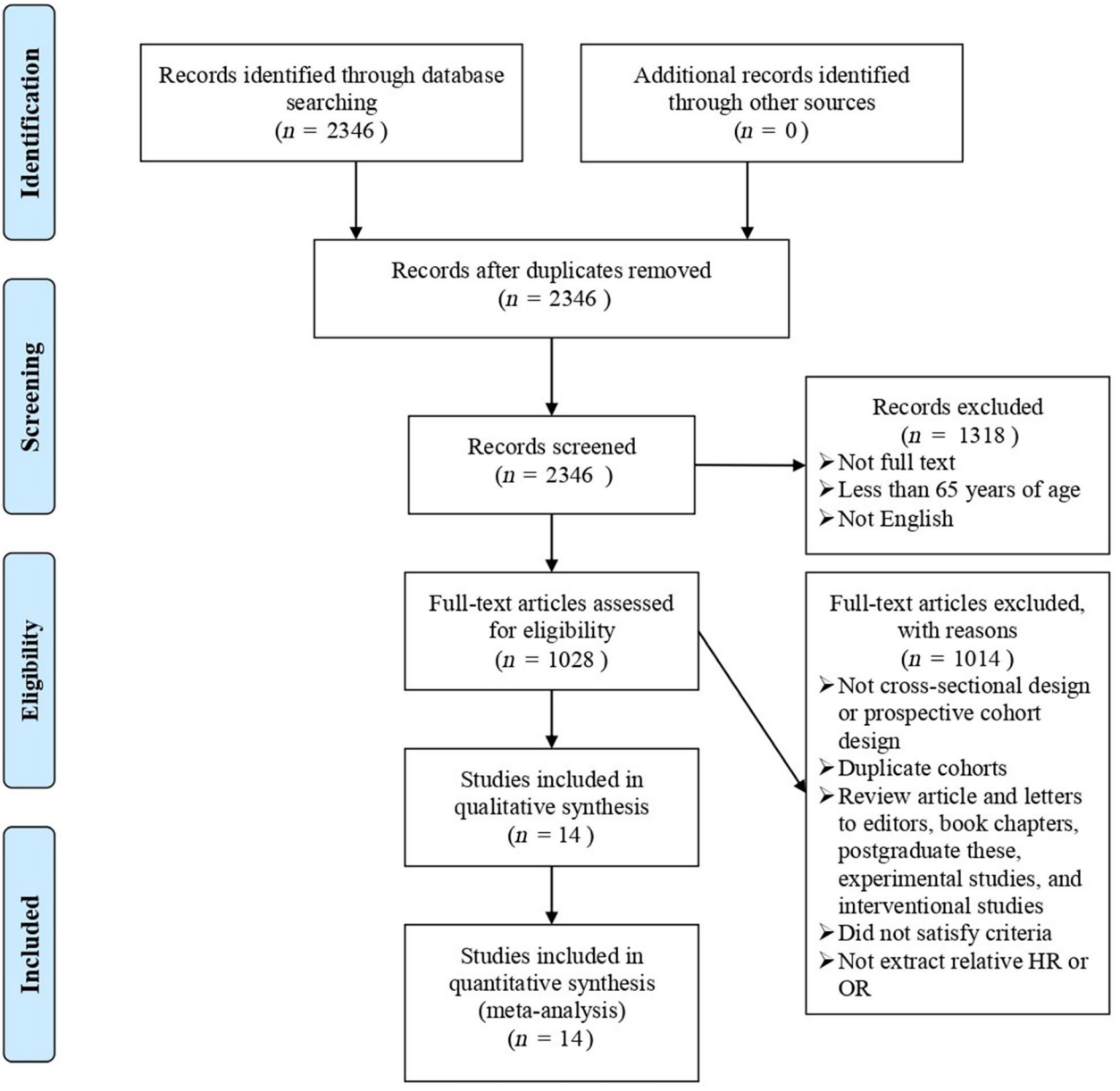

Figure 1. PRISMA flow-diagram showing identification and selection of the pertinent studies.

determine depression criteria (Almeida et al., 2015; Chang et al., 2010; de Albuquerque Sousa et al., 2012; Espinoza & Hazuda, 2015; Fugate Woods et al., 2005; Gurina et al., 2011; Jürschik et al., 2012; Lakey et al., 2012; Lohman et al., 2014; Lohman et al., 2014; Pegorari & Tavares, 2014; Sánchez-García et al., 2013), whereas the remaining two used a structured instrument (DSM-IV; Bilotta et al., 2010; Collard et al., 2014). Six effect sizes (ORs) were retrieved from the multivariate logistic regression analyses and eight were calculated according to the cross-table of depression by frailty without adjustment for confounding factors.

Among the analyzed studies, eight adopted the CHS as frailty criteria (Collard et al., 2014; de Albuquerque Sousa et al., 2012; Gurina et al., 2011; Jürschik et al., 2012; Lakey et al., 2012; Lohman et al., 2014, 2015; Pegorari & Tavares, 2014), two used SOF criteria (Bilotta et al., 2010; Espinoza & Hazuda, 2015), and four used other criteria (Almeida et al., 2015; Chang et al., 2010; Fugate Woods et al., 2005; Sánchez-García et al., 2013). Four studies analyzed only female

Table 1. Characteristics of the Included Studies for Meta-Analysis

Study	Study design	Nationality	Participant	Frailty criteria	Depression criteria	Sample size	Sex	Age (years)	Length of follow-up	No. of covariates	OR (95% CI)
Almeida et al. (2015)	Prospective	Australia	Community-dwelling	IANA Task Force definition of frailty	PHQ-9 ≥ 5	2,565	M	≥75	4.2±1.1 years	0	4.76 (3.61, 6.27)
Lakey et al. (2012)	Prospective	United States	Clinical centers	CHS	CES-D cutpoints to indicate low (0.009), medium (0.009–0.06), and high (0.06) depressive symptoms	27,652	F	65–79	3 year	0	2.12 (1.89, 2.36)
Lohman et al. (2014)	Prospective	United States	Community-dwelling	CHS	CES-D 8 item ≥ 4 symptoms	3,453	M/F	≥65	2 years	0	2.59 (2.00, 3.35)
Fugate Woods et al. (2005)	Prospective	United States	Clinical centers	WHI-OS	CES-D 6-item ≥ 5	40,657	F	65–79	3 years	0	1.35 (1.24, 1.46)
Bilotta et al. (2010)	Cross-sectional	Italy	Community-dwelling	SOF	DSM-IV	302	M/F	65–89	N/A	8/10[a]	Living alone: 10.55 (2.35, 47.44); not living alone: 1.45 (0.66, 3.20)
Chang et al. (2010)	Cross-sectional	United States	Community-dwelling	mCHS	GDS 30 items > 9	620	F	70–79	N/A	3	4.74 (2.62, 8.55)
Collard et al. (2014)	Cross-sectional	Netherlands	Mental health institutes	CHS	DSM-IV	510	M/F	≥60	N/A	0	3.69 (1.96, 6.97)
de Albuquerque Sousa et al. (2012)	Cross-sectional	Brazil	Community-dwelling	CHS	GDS-15 item > 5	391	M/F	≥65	N/A	5	1.782 (0.820, 3.870)
Espinoza & Hazuda (2015)	Cross-sectional	Mexican Americans	Community-dwelling	SOF	GDS 30-item > 10 (probable depression)	394	M/F	65–80	N/A	6	2.84 (1.33, 6.03)
Gurina et al. (2011)	Cross-sectional	Russia	Community-dwelling	CHS	CES-D 20-item > 16 or GDS 15-item > 5	611	M/F	65–91	N/A	5	2.62 (1.60, 4.23)
Jürschik et al. (2012)	Cross-sectional	Spain	Community-dwelling	CHS	CES-D 20-item ≥ 16	640	M/F	≥75	N/A	5	
Lohman et al. (2014)	Cross-sectional	United States	Community-dwelling	CHS	CES-D 8-item ≥ 4	3,665	F	≥65	N/A	0	4.72 (3.65, 6.11)
Pegorari & Tavares (2014)	Cross-sectional	Brazil	Urban area	CHS	GDS 15-item > 5	958	M/F	≥60	N/A	0	2.80 (1.90, 4.14)
Sánchez-García et al. (2013)	Cross-sectional	Mexico	Community-dwelling	mCHS	CES-D 20-item > 16	1,933	M/F	≥60	N/A	0	5.71 (4.40, 7.41)

Note: CES-D = Center for Epidemiologic Studies Depression Scale; CHS = Cardiovascular Health Study; CI = confidence interval; DIS = Diagnostic Interview Schedule; DSM-IV = ***Diagnostic and Statistical Manual of Mental Disorders,*** 4th edition; GDS = Geriatric Depression Scale; IANA = International Association of Nutrition and Aging; mCHS = Modified Cardiovascular Health Study Frailty Index; OR = odds ratio; PHQ-9 = Patient Health Questionnaire-9; SOF = Study of Osteoporotic Fractures; WHI-OS = Women's Health Initiative Observational Study.

Table 2. Newcastle–Ottawa Scale Quality Assessment for Prospective Cohort Studies

	Selection				Comparability	Outcome			
Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up of cohorts	Overall quality score (maximum = 9)
Almeida et al. (2015)	★	★	★	★	★★	★	★	★	9
Lakey et al. (2012)	★		★	★	★★	★	★	★	8
Lohman et al. (2014)	★	★	★	★	★★	★	★	★	9
Fugate Woods et al. (2005)	★	★	★	★	★★	★	★	★	9

Note: ★= 1 score; ★★= 2 scores.

participants and one analyzed only male participants.

Quality Assessment

The NOS was used to score 4 prospective cohort studies, and 10 cross-sectional studies were scored using the AHRQ scale. Of the studies scored by NOS, all of them indicated a low risk of bias; the minimum score was 8, the maximum score was 9, and the average score was 8.8 (Table 2). Of the studies scored by the AHRQ scale, most of them indicated medium to high quality; the minimum score was 7, the maximum score was 9, and the average score was 8.2 (Table 3).

Association Between Depression and Frailty

Figure 2 contains a summary of the results of comparing the depression groups by using a random effects model. Of the individual studies, 13 of 14 had significant ORs with CIs above 0. After the ORs of the 14 studies had been pooled, the results revealed that the risk for frailty in the depression group was greater than that in the nondepression group (pooled OR = 2.99; 95% CI = 2.19–4.08). The between-study heterogeneity in the meta-analysis was extremely high (I^2 = 94.9%).

Subgroup Analysis of Depression Study Characteristics

Figure 3 presents the results of comparing the depression groups subgrouped by study characteristics derived from a mixed effects model. The results revealed that no significantly increased risk for frailty due to depression was evident among the subgroups according to study design (p for heterogeneity = .149), region (p = .429), depression criteria (p = .934), covariate adjustment (p = .702), or frailty criteria (p = .661). Notably, men had a significantly higher risk for frailty due to depression than did women (pooled ORs for men and women: 2.25 and 4.76, respectively; Qbetween χ^2 = 9.93, p = .002).

Heterogeneity and Publication Bias

Figure 4 displays the funnel plot and results of Egger's test. No evident asymmetrical pattern was observed in the funnel plot. However, Egger's test indicated that publication bias may have been present in this meta-analysis (p = .019). Using Duval and Tweedie's trim and fill method, seven studies were trimmed and the corrected pooled OR was 1.82 (95% CI = 1.33–2.49). Therefore, the main conclusions did not change when publication bias was considered.

Discussion

Regarding correlation between depression and frailty, the present evidence-based study revealed that people 65 years of age or older with depression had a higher risk for frailty than did those without depression, indicating that depression and frailty are strongly correlated in older adults. This result was consistent with those of relevant individual studies (Almeida et al., 2015; Bilotta et al., 2010; Chang et al., 2010; Collard et al., 2014; de Albuquerque Sousa et al., 2012; Espinoza &

Table 3. Agency for Healthcare Research and Quality (AHRQ) Checklist to Assess Quality of the Cross-Sectional Studies

AHRQ Methodology Checklist for Cross-sectional Study (http://www.ncbi.nlm.nih.gov/books/NBK35156/)	Bilotta et al. (2010)	Chang et al. (2010)	Collard et al. (2014)	de Albuquerque Sousa et al. (2012)	Espinoza & Hazuda (2015)	Gurina, et al. (2011)	Jürschik et al. (2012)	Lohman et al. (2014)	Pegorari & Tavares (2014)	Sánchez-García et al. (2013)
1. Define source of information (survey, record, review)	★	★	★	★	★	★	★	★	★	★
2. List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications	★	★	★	★	★	★	★	★	★	★
3. Indicate time period used for identifying patients	★	★	★	★	★	★	★	★	★	★
4. Indicate whether or not subjects were consecutive if not population-based	-	★	U	U	★	★	★	★	★	-
5. Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants	★	★	★	★	-	★	-	-	★	★
6. Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements)	★	★	★	★	★	★	★	★	★	★
7. Explain any patient exclusions from analysis	★	★	★	★	-	★	★	★	★	★
8. Describe how confounding was assessed and/or controlled	★	★	★	★	★	★	★	★	★	★
9. If applicable, explain how missing data were handled in the analysis	-	-	-	-	-	-	-	-	-	-
10. Summarize patient response rates and completeness of data collection	★	★	★	★	★	★	★	★	★	★
11. Clarify what follow-up, if any, was expected and the percentage of patients for whom incomplete data or follow-up was obtained	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Overall quality score (maximum = 11)	8	9	8	8	7	9	8	8	9	8

Note: ★ = yes; **-** = no; NA = not applicable = NA; U = unclear.

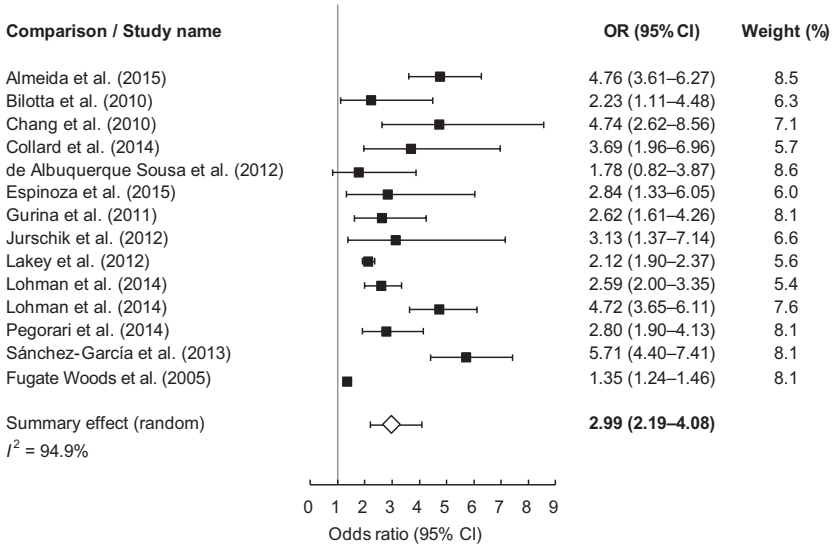

Figure 2. Summary effect on the increased risk for frailty in contrasting the groups of depression status derived from random effect model. CI = confidence interval; OR = odds ratio.

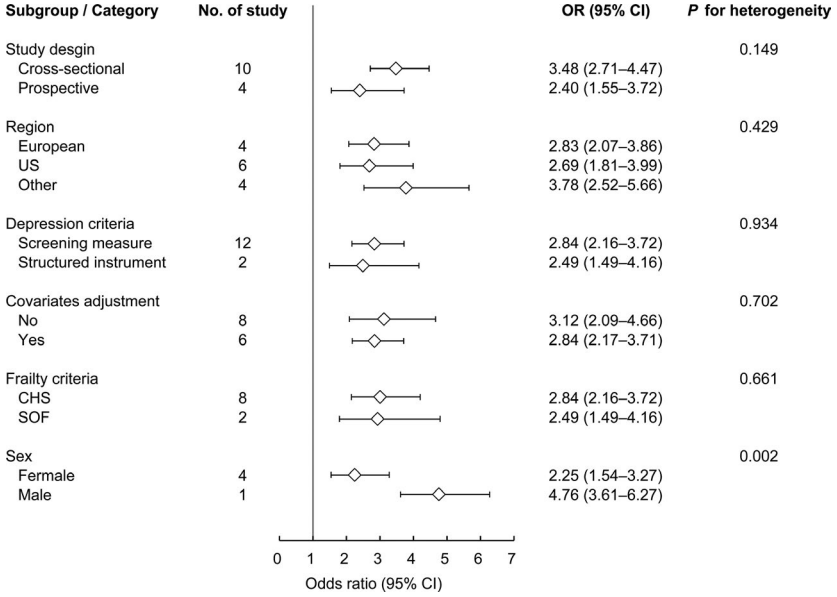

Figure 3. Comparing groups of depression subgroup on the risk for frailty derived from mixed effect model. CHS = Cardiovascular Health Study; CI = confidence interval; OR = odds ratio; SOF = Study of Osteoporotic Fractures.

Hazuda, 2015; Fugate Woods et al., 2005; Gurina et al., 2011; Jürschik et al., 2012; Lakey et al., 2012; Lohman et al., 2014, 2015; Pegorari & Tavares, 2014; Sánchez-García et al., 2013). Based on the findings of Pegorari and Tavares (2014), the probability of older adults with depression being frail is as high as 80%; this implies that depression symptoms may increase the risk for frailty. In addition, Pegorari and Tavares noted that depression affects behavior and performance, reduces social participation, leads to deterioration with respect to functional status, and increases frailty in older adults. Furthermore, studies have shown that antidepressants are commonly used by older adults with depression. Lakey et al. (2012) investigated older adults with depression treated with antidepressants and found that their risk for frailty was 3.63 times higher than that of nondepressed older adults. Additionally, older adults with depression who were not treated with antidepressant medication exhibited a 2.05-fold higher risk for frailty than nondepressed older adults. Therefore, use of

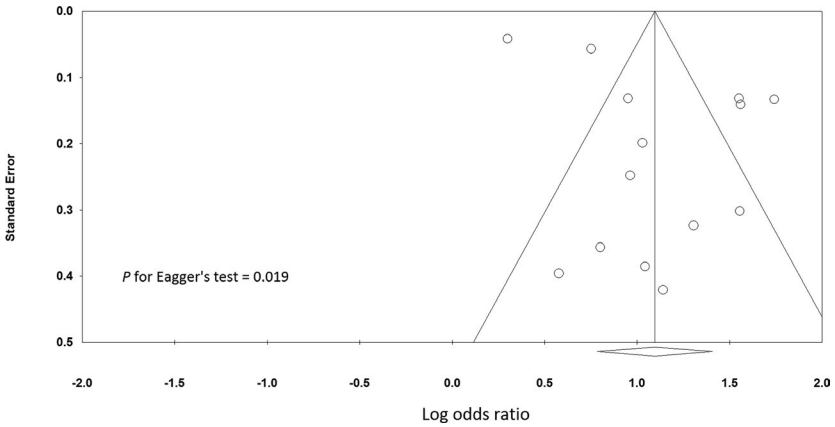

Figure 4. Funnel plot of standard error by log odds ratio.

antidepressants had a considerable effect on frailty in older adults; that is, use of antidepressants can increase the risk for frailty in older adults with depression.

As stated, this study was the first meta-analysis to explore the correlation between depression and frailty in people 65 years of age or older according to different study designs (prospective vs. cross-sectional), regions, depression indices, frailty indices, covariance corrections, and sexes. The systematic literature review and meta-analysis conducted in this study revealed that most studies used cross-sectional methods. The results obtained were similar to those obtained through prospective methods, indicating that different research methods do not cause discrepancies when analyzing the risk for frailty in older adults with depression. As stated, 6 of the 14 analyzed studies were conducted in the United States (Chang et al., 2010; Espinoza & Hazuda, 2015; Fugate Woods et al., 2005; Lakey et al., 2012; Lohman et al., 2014, 2015), two were conducted in Brazil (de Albuquerque Sousa et al., 2012; Pegorari & Tavares, 2014), and one each were conducted in Australia (Almeida et al., 2015), Italy (Bilotta et al., 2010), the Netherlands (Collard et al., 2014), Russia (Gurina et al., 2011), Spain (Jürschik et al., 2012), and Mexico (Sánchez-García et al., 2013). The results of our evidence-based study revealed that regardless of region, no substantial differences were observed among the analyzed studies in terms of their outcomes related to frailty risk in older adults with depression.

The criteria used in the 14 studies to discriminate depression differed. The CESD scale was used in seven studies, whereas other studies used the GDS, PHQ-9, DSM-IV, and DIS. The findings revealed no differences in analysis outcomes for risk for frailty among the various depression indices used. The criteria used for frailty assessment differed; of the 14 studies, 8 used the CHS indicator, whereas others used SOF indicators, the IANA Task Force definition of frailty, the mCHS, and the WHI-OS instrument. However, no contrasting results were obtained for the discrimination of frailty, regardless of the indicators used. Furthermore, the analysis of covariance corrections revealed that six of the analyzed studies applied covariance corrections (Bilotta et al., 2010; Chang et al., 2010; de Albuquerque Sousa et al., 2012; Espinoza & Hazuda, 2015; Gurina et al., 2011; Jürschik et al., 2012), whereas the other eight did not (Almeida et al., 2015; Collard et al., 2014; Fugate Woods et al., 2005; Lakey et al., 2012; Lohman et al., 2014, 2015; Pegorari & Tavares, 2014; Sánchez-García et al., 2013). However, the results of the present study revealed no significant differences in the analysis of depressed older adults with frailty, regardless of whether covariance corrections were applied. In addition to whether covariance corrections were employed, different study designs, regions, depression indices, and frailty indices yielded no differences in risk for frailty among older adults with depression, possibly because the subjects of this study (community-dwelling older adults) had high homogeneity, resulting in no differences in the subgroup analysis.

Cole and Dendukuri (2003) conducted a systematic review and meta-analysis and suggested that disability, prior depression, and being female could be crucial risk factors for depression. In short, the researchers posited that women are at higher risk for developing depression than are men. However, the results of this study demonstrated that male and female older adults had different outcomes related to depression and frailty. The risk for frailty in older men with depression increased markedly compared with that in older women with depression. In other words, older men with depression are more likely to experience frailty than are

older women with depression. This might be true because people of different sexes exhibit different treatment responses, side effects, and degrees of frailty when treated with antidepressants (Diem et al., 2007; Haney et al., 2007; Keers & Aitchison, 2010; Ryan et al., 2008). According to Keers and Aitchison (2010), differences exist in the effects on metabolism and distribution of antidepressants between men and women; women exhibit fewer adverse reactions than men. Thus, men are more likely to experience adverse reactions to antidepressants in terms of subsequent frailty.

Collard et al. (2014) posited that depression and frailty both have many comorbidities, and Brown et al. (2014) highlighted that depression and frailty have some common risk factors that render distinction difficult. Chang (2017) and Fugate Woods et al. (2005) have stated that frailty is a multifactorial geriatric syndrome that can be affected by pain, weakness, and low endurance. These risk factors might cause disability or functional deterioration, leading to sadness and helplessness, and resulting in depression. Depression may also induce frailty because of the negative factors associated with it, including a sedentary lifestyle, risk for fall, and weight loss, all of which may increase the risk for frailty (Lohman et al., 2015). Pegorari and Tavares (2014) revealed that depression can affect older adults' behaviors and activity levels, thereby reducing social participation, causing deterioration in functional status, and increasing frailty. Therefore, understanding the relationship between frailty and depressive symptoms is crucial.

This study was the first to perform a systematic literature review and meta-analysis in order to determine a correlation between people 65 years of age and older with depression and concurrent frailty in studies that have employed various research methods, regions, depression indices, frailty indices, covariance corrections, and sex for analysis. Therefore, the results of this study could serve as a valuable reference for nursing personnel. However, some research limitations were identified. First, although subgroup analyses (study design, regions, depression indices, frailty indices, and covariance corrections) were conducted to examine the correlation between depression and frailty in older adults, meta-analyses and statistical analyses revealed that statistical analysis errors occurred even when the risk levels of frailty among older adults in these subgroups were similar. Second, the analyzed studies differed in terms of follow-up duration; time errors may have occurred because some studies had follow-up periods of 2 to 4 years, whereas others did not state their follow-up durations. Nevertheless, although these limitations may have affected the conclusions and correlation inferences of the meta-analysis, the findings may still provide a favorable reference for professional medical personnel and could be used to understand the risk for frailty in older adults with depression. In turn, these benefits could provide a crucial basis for the development of relevant care plans.

Conclusions

Depression in older adults is a crucial indicator of geriatric syndrome. Evidence-based studies have shown that older adults experiencing frailty due to depression is a pertinent concern. The results of this study confirmed that depression in older adults is associated with frailty. The results of the analyzed studies were unaffected by research methods, region, depression indices, frailty indices, or covariance corrections. Furthermore, comparing older men and older women with depression and concurrent frailty revealed that the older men with depression were at a higher risk for developing frailty than were their female counterparts. This finding could provide an essential reference for nursing practice.

Nursing Implications

Evidence-based studies have confirmed that depression in older adults is strongly correlated with frailty. Nursing personnel should apply depression indices as early as possible to screen older adults for depression. In particular, the association between depression and frailty was more apparent in older men than in older women. Therefore, nursing personnel are recommended to pay close attention to the conditions of older men with depression and design appropriate care programs to improve depression symptoms and the quality of life of older adults.

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Clinical Resources

- Equator Network. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist: The PRRHQISMA Statement. http://www.equator-network.org/reporting-guidelines/prisma/
- National Center for Biotechnology Information. ARHQ methodology checklist for cross-sectional study. http://www.ncbi.nlm.nih.gov/books/NBK35156/

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