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Global Comparison of Readmission Rates for Patients With Heart Failure

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ABSTRACT

BACKGROUND Heart failure (HF) readmission rates are low in some jurisdictions. However, international comparisons are lacking and could serve as a foundation for identifying regional patient management strategies that could be shared to improve outcomes.

OBJECTIVES This study sought to summarize 30-day and 1-year all-cause readmission and mortality rates of hospitalized HF patients across countries and to explore potential differences in rates globally.

METHODS We performed a systematic review and meta-analysis using MEDLINE, Embase, and CENTRAL for observational reports on hospitalized adult HF patients at risk for readmission or mortality published between January 2010 and March 2021. We conducted a meta-analysis of proportions using a random-effects model, and sources of heterogeneity were evaluated with meta-regression.

RESULTS In total, 24 papers reporting on 30-day and 23 papers on 1-year readmission were included. Of the 1.5 million individuals at risk, 13.2% (95% CI: 10.5%-16.1%) were readmitted within 30 days and 35.7% (95% CI: 27.1%-44.9%) within 1 year. A total of 33 papers reported on 30-day and 45 papers on 1-year mortality. Of the 1.5 million individuals hospitalized for HF, 7.6% (95% CI: 6.1%-9.3%) died within 30 days and 23.3% (95% CI: 20.8%-25.9%) died within 1 year. Substantial variation in risk across countries was unexplained by countries' gross domestic product, proportion of gross domestic product spent on health care, and Gini coefficient.

CONCLUSIONS Globally, hospitalized HF patients exhibit high rates of readmission and mortality, and the variability in readmission rates was not explained by health care expenditure, risk of mortality, or comorbidities.
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Heart failure (HF) is a global pandemic affecting approximately 64 million persons worldwide.[1] Within both the United States and Europe, >1 million hospitalizations are attributed to HF.[2] The global cost of HF is approximately U.S. $346 billion per year,[1] a large portion of which is attributed to HF hospitalizations. The high prevalence and costs of HF hospitalizations warrant consideration and evaluation of factors associated with admissions on a global scale.

SEE PAGE 445

To date, efforts to understand HF readmission rates have been conducted in silos for each country separately. Such studies attribute readmission rates to factors such as patients' environment, ethnicity, and socioeconomic status.[3-5] There remains no global comparison of HF readmission rates across all countries. However, several recent global clinical trials (eg, PARAGON-HF [Prospective Comparison of ARNI (angiotensin receptor-neprilysin inhibitor) with ARB (angiotensin-receptor blockers) Global Outcomes in HF with Preserved Ejection Fraction], EMPULSE [Empagliflozin in Patients Hospitalized for Acute Heart Failure], ASIAN-HF [Asian Sudden Cardiac Death in Heart Failure]) have identified regional and country-level differences in readmission and mortality rates.[6-9] Through comparison across countries, it may be possible to identify those with lower readmission rates and potentially identify mitigating factors that may be adopted by countries with higher readmission rates to improve care and outcomes.

Beyond identifying and understanding mitigating factors that may be adopted across countries, we sought to explore HF outcomes as a function of health care expenditure. A previous systematic review observed that amongst 61 studies reporting on health care cost and health care quality, 34% reported a positive association (higher cost associated with higher quality).[10] Therefore, we sought to test the hypothesis that countries with greater health care spending, per capita, may observe lower rates of HF readmission and mortality.

The objectives of our systematic review were as follows: to identify the best estimates of HF readmission and mortality rates internationally, to combine these observations in a meta-analysis to obtain a global estimate of readmission and mortality, and to compare readmission and mortality rates across all identified countries to note and understand patterns of readmission and mortality.

METHODS

SEARCH STRATEGY. The search strategy of this systematic review and meta-analysis is summarized in the following text. With the help of an experienced information specialist, we performed a systematic search of MEDLINE, PubMed, Embase, Cochrane Database of Systematic Reviews, and Cochrane Central from January 1, 2010, to March 9, 2021. We restricted our search to capture only papers published after 2010 to evaluate the most current rates of readmission and mortality. We excluded citations for research in progress, conference proceedings and abstracts, dissertations and theses, and books. Our full search strategy is shown in Supplemental Appendix 1. Ethics approval was not required because this study was based exclusively on published literature.

SELECTION CRITERIA. We included studies that followed adult (age ≥18 years) HF patients who were previously hospitalized for HF. We included studies reporting 30-day or 1-year all-cause hospital readmission rates (planned and unplanned) or all-cause mortality rates. To ensure that patients from a given country were not counted twice in our review, for all outcomes, we selected studies that were most representative of the HF population from each country. For each country, we selected studies based on an algorithm with the following principles: 1) whenever possible, select studies that used national administrative databases to maximize generalizability and comprehensiveness; 2) exclude studies that required patient consent for participation to minimize volunteer bias and maximize representativeness; 3) prioritize studies with more recent data; and 4) when 2 studies used the same source of data and sampling period, include the study with the larger sample size. Our selection algorithm is summarized in Supplemental Appendix 2. Two teams of reviewers, working in pairs, screened the titles and abstracts and, from those not excluded during this phase, determined eligibility through full text review.

DATA EXTRACTION AND QUALITY ASSESSMENT. Two reviewers (F.F., D.G.R., T.E., A.S., S.S., A.M., H.B., T.H.A.L.) independently extracted data on the characteristics of the study cohort; the number or proportion of patients with readmission or mortality, at both 30 days and 1 year; and selected HF comorbidities, such as chronic obstructive pulmonary disease (COPD), diabetes, hypertension, atrial fibrillation, and renal disease. Our full list of extracted variables can be found in Supplemental Appendix 3.

ABBREVIATIONS AND ACRONYMS

COPD = chronic obstructive pulmonary disease

GDP = gross domestic product

HF = heart failure

To determine risk of bias, 2 reviewers (F.F., D.G.R.) independently applied a modified Newcastle-Ottawa Scale on the selected studies which is outlined in Supplemental Appendix 4. A total score was calculated by adding each item given a star rating, with higher scores indicating lower risk of bias.

STATISTICAL ANALYSIS. We conducted 4 different meta-analyses, 1 for each of the following outcomes: 30-day or 1-year all-cause hospital readmission and 30-day or 1-year all-cause mortality. For each meta-analysis, we used the number of events and the sample size of each cohort to calculate the incidence rate for 30-day and 1-year outcomes. We pooled these incidence rates using STATA's Metaprop package, applying the DerSimonian and Laird random effects model with a Freeman-Tukey double arcsine transformation, and a back transformation was performed to visualize results.[11,12]

Our review assessed heterogeneity through visual inspection of the individual studies' point-estimates and 95% CIs. We did not rely on the I^2 as this measure overestimates heterogeneity in meta-analyses of large observational studies.[13] To identify sources of heterogeneity, we generated 11 a priori subgroup hypotheses. To assess the impact of countries' socioeconomic status on readmission and mortality rates, we explored the impact of national gross domestic product (GDP), proportion of GDP spent on health care, and the country's Gini coefficient.[14,15] We also explored the effect of established prognostic factors for readmission and mortality, including age, proportion of women, proportion of patients with COPD, diabetes, hypertension, atrial fibrillation, and renal disease.[16-18] Furthermore, we assessed the effects of time periods and study quality by exploring the effect of the last year of patient recruitment and Newcastle-Ottawa Scale scores. Finally, to account for competing risks, we assessed the impact of 30-day or 1-year all-cause mortality on 30-day or 1-year readmission rates, respectively. We estimated a country's GDP per capita (2018 estimates) from the International Monetary Fund's World Economic Outlook (April 2019).[19] We obtained health care spending using 2015 estimates of health expenditure from the World Health Organization's Global Health Expenditure Database.[20] For Taiwan, however, we utilized Taiwan's National Health Insurance Administration to obtain 2015's estimates for health expenditure.[21] Gini coefficients (2010-2018 estimates) were obtained from the United Nation's 2020 Human Development Report.[22]

We postulated that risk of 30-day and 1-year hospitalization or mortality would be lower in countries with the following: 1) a higher GDP; 2) a higher proportion of GDP spent on health care; 3) a lower Gini coefficient; and 4) a larger number of contemporary HF patients. When evaluating risk of bias, we hypothesized that there would be a lower risk of 30-day and 1-year all-cause hospitalization or mortality in studies with lower Newcastle-Ottawa scale score (higher risk of bias) compared with those with higher scores (lower risk of bias). Moreover, we postulated higher risk in studies with older mean age, lower proportion of women, and greater proportion of patients with HF comorbidities. Finally, because all-cause mortality is a competing event for hospital readmission, we postulated lower incidence of readmission in countries with higher risk of all-cause mortality, compared with those with lower risks. If 10 or more studies reported on the potential mediators, we explored its effect on the risk of 30-day and 1-year hospital readmission or mortality with the use of random effects meta-regression. Stata/SE version 17.0 provided the platform for all our statistical analyses.

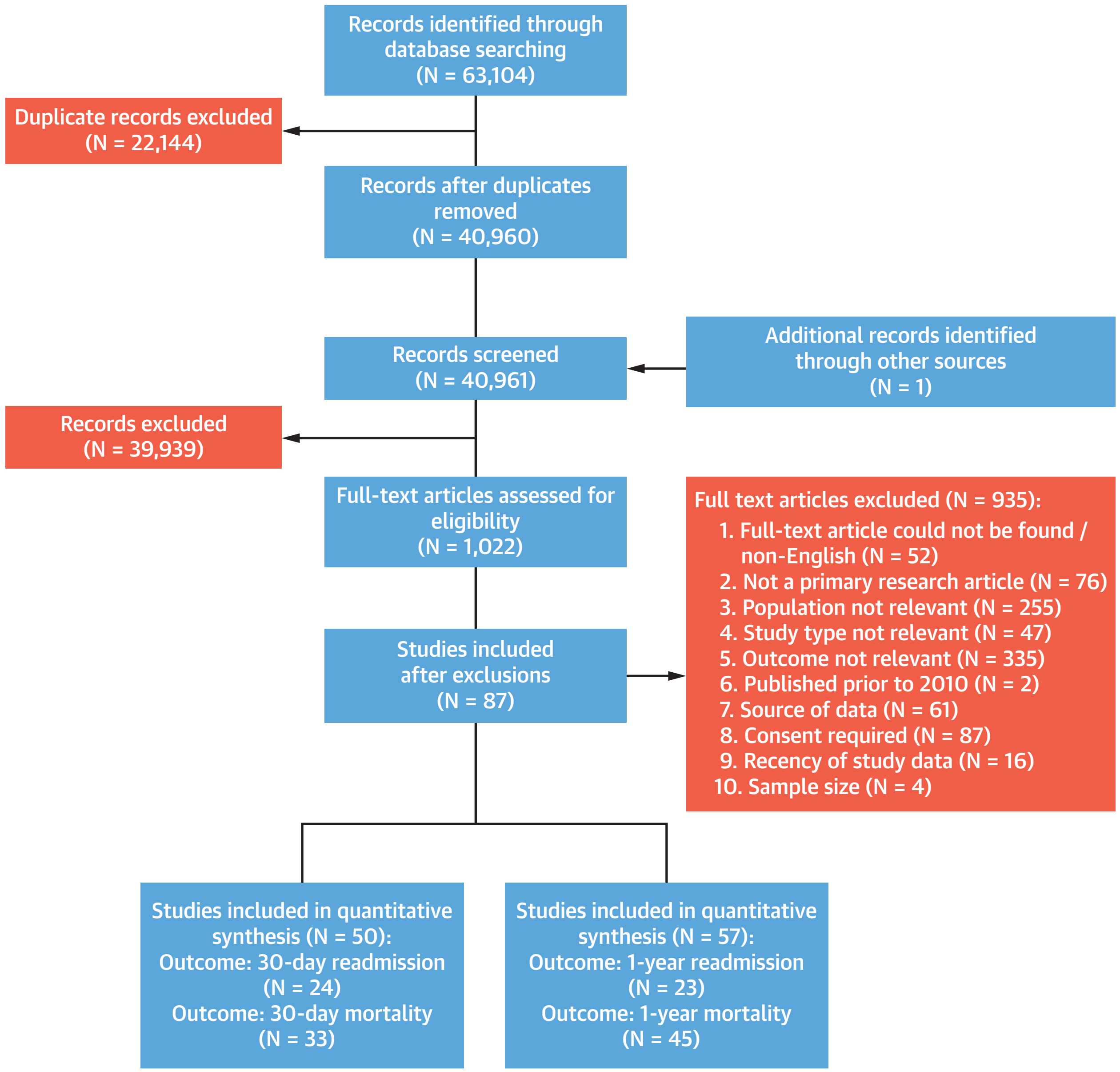
GRADE ASSESSMENT. To assess our certainty in the evidence, we applied GRADE guidance for overall prognosis.[13] This certainty is influenced by the risk of bias of individual studies, imprecision around the pooled estimate, inconsistency across studies, indirectness of evidence identified, and the risk of publication bias. Depending on the consideration of these 5 domains, confidence in the evidence is designated as very low (untrustworthy), low, moderate, or high (very trustworthy).

RESULTS

Our literature search yielded 63,104 papers, of which 22,144 were duplicates. Of the remaining 40,960 citations we screened, 1,021 papers were relevant for full-text review. Among these, 87 papers reporting 30-day and/or 1-year readmission or mortality rates for hospitalized HF patient cohorts were included.[23-109] 24 papers (representing 18 countries)[23-46] and 23 papers (16 countries)[23,30,37,39,40,43,47-63] were included in the meta-analyses for the 30-day and 1-year readmission outcomes, respectively. Meanwhile, 33 papers (24 countries)[23,30,32,41-43,45,60,64-88] and 45 papers (33 countries)[23-25,30,40,42,54,55,57,60,61,63,64,66,69,71-74,77,79,81,86,88-109] were included in the meta-analyses for the 30-day and 1-year mortality outcomes, respectively. The study characteristics of the included studies are reported in Supplemental Appendixes 5 and 6. The PRISMA flow diagram is shown in **Figure 1**.

30-DAY READMISSION RATES. The studies reporting on 30-day readmission followed a total of 1,417,462 persons with HF. The median age reported across

FIGURE 1 PRISMA Flow Diagram for Study Selection



Prisma flow diagram for systematic review showing study inclusion and exclusion criteria. We screened 40,961 unique papers for study eligibility, examined the full text for 1,022 studies, and included 87 studies in the final study.

studies was 76.8 years (25th to 75th percentile: 70.2-79.3 years), with equal numbers of men and women, with the median proportion of women being 50.6% (25th to 75th percentile: 49.5%-54.0%). The highest mean age was observed in Italy, whereas the lowest was in Uganda. The highest proportion of women was reported by Uganda, whereas the highest proportion of men was reported by Greece. The most prevalent HF comorbidity was hypertension, followed by atrial fibrillation, diabetes, renal disease, and COPD (Supplemental Appendix 5A).

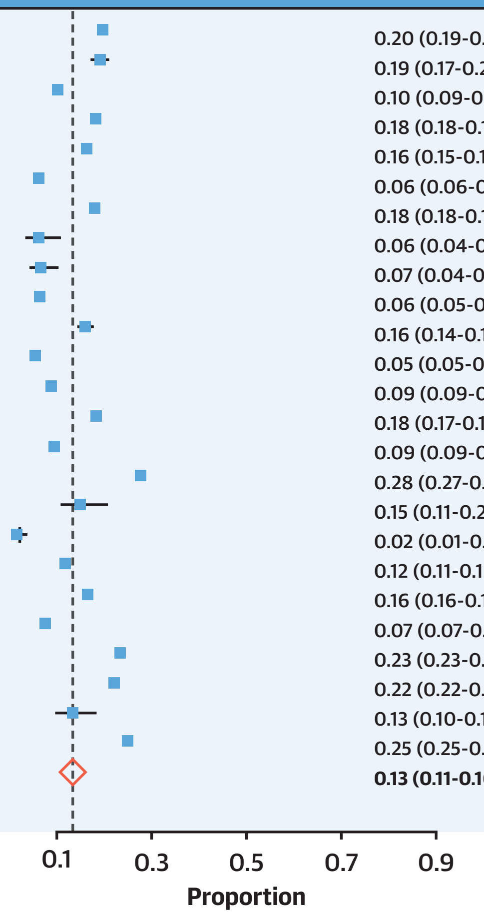
Of the 1,417,462 individuals hospitalized for HF, 222,447 were readmitted within 30 days, resulting in a pooled 30-day readmission rate of 13.2% (95% CI: 10.5%-16.1%, moderate certainty caused by inconsistency) (**Figure 2**). There was substantial variability both globally and within continents; the highest readmission was rate observed in South Korea (27.6%;

JACC VOL. 82, NO. 5, 2023
AUGUST 1, 2023:430–444

FIGURE 2 Meta-Analysis of 30-Day Readmission Rates Globally

30-Day Hospital Readmission Rate

Study	Continent	Country	Proportion (95% CI)	Numerator	Denominator
Al-Omary 2017	Oceania	Australia	0.20 (0.19-0.20)	2,120	10,840
Huynh 2015	Oceania	Australia	0.19 (0.17-0.21)	293	1,537
Islam 2012	Oceania	Australia	0.10 (0.09-0.11)	630	6,252
McAlister 2017	North America	Canada	0.18 (0.18-0.18)	39,368	217,039
Huang 2017	Asia	China	0.16 (0.15-0.17)	1,274	7,847
Bottle 2017	Europe	England	0.06 (0.06-0.06)	11,699	194,983
Tuppin 2013	Europe	France	0.18 (0.18-0.18)	11,235	62,417
Stafylas 2017	Europe	Greece	0.06 (0.04-0.11)	11	177
Kwan 2016	North America	Haiti	0.07 (0.04-0.10)	18	274
Novack 2011	Asia	Israel	0.06 (0.05-0.07)	138	2,182
Avaldi 2015	Europe	Italy	0.16 (0.14-0.18)	300	1,873
Degli Esposti 2020	Europe	Italy	0.05 (0.05-0.05)	3,596	69,164
Roshanghalb 2019	Europe	Italy	0.09 (0.09-0.09)	5,363	60,771
Tellini 2015	Europe	Italy	0.18 (0.17-0.19)	1,291	7,056
Chen 2021	Asia	Japan	0.09 (0.09-0.10)	2,503	26,365
Chung 2017	Asia	Korea	0.28 (0.27-0.28)	5,286	19,128
Deek 2018	Asia	Lebanon	0.15 (0.11-0.21)	28	187
Ogah 2014	Africa	Nigeria	0.02 (0.01-0.04)	4	262
Omersa 2019	Europe	Slovenia	0.12 (0.11-0.12)	4,116	35,371
Zapatero 2012	Europe	Spain	0.16 (0.16-0.17)	61,008	370,983
Chou 2019	Asia	Taiwan	0.07 (0.07-0.08)	2,987	40,541
Tung 2017	Asia	Taiwan	0.23 (0.23-0.24)	3,169	13,577
Sundaram 2021	Asia	Taiwan	0.22 (0.22-0.22)	8,100	36,900
Okello 2014	Africa	Uganda	0.13 (0.10-0.18)	30	224
Sundaram 2021	North America	USA	0.25 (0.25-0.25)	57,880	231,512
Overall			**0.13 (0.11-0.16)**		



Forest plot summarizing the pooled proportions for 30-day readmission rates. For each study, **blue squares** and **horizontal lines** correspond to the respective point estimate and accompanying 95% CI. The **vertical dashed line** on the forest plot represents the point estimate of the summary estimate. The **red diamond** represents the 95% CI of the summary estimate.

95% CI: 27.0%-28.3%), whereas the lowest readmission rate was observed in Nigeria (1.5%; 95% CI: 0.6%-3.9%).

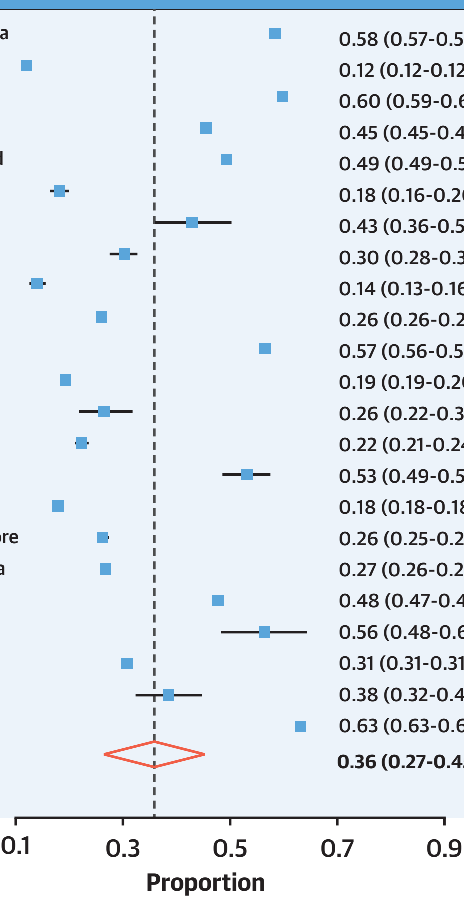
Among the prespecified subgroup hypotheses (Supplemental Appendix 7), the proportion of patients with COPD and diabetes explained some of the observed heterogeneity. Specifically, for every 1% increase in the proportion of patients with COPD, we observed a 0.4% (95% CI: 0.1%-0.7%) increase in the absolute risk of 30-day all-cause hospitalization (adjusted $R^2 = 43.73\%$). Likewise, for every 1% increase in the proportion of patients with diabetes, we observed a 0.3% (95% CI: 0.03%-0.5%) increase in the absolute risk of 30-day all-cause hospitalization (adjusted $R^2 = 20.81\%$). As well, the observed heterogeneity was not explained by the countries' GDP, proportion of GDP spent on health care, Gini coefficient, or 30-day mortality rates.

1-YEAR READMISSION RATES. The studies reporting on 1-year readmission followed a total of 1,036,771 patients. The median age reported across studies was 77.2 years (25th to 75th percentile: 70.1-78.7 years), and there were equal numbers of men and women, with the median proportion of women being 49.7% (25th to 75th percentile: 46.2%-52.4%). The highest mean age was observed in the United States, whereas

FIGURE 3 Meta-Analysis of 1-Year Readmission Rates Globally

1-Year Hospital Readmission Rate

Study	Continent	Country	Proportion (95% CI)	Numerator	Denominator
Al-Omary 2017	Oceania	Australia	0.58 (0.57-0.59)	6,312	10,840
Sun 2018	North America	Canada	0.12 (0.12-0.12)	11,030	90,707
Wong 2017	North America	Canada	0.60 (0.59-0.60)	16,605	27,791
Yeung 2012	North America	Canada	0.45 (0.45-0.46)	6,580	14,462
Bottle 2015	Europe	England	0.49 (0.49-0.50)	51,982	105,441
Vorilhon 2015	Europe	France	0.18 (0.16-0.20)	332	1,825
Stafylas 2017	Europe	Greece	0.43 (0.36-0.50)	76	177
Harikrishnan 2017	Asia	India	0.30 (0.28-0.33)	333	1,103
Novack 2011	Asia	Israel	0.14 (0.13-0.16)	306	2,182
Degli Esposti 2020	Europe	Italy	0.26 (0.26-0.26)	17,941	69,164
Maggioni 2016	Europe	Italy	0.57 (0.56-0.57)	23,431	41,413
Spreafico 2020	Europe	Italy	0.19 (0.19-0.20)	2,496	12,938
Setoguchi 2015	Asia	Japan	0.26 (0.22-0.32)	82	310
Yoshikawa 2020	Asia	Japan	0.22 (0.21-0.24)	829	3,717
Balsam 2016	Europe	Poland	0.53 (0.49-0.58)	255	480
Niedziela 2018	Europe	Poland	0.18 (0.18-0.18)	12,729	71,002
Chang 2014	Asia	Singapore	0.26 (0.25-0.27)	1,494	5,703
Omersa 2019	Europe	Slovenia	0.27 (0.26-0.27)	9,497	35,371
Farre 2017	Europe	Spain	0.48 (0.47-0.49)	6,121	12,806
Martinez 2017	Europe	Spain	0.56 (0.48-0.64)	80	142
Wang 2020	Asia	Taiwan	0.31 (0.31-0.31)	35,275	114,253
Okello 2014	Africa	Uganda	0.38 (0.32-0.45)	86	224
Dharmarajan 2017	North America	USA	0.63 (0.63-0.63)	261,274	414,720
Overall			**0.36 (0.27-0.45)**		



Forest plot summarizing the pooled proportions for 1-year readmission rates. For each study, **blue squares** and **horizontal lines** correspond to the respective point estimate and accompanying 95% CI. The **vertical dashed line** on the forest plot represents the point estimate of the summary estimate. The **red diamond** represents the 95% CI of the summary estimate.

the lowest was reported in Uganda. Similar to the demographic of countries reporting on 30-day readmission, among countries reporting on 1-year readmission, the highest proportion of women was in Uganda, whereas the highest proportion of men was in Greece. Amongst patients at risk for 1-year readmission, the most prevalent HF comorbidity was hypertension, followed by diabetes, atrial fibrillation, COPD, and renal disease (Supplemental Appendix 5B).

Of the 1,036,771 individuals hospitalized for HF, 465,146 were readmitted within 1 year. The pooled estimate of 1-year readmission was 35.7% (95% CI: 27.1%-44.9%), with moderate certainty caused by inconsistency (**Figure 3**). There was substantial variability in risk within continents and globally; the highest readmission rate was observed in the United States (63.0%; 95% CI: 62.9%-63.1%), whereas the lowest readmission rate was observed in Israel (14.0%; 95% CI: 12.6%-15.5%).

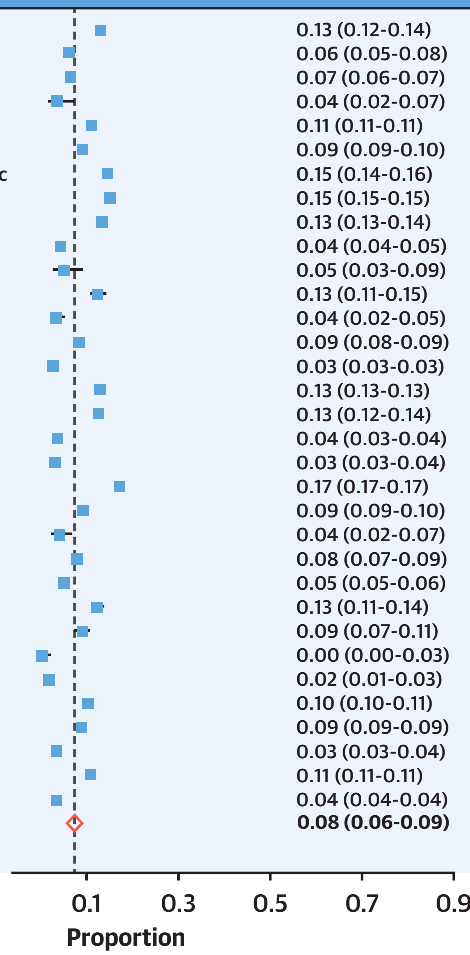
Our subgroup analyses (Supplemental Appendix 8) found that only the proportion of patients with COPD was significantly associated with 1-year readmission. Specifically, for every 1% increase in the proportion of patients with COPD, we observed a 1.0% (95% CI: 0.5%-1.6%) increase in the absolute risk of 1-year all-cause hospitalization (adjusted $R^2 = 62.09\%$). Similar to the 30-day readmission rates, the observed heterogeneity among the studies reporting on 1-year readmission was not explained by the countries'

JACC VOL. 82, NO. 5, 2023
AUGUST 1, 2023:430-444

FIGURE 4 Meta-Analysis of 30-Day Mortality Rates Globally

30-Day Mortality Rate

Study	Continent	Country	Proportion (95% CI)	Numerator	Denominator
Al-Omary 2017	Oceania	Australia	0.13 (0.12-0.14)	1,575	12,114
Huynh 2015	Oceania	Australia	0.06 (0.05-0.08)	97	1,537
Teng 2015	Oceania	Australia	0.07 (0.06-0.07)	1,144	17,379
Mwita 2017	Africa	Botswana	0.04 (0.02-0.07)	7	190
Raslan 2021	North America	Canada	0.11 (0.11-0.11)	19,949	178,997
McAlister 2020	North America	Canada	0.09 (0.09-0.10)	2,455	26,426
Littnerova 2015	Europe	Czech Republic	0.15 (0.14-0.16)	738	5,057
Zareini 2019	Europe	Denmark	0.15 (0.15-0.15)	18,922	124,113
Bottle 2018	Europe	England	0.13 (0.13-0.14)	10,497	77,801
Tuppin 2013	Europe	France	0.04 (0.04-0.05)	3,078	69,958
Stafylas 2017	Europe	Greece	0.05 (0.03-0.09)	9	177
Harikrishnan 2015	Asia	India	0.13 (0.11-0.15)	151	1,205
Roy 2013	Europe	Ireland	0.04 (0.02-0.05)	23	637
Novack 2010	Asia	Israel	0.09 (0.08-0.09)	701	8,246
Degli Esposti 2020	Europe	Italy	0.03 (0.03-0.03)	1,920	69,164
Roshanghalb 2019	Europe	Italy	0.13 (0.13-0.13)	9,480	72,083
Tellini 2015	Europe	Italy	0.13 (0.12-0.14)	903	7,056
Wakabayashi 2018	Asia	Japan	0.04 (0.03-0.04)	184	4,842
Lee 2017	Asia	Korea	0.03 (0.03-0.04)	177	5,356
van Oeffelen 2014	Europe	Netherlands	0.17 (0.17-0.17)	32,502	189,069
Wasywich 2010	Oceania	New Zealand	0.09 (0.09-0.10)	503	5,413
Ogah 2014	Africa	Nigeria	0.04 (0.02-0.07)	12	285
AlHabib 2015	Asia	Saudi Arabia	0.08 (0.07-0.09)	212	2,610
Omersa 2016	Europe	Slovenia	0.05 (0.05-0.06)	1,578	29,510
Fernandez-Berges 2013	Europe	Spain	0.13 (0.11-0.14)	278	2,220
Formiga 2018	Europe	Spain	0.09 (0.07-0.11)	89	985
Iranzo 2017	Europe	Spain	0.00 (0.00-0.03)	1	221
Minana 2017	Europe	Spain	0.02 (0.01-0.03)	40	2,110
Santos 2019	Europe	Spain	0.10 (0.10-0.11)	8,076	77,652
Ghith 2016	Europe	Sweden	0.09 (0.09-0.09)	3,312	36,943
Wang 2020	Asia	Taiwan	0.03 (0.03-0.04)	3,979	114,253
Krittayaphong 2018	Asia	Thailand	0.11 (0.11-0.11)	22,175	201,709
DeVore 2016	North America	USA	0.04 (0.04-0.04)	3,663	100,189
Overall			**0.08 (0.06-0.09)**		



Forest plot summarizing the pooled proportions for 30-day mortality rates. For each study, **blue squares** and **horizontal lines** correspond to the respective point estimate and accompanying 95% CI. The **vertical dashed line** on the forest plot represents the point estimate of the summary estimate. The **red diamond** represents the 95% CI of the summary estimate.

GDP, proportion of GDP spent on health care, Gini coefficient, or 1-year mortality rates.

30-DAY MORTALITY RATES. The studies reporting on 30-day mortality followed a total of 1,445,507 patients, and the median age across studies was 76.3 years (25th to 75th percentile: 70.1-78.4 years), with equal numbers of men and women with the reported median proportion of female patients being 49.3% (25th to 75th percentile: 42.3%-51.8%). The highest mean age was observed in Italy, whereas the youngest was observed in Botswana. The highest proportion of women was reported by Slovenia, whereas the highest proportion of men was reported by Greece. The most prevalent HF comorbidity was hypertension, followed by ischemic heart disease, atrial fibrillation, dyslipidemia, diabetes, renal disease, COPD, MI, and stroke/transient ischemic attack (Supplemental Appendix 5C).

Of the 1,445,507 individuals hospitalized for HF, 148,430 died within 30 days. The pooled estimate of 30-day mortality was 7.6% (95% CI: 6.1%-9.3%), with moderate certainty caused by inconsistency (**Figure 4**). There was substantial variability in 30-day mortality rates globally and within continents; the highest mortality rate was observed in the Netherlands (17.2%; 95% CI: 17.0%-17.4%), whereas the lowest mortality rate was observed in South Korea (3.3%; 95% CI: 2.9%-3.8%). Prevalence of HF comorbidities, age, proportion of women, study quality, final study recruitment year, GDP, proportion of GDP spent on health care, and Gini coefficients did not explain the observed heterogeneity (Supplemental Appendix 9).

1-YEAR MORTALITY RATES. The studies reporting on 1-year mortality followed a total of 1,538,776 patients and the median age across studies was 75.4 years (25th to 75th percentile: 68.0-78.2 years), with equal numbers of men and women; the median proportion of women across included studies was 49.5% (25th to 75th percentile: 42.4%-54.2%). The oldest age distribution was observed in Spain, whereas the youngest age distribution was reported by Slovakia. Among countries reporting on 1-year mortality, the highest proportion of women was reported by Spain, whereas the highest proportion of men was reported by Slovakia. Among patients at risk for 1-year mortality, the most prevalent HF comorbidity was hypertension, followed by ischemic heart disease, CAD, atrial fibrillation, dyslipidemia, diabetes, renal disease, MI, COPD, and stroke/transient ischemic attack (Supplemental Appendix 5D).

Of the 1,538,776 individuals hospitalized for HF, 384,718 died within 1 year. The pooled estimate of 1-year mortality was 23.3% (95% CI: 20.8%-25.9%), with moderate certainty caused by inconsistency (**Figure 5**). There was substantial variability in 1-year mortality rates between countries within continents as well as globally; the highest mortality rate was observed in the Netherlands (36.9%; 95% CI: 36.4%-37.5%), whereas the lowest mortality rate was observed in Ireland (8.2%; 95% CI: 6.3%-10.5%).

Our subgroup analyses found that the proportion of patients with COPD and the average age of patients was associated with 1-year mortality (Supplemental Appendix 10). Specifically, for every 1% increase in the proportion of patients with COPD, we observed a 0.2% (95% CI: 0.0%-0.05%) increase in the absolute risk of 1-year all-cause mortality (adjusted $R^2 = 12.97\%$). For every 1-year increase in average patient age, we observed a 0.3% (95% CI: 0.03%-0.6%) increase in the absolute risk of 1-year all-cause mortality (adjusted $R^2 = 8.96\%$). The observed heterogeneity was not explained by the countries' GDP, proportion of GDP spent on health care, or Gini coefficient.

DISCUSSION

In this systematic review and meta-analysis of data from 38 countries, we identified the global estimates of 30-day and 1-year hospital readmission and mortality amongst patients with HF. Within 30-days of discharge from their index HF admission, 13% (range: 1.5%-27.6%,) were readmitted to hospital (**Central Illustration**) and 7.5% (range: 3.3%-17.2%) died. By 1-year postdischarge, the risk of readmission increased to 36% (range: 14.0%-63.0%) and mortality rate was 23% (range: 8.2%-36.9%). For both 30-day and 1-year readmission and mortality rates, visual inspection of our forest plots indicated considerable heterogeneity not only globally, but also between countries on the same continent.

HF hospitalization is an important event with implications on downstream survival.[110] The observed variability in readmission or mortality rates were largely unexplained by our subgroup investigations. Among HF comorbidities, only the proportion of HF patients living with COPD was associated with both 30-day and 1-year readmission. This observation is complementary to the large breadth of literature, including OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure), supporting the association between COPD or respiratory decompensation and the increased hospitalization risk among HF patients.[111,112] This may be reflective of the similarity in clinical presentation of COPD and HF, potential for misdiagnosis, or additive comorbidity burden of a concomitant respiratory disease atop that of HF.[113,114]

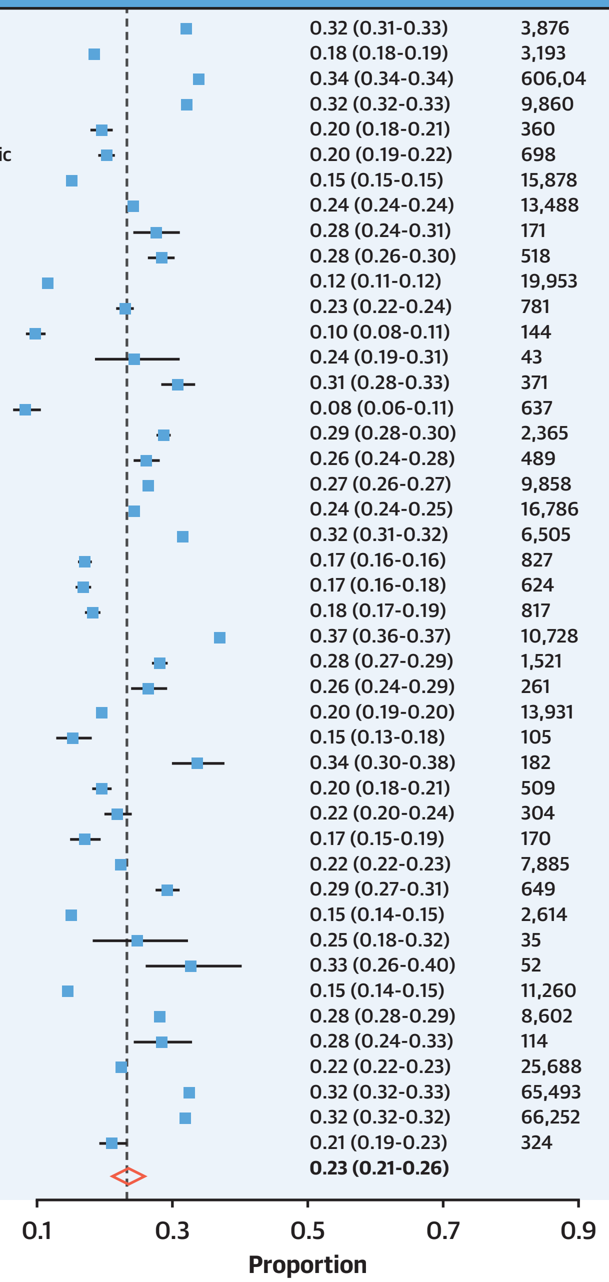
The observed variability in readmission rates was not associated with the countries' economic metrics, health care expenditure, or the competing risk of mortality. There may, however, be myriad of interacting factors that are difficult to capture through national/regional reports, including variability in hospital-level policies and prescribing practices, clarity of discharge instructions and patient education, and sociodemographic factors, which may explain the observed between-country heterogeneity.[115-117] Notably, North America was the region with the highest 1-year readmission rates. Despite the enactment of the Hospital Readmissions Reductions Program established under the Affordable Care Act in 2010, readmission rates in the United States remained among the highest in the world.[117] More broadly, global systemic disparities in health care settings, access to care, financial and human resources, availability of affordable prescription medication, programs for HF management, as well as cultural and

JACC VOL. 82, NO. 5, 2023
AUGUST 1, 2023:430-444

FIGURE 5 Meta-Analysis of 1-Year Mortality Rates Globally

1-Year Mortality Rate

Study	Continent	Country	Proportion (95% CI)	Numerator	Denominator
Al-Omary 2017	Oceania	Australia	0.32 (0.31-0.33)	3,876	12,114
Teng 2015	Oceania	Australia	0.18 (0.18-0.19)	3,193	17,379
Raslan 2021	North America	Canada	0.34 (0.34-0.34)	606,04	178,997
Wong 2017	North America	Canada	0.32 (0.32-0.33)	9,860	30,602
Hai 2016	Asia	China	0.20 (0.18-0.21)	360	1,845
Parenica 2013	Europe	Czech Republic	0.20 (0.19-0.22)	698	3,438
Zareini 2019	Europe	Denmark	0.15 (0.15-0.15)	15,878	104,522
Taylor 2019	Europe	England	0.24 (0.24-0.24)	13,488	55,959
Lassus 2013	Europe	Finland	0.28 (0.24-0.31)	171	620
Eschalier 2015	Europe	France	0.28 (0.26-0.30)	518	1,825
Jacob 2019	Europe	Germany	0.12 (0.11-0.12)	19,953	172,394
Ohlmeier 2015	Europe	Germany	0.23 (0.22-0.24)	781	3,395
Bonsu 2017	Africa	Ghana	0.10 (0.08-0.11)	144	1,488
Stayfylas 2017	Europe	Greece	0.24 (0.19-0.31)	43	177
Harikrishnan 2017	Asia	India	0.31 (0.28-0.33)	371	1,205
Roy 2013	Europe	Ireland	0.08 (0.06-0.11)	637	637
Novack 2010	Asia	Israel	0.29 (0.28-0.30)	2,365	8,246
Avaldi 2015	Europe	Italy	0.26 (0.24-0.28)	489	1,873
Bottle 2017	Europe	Italy	0.27 (0.26-0.27)	9,858	37,185
Degli Esposti 2020	Europe	Italy	0.24 (0.24-0.25)	16,786	69,164
Spreafico 2020	Europe	Italy	0.32 (0.31-0.32)	6,505	20,809
Wakwabayashi 2018	Asia	Japan	0.17 (0.16-0.16)	827	4,842
Yashikawa 2020	Asia	Japan	0.17 (0.16-0.18)	624	3,717
Lee 2017	Asia	Korea	0.18 (0.17-0.19)	817	4,487
Vaartjes 2010	Europe	Netherlands	0.37 (0.36-0.37)	10,728	29,053
Wasywich 2010	Oceania	New Zealand	0.28 (0.27-0.29)	1,521	5,413
Panduranga 2016	Asia	Oman	0.26 (0.24-0.29)	261	988
Niedziela 2018	Europe	Poland	0.20 (0.19-0.20)	13,931	71,002
Ozieranski 2016	Europe	Poland	0.15 (0.13-0.18)	105	689
Lourence 2016	Europe	Portugal	0.34 (0.30-0.38)	182	541
AlHabib 2015	Asia	Saudi Arabia	0.20 (0.18-0.21)	509	2,610
Yap 2019	Asia	Singapore	0.22 (0.20-0.24)	304	1,392
Lesny 2016	Europe	Slovakia	0.17 (0.15-0.19)	170	1,000
Omersa 2016	Europe	Slovenia	0.22 (0.22-0.23)	7,885	35,371
Fernandez-Berges 2013	Europe	Spain	0.29 (0.27-0.31)	649	2,220
Gracia Gutiérrez 2020	Europe	Spain	0.15 (0.14-0.15)	2,614	17,516
Martinez 2017	Europe	Spain	0.25 (0.18-0.32)	35	142
Parada 2012	Europe	Spain	0.33 (0.26-0.40)	52	159
Santos 2019	Europe	Spain	0.15 (0.14-0.15)	11,260	77,652
Ohlsson 2019	Europe	Sweden	0.28 (0.28-0.29)	8,602	30,721
Sotiropoulos 2016	Europe	Switzerland	0.28 (0.24-0.33)	114	402
Wang 2020	Asia	Taiwan	0.22 (0.22-0.23)	25,688	114,253
Kritlayaphong 2018	Asia	Thailand	0.32 (0.32-0.33)	65,493	201,709
Khera 2017	North America	USA	0.32 (0.32-0.32)	66,252	207,687
Munibari 2017	Asia	Yemen	0.21 (0.19-0.23)	324	1,536
Overall			**0.23 (0.21-0.26)**		

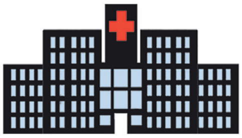


Forest plot summarizing the pooled proportions for 1-year mortality rates. For each study, **blue squares** and **horizontal lines** correspond to the respective point estimate and accompanying 95% CI. The **vertical dashed line** on the forest plot represents the point estimate of the summary estimate. The **red diamond** represents the 95% CI of the summary estimate.

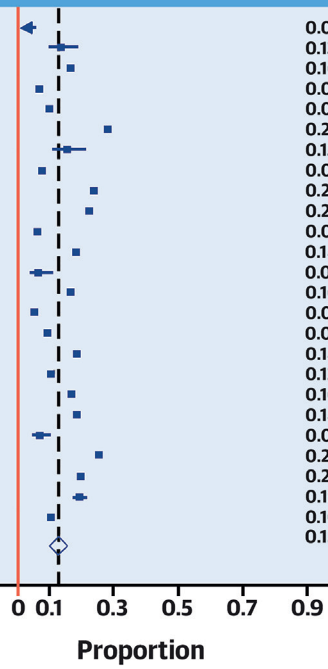
CENTRAL ILLUSTRATION Systematic Review of 30-Day Readmission Outcomes Globally

Global 30-Day Readmission for Patients With HF

13% (95% CI: 10%-16%)
1,417,462 HF Patients
18 Countries



Study	Continent	Country	Proportion (95% CI)	Numerator	Denominator
Ogah 2014	Africa	Nigeria	0.02 (0.01-0.04)	4	262
Okello 2014	Africa	Uganda	0.13 (0.10-0.18)	30	224
Huang 2017	Asia	China	0.16 (0.15-0.17)	1,274	7,847
Novack 2011	Asia	Israel	0.06 (0.05-0.07)	138	2,182
Chen 2021	Asia	Japan	0.09 (0.09-0.10)	2,503	26,365
Chung 2017	Asia	Korea	0.28 (0.27-0.28)	5,286	19,128
Deek 2016	Asia	Lebanon	0.15 (0.11-0.21)	28	187
Chou 2019	Asia	Taiwan	0.07 (0.07-0.08)	2,987	40,541
Tung 2017	Asia	Taiwan	0.23 (0.23-0.24)	3,169	13,577
Sundaram 2021	Asia	Taiwan	0.22 (0.22-0.22)	8,100	36,900
Bottle 2017	Europe	England	0.06 (0.06-0.06)	11,699	194,983
Tuppin 2013	Europe	France	0.18 (0.18-0.18)	11,235	62,417
Stafylas 2017	Europe	Greece	0.06 (0.04-0.11)	11	177
Avaldi 2015	Europe	Italy	0.16 (0.14-0.18)	300	1,873
Degli Esposti 2020	Europe	Italy	0.05 (0.05-0.05)	3,596	69,164
Roshanghalb 2019	Europe	Italy	0.09 (0.09-0.09)	5,363	60,771
Tellini 2015	Europe	Italy	0.18 (0.17-0.19)	1,291	7,056
Omersa 2019	Europe	Slovenia	0.12 (0.11-0.12)	4,116	35,371
Zapatero 2012	Europe	Spain	0.16 (0.16-0.17)	61,008	370,983
McAlister 2017	North America	Canada	0.18 (0.18-0.18)	39,368	217,039
Kwan 2016	North America	Haiti	0.07 (0.04-0.10)	18	274
Sundaram 2021	North America	USA	0.25 (0.25-0.25)	57,880	231,512
Al-Omary 2018	Oceania	Australia	0.20 (0.19-0.20)	2,120	10,840
Huynh 2015	Oceania	Australia	0.19 (0.17-0.21)	293	1,537
Islam 2012	Oceania	Australia	0.10 (0.09-0.11)	630	6,252
Overall			0.13 (0.11-0.16)		



Foroutan F, et al. J Am Coll Cardiol. 2023;82(5):430-444.

We examined >1.4 million people with heart failure in 18 countries. The pooled average 30-day readmission rate was 13% (95% CI: 10%-16%) worldwide.

personal views of medical care and health may all vary from country to country, further underlying the complex relationship between patient care, resources, and hospital readmission.[118]

The findings of our review partially agree with a previous attempt to explore HF readmission and mortality in a global setting.[119] The authors of this review also found that HF patients had high rates of mortality and readmission globally, which were partially explained by the usage of oral cardiovascular therapies. However, our review differs significantly in our approach for estimating and exploring variability in global readmission rates. We explored several potential sources of heterogeneity between studies that were not investigated by Kimmoun et al,[119] including HF-related comorbidities, study quality, and the countries' socioeconomic condition (captured through GDP, percent of GDP spent on health care, and the Gini coefficient). Moreover, we utilized a more population-based approach, and opted to only include studies that were the best representation of each countries' population. As a result, nearly all studies included in our review were assessed as having a low risk of bias. The review by Kimmoun et al[119] adopted a broader selection criterion and included all studies with a sample size ≥100 (inclusive of hospital-based cohort studies as opposed to regional or national data). These smaller studies may not be a good representation of the population and may mitigate generalizability to all HF patients within a given nation.[120]

Our results emphasize the immense burden of HF readmissions as a worldwide problem. The geographic variations in readmission rates suggest that there may be substantial opportunity to reduce readmission rates in many countries, in part by learning and adopting strategies of patient management from better performing countries. Future research should aim to identify the infrastructure or processes of care used by different countries, to potentially "unmask" the determinants of improved outcomes manifested as lower mortality and readmission rates at national level. These factors may be complex, and may include differences in rehabilitation programs, social inequality, economic instability, and crime rates between countries. Identifying these factors may not only improve care within these countries, but may also be adopted by other, worse performing countries.

The findings of our review have several implications for clinical practice and research related to HF care. The observed unexplained inconsistency in outcome rates may, in part, be caused by the differing definitions of the thresholds that can trigger hospitalization for HF with reduced and preserved ejection fraction (EF) across various countries and regions. This finding emphasizes the importance of establishing a uniform HF definition based on objective markers (eg, natriuretic peptides or ejection fraction) for the standardization of patient enrollment in global trials. Moreover, our findings are relevant for clinical trial planning. Trialists can use our estimates to anticipate readmission and mortality rates, which may inform power calculations and sample size estimations in prospective countries. Finally, the comparative regional and national data presented in our review may help policymakers in different countries understand the potential effects of interventions at the population level vis-à-vis the relative effects on mortality vs hospitalization outcomes. These data may inform countries performing more poorly compared with global benchmarks on the urgency of adopting new HF therapies shown to provide benefit.

Our review has several strengths. We conducted a comprehensive search for studies most representative of countries' national data on HF patients. As well, we conducted meta-regression analyses to explore the impact of risk of bias, metrics of countries' economic performance, health care expenditure, competing risk of mortality, and the prevalence of select HF comorbidities on both 30-day and 1-year readmission and mortality rates.

STUDY LIMITATIONS. A potential limitation of our study is that we only considered primary peer-reviewed articles in our review. We excluded gray literature and, as such, may have potentially missed reports on countries that may have published readmission and mortality rates in the form of abstracts or national/regional reports. Such reports may have provided estimates of readmission and mortality rates for countries not included in our review. For countries that did not provide national reports, we relied on regional estimates of HF readmission and mortality rates. These regions may not be a true representation of the national rates of readmission and mortality. The regions reporting on readmission or mortality rates may be more representative of subpopulations with better socioeconomic status, where there is infrastructure for capturing readmission or mortality data. Such regions may have systematically lower rates of readmission or mortality than regions where lower socioeconomic status and worse HF care could lead to higher readmission and mortality rates. Alternatively, one may also expect systematically higher readmission and mortality rates amongst the more urbanized regions within a country compared with the rural regions. We did not have access to adequate studies to further explore the extent to which regional estimates underestimate or overestimate the true incidence of HF readmission and mortality as a potential source of bias. Our review focused on contemporary global readmission and mortality data. We did not design our review to explore readmission and mortality trends over time. In addition, we were unable to explore the impact of HF phenotypes (HF with reduced EF vs preserved EF vs mildly reduced EF) on readmission and mortality rates because of a lack of reporting, which may be one potential explanation of the substantial heterogeneity observed in our meta-analyses. Furthermore, an additional limitation may be the variation in how hospital readmission is classified on a global scale. The individual studies did not provide details on how they define HF readmission and the thresholds used for necessitating a readmission. This may also be another potential explanation for the observed heterogeneity. In this review, we strived to capture this reporting bias limitation in our risk of bias assessments of included studies.

Furthermore, we were unable to fully explore the underlying reasons for the heterogeneity we observed, including not only potential variations in health care systems, but also differences in diagnostic ascertainment and varying thresholds in the decision to admit patients to hospital.[121,122] In some cases, there were variations within countries, indicating that the latter factors or regional differences in health systems or organization may have been contributing factors. Finally, completeness of follow-up may have contributed to unexplained variations because not all countries had access to comprehensive outcomes data at a population level. Nevertheless, we show that there are marked international disparities in HF hospitalization and mortality rates. Further exploration for the underlying causes of these variations at both the country- and region-level should be conducted.

CONCLUSIONS

In this systematic review and meta-analysis, we found substantial global heterogeneity in 30-day and 1-year readmission rates for hospitalized HF patients. We demonstrated that the substantial variability across countries is not simply explained by health care expenditure, risk of mortality, or prevalence of HF comorbidities. Future studies are required to evaluate differences in structure and processes of care delivery, as well as social and cultural differences across countries that may be contributing to the risk of readmission. Successfully addressing this research goal could lead to the implementation of readmission reduction programs in health care centers around the world.

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PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE: Differences between countries in rates of hospital readmission and mortality among patients with HF are unexplained by health care expenditures.

TRANSLATIONAL OUTLOOK: Future studies should explore how differences in health care delivery processes and social and cultural factors between countries contribute to the variation in readmission rates and develop strategies to improve outcomes.

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KEY WORDS heart failure, hospitalization, meta-analysis, readmission

APPENDIX For supplemental data, please see the online version of this paper.