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Editorial Board Member of *World Journal of Clinical Cases*, Potluri Leela Ravishankar, MDS, Professor, Department of Periodontics, SRM Kattankulathur Dental College and Hospital, SRM University, Chennai 603203, Tamil Nadu, India. plrs6@yahoo.com

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META-ANALYSIS

Risk factors for hospital readmissions in pneumonia patients: A systematic review and meta-analysis

Yuan-Yuan Fang, Jian-Chao Ni, Yin Wang, Jian-Hong Yu, Ling-Ling Fu

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Yuan-Yuan Fang, Jian-Chao Ni, Jian-Hong Yu, Department of Geriatrics, Affiliated Hospital of Shaoxing University, Shaoxing 312000, Zhejiang Province, China

Yin Wang, Department of Internal Medicine, Yuecheng People's Hospital, Shaoxing 312000, Zhejiang Province, China

Ling-Ling Fu, Department of Respiratory Medicine, Zhuji Affiliated Hospital of Shaoxing University, Zhuji 311800, Zhejiang Province, China

Corresponding author: Ling-Ling Fu, MD, Chief Doctor, Department of Respiratory Medicine, Zhuji Affiliated Hospital of Shaoxing University, No. 9 Jianmin Road, Zhuji 311800, Zhejiang Province, China. fu198609262021@sina.com

Abstract

BACKGROUND

Factors that are associated with the short-term rehospitalization have been investigated previously in numerous studies. However, the majority of these studies have not produced any conclusive results because of their smaller sample sizes, differences in the definition of pneumonia, joint pooling of the in-hospital and post-discharge deaths and lower generalizability.

AIM

To estimate the effect of various risk factors on the rate of hospital readmissions in patients with pneumonia.

METHODS

Systematic search was conducted in PubMed Central, EMBASE, MEDLINE, Cochrane library, ScienceDirect and Google Scholar databases and search engines from inception until July 2021. We used the Newcastle Ottawa (NO) scale to assess the quality of published studies. A meta-analysis was carried out with random-effects model and reported pooled odds ratio (OR) with 95% confidence interval (CI).

RESULTS

In total, 17 studies with over 3 million participants were included. Majority of the studies had good to satisfactory quality as *per* NO scale. Male gender (pooled OR = 1.22; 95%CI: 1.16-1.27), cancer (pooled OR = 1.94; 95%CI: 1.61-2.34), heart failure (pooled OR = 1.28; 95%CI: 1.20-1.37), chronic respiratory disease (pooled OR = 1.37; 95%CI: 1.19-1.58), chronic kidney disease (pooled OR = 1.38; 95%CI: 1.23-

1.54) and diabetes mellitus (pooled OR = 1.18; 95%CI: 1.08-1.28) had statistically significant association with the hospital readmission rate among pneumonia patients. Sensitivity analysis showed that there was no significant variation in the magnitude or direction of outcome, indicating lack of influence of a single study on the overall pooled estimate.

CONCLUSION
Male gender and specific chronic comorbid conditions were found to be significant risk factors for hospital readmission among pneumonia patients. These results may allow clinicians and policymakers to develop better intervention strategies for the patients.

Key Words: Hospital readmission; Meta-analysis; Pneumonia; Prediction; Systematic review

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Core Tip: The main goal of this review is to estimate the effect of various risk factors on the rate of hospital readmissions in patients with pneumonia. In total, 17 studies with over 3 million participants were included. Most studies had good to satisfactory quality. Male gender and specific chronic comorbid conditions were found to be significant risk factors for hospital readmission among pneumonia patients. These results may allow clinicians and policymakers to develop better intervention strategies for the patients.

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INTRODUCTION

The burden and incidence of acute infectious diseases, such as pneumonia, that have traditionally led to hospital admissions are expected to rise over the next few decades, mainly due to the increase in the population aged above 80 years[1,2]. Older patients with pneumonia often require hospital admissions [3]. The short-term rehospitalization and mortality rates are also found to be higher amongst those who survive the initial admission[3]. Most elderly patients require special attention from health care professionals after discharge to reduce short-term rehospitalization and mortality rates.

Studies also show higher short-term rehospitalization and mortality rates in pneumonia patients, with 12% to 22% of the patients readmitted within 30 d after initial hospitalisation for pneumonia[3-5]. Recent reports also show that rehospitalizations are associated with the increased risk of iatrogenic complications, resulting in additional financial burden on the health care system[6-8]. As a results of the general trend of having short hospital stays, the main responsibility of caring for older pneumonia patients after the discharge falls on the primary health care providers[9].

Yet, there is still a limited knowledge of how to identify the pneumonia patients who are at higher risk of having short-term rehospitalization following discharge[10-12]. Such knowledge is urgently required to ensure that the health care attention has been specifically given to the patients with the highest level of needs. Numerous studies attempted to investigate factors that are associated with the short-term rehospitalization[13-15]. However, the majority of these studies were inconclusive due to small sample sizes, differences in the definition of pneumonia, joint pooling of the in-hospital and post-discharge deaths and lower generalizability[16-18].

To the best of our knowledge, there has been no systematic effort to pool data on the risk factors for hospital readmissions in patients with pneumonia. The purpose of the present review is to pool data from individual studies to identify risk factors for hospital readmissions in patients with pneumonia.

MATERIALS AND METHODS

Design and registration

The protocol of the current systematic review and meta-analysis of observational studies was registered in PROSPERO under the registration number (CRD42021260284). "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement 2020" was utilized for reporting this systematic review incorporating the meta-analyses[19].

Eligibility criteria

Study design: Observational studies, irrespective of the study design (cross-sectional/case-control/cohort studies) reporting the relevant exposure and outcome were included. Only full-text publications were included while the studies published as conference abstracts/case reports/case series and unpublished data were excluded.

Participants: We have included the studies conducted among the adult pneumonia patients aged ≥ 18 years. Studies conducted among specific diseased population were excluded from the analysis.

Exposure: We have included studies assessing the association of any sociodemographic risk factors or comorbidity with hospital readmissions. At least three studies should have reported the particular risk factor to be eligible for inclusion in the review.

Outcome: Studies reporting the rate of hospital readmission across the different sociodemographic and comorbidity factors were included.

Search strategy

Systematic search of the literature was performed in the electronic databases such as PubMed Central, EMBASE, MEDLINE, and Cochrane library and search engines such as ScienceDirect and Google Scholar. Both medical subject headings (MeSH) and free-text words were used to search all these databases & search engines. The final search was carried out by combining the individual search results using appropriate Boolean operators ("OR" and "AND") and narrowed down using the available filters on time period (from January 2010 to July 2021), language (published in English language only) and study design (observational studies). The detailed search strategy with search terms and results has been reported in the Supplementary material.

Study selection process

The selection of the relevant studies was performed by two independent investigators by screening the title, abstract and keywords of the manuscripts identified by the literature search. Full-text articles were retrieved for the studies shortlisted based on the eligibility criteria and screened by the same two investigators. Only studies that satisfy all the eligibility criteria with respect to design, participants, exposure and outcome were included. Disagreements between the investigators were resolved and final consensus on inclusion of studies was reached with the help of another investigator.

Data extraction process

Manual extraction of data was done using a pre-defined structured data extraction form. Data extracted using the form were as follows: Author, year of publication, information related to methods section such as design, setting, sample size, sampling strategy, study participants, eligibility criteria, exposure and outcome assessment method, quality related information, number of participants in exposed and non-exposed group and number of exposed and non-exposed participants with hospital readmission. Data were entered by the primary investigator and it was double-checked by secondary investigators for correct entry.

Risk of bias assessment

The risk of bias assessment was performed by two independent investigators using the Newcastle Ottawa (NO) Quality Assessment Form for observational studies under the Selection (maximum 4 stars), Comparability (maximum 2 stars) and Outcome domains (maximum 2 stars) with the following criteria: Representativeness, Sample size justification, Non-response, Ascertainment of exposure, Control for confounding, Assessment of outcome and Statistical tests. The total score ranges from 0 to 8 stars. Studies having 7 to 8 stars were considered of "good" quality, 5 to 6 stars indicated "satisfactory" quality, and 0 to 4 stars indicated "unsatisfactory" quality[20].

Statistical analysis

Meta-analysis was executed using the software Review Manager 5.4 (The Cochrane Collaboration, 2020). Since all the outcomes were dichotomous, number of events and participants in each group were entered to obtain the pooled effect estimate in terms of odds ratio (OR) and were graphically depicted by the forest plot. We used the random effects model with inverse variance method to calculate the weight of individual studies. Evidence of heterogeneity was assessed through chi square test and I^2 statistics to quantify the inconsistencies[21]. We also performed sensitivity analysis to assess the robustness of results by removing the studies one by one and checking for any significant variation in the results. We have assessed publication bias through funnel plot for the outcomes with minimum of 10 included studies.

Quality of evidence

Two independent investigators assessed the risk of bias and quality of evidence for included studies

using Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines [21]. GRADE approach consists of five components: (1) Risk of bias assessment: "Newcastle Ottawa Scale"; (2) Indirectness: Assessed in terms of population, exposure or outcomes; (3) Imprecision: To find how precise the estimate obtained–based on sample size and confidence interval; (4) Inconsistency: Evidence of heterogeneity using I^2 statistic and chi square test of heterogeneity; and (5) Publication bias: Egger's test and funnel plot.

Finally, the quality of the included studies was classified as "Very Low", "Low", "Moderate" and "High" based on certainty of evidence.

RESULTS

Study selection

In total, 2421 records were retrieved through the literature search. Of them, 110 studies were eligible for the full-text retrieval, including four studies identified through the hand-search of references in the 106 retrieved articles from the primary screening. During the final stage of the screening, 17 studies with nearly 3 million participants were included (Figure 1)[11,12,22-36].

Characteristics of the included studies

Almost all the studies (16 out of 17 studies) were retrospective in nature. Majority of the included studies were conducted in the United States of America followed by European countries such as Italy, Denmark, United Kingdom, and Spain. The sample sizes of the included studies ranged from 771 to 1472070. Mean age of the participants ranged from 60 to 79 (Table 1). All the included studies had good to satisfactory quality (Table 2).

Predictors of hospital readmissions among pneumonia patients

Age and hospital readmissions: Three studies have reported on the risk of readmissions among elderly pneumonia patients aged 65+ years. The pooled OR was 0.90 (95%CI: 0.58-1.39; I^2 = 92%), indicating no difference in terms of hospital readmissions based on age group (Figure 2A). The quality of evidence was found to be very low as *per* GRADE approach.

Gender and hospital readmissions: A total of 13 studies looked at the risk of readmissions in male and female pneumonia patients. The pooled OR was 1.22 (95%CI: 1.16-1.27; I^2 = 79%), indicating that the males have 1.19 times higher odds of having hospital readmissions when compared to female pneumonia patients and this association was statistically significant (P < 0.001) (Figure 2B). The quality of evidence was found to be low as *per* GRADE approach.

Dementia and hospital readmissions: Nine studies compared risk of readmissions between dementia and non-dementia pneumonia patients. The pooled OR was 1.11 (95%CI: 0.96-1.29; I^2 = 99%), indicating that there was no between dementia and hospital readmissions among pneumonia patients (Figure 2C). The quality of evidence was found to be very low as *per* GRADE approach.

Diabetes mellitus and hospital readmissions: Seven studies have reported on the risk of readmissions between diabetes and non-diabetes pneumonia patients. The pooled OR was 1.18 (95%CI: 1.08-1.28; I^2 = 34%), indicating that the diabetes patients have 1.18 times higher odds of having hospital readmissions when compared to non-diabetes pneumonia patients (Figure 2D). The quality of evidence was found to be low as *per* GRADE approach.

Chronic respiratory disease and hospital readmissions: Ten studies showed the risk of readmissions in patients with and without chronic respiratory disease. The pooled OR was 1.37 (95%CI: 1.19-1.58; I^2 = 93%), indicating that the patients with chronic respiratory disease have significantly (1.37 times) higher odds of having hospital readmissions when compared to patients without chronic respiratory disease (P < 0.001) (Figure 2E). The quality of evidence was found to be low as *per* GRADE approach.

Chronic kidney disease and hospital readmissions: Seven studies have reported on the risk of readmissions between patients with and without chronic kidney disease. The pooled OR was 1.38 (95%CI: 1.23-1.54; I^2 = 47%), indicating that the patients with chronic kidney disease have 1.38 times higher odds of having hospital readmissions when compared to patients without chronic kidney disease (P < 0.001) (Figure 2F). The quality of evidence was found to be low as *per* GRADE approach.

Chronic liver disease and hospital readmissions: Five studies evaluated the risk of readmissions in patients with and without chronic liver disease and showed the pooled OR of 1.39 (95%CI: 0.98-1.98; I^2 = 75%), indicative of no significant association between chronic liver disease and readmission risk (Figure 2G). The quality of evidence was found to be very low as *per* GRADE approach.

Heart failure and hospital readmissions: Nine studies have reported on the risk of readmissions between patients with and without heart failure. The pooled OR was 1.28 (95%CI: 1.20-1.37; I^2 = 19%),

Table 1 Characteristics of the studies included (*n* = 17)

No.	Ref.	Country	Study design	Sample size	Mean age (in years)	Study participants	Risk factors reported
1	Ahmedani *et al*[33], 2015	United States	Retrospective analysis of data	72438	NR	All health plan patients at the participating health systems with an index inpatient hospitalization for pneumonia between January 2009 and December 2011	Dementia
2	Buja *et al*[36], 2020	Italy	Retrospective cohort study	6258	NR	Residents aged ≥ 65 yr with diagnosis related groups pneumonia (DRG 89 or 90)	Gender
3	Chakrabarti *et al*[22], 2021	United Kingdom	Retrospective analysis of data	10366	73	All community acquired pneumonia cases submitted by the nine participating hospitals in the AQ Pneumonia Programme between January 1, 2017 and March 31, 2019	Gender, Dementia, Heart failure, Cancer, CRD, CKD, DM, IHD, Cerebrovascular disease
4	Dharmarajan *et al*[29], 2013	United States	Retrospective analysis of data	214239	NR	Hospitalizations among patients 65 yr or older with a complete claims history for 1 yr preceding admission	Gender
5	Dong *et al*[30], 2017	United States	Retrospective cohort study	2892	61	Medical records of all 2892 patients coded with a principal diagnosis of pneumonia admitted to the University of Chicago	Age, Gender, Cancer, Heart Failure, CKD, CRD, Cerebrovascular disease
6	Faverio *et al*[31], 2020	Italy	Retrospective cohort study	203768	71.2	NHS eligible residents in Lombardy who had experienced at least one hospital admission with pneumonia as primary or secondary diagnosis during the years 2003 to 2012	Gender, Cancer, CKD, CRD, CLD, Cerebrovascular disease, Mechanical ventilation
7	Graversen *et al*[23], 2020	Denmark	Retrospective analysis of data	298564	NR	All Danish residents aged 65-99 yr, who had been discharged after a pneumonia-related hospital admission, referred to as index admission, during our study period	Gender, Dementia, Heart failure, Cancer, CRD, DM
8	Graversen *et al*[24], 2021	Denmark	Retrospective analysis of data	298872	NR	All Danish citizens aged 65–99 yr, who were discharged after a hospital admission (index admission) with a primary or secondary diagnosis of pneumonia as defined by the allocation of diagnostic codes (ICD-10: J12-J18, A709, or A481)	Dementia
9	Jain *et al*[34], 2018	United States of America	Retrospective analysis of data	1472070	68.9	All adults discharged alive after a hospitalization with the primary diagnosis of pneumonia	Age
10	Jang *et al*[35], 2020	Korea	Retrospective cohort	862	68.5	Patients with community acquired pneumonia hospitalized at Yeungnam University Hospital from March 2012 to February 2014	Age, Gender, Dementia, Heart failure, Cancer, CRD, DM, CKD, CLD, Cerebrovascular disease, ICU admission, Mechanical ventilation
11	Knox[32], 2019	United States	Retrospective analysis of data	389956	79	Pneumonia patients ranging in age from 65 to 90 yr of age	Dementia
12	Lee *et al*[25], 2017	Republic of Korea	Retrospective cohort	7446	NR	Patients older than 65 yr who were hospitalized with pneumonia between 2003 and 2013	Gender, Dementia, Heart failure, Cancer, CRD, CKD
13	Mather *et al*[11], 2013	United States	Retrospective cohort	956	NR	Adult patients admitted to Hartford Hospital from January 2009 to March 2012 with principal diagnosis of pneumonia (International Classification of Diseases, 9th Revision, Clinical Modification codes 480.XX, 481, 482.XX, 483.X, 485, 486, and 487.0) as potential index pneumonia admission	Gender, Dementia, Heart failure, Cancer, CRD, CKD, DM, IHD
14	Nagasako *et al*[27], 2014	United States	Retrospective analysis of data	29849	NR	Hospital readmissions for patients discharged from non-federal Missouri acute care or critical access hospitals between June 1, 2009 and May 31, 2012, with principal diagnoses of pneumonia	Gender
15	Shams *et al*[28], 2014	United States	Retrospective cohort	1306	68.3	Adult patients with principal (or secondary) discharge diagnoses of pneumonia	Gender, Cancer, Heart Failure, CRD, DM, IHD
16	Shorr *et al*[12], 2013	United States	Retrospective cohort	771	60	All adult subjects with bacterial pneumonia admitted to a single institution between January and December 2010	Gender, Cancer, Dementia, Heart Failure, ICU admission, Mechanical ventilation, Cerebrovascular disease,

							CRD, DM, IHD
17	Toledo *et al* [26], 2018	Spain	Cross-sectional	1756	NR	Patients included were aged ≥ 65 yr admitted through the emergency department to any of the participating hospitals for ≥ 24 h with a chest X ray showing pulmonary infiltrate compatible with pneumonia and ≥ 1 of the following symptoms or signs of acute lower respiratory tract infection: Cough, pleural chest pain, dyspnoea, fever > 38 °C, hypothermia < 35 °C and abnormal auscultator respiratory sounds unexplained by other causes	Gender, Heart failure, Cancer, CRD, CKD, DM

NR: Not reported; CRD: Chronic respiratory diseases; CKD: Chronic kidney disease; CLD: Chronic liver disease; DM: Diabetes mellitus; IHD: Ischaemic heart disease; NHS: National Health Service.

Table 2 Quality assessment of the included studies (*n* = 17)

No.	Ref.	Representativeness	Sample size justification	Non-response	Ascertainment of exposure	Control for confounding	Assessment of outcome	Statistical tests	Overall quality
1	Ahmedani *et al*[33], 2015	1 star	0 star	0 star	1 star	2 stars	1 star	1 star	Satisfactory
2	Buja *et al*[36], 2020	1 star	1 star	1 star	1 star	2 stars	1 star	1 star	Good
3	Chakrabarti *et al*[22], 2021	1 star	0 star	1 star	1 star	2 stars	1 star	1 star	Good
4	Dharmarajan *et al*[29], 2013	1 star	1 star	0 star	1 star	2 stars	1 star	1 star	Good
5	Dong *et al* [30], 2017	0 star	0 star	0 star	1 star	2 stars	1 star	1 star	Satisfactory
6	Faverio *et al* [31], 2020	1 star	0 star	0 star	1 star	2 stars	1 star	1 star	Satisfactory
7	Graversen *et al*[23], 2020	1 star	1 star	1 star	1 star	2 stars	1 star	1 star	Good
8	Graversen *et al*[24], 2021	1 star	0 star	1 star	1 star	2 stars	1 star	1 star	Good
9	Jain *et al*[34], 2018	1 star	1 star	0 star	1 star	2 stars	1 star	1 star	Good
10	Jang *et al* [35], 2020	1 star	1 star	1 star	1 star	2 stars	1 star	1 star	Good
11	Knox[32], 2019	0 star	0 star	0 star	1 star	0 star	1 star	0 star	Unsatisfactory
12	Lee *et al*[25], 2017	1 star	1 star	1 star	1 star	2 stars	1 star	1 star	Good
13	Mather *et al* [11], 2013	1 star	0 star	1 star	1 star	2 stars	1 star	1 star	Good
14	Nagasako *et al*[27], 2014	0 star	1 star	0 star	0 star	0 star	1 star	1 star	Unsatisfactory
15	Shams *et al* [28], 2014	0 star	1 star	0 star	1 star	0 star	1 star	0 star	Unsatisfactory
16	Shorr *et al* [12], 2013	1 star	1 star	1 star	1 star	2 stars	1 star	1 star	Good
17	Toledo *et al* [26], 2018	1 star	0 star	1 star	1 star	2 stars	1 star	1 star	Good

indicating that the patients with heart failure have 1.28 times higher odds of having hospital readmissions when compared to patients without heart failure (Figure 2H). The quality of evidence was found to be low as *per* GRADE approach.

Ischaemic heart disease and hospital readmissions: A total of 4 studies evaluated the risk of readmissions in patients with and without ischaemic heart disease. The pooled OR was 1.15 (95%CI:

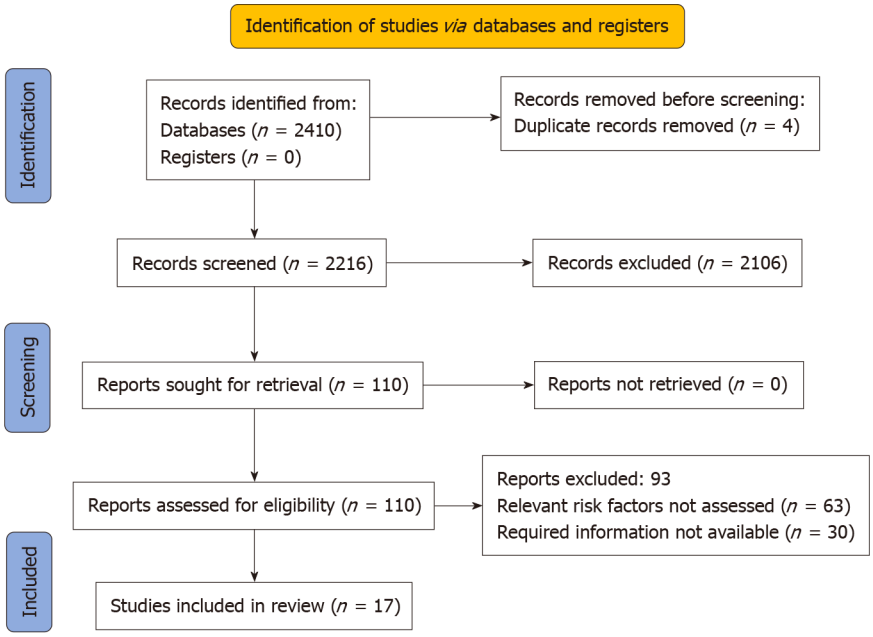

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Figure 1 PRISMA flowchart.

0.94-1.40; I^2 = 42%), indicating that there is no association between ischaemic heart disease and hospital readmissions (Figure 2I). The quality of evidence was found to be low as *per* GRADE approach.

Cerebrovascular disease and hospital readmissions: Five studies have reported on the risk of readmissions between patients with and without cerebrovascular disease. The pooled OR was 1.08 (95%CI: 0.85-1.38; I^2 = 71%), indicating there is no association between cerebrovascular disease and hospital readmissions (Figure 2J). The quality of evidence was found to be low as *per* GRADE approach.

Cancer and hospital readmissions: Risk of readmissions in patients with and without cancer was discussed in 10 studies. The pooled OR was 1.94 (95%CI: 1.61-2.34; I^2 = 96%), indicating that the patients with cancer have significantly higher (1.94 times) odds of having hospital readmissions when compared to patients without cancer (P < 0.001) (Figure 2K). The quality of evidence was found to be very low as *per* GRADE approach.

Intensive care units admission and hospital readmissions: Three studies have reported on the risk of readmissions between patients with and without intensive care units (ICU) admission during their hospital stay for primary diagnosis. The pooled OR was 1.21 (95%CI: 0.69-2.13; I^2 = 46%), indicating there is no association between ICU admission and hospital readmissions (Figure 2L). The quality of evidence was found to be low as *per* GRADE approach.

Mechanical ventilation and hospital readmissions: Four studies have reported on the risk of readmissions between patients with and without mechanical ventilation requirement during their hospital stay for primary diagnosis. The pooled OR was 1.36 (95%CI: 0.96-1.93; I^2 = 74%), indicating there is no association between mechanical ventilation and hospital readmissions (Figure 2M). The quality of evidence was found to be low as *per* GRADE approach.

Additional analysis

Sensitivity analysis has revealed that the estimates obtained for all the outcomes were robust to small study effects in terms of magnitude or direction of the outcomes. Funnel plot for the risk factors such as gender, cancer and chronic respiratory disease showed asymmetrical plot indicating the possibility of publication bias (Supplementary Figures 1-3).

DISCUSSION

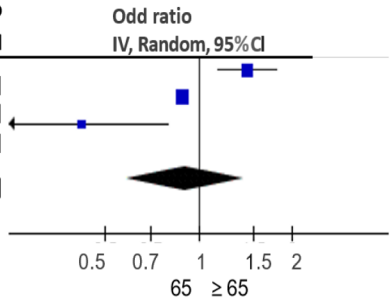
Almost one in five pneumonia patients have to be readmitted to the hospital[37]. Hospital readmissions following an episode of pneumonia are becoming a relatively frequent event, specifically among the older adults and patients with various co-morbidities[38]. It is important, therefore, to identify the patients at high-risk of getting readmitted as early as possible and prevent the development of future

A

Study or subgroup	Age < 65 yr Events	Total	Age ≥ 65 yr Events	Total	Weight	Odds ratio IV, Random, 95%CI
Dong *et al*, 2017	288	1728	143	1164	37.2%	1.43 [1.15, 1.77]
Jain *et al*, 2018	80438	532481	156911	939589	41.0%	0.89 [0.88, 0.90]
Jang *et al*, 2020	12	266	60	596	21.7%	0.42 [0.22, 0.80]
Total (95%CI)		**534475**		**941349**	**100.0%**	**0.90 [0.58, 1.39]**
Total events	80738		157114			

Heterogeneity: Tau² = 0.12; Chi² = 23.83, df = 2 (P < 0.00001); I² = 92%

Test for overall effect Z = 0.47 (P = 0.64)

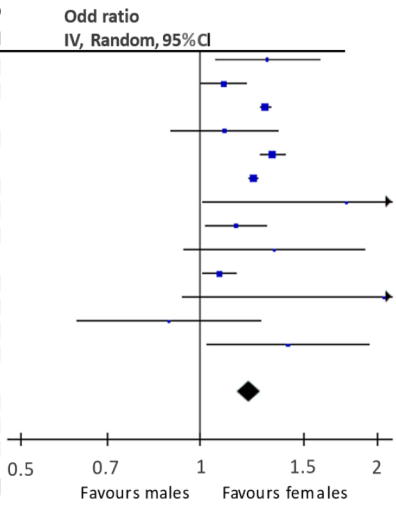


B

Study or subgroup	Male Events	Total	Female Events	Total	Weight	Odds ratio IV, Random, 95%CI
Buja *et al*, 2020	235	3220	173	3038	4.0%	1.30 [1.06, 1.60]
Chakrabarti *et al*, 2021	1308	4856	1381	5504	11.2%	1.10 [1.01, 1.20]
Dharmarajan *et al*, 2013	24118	100077	22490	114162	18.3%	1.29 [1.27, 1.32]
Dong *et al*, 2017	234	1510	197	1382	3.9%	1.10 [0.90, 1.35]
Faverio *et al*, 2020	4509	112698	2766	91070	15.7%	1.33 [1.27, 1.40]
Graversen *et al*, 2020	36827	148265	31724	150299	18.5%	1.24 [1.21, 1.26]
Jang *et al*, 2020	55	565	17	297	0.6%	1.78 [1.01, 3.12]
Lee *et al*, 2017	782	3883	639	3563	8.6%	1.15 [1.03, 1.30]
Mather *et al*, 2013	73	413	75	543	1.6%	1.34 [0.94, 1.90]
Nagasako *et al*, 2014	2030	13014	2458	16835	13.9%	1.08 [1.01, 1.15]
Shams *et al*, 2014	182	1217	7	89	0.3%	2.06 [0.94, 4.53]
Shorr *et al*, 2013	79	427	70	344	1.5%	0.89 [0.62, 1.27]
Toledo *et al*, 2018	136	1070	64	686	1.9%	1.42 [1.03, 1.94]
Total (95%CI)		**391215**		**387812**	**100.0%**	**1.22 [1.16, 1.27]**
Total events	70568		62061			

Heterogeneity: Tau² = 0.00; Chi² = 57.89, df = 12 (P < 0.00001); I² = 79%

Test for overall effect Z = 8.33 (P < 0.00001)

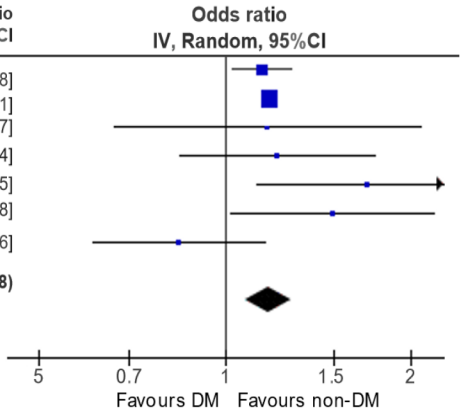


C

Study or subgroup	DM Events	Total	non-DM Events	Total	Weight	Odds ratio IV, Random, 95%CI
Chakrabarti *et al*, 2021	561	1993	2130	8373	28.0%	1.15 [1.03, 1.28]
Graversen *et al*, 2020	9417	36786	59134	261778	50.2%	1.18 [1.15, 1.21]
Jang *et al*, 2020	17	182	55	680	2.1%	1.17 [0.66, 2.07]
Mather *et al*, 2013	58	338	90	618	5.0%	1.22 [0.85, 1.74]
Shams *et al*, 2014	35	167	154	1139	4.0%	1.70 [1.13, 2.55]
Shorr *et al*, 2013	53	221	96	550	4.6%	1.49 [1.02, 2.18]
Toledo *et al*, 2018	61	594	139	1162	6.2%	0.84 [0.61,1.16]
Total (95%CI)		**40281**		**274300**	**100.0%**	**1.18 [1.08, 1.28]**
Total events	10202		61798			

Heterogeneity: Tau² = 0.00; Chi² = 9.03, df = 6 (P = 0.17) ;I² = 34%

Test for overall effect Z = 3.77 (P = 0.0002)

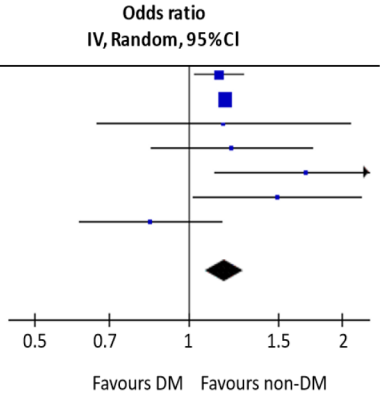


D

Study or subgroup	DM Events	Total	Non-DM Events	Total	Weight	Odds ratio IV, Random, 95% CI
Chakrabarti *et al*, 2021	561	1993	2130	8373	28.0%	1.15 [1.03, 1.28]
Graversen *et al*, 2020	9417	36786	59134	261778	50.2%	1.18 [1.15, 1.21]
Jang *et al*, 2020	17	182	55	680	2.1%	1.17 [0.66, 2.07]
Mather *et al*, 2013	58	338	90	618	5.0%	1.22 [0.85, 1.74]
Shams *et al*, 2014	35	167	154	1139	4.0%	1.70 [1.13, 2.55]
Shorr *et al*, 2013	53	221	96	550	4.6%	1.49 [1.02, 2.18]
Toledo *et al*, 2018	61	594	139	1162	6.2%	0.84 [0.61, 1.16]
Total (95%CI)		**40281**		**274300**	**100.0%**	**1.18 [1.08, 1.28]**
Total events	10202		61798			

Heterogeneity: Tau² = 0.00; Chi² = 9.03, df = 6 (P = 0.17); I² = 34%

Test for overall effect Z = 3.77 (P = 0.0002)

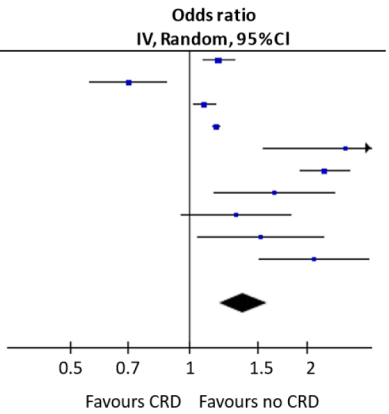


E

Study or subgroup	CRD Events	CRD Total	No CRD Events	No CRD Total	Weight	Odds ratio IV, Random, 95%CI
Chakrabarti *et al*, 2021	966	3422	1725	6944	13.4%	1.19 [1.09, 1.30]
Dong *et al*, 2017	123	1015	308	1877	10.4%	0.70 [0.56, 0.88]
Faverio *et al*, 2020	1205	31369	6070	172399	13.8%	1.09 [1.03, 1.17]
Graversen *et al*, 2020	21961	87747	46590	210817	14.2%	1.18 [1.16, 1.20]
Jang *et al*, 2020	38	281	34	581	5.2%	2.52 [1.55, 4.09]
Lee *et al*, 2017	348	1117	1073	6329	12.4%	2.22 [1.92, 2.56]
Mather *et al*, 2013	85	448	63	508	7.4%	1.65 [1.16, 2.36]
Shams *et al*, 2014	69	408	120	898	8.1%	1.32 [0.96, 1.82]
Shorr *et al*, 2013	92	412	57	359	7.2%	1.52 [1.06, 2.20]
Toledo *et al*, 2018	64	351	136	1405	8.1%	2.08 [1.51, 2.88]
Total (95%CI)		**126570**		**402117**	**100.0%**	**1.37 [1.19, 1.58]**
Total events	24951		56176			

Heterogeneity: Tau² = 0.04; Chi² = 127.96, df = 9 (P < 0.00001); I² = 93%

Test for overall effect Z = 4.46 (P < 0.00001)

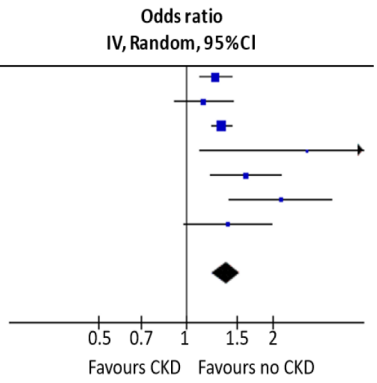


F

Study or subgroup	Chronic kidney disease Events	Chronic kidney disease Total	No chronic kidney disease Events	No chronic kidney disease Total	Weight	Odds ratio IV,Random,95% CI
Chakrabarti *et al*, 2021	428	1423	2263	8943	26.3%	1.27 [1.12, 1.44]
Dong *et al*, 2017	107	654	324	2238	14.2%	1.16 [0.91, 1.47]
Faverio *et al*, 2020	680	14765	6595	189003	31.9%	1.34 [1.23, 1.45]
Jang *et al*, 2020	7	38	65	824	1.7%	2.64 [1.12, 6.22]
Lee *et al*, 2017	68	250	1353	7196	11.2%	1.61 [1.21, 2.15]
Mather *et al*, 2013	41	164	107	792	6.4%	2.13 [1.42, 3.21]
Toledo *et al*, 2018	49	342	151	1414	8.3%	1.40 [0.99, 1.98]
Total(95%CI)		**17636**		**210410**	**100.0%**	**1.38 [1.23,1.54]**
Total events	1380		10858			

Heterogeneity: Tau² = 0.01; Chi² = 11.31, df = 6 (P = 0.08); I² = 47%

Test for overall effect Z = 5.57 (P < 0.00001)

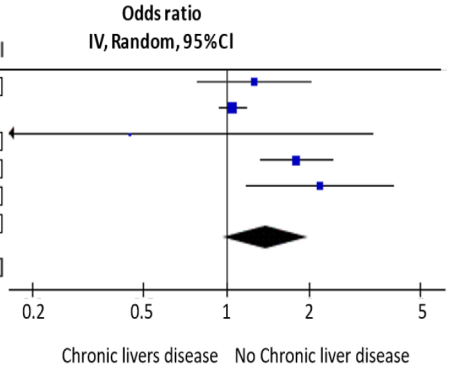


G

Study or subgroup	Chronic liver disease Events	Chronic liver disease Total	No chronic liver disease Event	No chronic liver disease Total	Weight	Odds ratio IV,Random,95% CI
Chakrabarti *et al*, 2021	25	85	2558	10281	21.0%	1.26 [0.79, 2.01]
Faverio *et al*, 2020	343	9154	6932	194614	32.4%	1.05 [0.94, 1.18]
Jang *et al*, 2020	1	25	71	837	2.8%	0.45 [0.06, 3.37]
Lee *et al*, 2017	63	215	1358	7231	27.0%	1.79 [1.33, 2.42]
Toledo *et al*, 2018	14	66	186	1690	16.7%	2.18 [1.18, 4.00]
Total(95% CI)		**9545**		**214653**	**100.0%**	**1.39 [0.98,1.98]**
Total events	446		11105			

Heterogeneity: Tau² = 0.10; Chi² = 16.01, df = 4 (P = 0.003); I² = 75%

Test for overall effect Z = 1.84 (P = 0.07)

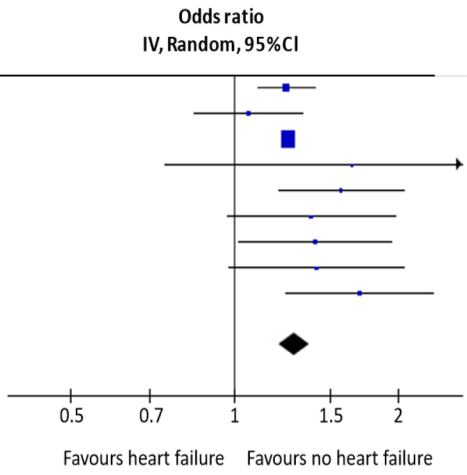


H

Study or subgroup	Heart failure Events	Heart failure Total	No heart failure Events	No heart failure Total	Weight	Odds ratio IV,Random,95%CI
Chakrabarti *et al*, 2021	450	1515	2241	8851	19.1%	1.25 [1.11, 1.41]
Dong *et al*, 2017	118	763	313	2129	6.9%	1.06 [0.84, 1.34]
Graversen *et al*, 2020	55742	234282	12809	64282	54.1%	1.25 [1.23, 1.28]
Jang *et al*, 2020	8	64	64	798	0.7%	1.64 [0.75, 3.59]
Lee *et al*, 2017	80	301	1341	7145	5.4%	1.57 [1.20, 2.04]
Mather *et al*, 2013	64	351	84	605	3.1%	1.38 [0.97, 1.97]
Shams *et al*, 2014	71	406	118	900	3.8%	1.40 [1.02, 1.94]
Shorr *et al*, 2013	59	256	90	515	2.9%	1.41 [0.98, 2.05]
Toledo *et al*, 2018	72	460	128	1296	4.0%	1.69 [1.24, 2.31]
Total(95% Ct)		**238398**		**86521**	**100.0%**	**1.28 [1.20, 1.37]**
Total events	56664		17188			

Heterogeneity: Tau² = 0.00; Chi² = 9.93, df = 8 (P = 0.27); I² = 19%

Test for overall effect Z = 7.63 (P < 0.00001)



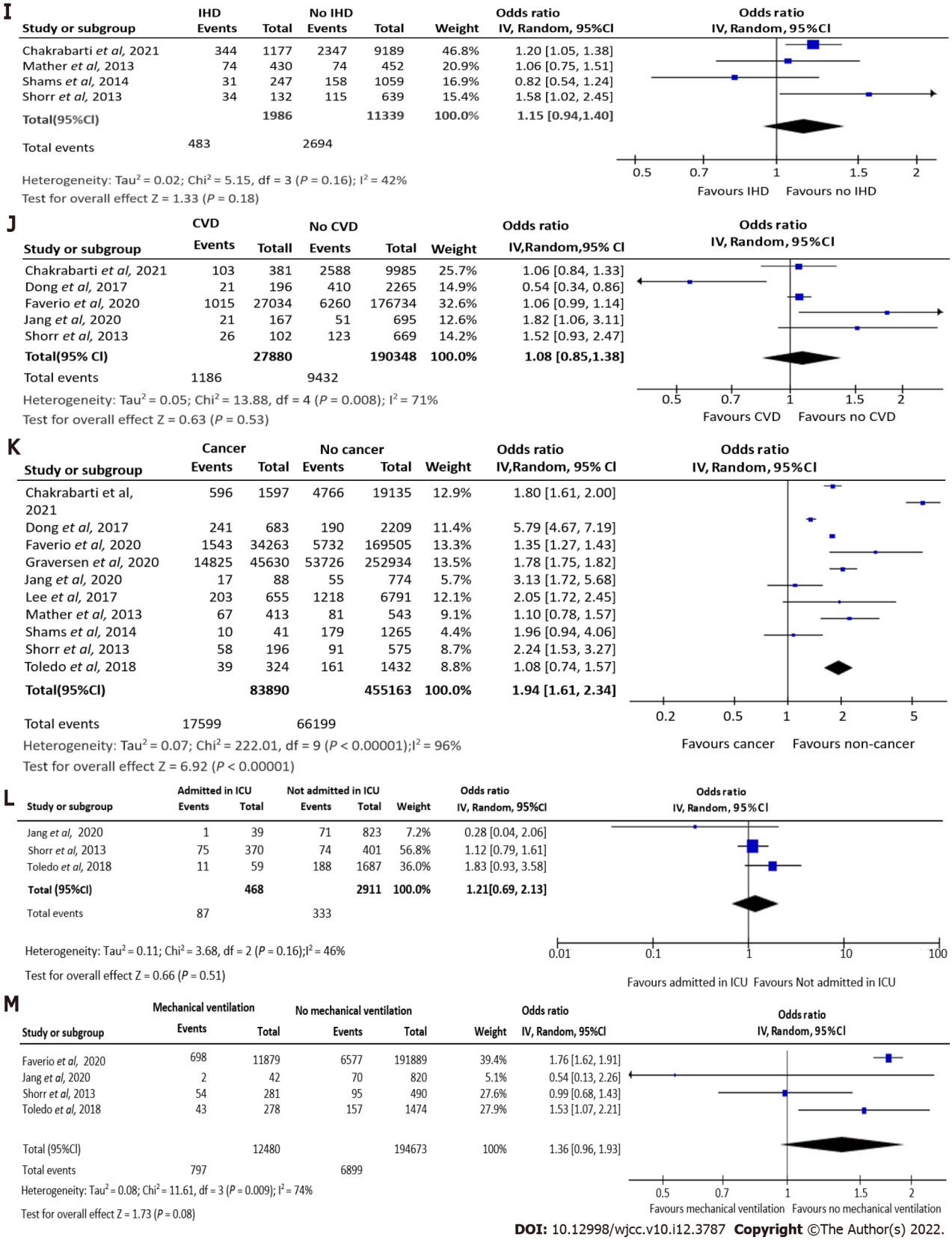


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Figure 2 Forest plot showing the risk factors of hospital readmission rate among pneumonia patients. A: Age and hospital readmission; B: Gender and hospital readmission; C: Dementia and hospital readmission; D: Diabetes mellitus and hospital readmission; E: Chronic respiratory disease and hospital readmission; F: Chronic Kidney disease and hospital readmission; G: Chronic liver disease and hospital readmission; H: Heart failure and hospital readmission; I: Ischaemic heart disease and hospital readmission; J: Cerebrovascular disease and hospital readmission; K: Cancer and hospital readmission; L: ICU admission and hospital readmission; M: Mechanical Ventilation and hospital readmission.

complications. Despite its importance, the role of various risk factors on the hospital readmission rate among pneumonia patients remains unclear. The goal of this review was to study the association of various risk factors on hospital readmission rate among pneumonia patients.

We have found a total of 17 studies matching the eligibility criteria of the review. Most of these studies were conducted in American and European region. Though, almost all the studies were retrospective in nature, all of them were of good to satisfactory quality. We found that males had significantly higher odds of having hospital readmissions when compared to female pneumonia patients. Co-morbidities, such as diabetes mellitus, cancer, heart failure, chronic respiratory disease and chronic kidney disease were also significantly associated with the risk of readmissions among pneumonia patients. Sensitivity analysis revealed that there was no significant single-study effect on the magnitude or direction of association.

Although, there was no previous reviews to compare our study findings, the possible impact of various risk factors on hospital readmission rate among pneumonia patients has been explored using the previous literature. Studies show that in one in six patients pneumonia might fail to resolve completely in spite of appropriate treatment[39]. Such patients might end up developing serious complications that require hospital readmissions[39]. Our study showed that several host factors like gender, immunocompromising conditions (cancer, diabetes mellitus), heart failure, and chronic respiratory and kidney diseases are associated with the failure to resolve completely and increased risk of readmission.

Since the most frequent reason for the 30-d hospital readmission amongst pneumonia patients is the decompensation of the associated comorbid conditions[29,34], it is important to develop interventions that are aimed at reducing the all-cause readmission rates. This, in turn, would have a significant impact on the pneumonia readmission rate. Almost all the top five diagnoses of the potentially avoidable readmissions for each comorbidity were either a direct or an indirect complication of that comorbidity. For example, in patients with diabetes mellitus, atrial fibrillation, heart failure, ischemic heart disease, or chronic kidney disease, the most common cause and diagnosis of the potentially avoidable hospital readmission was the acute heart failure. Therefore, ensuring stability of comorbidities at the time of discharge in high risk patients with heart failure, kidney failure, cancer, *etc*., would impact not only the all-cause readmission rate but also the pneumonia readmission rate. Further research is required to explore potential interventions to evaluate and ensure clinical stability at the level of discharge, particularly in patients with the multiple and interrelated comorbidities.

In other cases, pneumonia readmissions may not be related to the initial pneumonia episode or the comorbidity decompensation, but rather to other causes, such as hospital-acquired infections, acute conditions, or trauma. With enhanced care, numbers of readmission due to hospital-acquired infections decreases. However, a significant number of these cases may remain as potentially unavoidable readmissions. Further studies are needed to assess how these factors may impact readmission rates in pneumonia patients, and to develop appropriate intervention plans.

The major strength of our review is the rigorous literature search and methodology used to provide reliable estimates. Additionally, this was the first review providing the association between sociodemographic and comorbid risk factors and hospital readmissions among pneumonia patients. Most studies included in our review were of higher quality and had a standard-criteria for defining hospital readmission (30-d hospital readmission), which might further enhance the generalisability of our study findings. Moreover, sensitivity analysis did not show any significant changes in magnitude and direction of association with respect to any of the exposure-outcome relationships.

However, our study has some limitations. There was a significant between-study variability that may limit the extrapolation of the study results. Most of the included studies were retrospective in nature, which makes it difficult to establish causation between the exposure and the disease. Hence, more longitudinal studies are needed to identify accurate and reliable effect estimates and make evidence-based recommendation for developing potential interventions in hospital setting.

CONCLUSION

Male gender and specific chronic comorbid conditions were found to be significant risk factors for hospital readmission among pneumonia patients. These results may allow clinicians and policymakers to develop better intervention strategies for the patients.

ARTICLE HIGHLIGHTS

Research background

Factors that are associated with the short-term rehospitalization have been investigated previously in numerous studies. However, the majority of these studies have not produced any conclusive results because of their smaller sample sizes, differences in the definition of pneumonia, joint pooling of the in-

hospital and post-discharge deaths and lower generalizability.

Research motivation

To the best of our knowledge, there has been no systematic effort to pool data on the risk factors for hospital readmissions in patients with pneumonia.

Research objectives

To pool data from individual studies to identify risk factors for hospital readmissions in patients with pneumonia.

Research methods

Systematic search was conducted in PubMed Central, EMBASE, MEDLINE, Cochrane library, ScienceDirect and Google Scholar databases, and search engines from inception until July 2021.

Research results

In total, 17 studies with over 3 million participants were included. Majority of the studies had good to satisfactory quality as *per* Newcastle Ottawa scale. Male gender, cancer, heart failure, chronic respiratory disease, chronic kidney disease and diabetes mellitus had statistically significant association with the hospital readmission rate among pneumonia patients.

Research conclusions

Male gender and specific chronic comorbid conditions were found to be significant risk factors for hospital readmission among pneumonia patients. These results may allow clinicians and policymakers to develop better intervention strategies for the patients.

Research perspectives

More longitudinal studies are needed to identify accurate and reliable effect estimates and make evidence-based recommendation for developing potential interventions in hospital setting.

FOOTNOTES

Author contributions: Fang YY and Ni JC conceived and designed the study; Wang Y and Yu JH were involved in literature search and data collection; Yu JH and Fu LL analyzed the data; Fang YY and Ni JC wrote the paper; Wang Y and Yu JH reviewed and edited the manuscript; all authors read and approved the final manuscript.

Conflict-of-interest statement: The authors deny any conflict of interest.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2020 Checklist, and manuscript was prepared and revised according to the PRISMA 2020 Checklist.

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Country/Territory of origin: China

ORCID number: Yuan-Yuan Fang 0000-0003-2104-6932; Jian-Chao Ni 0000-0003-1723-1182; Yin Wang 0000-0003-0493-3150; Jian-Hong Yu 0000-0002-2096-0506; Ling-Ling Fu 0000-0002-6613-2271.

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L-Editor: A
P-Editor: Fan JR

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