Research Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2024.59.009372

Socioeconomic and Geographic Differences Between HFpEF and HFrEF: A Systematic Review

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ARTICLE INFO

Received: October 09, 2024

Published: December 13, 2024

Citation: Kiki J Estes Schmalzl MBA-MIS, RN, Ph.D. Student and Kristin M Lefebvre PT, Ph.D., CCS. Socioeconomic and Geographic Differences Between HFpEF and HFrEF: A Systematic Review. Biomed J Sci & Tech Res 59(5)-2024. BJSTR. MS.ID.009372.

ABSTRACT

Background: This systematic review examines the impact of socioeconomic status and geographic location on the diagnosis, management, and outcomes of heart failure with preserved ejection fraction (HFpEF) versus heart failure with reduced ejection fraction (HFrEF).

Methods and Results: A comprehensive search of PubMed, EMBASE, CINAHL, and Cochrane Library (2008-2023) identified 11 studies meeting inclusion criteria, involving 182,540 patients. HFpEF patients were typically older, more often female, and had higher rates of comorbidities, particularly hypertension and metabolic diseases. Socioeconomic disparities were noted, with HFpEF more commonly diagnosed in higher-income groups, likely due to better access to healthcare services. Geographic differences influenced treatment utilization and outcomes, with the highest mortality rates observed in Africa and India. Sensitivity analysis confirmed the significant role of socioeconomic and geographic factors in mortality and medication adherence.

Conclusions: The review underscores the importance of considering social determinants and regional differences in heart failure management. Tailored approaches and improved healthcare access in underserved areas are crucial to addressing disparities between HFpEF and HFrEF. Further research is needed to clarify the drivers of these inequalities, particularly in underrepresented regions.

Keywords: Heart Failure with Preserved Ejection Fraction (HFpEF); Socioeconomic Disparities; Geographic Differences; Social Determinants of Health

Introduction

Heart failure (HF) affects approximately 64 million people worldwide, imposing substantial morbidity, mortality, and healthcare costs [1]. The two principal types, heart failure with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF) exhibit distinct etiologies, patient demographics, treatment responses, and outcomes, necessitating tailored management approaches [2]. Since its redefinition in 2007, diagnoses of HFpEF have surpassed those of HFrEF globally yet remain challenging to diagnose due to subtle clinical presentations [3-5]. HFpEF patients often experience pronounced exertional symptoms and higher rates of comorbidities, including hypertension, obesity, and atrial fibrillation. Conversely, HFrEF typically presents with classic congestion signs, even at rest [6,7]. These distinctions reflect underlying pathophysiological differences: impaired ventricular relaxation and increased stiffness in HFpEF versus reduced contractility in HFrEF [8]. Despite recognizing the impact of socioeconomic status and geographic location on cardiovascular health, their specific relationship to HFpEF versus HFrEF still needs to be studied. Most clinical guidelines and medical textbooks do not identify these demographic factors as pertinent for differentially diagnosing heart failure types [1,9].This systematic review aims to synthesize current literature on socioeconomic and geographic factors in HFpEF and HFrEF. By elucidating how these factors intersect with HF subtypes, we aim to inform diagnosis, treatment, outcomes, and healthcare policymaking, advancing health equity.

Methods

Protocol and Registration

The review was conducted following the Preferred Reporting Items for Systematic Reviews (PRISMA) [10]. This review protocol is registered with the PROSPERO database (Registration number: CRD42024497619).

Search Strategy

A comprehensive literature search of PubMed, EMBASE, CINAHL, and Cochrane Library using a combination of Medical Subject Headings (MeSH) terms and keywords related to heart failure (HF), heart failure with preserved ejection fraction (HFpEF), heart failure with reduced ejection fraction (HFrEF), socioeconomic factors, geographic disparities, and healthcare access. The search strategy was reviewed by the graduate school librarian at the University of Jamestown, Jamestown, ND, and suggestions were incorporated.

Study Selection Process

This systematic review included studies that satisfied the inclusion-exclusion criteria. Observational or cross-sectional studies on adults 18 years of age and older; populations with clearly defined HFpEF (LVEF ≥ 50%) or HFrEF (LVEF ≤ 40%); studies that included analysis of outcomes related to socioeconomic and geographic factors and HFpEF prognostic outcomes based on multivariate analysis; literature was restricted to the English.

Studies were included if they:

1. Were original research articles or systematic reviews published in peer-reviewed journals,
2. Focused on adults (aged 18 and older) with HFpEF or HFrEF,
3. Examined the association between socioeconomic or geographic factors and HF outcomes, and
4. Were published in English.

Exclusion criteria included studies focusing on pediatric populations, studies without clear differentiation between HFpEF and HFrEF, and studies published in languages other than English. The Rayyan QCRI tool was used for the initial screening of titles and abstracts, followed by full-text screening and data extraction by two independent reviewers [11] Discrepancies were resolved through discussion or by a third reviewer if necessary.

Data Extraction

The data included study characteristics (e.g., design, sample size, and location), participant characteristics (e.g., age, sex, and comorbidities), and outcomes related to HFpEF and HFrEF (e.g., mortality, hospitalization, and quality of life) [12]

Risk of Bias

The risk of bias was assessed using the Cochrane Risk of Bias Tool for randomized controlled trials and the ROBINS-E tool for observational studies [13]. Due to the heterogeneity of the included studies, data synthesis was narrative. Any differences in opinions during the assessment were resolved through discussion and consensus. The reviewers reported no conflicts of interest, and no support or grants were associated with this systematic review. Figures 1 & 2 provide visual summaries of the risk of bias assessments, indicating the distribution of risk levels across the different domains evaluated.

Summary Measures and Narrative Synthesis

Summary measures included odds ratio (ORs) for specific outcomes, 95% confidence intervals (CIs), and p-values for various outcomes related to HFpEF and HFrEF. Due to the heterogeneity of the included studies and their observational nature, a meta-analysis was not conducted. The I^2 statistic for key outcomes exceeded 75%, indicating high heterogeneity. Instead, a narrative synthesis was performed to summarize the findings qualitatively [14]. This approach allowed for a more nuanced interpretation of the complex relationships between socioeconomic status, geographic factors, and heart failure outcomes.

Sensitivity Analysis

The sensitivity analysis conducted in this systematic review aimed to assess the robustness of the findings by examining the impact of geographical location, income levels, and neighborhood socioeconomic status (nSES) on mortality rates and medication adherence among heart failure patients [15]. Manual calculations and spreadsheet software were used to organize and code the extracted data for the sensitivity analyses.

Results

Literature Search and Screening

The GRADE approach and the ROBINS-E and STROBE tools were used to assess the risk of bias in observational and cross-sectional studies.[16-18] Most studies demonstrated a low to moderate risk of bias, with one study identified as having a high risk. Common sources of bias included selection bias due to non-random sampling, information bias from self-reported data, and potential confounding factors not accounted for in the study design. The variability in study quality suggests caution when interpreting pooled results. Using standardized tools like ROBINS-E enhances the reliability of our findings by systematically evaluating potential biases across studies. The assessed risk of bias was summarized using the Cochran Robvis tool and the ROBINS-E dataset template (Figures 1 & 2). The initial search revealed 4686 potentially eligible articles, of which 486 were duplicates and removed [19]. After reading titles and abstracts, we excluded 4000 references, and after reading the full-text versions, 189 articles were excluded. The PRISMA diagram outlines the review and study selection process (Figure 3) [20]. A list of excluded studies and reasons for exclusion was maintained.

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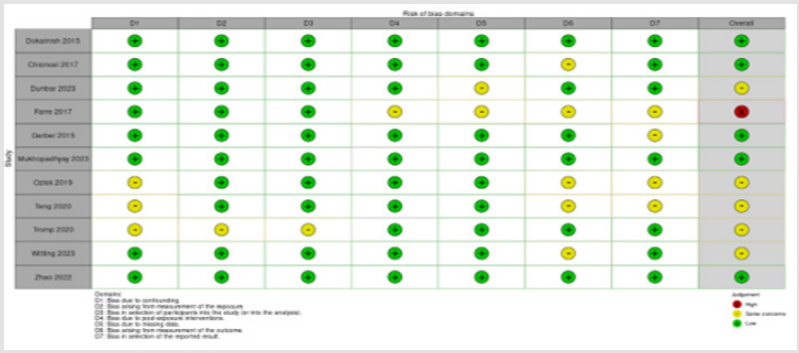

Figure 1: Risk of Bias Traffic Light Plot.

Figure 2: Risk of Bias Summary Plot.

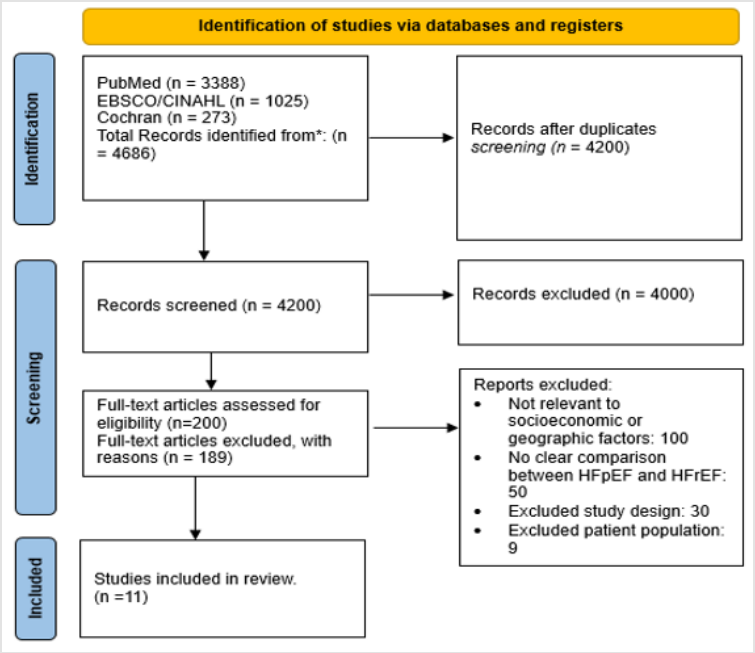

Figure 3: PRISMA Diagram.

Characteristics of the Included Studies

The eleven included studies were observational study designs, with sample sizes ranging from 512 to 126,670. Only one study was identified as having a high risk of bias. Table 1 below provides the characteristics of the included studies.

Table 1: Characteristics of Included Studies.

Study	Year	Country/ Region	Study Design	Sample Size	Population	HF Types Studied	Key Outcomes Measured
Chioncel et al. [21]	2017	Europe	Observational	9,134	HF patients	HFpEF, HFrEF	Patient characteristics, comorbidities
Dokainish, et al. [26]	2015	16 countries (LIC and MIC)	Observational	5,813	HF patients	HFpEF, HFrEF	Prevalence, comorbidities
Farre, et al. [22]	2017	Spain	Observational	3,580	HF patients	HFpEF, HFrEF, HFmrEF	Patient characteristics, outcomes
Gerber, et al. [24]	2015	USA (Olmsted County, MN)	Observational	2,762	HF patients	HFpEF, HFrEF	Incidence, mortality, hospitalizations
Zhao, et al. [23]	2022	USA (counties: Hinds, Madison, Rankin) Jackson, MS	Observational	4,361	Black adults	HFpEF, HFrEF	Risk factors
Tromp, et al. [25]	2020	44 countries	Observational	18,102	HF patients	HFpEF, HFrEF, HFmrEF	Mortality, regional variations
Mukhopadhyay, et al. [29]	2023	USA (New York)	Observational	6,247	HFrEF patients	HFrEF	Medication adherence, socioeconomic factors
Dunbar, et al. [30]	2023	USA	Survey	512	HFrEF patients	HFrEF	Treatment satisfaction, health status
Özlek ,et al. [27]	2019	Turkey	Observational	819	HFpEF patients	HFpEF	Regional differences in clinical profiles
Teng, et al. [28]	2021	11 Asian regions	Observational	4,540	HF patients	Not specified	Treatment adherence
Witting, et al. [31]	2023	USA	Observational	126,670	HFrEF patients (VA)	HFrEF	Treatment rates, sociodemographic factors

Patient Characteristics in HFpEF vs. HFrEF

HFpEF and HFrEF exhibit distinct clinical patient characteristics. Chioncel, et al. [21-22]) consistently reported HFpEF patients to be older (mean age 69-73.5 years) compared to HFrEF patients (64-66.2 years) [23,24] Chioncel, et al. [21] found that 78% of HFpEF patients were female versus 52% of HFrEF patients. Farre, et al. [22] reported that 56% of HFpEF patients were female, compared to 24.3% of HFrEF patients. These differences highlight the variability in patient populations across studies [21] Regarding etiology and comorbidities, ischemic etiology was more prevalent in HFrEF (49-52.6%) than in HFpEF (19.5-24%) [21,22]. Conversely, HFpEF patients showed higher rates of hypertension (67-81.2% vs. 56-64.2% in HFrEF) and atrial fibrillation (32-48.2% vs. 18-19.5% in HFrEF) [21,22] These findings suggest that HFpEF patients often present with a different constellation of comorbidities than HFrEF patients, which may influence diagnosis and treatment approaches. Zhao, et al. [23] identified distinct risk profiles in Black adults, further elucidating the differences between HFpEF and HFrEF.23 HFpEF was associated with a greater left atrial diameter (HR, 1.23; 95% CI, 1.03-1.47; P = .02), higher pulse pressure (HR, 1.23; 95% CI, 1.05-1.44; P = .009), lower Forced Expiratory Volume in 1 second (FEV1) (HR, 1.22; 95% CI, 1.04-1.43; P = .02), lower estimated Glomerular Filtration Rate (eGFR) (HR, 1.43; 95% CI, 1.19-1.72; P < .001), higher Hemoglobin A1c (HbA1c) (HR, 1.25; 95% CI, 1.07-1.45; P = .005), and higher waist circumference (HR, 1.41; 95% CI, 1.18-1.69; P < .001). In contrast, HFrEF was characterized by greater left ventricular mass index (HR, 1.25; 95% CI, 1.07-1.46; P = .005), lower left ventricular ejection fraction (HR, 1.65; 95% CI, 1.42-1.91; P < .001), lower FEV1 (HR, 1.19; 95% CI, 1.00-1.42; P = .047), and lower eGFR (HR, 1.27; 95% CI, 1.04-1.55; P = .02).

Clinical Outcomes in HFpEF vs. HFrEF

Gerber, et al. [24] reported lower cardiovascular mortality for HFpEF compared to HFrEF (HR 0.79; 95% CI, 0.67-0.93) but similar non-cardiovascular mortality rates [24]. The study noted frequent hospitalizations in HFpEF and HFrEF patients, with non-cardiovascular causes accounting for 63.0% of all hospitalizations [24] This observation suggests that the pathophysiological mechanisms and disease progression in HFpEF may differ from HFrEF, necessitating distinct treatment approaches [23]. Tromp, et al. [25]corroborated these findings, reporting better 1-year mortality rates for HFpEF patients (HR 0.67; 95% CI 0.61-0.74) compared to HFrEF patients [24]. This highlights the complex nature of heart failure management across both subtypes and emphasizes the need for comprehensive care approaches that address cardiovascular and non-cardiovascular

aspects of patient health, regardless of ejection fraction classification. The consistency in findings between these studies strengthens the argument for differentiated care approaches in HFpEF and HFrEF.

Outcomes in the Management of HFpEF and HFrEF

Prevalence and outcomes varied significantly across regions. Dokainish, et al. [26] reported that 29% of heart failure patients in low and middle-income countries had HFpEF, while 71% had HFrEF.25 The INTER-CHF study revealed substantial inter-regional differences in HF outcomes, with the highest mortality rates in Africa (34%) and India (23%), and the lowest in China (7%), South America (9%), and the Middle East (9%).Tromp, et al. [25] found that patients from low-income countries had higher 1-year all-cause mortality (HR 1.58; 95% CI 1.41-1.77), with Southeast Asia (HR 2.04; 95% CI 1.74-2.38), Central and South America (HR 1.70; 95% CI 1.48-1.95), and eastern Mediterranean and Africa (HR 1.77; 95% CI 1.53-2.04) showing the worst outcomes.26 However, HFpEF patients had better 1-year mortality rates than HFrEF patients (HFpEF HR 0.67; 95% CI 0.61-0.74; HFmrEF HR 0.83; 95% CI 0.74-0.92) [26].These results reveal significant global variations in heart failure outcomes, with notably higher mortality rates in low-income countries. The stark differences in outcomes across regions highlight the need for a nuanced, global approach to heart failure management.

Regional Differences in Clinical Profiles and Treatment Adherence

Regional differences were also observed in clinical profiles and treatment adherence. Özlek, et al. [27] reported that HFpEF patients in Turkey exhibited significant regional differences, with a higher prevalence of hypertension observed in the Mediterranean, Southeast Anatolia, and Black Sea region (P=0.002) [27].This variation suggests that regional disparities, such as access to healthcare, dietary habits, and socioeconomic status, influence the clinical profiles of HFpEF patients. Similarly, Teng et al. [28] found that 39% of patients lived in low-income regions, and 64.4% had low monthly household income (<US$1000). Patients from low-income areas were significantly less likely to receive B-blockers and device therapies than in high-income regions (P<0.001) [28].Adherence rates were 1.35 times higher in high-income regions than in lower-income areas (95% CI: 1.04-1.73, p=0.040).28 The study also found that lower household income and education status were strongly associated with worse clinical outcomes, especially in high-income regions (P<0.001 for both) [28].

Interconnectedness Clinical Profiles and Treatment Adherence

Regional differences in clinical profiles and treatment adherence appear interconnected. If these regions also face lower adherence rates, as seen in lower-income areas in Asia, the effectiveness of such a strategy could be compromised. This interplay between regional clinical profiles and treatment adherence highlights the need for region-specific interventions addressing the clinical and socioeconomic factors influencing heart failure outcomes. These findings underscore the significant regional disparities in heart failure outcomes, with low-income countries experiencing substantially higher mortality rates. The management of both conditions necessitates tailored approaches that consider regional contexts. The marked variations in outcomes across different geographical areas emphasize the critical importance of integrating socioeconomic factors and local healthcare infrastructure into global strategies for heart failure management. This approach is particularly crucial for improving outcomes in resource-limited settings, where healthcare access challenges and economic constraints often compound the burden of heart failure. Future research and policy initiatives should focus on developing and implementing region-specific interventions that address these disparities and enhance the quality of care for all heart failure patients, regardless of their geographical location or socioeconomic status.

Socioeconomic Factors in HFrEF and HFpEF

Socioeconomic factors are crucial in heart failure management and outcomes, influencing HFrEF and HFpEF patients. Several studies have provided insights into the socioeconomic factors affecting patients with heart failure with reduced ejection fraction (HFrEF). Mukhopadhyay, et al. [29] found that patients from lower socioeconomic neighborhoods had higher odds of medication nonadherence, with odds ratios ranging from 1.35 to 1.83 for the lowest quartile (p<0.001) [29] Having a care partner was associated with lower KCCQ-12 Overall Summary scores (9.6-point decrease, p<0.001), whereas perceived medication affordability correlated with higher scores (7.0-point increase, p=0.02) [30]. Additionally, Witting, et al. [31] reported that HFrEF patients from socially vulnerable neighborhoods had 3.4% lower rates of ARNI treatment, highlighting the impact of socioeconomic factors on treatment adherence and healthcare utilization [31]. Tromp, et al. [25] found that patients from low-income countries had higher 1-year all-cause mortality (HR 1.58; 95% CI 1.41-1.77) for both HFpEF and HFrEF, though HFpEF patients generally fared better (HR 0.67; 95% CI 0.61-0.74) [26]. Teng et al. [28] reported that among 4,540 HFrEF patients, 39% lived in low-income regions, and 64.4% had low monthly household income (<US$1000). 28 Higher socioeconomic indicators were associated with better quality of life and lower risk of adverse outcomes [28].

Dokainish, et al. [26]observed significant regional differences in HFrEF 1-year all-cause mortality, with the highest rates in Africa (34%) and India (23%), and the lowest in China (7%), South America (9%), and the Middle East (9%) [25]. Özlek ,et al. [27] reported regional differences in clinical profiles among HFpEF patients in Turkey, noting that hypertension prevalence varied significantly, from 60% in the eastern region to 70% in the western region (p<0.05), suggesting socioeconomic influences on disease presentation [27]. Zhao, et al. [23] identified distinct risk profiles for HFpEF and HFrEF in Black adults, hinting at potential socioeconomic implications, although direct socioeconomic data were not provided [23].These findings col-

lectively emphasize the profound impact of socioeconomic factors on heart failure outcomes, particularly in HFrEF. Future studies should focus on elucidating the socioeconomic determinants of HFpEF outcomes and developing targeted interventions to address these disparities (Table 2).

Table 2: Patient Characteristics, Clinical Outcomes, Treatment Adherence, and Socioeconomic Factors in HFpEF vs. HFrEF.

Study	Sample Size	Population/Location	Key Findings	95% CI	P-value
Chioncel et al. [21]	9,134	Patients, Europe; ESC Heart Failure Long-Term Registry	Higher age and female representation in HFpEF; Higher comorbidities in HFpEF	HFpEF: 1.3-2.6; HFrEF: 1.8-4.2	<0.006 (HFpEF); <0.001 (HFrEF)
Dokainish, et al. [26]	5,813	Patients, 16 countries (Low- and middle-income countries in Africa, Asia, Middle East, South America); INTER-CHF study	Significant inter-regional differences; variations in sociodemographic and clinical risk factors, HF etiologies, treatments, and outcomes; 1-year all-cause mortality: highest in Africa (34%) and India (23%); lowest in China (7%), South America (9%), Middle East (9%)	NR	<0.001
Farre, et al. [22]	3,580	Cases, Spain	Older HFpEF patients; Lower mortality in HFpEF; Fewer comorbidities in HFpEF	HFrEF: 1.0-3.9	0.037
Gerber, et al. [24]	2,762	Cases, Olmsted County, Minnesota	Declining HF incidence overall; Smaller decline in HFpEF; Lower CV mortality in HFpEF	HFpEF: -13% to -40%; HFrEF: 33% to -55%	<0.001
Zhao, et al. [23]	4,361	Adults >60, Black adults, Jackson, MS	Declining HFrEF incidence; Increasing HFpEF incidence; Consistent male predominance in HFrEF	HFrEF: 1.4-1.8	<0.001
Özlek ,et al. [27]	819	HFpEF patients, Turkey; APOLLON	Regional differences in clinical profiles and comorbidities	NR	<0.001 to 0.003
Mukhopadhyay, et al. [29]	6,247	HFrEF patients, New York	Higher medication non-adherence in low SES neighborhoods	Quartile 1 OR: 1.35-1.83; Quartile 2 OR: 1.16-1.56	<0.001
Teng, et al. [28]	4,540	Patients from 11 Asian regions	Reduced adherence to therapies in lower-income areas	1.04-1.73 (high-income regions)	<0.001, 0.040
Tromp, et al. [25]	18,102	Patients from 44 countries; REPORT-HF	Higher mortality in low-income countries and regions	1.41-1.77	<0.001
Witting, et al. [31]	126,670	VA HFrEF patients, USA	Lower ARNI treatment rates in socially vulnerable areas	NR	<0.001
Dunbar, et al. [30]	722	HFrEF patients, USA	Lower KCCQ-12 Overall Summary scores associated with having a care partner; Perceived medication affordability correlated with higher scores	9.6-point decrease; 7.0-point increase	<0.001; 0.02

Linking Outcomes to Socioeconomic and Geographic Factors

The disparities in outcomes between heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF) are not solely a reflection of biological differences but are significantly shaped by socioeconomic and geographic factors. Patients from lower socioeconomic backgrounds or residing in rural and underserved areas often face barriers to accessing advanced diagnostic tools and specialized care, which are crucial for managing complex conditions like HFpEF. For example, the better outcomes observed in HFpEF among wealthier populations may be skewed by their greater access to healthcare resources, leading to earlier diagnosis and more comprehensive management. The impact of socioeconomic factors also extends to HFrEF, albeit in different ways. This underscores the need for targeted interventions that address the unique challenges faced by both HFpEF and HFrEF patients across different socioeconomic strata. Regional variations in clinical profiles and treatment adherence further highlight the influence of geography and socioeconomic status on heart failure outcomes. Özlek ,et al. [27] reported significant differences in hypertension prevalence among HFpEF patients across different regions of Turkey [27].

Teng, et al. [28] found that patients from high-income regions were more likely to receive guideline-directed medical therapy than those from low- and middle-income regions across 11 Asian regions [28] Specifically, the odds of receiving such therapy were 1.35 times higher in high-income regions (95% CI: 1.04-1.73, p=0.040) [28]. A study by Witting et al. (2023) examining Veterans Affairs (VA) patients with recently diagnosed HFrEF provides nuanced insights into the relationship between sociodemographic characteristics and guideline-directed medical therapy (GDMT).31

1. Patients in socially vulnerable neighborhoods had 3.4% lower treatment rates with angiotensin receptor-neprilysin inhibitors (ARNIs) [31].

2. While patients living farther from specialty care had similar overall rates of GDMT, they were less likely to be taking at least 50% of the target doses of beta-blockers (4.0% less likely) or renin-angiotensin system inhibitors (5.0% less likely) compared to those closer to care [31].

Schultz, et al. [32] comprehensively reviewed the relationship between socioeconomic status (SES) and cardiovascular health, including heart failure [9].

1. SES has a measurable and significant effect on cardiovascular health, with biological, behavioral, and psychosocial risk factors more prevalent in disadvantaged individuals [9].

2. Four key measures are consistently associated with cardiovascular disease (CVD) in high-income countries: income level, educational attainment, employment status, and neighborhood socioeconomic factors.

3. While many interventions targeting low-SES patients have focused on modifying traditional CVD risk factors, emerging approaches show promise for implementation at individual, community, or population levels [9].

The COVID-19 pandemic has accelerated the adoption of telemedicine and demonstrated its usefulness across various healthcare settings. Salzano,et al. [32] conducted a study in Italy during the COVID-19 outbreak, implementing a telemedicine service (TMS) for heart failure patients. 32 Their findings demonstrated the effectiveness of telemedicine in managing heart failure patients during crises:

1. The TMS included phone numbers active 24/7, chat and video-conference services, and an email address.32

2. 58% of patients made at least one TMS access during the study period, with 51% of contacts leading to clinical decisions such as medication adjustments [32].

3. Compared to the same period in the previous year without TMS, patients with access to the TMS were significantly less likely to experience the primary outcome of heart failure hospitalization or death (p = 0.001) [32].

4. A significant reduction was observed specifically in heart failure hospitalizations (p = 0.001), although there was no difference in mortality[32].

5. Building on this, Tedeschi, et al. [33] highlighted the broader potential of telehealth in heart failure management [33]:

i. Telehealth can drive substantial qualitative improvements in clinical practice by developing patient-centered care and optimizing resources [33].

ii. It can lead to decreased outpatient visits, hospitalizations, and lengths of hospital stays, addressing some of the socioeconomic and geographic barriers to care [33].

iii. Emerging technologies, including artificial intelligence, show promise in anticipating patient deterioration and providing tailored care to various subsets of heart failure patients [33].

These findings emphasize the need for region-specific and socioeconomic-conscious approaches to heart failure management, particularly in under-resourced areas. Potential strategies could include:

1. Implementing telemedicine programs to improve access to specialized care in rural areas and for patients far from specialty care centers.

2. Developing community-based interventions to enhance medication adherence and proper dose titration in low-income neighborhoods and areas distant from specialty care.

3. Tailoring patient education materials to address cultural and socioeconomic factors that may influence treatment adherence and dose optimization.

4. Implementing structured physical activity programs tailored for low-SES populations.

5. Utilizing geo-mapping techniques to identify targets for large-scale interventions in areas with high social vulnerability.

6. Exploring task-shifting strategies to improve access to healthcare in underserved areas.

7. Integrating SES factors into CVD risk prediction models while accounting for cultural and regional differences.

By addressing the geographic and socioeconomic disparities in healthcare access, treatment adherence, and dose optimization, healthcare systems can work towards more equitable outcomes for patients with HFpEF and HFrEF. Implementing these strategies, particularly advanced telehealth solutions. As we move forward, it will be crucial to address the challenges associated with implementing telehealth solutions, ensure equitable access to these technologies, and continue to evaluate their effectiveness in diverse patient populations.

Sensitivity Analysis and Interpretation

We conducted a comprehensive sensitivity analysis to assess the robustness of our findings and explore the impact of various factors on heart failure outcomes. The analysis of mortality rates across studies demonstrated considerable variation, with rates ranging from 34% (95% CI: 32%-36%) in Dokainish, et al. [26] to 17% (95% CI: 15%-19%) in Tromp, et al. [25] To ensure the consistency of our data, we employed Z-scores and the Interquartile Range (IQR) method, which identified no significant outliers [34]. These findings strengthen the confidence in our overall conclusions.Geographical location emerged as a crucial factor influencing heart failure outcomes. Studies from low- to middle-income regions, particularly in Africa, Asia, and the Middle East, reported higher mortality rates and variations in clinical outcomes [35] For instance, Dokainish, et al. [26] observed an adjustment in in-hospital mortality rate from 85% to 80%, highlighting the influence of healthcare infrastructure and access disparities [25].Similarly, Tromp, et al. [25] showed a decrease in mortality rate from 17% to 15% after sensitivity adjustments, indicating significant regional differences in heart failure outcomes [26] .Income levels were found to influence both mortality rates and medication adherence significantly [26]. Lower-income regions consistently reported higher mortality and reduced adherence rates. Mukhopadhyay, et al. [29]highlighted higher medication non-adherence in low-income neighborhoods, with values adjusting from 33% to 30%. [29] These findings underscore the strong association between economic factors and heart failure outcomes.

Neighborhood socioeconomic status (nSES) also emerged as a critical factor. Lower nSES was associated with higher medication non-adherence and adverse outcomes. Studies focusing on socioeconomically disadvantaged populations showed significant reductions in adherence rates and increased health risks in low-nSES neighborhoods. [28,29].Heatmaps clearly illustrated variations in mortality rates across different regions and income levels, as well as differences in adherence rates across socioeconomic and geographical factors [35] This visual representation reinforces the importance of considering regional and economic factors in heart failure management. It underscores the importance of a nuanced, context-specific approach to heart failure management that considers different populations and regions' diverse needs and challenges [13]. Future research should aim to standardize data collection, analysis methods, and visualization practices to enhance the consistency and reliability of findings in this area. Addressing disparities through targeted interventions and policy changes can help healthcare providers and systems better manage heart failure and improve patient outcomes across diverse populations. The sensitivity analysis reinforces the main findings of our systematic review, highlighting the critical role of socioeconomic and geographic factors in heart failure outcomes. It emphasizes the need for a multifaceted approach to heart failure management that considers clinical factors and the broader socioeconomic and geographic context in which patients live and receive care.

Discussion

This systematic review reveals significant socioeconomic and geographic disparities in the diagnosis, management, and outcomes of HFpEF and HFrEF. These disparities are multifaceted and influenced by various factors, including income, neighborhood characteristics, and urban-rural divides.

Socioeconomic and Geographic Disparities

Patients from lower socioeconomic backgrounds or those residing in rural and underserved regions often face substantial barriers to accessing advanced diagnostic tools and specialized care, which are crucial for managing complex conditions like HFpEF. These barriers contribute to delayed or missed diagnoses, poorer management, and worse outcomes, particularly for HFrEF, where the disease progression tends to be more aggressive. In contrast, HFpEF, which often presents with more subtle symptoms, is more frequently diagnosed in wealthier populations and settings. This pattern suggests that access to comprehensive healthcare services, including advanced diagnostic testing and specialist consultations, is critical for identifying HFpEF. Additionally, Witting, et al. [31] found that patients residing in socially vulnerable neighborhoods had a 3.4% lower treatment rate with angiotensin receptor-neprilysin inhibitors (ARNIs), underscoring the impact of neighborhood-level socioeconomic factors on heart failure management [31]. Supporting literature underscores the need for healthcare systems to develop more effective and equitable strategies to address these disparities. Improving access to diagnostic tools and healthcare services in disadvantaged communities could help ensure that all patients, regardless of socioeconomic status or geographic location, receive timely and accurate diagnoses, leading to better management and outcomes for HFpEF and HFrEF.

Patient Characteristics

In this systematic review, patients with HFpEF tend to be older, female, and low-income, with different underlying etiology and comorbidities compared to those with the more commonly diagnosed HFrEF. When clinicians meet patients with risk factors for heart failure, those with the following demographic characteristics should be considered more closely based on the findings in the literature. Ensuring access to and follow-through with diagnostic testing and follow-up treatment could address disparities in HFpEF and HFrEF diagnosis and treatment.

- Age: Age is associated with increased rates of HF. Understanding the differences in age-related HF outcomes can help tailor screening and intervention strategies. For example, Chioncel, et al. [21] noted that HFpEF patients were generally older (mean age 69 vs. 64 years) compared to HFrEF patients, emphasizing the need to consider the patient's age in referral for testing and subsequent management of the condition [22] The increased prevalence of comorbidities such as hypertension and diabetes in olderpopulations further complicates HF and HF subtype man-

agement, necessitating comprehensive care plans that address multiple health issues simultaneously.

- Gender: Females tend to be a vulnerable population for underdiagnosis, and disparities across cardiovascular diagnoses and sex should be considered when deciding if screening is warranted for HFpEF. Studies such as Chioncel, et al. [21] and Farre, et al. [22] highlight that HFpEF is more prevalent in females (52% vs. 22% in HFrEF), and they often present with different symptoms compared to males, potentially leading to delays in diagnosis [21,22]. Addressing these sex-specific differences in HF presentation and management could improve diagnostic accuracy and treatment outcomes for female patients.

- Race/Ethnicity: While this systematic review identified some studies addressing racial and ethnic differences in HF outcomes, there remains a significant gap in the literature regarding how these factors specifically affect the diagnosis and management of HFpEF compared to HFrEF. Racial and ethnic minorities often face compounded barriers to healthcare, including limited access, socioeconomic challenges, and cultural differences, which can exacerbate disparities in HF outcomes. Further research must prioritize understanding how race and ethnicity intersect with other social determinants of health to impact HFpEF and HFrEF outcomes. This will not only enhance the accuracy of diagnosis but also improve the overall quality of care for underrepresented groups.

Geographic Variations

Our systematic review provides substantial evidence of significant urban-rural differences in cardiovascular disease diagnosis and outcomes, particularly in the context of heart failure. These findings align with and extend the current understanding of geographic disparities in heart failure care.Geographic location and socioeconomic factors are critical in shaping cardiovascular disease diagnosis, management, and treatment outcomes, including heart failure. [26-28,31] The influence of these factors on healthcare access, availability of specialized care, and social conditions can lead to significant disparities in patient outcomes. Yusuf, et al. [36] in their large-scale PURE study across 17 countries, demonstrated that cardiovascular risk factors and event rates vary substantially between low-, middle-, and high-income countries [36]. This study highlighted how economic development levels of countries significantly impact cardiovascular health outcomes, including heart failure.This is consistent with broader findings in the literature where geographic and socioeconomic disparities have been observed across various cardiovascular conditions. Similarly, Teng, et al. [28] demonstrated significant rural-urban differentials in 30-day and 1-year mortality following first-ever heart failure hospitalization in Western Australi [28] In the United States, Kulshreshtha, et al. [37] observed persistent urban-rural disparities in coronary heart disease mortality, with rural areas experiencing higher mortality rates [37] This is consistent with broader findings where geographic and socioeconomic disparities have been observed across various cardiovascular conditions.

Socioeconomic Impacts

This systematic review synthesizes current literature on socioeconomic disparities in HFpEF and HFrEF, revealing significant differences in diagnosis, management, and outcomes. The findings consistently demonstrate an association between lower socioeconomic status and poorer heart failure outcomes, particularly for patients with HFrEF. A landmark study by Dewan, et al. [38] provides robust evidence of the impact of income inequality on heart failure outcomes globally.38 They found that patients in countries with higher income inequality (higher Gini coefficients) had significantly worse outcomes, even after adjusting for standard prognostic variables and country-level factors was 1.46 (95% CI: 1.25 to 1.70) for countries with the highest income inequality compared to those with the lowest 1.30 (95% CI: 1.10 to 1.53), highlighting the substantial impact of societal, economic disparities on individual health outcomes [38].This global perspective is complemented by our review's findings from individual studies. Mukhopadhyay, et al. [29] found that patients from lower socioeconomic neighborhoods had higher odds of medication nonadherence [29]. This underscores the impact of socioeconomic status on treatment adherence, a critical factor in managing heart failure.

Tromp, et al. [25] reported that patients from low-income countries had higher 1-year all-cause mortality (HR 1.58; 95% CI 1.41-1.77) for both HFpEF and HFrEF, though HFpEF patients generally fared better (HR 0.67; 95% CI 0.61-0.74) [26] This further highlights the global impact of socioeconomic factors on heart failure outcomes. Interestingly, our review suggests that HFpEF, which is often more challenging to diagnose due to its subtle symptomatology, is more frequently diagnosed in wealthier populations. This pattern suggests that access to healthcare plays a crucial role in the timely and accurate diagnosis of HFpEF, potentially leading to underdiagnosis in less affluent communities.Understanding these socioeconomic disparities in HFpEF and HFrEF is crucial for identifying individuals needing early screening and intervention. Our review, supported by these studies, suggests that implementing community-based screening programs in regions with significant socioeconomic disadvantages could ensure more timely care. Additionally, integrating socioeconomic indicators into risk assessment and diagnostic models may help predict which patients would benefit most from intensified monitoring and personalized treatment plans, thereby addressing disparities and improving overall heart failure management.

Implications for Practice and Future Research

Our findings suggest a multi-faceted approach to address the unique challenges different patient populations face. Based on our review and additional supporting literature, we propose the following strategies:

1. Tailored Diagnostic Approaches: Increased screening for HFpEF in older female patients from lower socioeconomic backgrounds could improve early detection rates. Lam, et al. [39] emphasize the importance of sex-specific approaches in heart failure management, highlighting the unique risk factors and clinical presentations in women [39]. Additionally, Gupta, et al. [40] underscore the need for targeted strategies for African Americans with HFpEF [40].

2. Technology-Enabled Care: Expanding telemedicine services and mobile health units could bridge geographic gaps in HF care, particularly for rural populations. Ten Eyck et al. [41] demonstrated that comprehensive heart failure management programs can significantly improve outcomes in Medicare Advantage populations [41].

3. Community-Based Interventions: Partnerships with local organizations and culturally sensitive education and support groups can address the social determinants of health impacting HF outcomes. This aligns with Braveman, et al. [42] who highlight the importance of addressing socioeconomic health disparities [42].

4. Policy Advocacy: Sustainable funding of HF management programs and policy initiatives targeting vulnerable populations are crucial. Roth, et al. [43] emphasize the need for global strategies to reduce the burden of cardiovascular diseases, including heart failure [43].

5. Personalized Treatment Protocols: Developing personalized treatment protocols tailored to patients' specific needs with HFpEF and HFrEF while considering their socioeconomic context can improve outcomes.

Future Research Directions Should Include:

- Investigating the impact of obesity and diabetes on HFpEF and stroke risk, as Packer, et al. [44] highlighted .
- Exploring heart failure with preserved ejection fraction in younger populations, as Tromp, et al. [45] studied.
- Examining temporal trends in heart failure incidence across different populations, following the work of Conrad, et al. [46].

By integrating these strategies and research directions, healthcare systems can work towards more equitable and effective HF management, addressing the unique needs of diverse patient populations.

Limitations of Study

This study has several limitations. The heterogeneity in populations, healthcare systems, and HF subtype diagnostic criteria limits pooled analyses and may affect the generalizability of our findings. This heterogeneity is further complicated by differences in follow-up periods across studies and variability in how socioeconomic status is defined and measured across countries and regions. The variability in clinical endpoints complicates direct outcome comparisons between HF subtypes. Significant data gaps persist, particularly in low-to-middle-income countries, which restrict our ability to draw comprehensive conclusions. The quality of included studies varied, with some showing potential biases in patient selection or data collection methods. Assessing social determinants of health was challenging due to inconsistent reporting across studies. Our search strategy was limited to English-language publications, potentially excluding relevant studies from non-English-speaking countries and introducing language bias. Despite a comprehensive search strategy, some relevant studies may have been missed. Publication bias may also exist, as studies with significant findings are more likely to be published. Comparing studies from different periods presents challenges as diagnostic criteria and treatment standards may have evolved. These limitations highlight the complexities of drawing generalized conclusions about HF management disparities and emphasize caution when interpreting causality and applicability across diverse healthcare settings. Future research should standardize methodologies, include diverse populations, and focus on prospective longitudinal studies to better understand the long-term impact of socioeconomic and geographic factors on HF outcomes. Addressing these limitations through robust and diverse study designs will enhance the validity and applicability of future findings.

Conclusion

This systematic review underscores the significant influence of socioeconomic and geographic factors on the diagnosis, treatment, and outcomes of heart failure with preserved ejection fraction (HFpEF) and reduced ejection fraction (HFrEF). The disparities in healthcare access, treatment adherence, and clinical outcomes are tightly correlated with these factors, with those in lower socioeconomic groups or rural areas facing substantial barriers to receiving optimal care. These challenges exacerbate the underdiagnosis of HFpEF, particularly in marginalized communities where access to advanced diagnostic tools and specialist care is often lacking. The review highlights a complex interaction between environmental, sociodemographic, and intrinsic risk factors that shape the epidemiology and progression of heart failure. This complexity underscores the urgent need for targeted interventions to mitigate these disparities and identifies key variables to help pinpoint individuals at higher risk for HFpEF.

Addressing these disparities requires a comprehensive approach, including targeted interventions for low-income populations, enhanced access to specialized care in underserved areas, and policies that tackle broader social determinants of health. Implementing telehealth, alongside strategies such as community-based multidisciplinary teams and comprehensive prevention programs, could significantly reduce the socioeconomic and geographic disparities in heart failure outcomes highlighted in this review. Future research should prioritize prospective cohort studies that directly compare HFpEF and HFrEF outcomes across different socioeconomic strata and geo-

graphic regions using standardized endpoints and data collection methods. Research from low- and middle-income countries is critical to fill knowledge gaps. This review emphasizes the pivotal role of socioeconomic and geographic factors in shaping heart failure outcomes. By adopting the strategies and research directions outlined, healthcare systems can advance toward more equitable and effective heart failure management, better addressing the diverse needs of patient populations and ultimately improving outcomes for all those affected by this complex condition.

Ethics Committee & Informed Consent

Not required for systematic review.

Conflicts of Interest

The authors declare no potential conflicts of interest.

Acknowledgments

We want to thank the University of Jamestown Clinical Research program team for their unwavering support and valuable resources throughout this study. Special thanks to the librarians at the University of Jamestown for their expert assistance in sourcing and organizing the extensive literature required for this systematic review.

Funding

This work did not receive any public or private funding.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2024.59.009372

Kiki Estes Schmalzl. Biomed J Sci & Tech Res