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Review article

The impact of perceived and objective social isolation on hospital readmission in patients with heart failure: A systematic review and meta-analysis of observational studies☆

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ABSTRACT

Objective: Several psychosocial risk factors have been identified that increase the rate of readmission in heart failure (HF) patients. However, the impact of social isolation (SI) on the rate of readmission is unclear. Therefore, the current review focused on the impact of SI on readmission rates of patients with HF.

Methods: A Medline-based strategy was applied to search PubMed, SCOPUS, Cochrane library, ProQuest, and Embase from inception until November 15, 2018. We performed a meta-analysis and pooled results using random effects model. The primary outcome was the odds ratio of readmission in HF patients suffering from SI. We examined the impact of both perceived and objective SI on readmission rates. We also examined the differences in readmission rates between these concepts. The secondary outcomes were the incidence of readmission and the prevalence of SI.

Results: From 3326 titles, 13 studies (n = 6468 participants) were eligible. The mean follow-up period was 13 months. The cumulative incidence for HF-related hospital readmission was 35.47% (95% CI: 34.29–36.67). The pooled prevalence ratio (PR, (95% CI)) was 37.31% (36.14–38.49), 31.51% (30.36–32.68), 32.82% (29.90–35.88), and 39.57% (37.73–41.45) for SI, living alone, lack of social support, and poor social network, respectively. SI was associated with a 55% greater risk of hospital readmission in patients with HF (OR = 1.55; 95% CI = 1.39–1.73; p < .001). Our analysis did not show a significant difference in the rate of hospital readmission between perceived and objective SI.

Conclusion: SI is prevalent in patients with HF and seems to be consistently linked to hospital readmission in HF patients, regardless of how it is measured. Therefore, it is necessary to develop interventions to reduce the burden of SI in patients with HF.

1. Introduction

Heart failure (HF) is a major health problem worldwide. Globally, > 25 million are living with HF [1]. Despite significant advances in the treatment of HF, the rate of hospital readmission is high. Estimates indicate that approximately 25% [2,3] and 67% [4] of patients with HF are readmitted within 30 days and one year after index hospitalization, respectively. Several risk factors, such as psychosocial factors, have been identified that increase the rates of readmission and death in these patients [3,5,6]. Previous research has shown that social isolation, poor social support, poor social network, lack of social relationship and living alone are associated with poor outcomes in patients with HF [5,7–10]. Among these risk factors, it has been reported that social isolation might increase the mortality risk similar to biological factors, such as smoking and high cholesterol [11]. However, the burden of social isolation on patients with HF and the extent to which it affects the readmission rates of these patients is unclear. Therefore, the current systematic review and meta-analysis focused on the impact of social isolation on readmission rates of patients with HF. The underlying hypothesis is that social isolation could increase the odds of hospital readmission in patients with HF.

2. Background

In the literature, social isolation, loneliness, lack of social support, poor social network, social disconnectedness, and living alone have

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been used interchangeably [12,13]. In addition, these concepts have been defined inconsistently across the disciplines and there are ambiguities regarding their definitions and characteristics [14]. Zavaleta, Samuel and Mills [15] defined social isolation as "the inadequate quality and quantity of social relations with other people at the different levels where human interaction takes place". The inadequate quantity of social relations, as objective social isolation, refers to the small number of interactions with others. The inadequate quality of social relations, as subjective social isolation, refers to the lack of meaningful social relations. It occurs when perceived social relationships of individuals are inconsistent with their ideal standards [15]. Cornwell and Waite [12] have suggested two types of social isolation: social disconnectedness (quantifiable or objective) and perceived isolation (subjective). Social disconnectedness is defined as "lack of contact with others due to situational factor, such as the small size of the social network, infrequent social interaction, or lack of participation in social activity". Perceived isolation is defined as "loneliness and a perceived lack of social support" [12]. Based on what is stated, a consensus has emerged that there are two types of social isolation: objective (quantifiable) and subjective (perceived) [13,15,16].

Several indicators have been proposed for assessing and measuring social isolation such as rare social contact, poor social network, low participation in social activities, living alone, being unmarried, feelings of loneliness, and lack of social support [12,13,17,18]. Cornwell and Waite (2009) suggested that small social network, infrequent interaction and lack of participation in social activities are characteristics of social disconnectedness (objective), whereas feelings of loneliness and lack of perceived social support are characteristics of perceived isolation [13]. In addition, Holt-Lunstad and colleagues suggested that living alone, poor social network, and rare social contact are indicative of objective social isolation [17].

This systematic review was guided by the abovementioned definitions and categorization. For the purpose of this review, we determined the status of each indicator of social isolation, and then we consolidated those indicators to obtain a general view of social isolation in patients with HF.

3. Methods

The recommendations of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group [19] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [20] were followed for conducting this review and meta-analysis.

3.1. Study question

To what extent social isolation (condition/exposure) can affect the hospital readmission rate (outcome) for heart failure patients (population)?

3.2. Eligibility criteria

Observational studies were included if they met each of the following criteria: (1) studies done in HF patient > 18 years; (2) prospective studies (longitudinal, follow-up, and cohort study) published in peer-reviewed journals; (3) studies providing data regarding the HF-related readmission; (4) studies presenting data on social isolation and its related concepts including loneliness, living alone, marital status, living status, social support, social network, social relationship, or social connectedness; (5) studies presenting sufficient data to calculate readmission rate and social status of patients; and (6) studies published in English.

Exclusion criteria: we excluded those studies that included new cases of HF; studies in which the outcome could not be isolated to HF-related readmission, studies with retrospective design and those studies that did not report sufficient data. Discussions, editorials, case reports, reviews, letters, commentaries or critiques were also excluded.

3.3. Outcomes

The primary outcome was the odds ratio of hospital readmission in HF patients who were socially isolated. As we explained earlier, we considered two types of social isolation, including objective and subjective (perceived). Social isolation was operationalized as the number of persons who (a) were socially isolated; (b) had a poor social network; (c) had a lack of perceived social support; (d) had low participation in social activities; (e) were living alone; or (f) had a feeling of loneliness. The secondary outcomes were the cumulative incidence of readmission and the prevalence of social isolation or its indicators in patients with HF.

3.4. Information sources and search strategy

A Medline-based strategy was applied to search the following databases: PubMed, SCOPUS, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, ProQuest, and Embase. To find additional articles, we manually examined the reference section of retrieved studies. To reduce unintentional omissions, we searched each database twice. The search plan included three general components: (1) heart failure; (2) readmission OR rehospitalization OR hospital-admission OR hospitalization; and (3) social isolation OR social deprivation OR social network OR social support OR social relationship OR loneliness OR social life OR social limitation OR living alone. All three components were combined using the Boolean operator, "AND", to obtain any link between them. We searched the databases from their inception to 15 November 2018.

3.5. Study selection and data collection process

Two authors (MHG, AAF) with the assistance of two librarians searched the databases. They individually screened the titles and abstracts of retrieved studies against the predetermined inclusion criteria for choosing relevant articles. The full text of potentially relevant studies was evaluated and reviewed for inclusion according to the eligibility criteria. The disagreement was resolved by discussion and consensus with the other author (AAF). In cases that supplementary data was required, we contacted the corresponding author of the article for more information. All three authors completed the data extraction table by relevant data of studies that met the inclusion criteria. The authors were not blinded to details during the study selection process.

3.6. Assessing the risk of bias (quality assessment)

All three authors were independently involved in the process of quality assessment. The quality of included studies was assessed by the CASP Checklist for Cohort study (Table 1) [21]. This scale is used to assess the methodological quality of prospective observational studies and has acceptable validity and reliability. The disagreement was resolved by discussion and consensus among the authors.

3.7. Data synthesis and analysis

We extracted baseline data of eligible articles. In cases where data was not available, we estimated them based on other available data. The cumulative incidence rate and the prevalence ratio were provided for readmission and social isolation (including related indicators), respectively. To estimate the odds ratio (with 95% CI), we either used the primary data provided by the authors or we used the estimated effect size reported by the authors. Meta-analysis was done using Comprehensive Meta-analysis version 2 (Biostat, Inc., USA). A p-value ≤ .05 was considered for statistical significance. Statistical heterogeneity was evaluated using the Q test and I^2 with values below 50%

Table 1
CASP checklist for assessing the quality of analytical studies.

Study	Q1	Q2	Q3	Q4	Q5-a	Q5-b	Q6-a	Q6-b
Chung 2011	Y	Y	Y	Y	Y	Y	Y	Y
Heo 2012	Y	Y	Y	Y	Y	Y	Y	Y
Huynh 2015	Y	Y	Y	N	Y	Y	Y	Y
Huynh 2018	Y	Y	Y	Y	Y	Y	Y	Y
Luttik 2006	Y	C	C	N	N	Y	Y	Y
Manemann 2018	Y	Y	Y	Y	Y	Y	Y	Y
Rodríguez-Artalejo 2006	Y	Y	Y	Y	Y	Y	Y	Y
Saito 2018	Y	Y	Y	Y	Y	Y	Y	Y
Sokoreli 2018	Y	Y	Y	Y	Y	Y	Y	Y
Tsuchihashi-Makaya 2009	Y	Y	Y	Y	Y	Y	Y	Y
Vinson1990	Y	C	C	N	Y	Y	Y	Y
Volz 2011	Y	Y	Y	Y	Y	Y	Y	Y
Wu 2013	Y	Y	Y	N	Y	Y	Y	Y

Questions:

1. Did the study address a clearly focused issue
2. Was the cohort recruited in an acceptable way
3. Was the exposure accurately measured to minimize bias
4. Was the outcome accurately measured to minimize bias
5. (a) Have the authors identified all important confounding factors
(b) Have they take account of the confounding factors in the design and/or analysis
6. (a) Was the follow up of subjects complete enough
(b) Was the follow up of subjects long enough

Note: Every item use "Yes (Y)", "Can't tell (C)", or "No (N)" to judge

was considered as low heterogeneity; 50% - 75% as moderate heterogeneity, and 75% and more considered as substantial heterogeneity [22]. We expected moderate to high heterogeneity among studies due to variation in data sampling and therefore planned to pooled data by random effects model. In addition, subgroup analyses were done based on two types of social isolation and follow-up periods. The publication bias was assessed by Egger's test. Ethical approval was not required for the study.

4. Results

4.1. Study selection

Fig. 1 shows the PRISMA flow chart. A total of 3326 articles were located and the titles and abstracts were screened. Of those, 126 full-text articles were reviewed and subsequently, 13 studies (n = 6468 participants) were included in the systematic review [9,23–34]. The articles spanned 7 countries.

4.2. Study characteristics

Table 2 shows the demographic and clinical characteristics of the included studies and Table 3 shows the overall statistics related to the sample. The concepts studies were social isolation, lack of social support, poor social network, and living alone. We categorized these concepts into two groups: perceived (subjective) and objective social isolation.

Except one, 12 studies (n = 6321) reported the number of HF-related hospital readmission. Overall, 2242 patients were readmitted during the mean follow-up period of 13 months (min 1, max 48 months). During this period, the cumulative incidence (incidence proportion) for hospital readmission was 35.47% (95% CI: 34.29–36.67). Table 4 shows the pooled prevalence ratio with 95% CI for each concept.

4.3. Qualitative review

A limited number of authors have operationally defined the concept of social isolation. In addition, the measurement of social isolation was heterogeneous and only a small number of studies used special instruments (Table 2).

4.3.1. Social isolation

Two studies showed that both perceived and objective social isolation are associated with increased risk of hospital readmission in patients with HF [23,33]. Manemann *et al* [23] examined the relationship between perceived social isolation and associated health outcomes among patients with HF. The authors found that patients with high perceived social isolation had a 68% increased risk of readmission. In addition, Saito *et al* [33] determined the prevalence of social isolation in HF patients and whether it is associated with readmission within 90 days after discharge. About 50% of the patients reported social isolation. The authors found that patients with social isolation had about 2.5 times higher odds of hospital readmission than those without social isolation. This study evaluated the social network of HF patients and thus measured the objective social isolation.

4.3.2. Poor social network

Rodriguez-Artalejo *et al* [9] examined the relationship between the quality of social network and hospital readmission. The authors found that patients who had poor social network were readmitted about 87% and 98% more compared to patients who had moderate or high social network, respectively.

4.3.3. Lack of perceived social support

Four studies found that perceived social support was significantly associated with increased risk of hospital readmission in patients with HF [24,28,29,31]. Chung *et al* [24] and Wu *et al* [31] found that patients with low perceived social support had 50% and 89% increased risk of readmission, respectively, compared with those who had high perceived social support. In addition, Tsuchihashi-Makaya *et al* [28] and Vinson *et al* [29] found that low social support was independently associated with a two-fold higher risk of hospital readmission.

As reported in two studies, lack of perceived social support was not significantly associated with increased risk of readmission. Heo *et al* [32] evaluated the relationship between the individual's social status and the risk of hospital readmission. The authors conceptualized social support as the quality of perceived support, perception of emotional

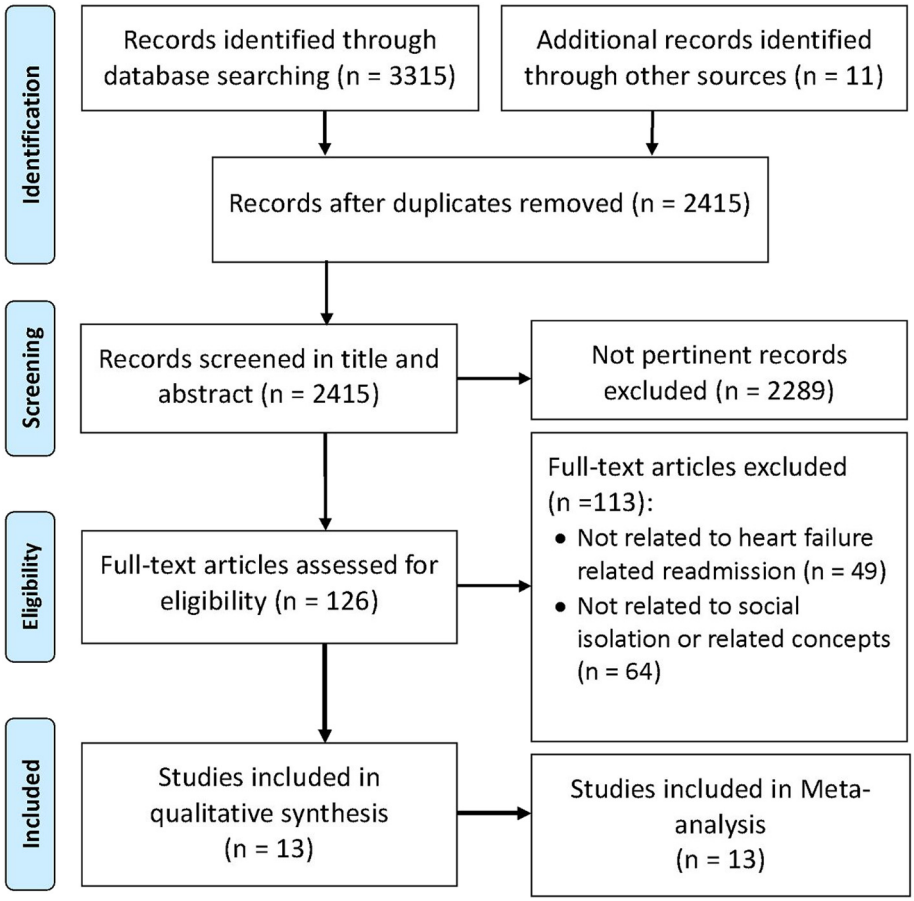

Fig. 1. PRISMA 2009 flow diagram for the selection of studies.

support, and marital status. They found that low perceived social support was not significantly associated with risk of hospital readmission. Volz *et al* [30] also found that low perceived social support was not significantly associated with the risk of hospital readmission. In this study, about 21% of patients were readmitted and the proportion of patients who had low perceived social support was about 6%.

4.3.4. Living alone

Four studies found a significant relationship between living alone and the risk of readmission [25–27,34]. Huynh *et al* [26] (2015) found that living alone is one of the strong predictors for 30-day readmission in patients with HF. The authors reported that > 25% of patients with HF were readmitted within the 30-day after hospital discharge. Among studied risk factors, the odds of readmission were 70% higher in those patients who were living alone. In 2018, Huynh *et al* [25] found that living alone could increase the odds of 30-day and 90-day readmission about 37% and 91%, respectively.

Luttik *et al* [27] investigated the impact of having a partner on hospital readmission. The proportion of patients who were living alone was 46%. > 57% of patients experienced an event (readmission or death) in the follow-up period. The authors found that the odds of readmission were 55% higher in patients who were living alone.

Sokoreli *et al* [34] investigated the prognostic value of psychosocial factors for predicting the readmission or death risk in HF patients. Of the 671 patients, > 66% had one or more unplanned readmissions and about 30% were living alone. The authors found that patients who were living alone have a 40% higher risk of having multiple events after discharge.

4.4. Quantitative synthesis

In order to pool the odds of hospital readmission for HF patients who were socially isolated, we estimated the odds ratio with 95% CI from the reported data or we used the reported odds ratio by reviewed studies.

Subgroups analyses were performed based on both follow-up period and two types of social isolation – objective (social network and living alone) and subjective (perceived social support and perceived social isolation). Considering that the follow-up periods of patients varied across studies, the follow-up periods were categorized into three groups (≤ 1 month, 1–3 months and > 3 months).

4.5. Objective social isolation

Regarding objective social isolation, we pooled the data of six studies (n = 3812) related to the two concepts of social network and living alone [9,25–27,33,34]. We found that HF patients who were socially isolated had 52% higher odds of being readmitted compared to those who were not socially isolated (OR = 1.52; 95% CI = 1.24–1.86; $p < .001$; Fig. 2). The statistical heterogeneity was not significant ($\chi^2 = 7.50$, df = 6, p = .28, $I^2 = 20.04\%$). Subgroup analyses by three follow-up periods showed that the odds of readmission for patients with objective social isolation were higher during the first month after discharge. As depicted in Fig. 2, the odds of readmission for socially isolated patients were 81%, 32%, and 52% during the < 1 month, 1–3 months, and > 3 months follow-up periods, respectively. However, the difference was not statistically significant ($\chi^2 = 3.79$, p = .15).

4.5.1. Subjective (perceived) social isolation

Regarding subjective social isolation, we pooled the data of seven

Table 2
Demographic and clinical characteristics of included studies.

Author, year	Country	Sample (n)	Age (mean)	Male (n)	Single (n)	Ejection fraction (%)	Follow-up (months)	Poor social network (n)	Living alone (n)	Socially isolated (n)	Total readmission (n)	Type of social isolation	Scale
Chung 2011	USA	220	61	146	96	34.5	48	111	62	111	96	Perceived Social Isolation	Multidimensional perceived social support scale (MPSSS)
Heo 2012	USA	147	61.2	103	63	34.6	11	11	44	NR	NR	Perceived Social Isolation	Quality of perceived support was defined as patients' subjective perception about the quality of support they received.
Huynh 2015	Australia	1537	80	760	868	NR	1	73	771	NR	293	Objective social isolation	Administrative data form
Huynh 2018	Australia	906	72.5	525		38	3	NR	311	NR	596	Objective social isolation	Self-reported questionnaire
Luttik 2006	Netherlands	179	73	102	83	34	9	NR	83	NR	78	Objective social isolation	Structured interview
Manemann 2018	USA	1681	73.29	898	703	NR	8	693	222	420	533	Perceived Social Isolation	PROMIS Item Bank v2.0 - Social Isolation – Short Form 4a. Scores could range from 4 to 20, with a higher score indicating greater perceived social isolation.
Rodríguez-Artalejo 2006	Spain	371	77.2	155	191	NR	6.4	166	38	166	135	Objective social isolation	Social network was measured using a 4-item questionnaire (married, lived with another person, saw or had telephone contact with family members living apart daily or almost daily, and were at home alone for < 2 h per day).
Saito 2018	Japan	148	82	75	NR	48	3	19	28	73	25	Objective social isolation	Lubben social network scale (LSNS-6)
Sokoreli 2018	UK	671	76	441	NR	NR	12	NR	184	NR	346	Objective social isolation	Self-reported questionnaire
Tsuchihashi-Makaya 2009	Japan	139	67.6	91	43	48.2	12	6	22	70	36	Perceived Social Isolation	Perceived social support survey (PSSS)
Vinson1990	USA	140	80.5	59	NR	38	3	14	NR	14	66	Perceived Social Isolation	Self-reported questionnaire
Volz 2011	Switzerland	111	57	82	NR	NR	12	NR	NR	6	24	Perceived Social Isolation	EICHD social support instrument (ESSI)
Wu 2013	USA	218	60	141	NR	36	36	NR	160	108	48	Perceived Social Isolation	Multidimensional perceived social support scale (MPSSS)

Table 3
Overall statistics of sample.

				Number of studies
Sample (n, %)	Total	6468	100	13
	Europe	1332	20.59	4
	Asia	2730	42.21	4
	North America	2406	37.20	5
Age (mean, SD)		70.87	8.62	13
Sex (male; n, %)		3578	55.32	13
Marital status (single) (n, %)		2047	47.89	7 (n = 4274)
Systolic BP (mean, SD)		117	5	2
Diastolic BP (mean, SD)		65	6	2
Heart rate (mean, SD)		74	6	2
% of ejection fraction, (mean, SD)		38.91	5.87	8
Follow-up period (mean, median, min-max)		13, 9, 1—48 (month)		

studies (n = 2656) related to the two concepts of perceived social support and perceived social isolation [23,24,28–32]. We found that HF patients with perceived social isolation had 63% higher odds of being readmitted to hospital compared to those who were not socially isolated (OR = 1.63; 95% CI = 1.31–2.01; p < .001; Fig. 3). The statistical heterogeneity was not significant ($\chi^2 = 4.31$, df = 6, p = .63, $I^2 = 0\%$). As depicted in Fig. 3, subgroup analyses by follow-up periods (≤3 *vs* > 3 months) showed that perceived social isolation was slightly associated with higher odds of > 3-month readmission. However, the difference between the follow-up period and the odds of hospital readmission was not statistically significant ($\chi^2 = 2.06$, p = .15).

4.5.2. The overall effect of social isolation on hospital readmission

Regardless of how it was measured, a pooled analysis of 13 studies (n = 6468) demonstrated that social isolation was associated with a 55% greater odds of hospital readmission in patients with HF (OR = 1.55; 95% CI = 1.39–1.73; p < .001). The statistical heterogeneity was not significant ($p < .52$, $I^2 = 0\%$). As depicted in Fig. 4, subgroup analyses by two types of social isolation (objective *vs* subjective) showed that subjective social isolation was slightly associated with higher odds of readmission than objective isolation (63% *vs* 52%); however, the difference was not statistically significant ($\chi^2 = 0.26$, p = .61).

Subgroup analysis by follow-up periods (Fig. 5) showed that patients with social isolation had higher odds of readmission within 1-month of hospital discharge when compared with 1–3-month and > 3-month (81%, 27% and 53%, respectively). However, the difference was not statistically significant ($\chi^2 = 4.05$; df = 2; p = .13).

4.6. Quality and sensitivity analysis

Of 13 studies, the process of participants' recruitment in two studies was unclear [27,29]. When those studies were removed from the analysis, there was no significant difference in the odds ratio of hospital readmission.

4.7. Publication bias

Overall, as depicted in Table 1, the risk of bias was low across the included studies. To evaluate the publication bias, a funnel plot of the logarithm of effect size (log odds ratio) against the precision for each study was generated (Fig. 6). There was no significant publication bias (2-tailed p = .16 by the Egger test).

5. Discussion

To the best of our knowledge, this is the first meta-analysis on the association between social isolation and hospital readmission in patients with HF. Thirteen prospective studies involving 6468 patients with HF were reviewed. The overall prevalence of social isolation in patients with HF was about 37% and the cumulative incidence of readmission among 12 studies was estimated to be > 35%. Based on the findings of this review, social isolation seems to be consistently linked to rehospitalization, regardless of how it is measured. This systematic review and meta-analysis demonstrated that social isolation was associated with a 55% greater risk of hospital readmission. In addition, we found that subjective measures of social isolation were slightly more associated with increased risk of hospital readmission than objective measures (63% *vs.* 52%, respectively); however, statistical significance was not significant. Furthermore, our analysis did not show a significant difference between the follow-up period and the odds of hospital readmission in HF patients suffering from social isolation.

Other important findings of the current review are that the overall prevalence was 31%, 32%, and 39% for living alone, lack of social support, and poor social network, respectively. The mean age of patients was about 70 years, > 55% were male, and about 50% of the sample had single marital status. Furthermore, although there are a number of special scales for measuring social isolation, of the 13 included studies, only six studies used special scale [23,24,28,30,31,33].

In accordance with our results, previous studies have demonstrated that higher social isolation score is independently associated with more frequent hospital readmissions in older people with non-psychiatric chronic diseases [35,36]. In addition, retrospective studies have revealed that objective social isolation, as measured by living alone, is associated with increased risk of readmission by 14% [37].

There is robust evidence that social isolation is associated with increased all-cause mortality by involving the cardiovascular system and mental health [38]. Currently, the mechanism by which social isolation leads to hospital readmission in patients with HF is unknown. However, it has been postulated that social isolation leads to poor health outcomes through psychological and biological pathways [17,39,40].

From a psychological perspective, social isolation is associated with negative psychological states such as fatigue, depressive symptoms, vital exhaustion, demoralization, and cognitive decline [8,41]. In the long term, those psychological distress states can negatively affect health-promoting behaviors of person and may lead to cardiovascular diseases [39,42]. Previous studies have shown that psychological distress such as depression is associated with poor medication adherence among HF patients [43,44]. In contrast, having good social communication reduces readmission rates for HF patients [37]. Several reports have shown that HF patients with high perceived social support and good social network have better self-management skills and self-care behaviors [45].

From a biological perspective, social isolation is associated with

Table 4
The pooled prevalence ratio along with 95% CI for each concept.

State	Number of studies	Total sample	Affected patients	PR, % (95% CI)
Living alone	11	6217	1959	31.51 (30.36–32.68)
Lack of social network	7	2699	1068	39.57 (37.73–41.45)
Poor perceived social support	7	975	320	32.82 (29.90–35.88)
Social isolation (as a consolidated concept)	13	6484	2413	37.31 (36.14–38.49)

PR: prevalence ratio.

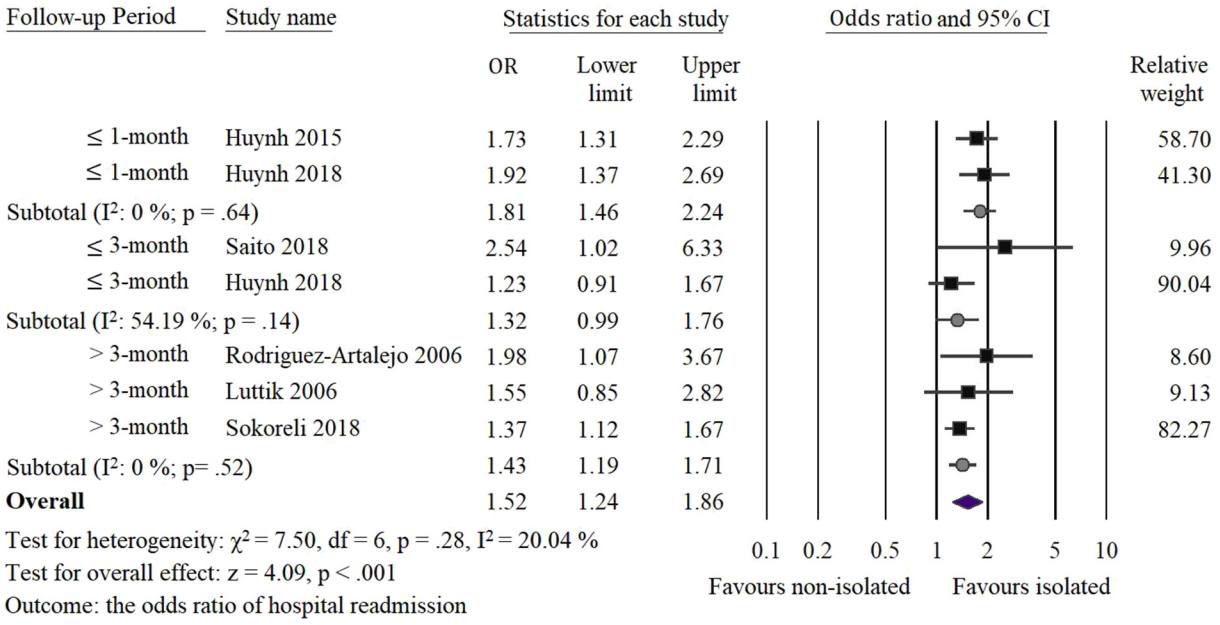

Fig. 2. The association of objective social isolation with readmission.

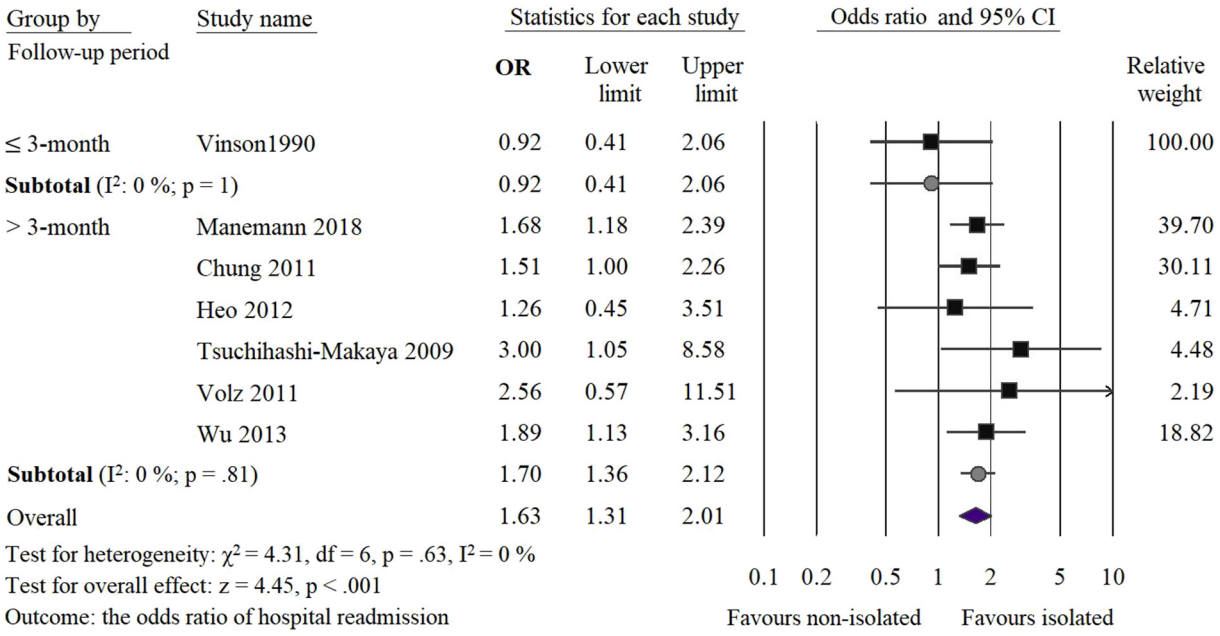

Fig. 3. The association of subjective social isolation with readmission.

increased risk of chronic disease, hypertension, coronary artery disease or cardiac failure [6,7,46]. The mechanisms underlying these associations are unclear; however, studies have suggested that perceived social isolation (loneliness) is associated with high levels of the stress hormone cortisol [47]. In addition, it can alter systemic inflammation biomarkers [48], and leads to increased vital exhaustion [6].

Based on the above-mentioned mechanisms, several interventions have been developed for healthy older adults in order to enhance their social connections; for example, access to technology-based applications [49], mindfulness training [50], tai chi exercise and meditation [51]. However, specific interventions designed to reduce the social isolation of HF patients are scarce.

5.1. Limitations

One of the most important limitations of our review was that the number of studies directly examining the concept of social isolation with specific scales was small. For this reason, we had to include studies with various concepts but related to social isolation. This issue caused a clinical heterogeneity in terms of outcomes, the definition of social isolation, measurement, and follow-up periods. To minimize this heterogeneity, we used the random effects model and performed subgroups analysis. However, due to the incomplete reporting of data, the heterogeneity across studies could not be completely explained through subgroups analysis. In addition, some authors used non-specific questionnaires so that those questionnaires did not conform to the definitions of social isolation. Furthermore, the hazard ratio of readmission was not available for some studies; hence, to create a unique dataset for

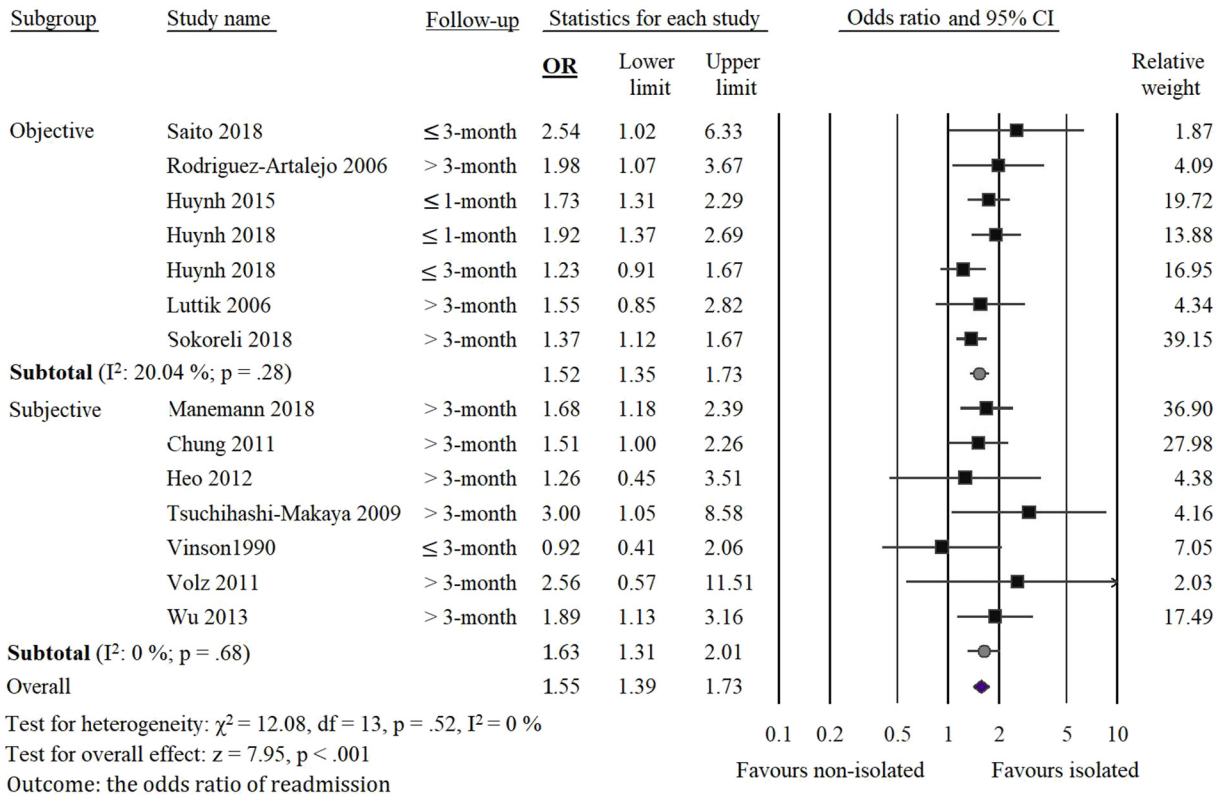

Fig. 4. The odds ratio of readmission by type of social isolation (objective *vs* subjective).

this analysis, we computed or extracted the odds ratio for all primary studies using available data.

6. Conclusion

Overall, the meta-analysis of 13 studies including 6468 patients with HF indicated that social isolation seems to be consistently linked to hospital readmission in patients with HF, regardless of how it is

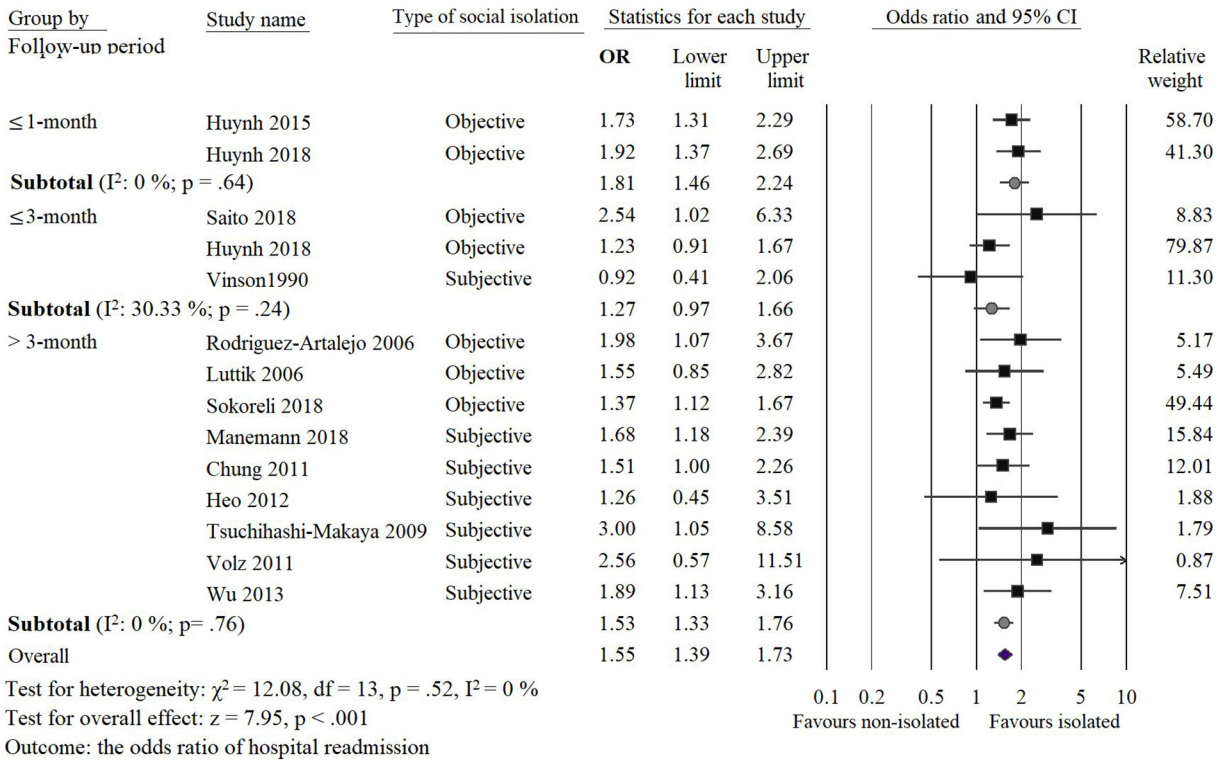

Fig. 5. The odds ratio of readmission by follow-up periods (≤1, ≤3, > 3 months).

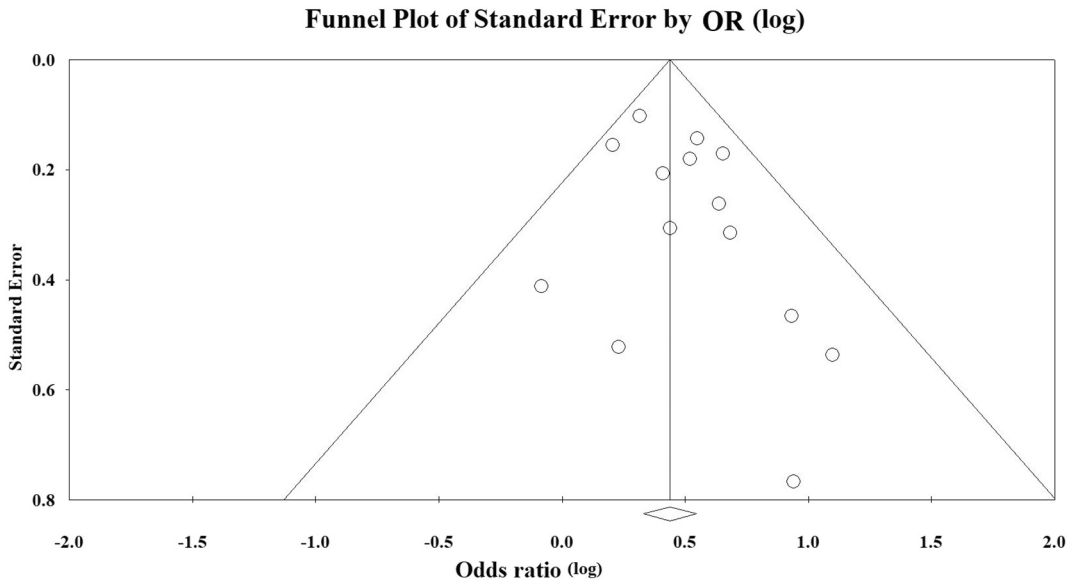

Fig. 6. Funnel plot of the logarithm of OR for publication bias.

measured. Social isolation was associated with a 55% greater risk of hospital readmission. In addition, we found that > 37% of HF patients suffered from social isolation. Furthermore, subjective social isolation was slightly associated with higher odds of readmission than objective isolation (63% *vs* 52%); however, the statistical difference was not significant.

7. Recommendation for future research

It is suggested that healthcare clinicians and researchers design high-quality interventional studies to reduce the social isolation of HF patients. Therefore, the development and implementation of social-psychological interventions to reduce social isolation are highly recommended. In addition, although several indicators of social isolation used across different disciplines, several validated scales also exist for measuring social isolation. Choosing a specific and valid scale, which conforms to the concept of social isolation, is recommended for future researchers.

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Statement of human and animal rights

This article does not contain any studies with human and animals performed by any of the authors.

Informed consent

None.

Declaration of Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this paper. In addition, they have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

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Appendix A. Supplementary data

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