


The role of comorbidities, medications, and social determinants of health in understanding urban-rural outcome differences among patients with heart failure

Emily P. Zeitler MD,MHS^{1,2}  | Joanna Joly MD³ | Christopher G. Leggett PhD² |
 Sandra L. Wong MD,MS^{2,4} | A. James O'Malley PhD² | Sally A. Kraft MD,MPH⁵ |
 Matthew B. Mackwood MD,MPH^{2,6} | Sarah T. Jones MPH^{1,2} | Jonathan S. Skinner PhD^{2,7}

¹Dartmouth-Hitchcock Medical Center, Heart and Vascular Center, Lebanon, New Hampshire, USA

²The Dartmouth Institute, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire, USA

³Division of Cardiovascular Disease, University of Alabama at Birmingham, Birmingham, Alabama, USA

⁴Department of Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, USA

⁵Dartmouth-Hitchcock Medical Center, Center for Population Health, Lebanon, New Hampshire, USA

⁶Department of General Internal Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, USA

⁷Department of Economics, Dartmouth College, Hanover, New Hampshire, USA

Correspondence

Emily P. Zeitler, Dartmouth-Hitchcock Medical Center, The Dartmouth Institute, 1 Medical Center Drive, Lebanon, NH 03766.
 Email: emily.p.zeitler@dartmouth.edu

Abstract

Purpose: There is now a 20% disparity in all-cause, excess deaths between urban and rural areas, much of which is driven by disparities in cardiovascular death. We sought to explain the sources of these disparities for Medicare beneficiaries with heart failure with reduced ejection fraction (HFrEF).

Methods: Using a sample of Medicare Parts A, B, and D, we created a cohort of 389,528 fee-for-service beneficiaries with at least 1 heart failure hospitalization from 2008 to 2017. The primary outcome was 30-day mortality after discharge; 1-year mortality, readmissions, and return emergency room (ER) admissions were secondary outcomes. We used hierarchical, logistic regression modeling to determine the contribution of comorbidities, guideline-directed medical therapy (GDMT), and social determinants of health (SDOH) to outcomes.

Results: Thirty-day mortality rates after hospital discharge were 6.3% in rural areas compared to 5.7% in urban regions ($P < .001$); after adjusting for patient health and GDMT receipt, the 30-day mortality odds ratio for rural residence was 1.201 (95% CI 1.164-1.239). Adding the SDOH measure reduced the odds ratio somewhat (1.140, 95% CI 1.103-1.178) but a gap remained. Readmission rates in rural areas were consistently lower for all model specifications, while ER admissions were consistently higher.

Conclusions: Among patients with HFrEF, living in a rural area is associated with an increased risk of death and return ER visits within 30 days of discharge from HF hospitalization. Differences in SDOH appear to partially explain mortality differences but the remaining gap may be the consequence of rural-urban differences in HF treatment.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](https://creativecommons.org/licenses/by-nc/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2023 The Authors. *The Journal of Rural Health* published by Wiley Periodicals LLC on behalf of National Rural Health Association.

INTRODUCTION

More than 60 million people, almost 1/5th of the US population, live in rural areas.¹ These individuals, on average, have higher rates of cardiovascular risk factors, including smoking,² obesity,³ and diabetes,⁴ which likely contribute to the higher prevalence of common cardiac conditions like heart failure (HF) in rural areas.⁵ While the overall incidence of HF in the United States has fallen over the last 3 decades, the incidence of new disease is actually rising again in some rural areas.⁵

Over the last 30 years, urban/rural disparities in health outcomes have worsened and there is now a 20% disparity in all-cause, excess deaths between urban and rural areas,⁶ much of which is driven by disparities in cardiovascular death.^{7,8} While HF mortality has been declining among patients in urban areas, HF mortality in rural areas has remained relatively stable, and in some areas, appears to be increasing.⁵ Recent data from 6 southeastern Minnesota counties found that among patients with HF, living in a rural area was independently associated with an 18% increased risk of death.⁹ Other work using the CDC's WONDER database found that age-adjusted mortality rates were consistently higher for rural residents with HF compared to urban residents with HF.¹⁰

The reasons for this higher mortality rate among rural residents with HF are not well understood. Higher comorbidity burdens,^{2-4,7} suboptimal implementation of guideline-directed medical therapy (GDMT),¹¹ and social determinants of health (SDOH)¹²⁻¹⁴ have all been proposed as potential explanations. The aim of this study is to investigate why rural HF mortality is higher than in urban areas. Furthermore, because HF decompensation events as identified by heart failure hospitalizations (HFH) and visits to the emergency room (ER)^{15,16} have long been associated with mortality in HF^{17,18} with relationships that appears to vary by rurality,^{9,19} differences on these measures were explored. We hypothesize that for patients with heart failure with reduced ejection fraction (HFrEF) aged 65 and over, the rural-urban gap could be explained in part by 3 general factors: differential comorbidity burdens, variation in the use of GDMT, and SDOH.

METHODS

Study population

We used the 100% national sample of patients enrolled in both Medicare Parts A and B and a random 40% sample for Part D enrollment to create a cohort of 389,528 fee-for-service (FFS) beneficiaries with at least 1 HFH (index admission) for HFrEF between 2008 and 2017. We required 1 year of FFS coverage prior to and after the index HFrEF admission to determine patient characteristics and outcomes. Only the patient's first HFH for HFrEF during the study period was included to avoid over-counting high utilizers. Patients who died during admission, were transferred to another facility, were in post-acute care 30 days after discharge (to enable determination

of drug use after discharge), left against medical advice, or received advanced therapies were excluded since we could not reliably assess their outcomes. Patients with a previously placed durable ventricular assist device or a prior cardiac transplant were also excluded as they represent more advanced disease which requires different management. HFrEF was defined using International Classification of Diseases (ICD) 9 and 10 codes and a previously validated methodology (Appendix S1).^{20,21}

Baseline characteristics

Age, sex, race/ethnicity, and dual-enrollment status were obtained directly from the Master Beneficiary Summary File. ZIP code-level estimates for socioeconomic variables were obtained using the patient's ZIP code and 5-year estimates from the 2012 American Community Survey data.²² Patient residence and geographic region of residence was ascertained using the patient's ZIP code and US Census regions.²³

Predetermined variables of interest

Comorbidities were determined using the well-validated Elixhauser comorbidity algorithm.²⁴ GDMT use was determined using National Drug Codes from Medicare Part D for beta-blockers, renin-angiotensin-aldosterone system inhibitors (RAASi) (including angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and angiotensin and neprilysin inhibitors) and mineralocorticoid receptor antagonists (MRAs). Sodium-glucose cotransporter-2 (SGLT-2) inhibitors were not included given that their United States Food and Drug Administration (FDA) approval date occurred after our study period. Use of these medications was determined based on the presence of a claim for a drug fill within 30 days of discharge from the index (ie, qualifying) hospitalization. SDOH were assessed using individual-level dual-eligibility status and the area deprivation index (ADI), which is a standardized 4-dimensional evaluation of a region's socioeconomic conditions encompassing poverty, housing, employment, and education.²⁵ Since ADI is based on census blocks, for purposes of this analysis, it was aggregated to ZIP codes by weighting each component tract's measure by how many of the ZIP's residences are in the tract.

Exposure

Rurality was assessed using the beneficiary's address at the time of the index HFrEF admission and rural-urban commuting areas (RUCA) codes.²⁶ RUCA codes classify ZIP codes using population density, urbanization, and commuting patterns. In this study, we classified ZIP codes as "urban" if the primary commuting flow was to, or within, an urban area, or if at least 30% of the secondary flow was to an urban area (Appendix S2).⁹

Outcomes

The primary outcome was 30-day mortality after hospital discharge. Secondary outcomes included 30-day readmission and 30-day ER visits (without hospitalization), and 1-year mortality and readmission rates. We also considered trends between 2008 and 2017 for outcome variables.

Statistical methods

Hierarchical, logistic regression modeling was used to examine the association between rurality and outcomes with increasing complexity from Model 1 to Model 4 as groups of independent variables were added serially. This approach was based on the a priori hypothesis that groups of independent variables (rather than single variables) would be associated with differential outcomes based on rurality. For example, GDMT was included as a group of independent variables in Models 3 and 4 since this might be meaningfully different between urban and rural groups based on access to HF specialists, whereas no such hypothesis exists for the individual components of GDMT. The models were as follows:

1. **Model 1 (base model): age + sex + race/ethnicity:** This model controls only for differences in age, sex, and race and serves as the baseline model for subsequent analyses.
2. **Model 2 (comorbidities): Model 1 + comorbidities:** In addition to the variables in Model 1, this model also includes patient-level comorbidities, prior HFHs (1, 2, or 3+), and the presence/absence of an implantable cardioverter defibrillator (ICD).
3. **Model 3 (GDMT): Model 2 + GDMT:** In addition to the variables in Model 2, this model also includes GDMT use before and after hospital discharge.
4. **Model 4 (SDOH): Model 3 + SDOH:** In addition to the variables in Model 3, this model also includes ADI and dual-eligibility status.

A full listing of the variables included in each model is included in Appendix S3.

These 4 models were used to better understand why outcomes differed according to urban/rural status. (In sensitivity analysis for the primary outcome of 30-day mortality, we also consider Model 1 with just the addition of SDOH.) All hypotheses were tested using 2-sided tests, and P values $<.05$ were considered significant. All analyses were performed between September 2021 and October 2022 using SAS version 9.4. This study is compliant with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies and was approved by the Institutional Review Board at Dartmouth Hitchcock Medical Center.

RESULTS

The study cohort included 389,528 patients with HFREF admitted for acute decompensated heart failure between January 31, 2008, and

December 31, 2017 (Table 1). Twenty-five percent ($n = 98,0447$) lived in rural areas, and 75% ($n = 2291,481$) lived in urban areas. Age distributions were similar, and 53% of patients in rural and urban areas were women. In rural areas, 6% of patients identified as Black, compared to 10% of patients in urban areas. On average, patients living in rural areas were more socioeconomically disadvantaged, as evidenced by greater likelihood of Medicaid-eligibility (dual eligibility), lower median income, and lower rates of bachelor's degree completion. Comorbidity rates are notable for modestly higher rates of peripheral vascular disease in urban areas (26% vs 21%) and chronic lung disease (34% vs 31%) in rural areas. A full description of all Elixhauser comorbidities is available in Appendix S4.

HF therapies prior to hospitalization were similar between urban and rural cohorts. A similar proportion of patients from urban and rural areas had an ICD in situ (13.2% vs 12.4%). GDMT use prior to HFH was slightly *higher* in rural areas: beta blocker 51.8% rural versus 51.2% urban; RAASi 50.7% rural versus 49.2% urban; and MRA 10.2% rural versus 8.8% urban areas (Table 1).

Unadjusted 30-day outcome rates are displayed in Table 2. Death within 30 days of discharge was higher in rural areas, 6.3% versus 5.7%, $P < .001$. ER visits within 30 days were also higher in rural areas, 11.9% versus 9.6% $P < .001$. Unadjusted 30-day readmission rates were lower in rural areas, 20.6% versus 21.3%, $P < .001$. At 1 year, mortality was similar between groups in urban and rural areas (32.3% vs 31.8%), and readmissions were higher among patients in urban areas (61.9% vs 63.9%).

Between 2008 and 2017, 30-day outcome trends are displayed in Figure 1 and show decreases in 30-day mortality (-0.8% rural; -1% urban) and readmission rates (-4.2% rural; -3.5% urban) and increases in 30-day ER visits ($+1.5\%$ rural; $+1.1\%$ urban). One-year outcome trends are shown in Figure 2. Mortality (-4% rural; -4.5% urban) and readmission (-7.9% rural; -7.1% urban) rates declined for all beneficiaries. Across the years, 30-day mortality and 30-day ER use remained higher in rural areas. The urban and rural 30-day and 1-year readmission trend lines began to separate between 2012 and 2013, which is when the Hospital Readmission Reduction Program was implemented.

Table 3 provides estimates for each of the models with an increasing number of covariates. For 30-day mortality, the baseline odds ratio for the rural variable was 1.152 (95% CI 1.128-1.188). With the addition of prior HFHs, comorbidities, and the presence of an ICD, the odds ratio rose to 1.178 (95% CI 1.143-1.215); adding GDMT further increased the odds ratio to 1.201 in Model 3 (95% CI 1.164-1.239). In Model 4, both the ADI measure (odds ratio 1.618, 95% CI 1.46-1.793) and the individual dual-eligibility variable (odds ratio 1.050, 95% CI 1.017-1.084) were positive and significant. Including SDOH variables (Model 4) reduced the odds ratio for rural residence by 0.061-1.140 (95% CI 1.103-1.178). In sensitivity analysis, we added the SDOH variables to just the baseline Model 1, leading to a mortality odds ratio for rural residence of 1.089 (95% CI 1.055-1.124), or a decline in the odds ratio of 0.063. When considering 1-year mortality, the baseline odds ratio for rurality (Model 1) is lower in magnitude (1.059, 95% CI 1.042-1.076) compared to the 30-day odds ratio. When all additional variables are included including SDOH, the odds ratio declines to 1.034 (95% CI 1.017-1.052).

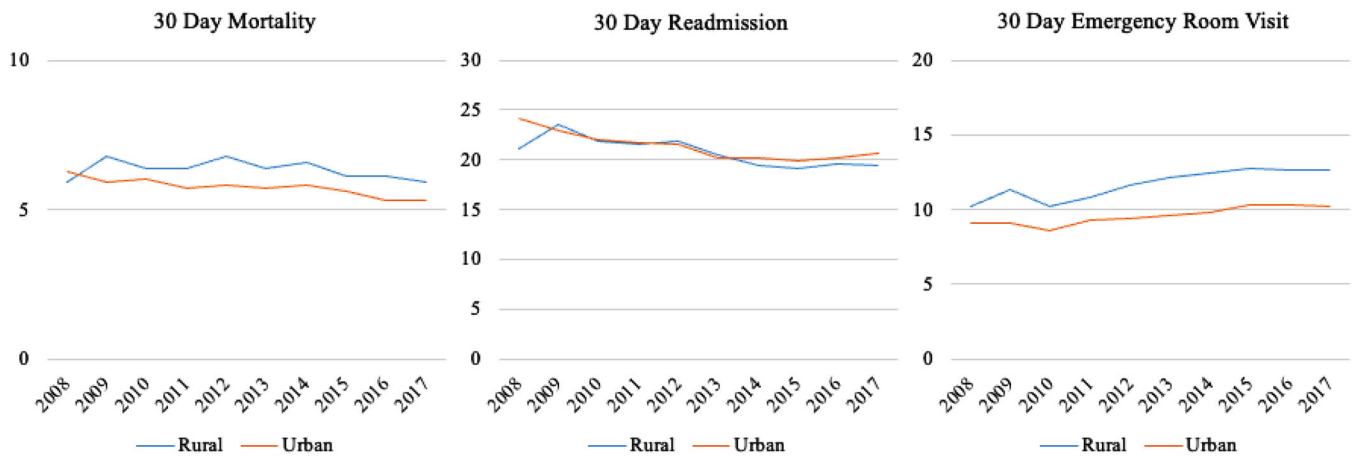


FIGURE 1 30-Day outcome trends, 2008-2017.

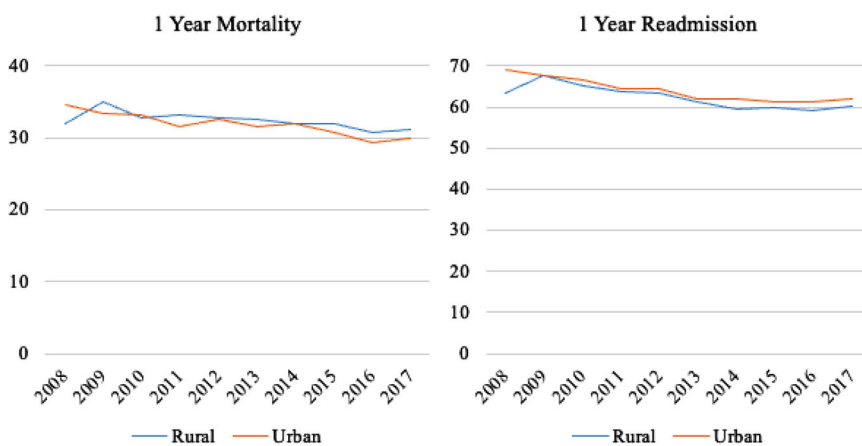


FIGURE 2 One-year outcome trends, 2008-2017.

In Table 3, we present additional model estimates for secondary outcome variables. The odds ratio for 30-day readmission in Model 1 was 0.969 (95% CI .951-.986), while for Model 4 with all covariates added, the odds ratio was essentially unchanged (0.954, 95% CI .935-.972); results were similar when considering 1-year readmission. For ER visits, the baseline estimates (Model 1) showed higher rates in rural areas (odds ratio 1.286, 95% CI 1.257-1.317), with similar findings for the other 3 Models (for Model 4 with all covariates, the odds ratio was 1.259, 95% CI 1.229-1.291).

DISCUSSION

While 20% of the US population lives in rural areas, approximately 25% of FFS Medicare beneficiaries with HFrEF live in rural areas. Compared to patients in urban areas, patients in rural areas with HFrEF are more likely to be White, live in the Midwest and South, and be socioeconomically disadvantaged. As previous studies had found, we also measured a rural disadvantage for patients with HFrEF, with a baseline 30-day odds ratio of death of 1.152. These findings confirm prior work^{9,27} and

extend those prior findings to a larger nationally representative sample. We also found that in rural areas, 30-day ER visit rates are higher, while 30-day readmission rates are lower.

We hypothesized that this excess mortality could be the consequence first of higher rates of comorbidities, including prior hospitalizations and rates of ICD presence. Prior work has demonstrated that, on average, comorbidity rates are higher in rural areas²⁸ and are known to be associated with outcomes as is the burden of prior HFH. Furthermore, the presence of an ICD would be expected to reduce the risk of mortality among eligible patients with HFrEF,^{29,30} but this treatment is applied less frequently among populations in rural areas. Second, we hypothesized that a lack of access to primary care could lead to lower use of guideline-directed medical therapy (GDMT) in rural areas, which could further explain the rural-urban gap in mortality. Finally, we hypothesized that rural areas could suffer from a larger health burden arising from SDOH.

We were surprised to find that the unexplained rural-urban gap in outcomes, as summarized by the rural odds ratio, became larger with the introduction of comorbidities and prior hospitalization and ICD use; this was because Medicare beneficiaries in rural areas are slightly healthier than their urban counterparts. For those baseline

TABLE 1 Beneficiary characteristics by rurality, 2008-2017.

	Rural		Urban	
	N	%	N	%
	98,047	25.24	291,481	74.75
Age (years)				
66-74	30,210	30.81	81,866	28.09
75-84	38,832	39.61	111,366	38.21
85+	29,005	29.58	98,249	33.71
Female sex	51,924	52.96	154,202	52.90
Race				
White	87,775	89.52	235,698	80.86
Black	6,058	6.18	29,624	10.16
Hispanic	2,436	2.48	17,036	5.84
Other	1,778	1.81	9,123	3.13
Geographic region				
Midwest	32,175	32.82	69,183	23.73
Northeast	10,252	10.46	71,103	24.39
South	45,679	46.59	108,556	37.24
West	9,941	10.14	42,639	14.63
Socioeconomic status				
Dual eligible	35,897		95,217	
% with bachelor's degree ^a		17.82		30.24
% Under federal poverty line ^a		18.39		14.68
Area deprivation index ^a (average)		106.47		97.19
# Hospitalizations in prior year				
0	45,400	46.30	138,471	47.51
1-2	40,043	40.84	116,574	40.00
3+	12,604	12.86	36,436	12.50
Elixhauser comorbidities^b				
Hypertension	79,755	81.3	241,352	82.8
Peripheral vascular disease	20,998	21.4	75,071	25.8
Chronic lung disease	33,145	33.8	91,449	31.4
Diabetes	43,426	44.3	129,212	44.3
Renal failure	25,720	26.2	81,548	28.0
ICD in place	12,186	12.4	38,599	13.2
GDMT use at admission^c				
Beta-blocker	50,745	51.8	149,121	51.2
RAAS inhibitor	49,720	50.7	143,540	49.2
MRA	9,980	10.2	25,721	8.8

(Continues)

TABLE 1 (Continued)

	Rural		Urban	
	N	%	N	%
GDMT use at discharge^d				
Beta-blocker	47,641	48.6	138,525	47.5
RAAS inhibitor	39,429	40.2	111,431	38.2
MRA ^c	12,544	12.8	33,989	11.7

Notes: GDMT is guideline-directed medical therapy (beta blocker + RAAS inhibitor + MRA); RAAS is renin-angiotensin aldosterone system; MRA is mineralocorticoid receptor antagonist; ICD is implantable cardioverter defibrillator.

Beta-blockers include: carvedilol, metoprolol, and bisoprolol (all HFrEF-specific beta-blockers).

RAAS inhibitors include: angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and angiotensin and neprolysin inhibitors (ARNIs).

MRA is mineralocorticoid receptor antagonists which include: spironolactone and eplerenone.

^aDetermined at the ZCTA-level.

^bSelect comorbidities, full comorbidity details in Appendix S3.

^cDefined by ≥ 1 drug fill during 90 days prior to admission.

^dDefined by ≥ 1 drug fill within 30 days of hospital discharge.

TABLE 2 Short- and long-term outcomes, by rurality, 2008-2017.

	Rural		Urban		P value
	N	%	N	%	
30d death	6,223	6.3%	16,676	5.7%	<0.001
30d readmission	20,208	20.6%	62,081	21.3%	<0.001
ER visit within 30d	11,712	11.9%	27,915	9.6%	<0.001
1 yr death	31,637	32.3%	92,809	31.8%	0.008
1 yr readmission	60,670	61.9%	186,389	63.9%	<0.001

Note: 30d is 30 days; 1 yr is 1 year; ER is emergency room.

comorbidities measured in the specific population in these analyses, some were more prevalent in the rural cohort (eg, chronic lung disease), while others were more prevalent in the urban cohort (eg, peripheral vascular disease), and others were nearly equal (eg, diabetes). Similarly, in this study, we showed that appropriate GDMT use rates are *higher* in rural areas; since GDMT use is associated with better outcomes,^{31,32} this widens the rural/urban gap and makes such differences harder to explain. Thus, our first 2 hypotheses seeking to explain excess mortality in rural areas were not supported by the data.

However, SDOH, which included both individual-level measures (eg, dual eligibility) and area-level measures (eg, ADI), do appear to partially explain the gap in rural and urban health outcomes for this sample of older patients with HFrEF. This is an intriguing result because at least some SDOH measures are modifiable to some degree. SDOH include socioeconomic status, education, environment, employment, support networks, and health care access, which are known to be strongly

TABLE 3 Hierarchical models for outcomes, by rurality, 2008-2017.

	Odds ratio for rural	Lower 95% CI	Upper 95% CI	P value
Death within 30 days				
Baseline Model 1: Age/Sex/Race	1.152	1.118	1.188	<0.001
Model 2: Age/Sex/Race + HFH + ICD + Comorbidities	1.178	1.143	1.215	<0.001
Model 3: Age/Sex/Race + HFH + ICD + Comorbidities + GDMT	1.201	1.164	1.239	<0.001
Model 4: Age/Sex/Race + HFH + ICD + Comorbidities + GDMT + SDOH	1.140	1.103	1.178	<0.001
Readmission within 30 days				
Baseline Model 1: Age/Sex/Race	0.969	0.951	0.986	<0.001
Model 2: Age/Sex/Race + HFH + ICD + Comorbidities	0.976	0.958	0.994	0.009
Model 3: Age/Sex/Race + HFH + ICD + Comorbidities + GDMT	0.979	0.961	0.997	0.020
Model 4: Age/Sex/Race + HFH + ICD + Comorbidities + GDMT + SDOH	0.954	0.935	0.972	<0.001
ER visit (without hospitalization) within 30 days				
Baseline Model 1: Age/Sex/Race	1.286	1.257	1.317	<0.001
Model 2: Age/Sex/Race + HFH + ICD + Comorbidities	1.292	1.262	1.323	<0.001
Model 3: Age/Sex/Race + HFH + ICD + Comorbidities + GDMT	1.291	1.262	1.322	<0.001
Model 4: Age/Sex/Race + HFH + ICD + Comorbidities + GDMT + SDOH	1.259	1.229	1.291	<0.001
Death within 1 year				
Baseline Model 1: Age/Sex/Race	1.059	1.042	1.076	<0.001
Model 2: Age/Sex/Race + HFH + ICD + Comorbidities	1.090	1.072	1.108	<0.001
Model 3: Age/Sex/Race + HFH + ICD + Comorbidities + GDMT	1.101	1.083	1.119	<0.001
Model 4: Age/Sex/Race + HFH + ICD + Comorbidities + GDMT + SDOH	1.034	1.017	1.052	<0.001
Readmission within 1 year				
Baseline Model 1: Age/Sex/Race	0.932	0.918	0.946	<0.001
Model 2: Age/Sex/Race + HFH + ICD + Comorbidities	0.936	0.922	0.951	<0.001
Model 3: Age/Sex/Race + HFH + ICD + Comorbidities + GDMT	0.937	0.923	0.952	<0.001
Model 4: Age/Sex/Race + HFH + ICD + Comorbidities + GDMT + SDOH	0.902	0.887	0.916	<0.001

Note: HFH is heart failure hospitalization categorized as 1, 2, or 3+; GDMT is guideline-directed medical therapy for heart failure; SDOH is social determinants of health including area deprivation index (ADI) at the ZIP code level and Medicare/Medicaid dual eligibility.

associated with health outcomes,³³⁻³⁵ and rural disparities have been described in other diseases.³⁶⁻³⁹ Additional work to describe which SDOH and combinations of SDOH are most strongly associated with patient outcomes in different types of rural areas could meaningfully inform regional quality improvement initiatives, system and community partnerships, and policy discussions focused on improving rural care. At a minimum, these findings based on aggregated SDOH measures reinforce a growing body of evidence supporting the evaluation of SDOH upon hospital discharge for HF patients.^{28,40,41}

Despite the importance of SDOH, there still remains an unexplained rurality gap of 1.140 in the 30-day mortality odds ratio. That it is so high (especially relative to the 1-year mortality odds ratio of 1.034) is suggestive of rural-urban differences in inpatient and ER care for HF patients. For example, this study and others have noted rising rates of ER use within 30 days of hospital discharge and lower readmission rates in rural areas.⁹ These 2 trends together raise concern about rural hospital bed capacity, which is known to be more limited than urban bed capacity and which has been negatively impacted by recent rural hospital closures.⁴² In practice, this may result in prolonged manage-

ment of patients with HF in the ER setting, deferring of admission by clinicians even when clinically indicated to reduce the risk of decompensation, or acting as a deterrent to community members with HF/EF who might otherwise seek inpatient care. Indeed, lower readmission rates at 30 days and 1 year among the rural cohort may partially reflect these pressures along with the potential impact of alternative payment programs which use readmission rates to determine financial penalties and may have inadvertently incentivized suboptimal outcomes in rural areas where hospital margins are thinner and the threat of financial penalties is, therefore, greater.

LIMITATIONS AND STRENGTHS

While this study presents new findings that expand our understanding of rural HF/EF care specifically and rural chronic disease management more broadly, it should be interpreted within the context of its limitations. The primary limitation of this study is its reliance on claims data. While this affords a large, national sample size, it does limit the

granularity of the data that can be examined; findings based on characteristics summarized by area (eg, ADI) cannot necessarily be applied to each individual patient in the cohort. Second, in the absence of a consensus on how to define rurality in claims data and to simplify the analyses, rurality was divided into only 2 categories: rural and urban based on associated RUCA codes. Future studies may explore different approaches to measuring rurality, as well as including additional health measures, including clinical lab values, imaging data, and cardiac resynchronization therapy.

The third key limitation is that our study relies on the FFS Medicare population. While highly reliable from a longitudinal perspective, the use of Medicare data restricts our findings to patients ≥ 65 years of age with continuous FFS coverage and Part D enrollment. Thus, the results may not be generalizable to younger, non-Medicare patients. Finally, as with any observational study, we cannot exclude the potential for unmeasured confounding.

Despite these limitations, the use of claims data in this study allows us to present large, nationally representative findings extending many prior studies that were smaller or limited to single centers or specific regions.^{5,9} The prior studies that did use larger samples did not separate reduced and preserved ejection fraction,^{43,44} thereby limiting the possibility of considering appropriate drug use. Finally, we used RUCA codes at the ZIP code level to define rurality. This allowed us to examine rural “pockets” within more metropolitan counties and vice versa and afforded us a more nuanced assessment of rurality as compared to country or hospital referral region-level approaches.²⁶

CONCLUSIONS

Among patients with HF rEF, the associations of HF outcomes with living in a rural area versus an urban one are mixed. On the one hand, despite greater odds of a return ER visit within 30 days of hospital discharge for HF exacerbation, living in a rural area is associated with a lower risk of hospital readmission at 30 days and 1 year. On the other hand, living in a rural area is associated with a significantly increased risk of death at 30 days and 1 year following HF hospitalization. When accounting for SDOH at the patient and area level, observed urban-rural differences in mortality among patients with HF rEF are diminished, but there is still a clinically important gap in mortality risk for patients in rural areas that may be related to differences in the management of HF in the ER and inpatient settings.

ACKNOWLEDGMENTS

The authors wish to acknowledge the dedication to populations of patients with heart failure in rural areas and the scientific work of Dr. Lauren Gilstrap who designed this study as part of an award by the NHLBI (K23HL142835) without which this work would never have been done. In addition to conceiving of this work and designing the protocol, Dr. Gilstrap interpreted the outputs and wrote the original draft of the manuscript. She also began revisions to this manuscript in

response to peer review, but her untimely death preceded resubmission. We are indebted to the work and friendship of Dr. Gilstrap and dedicate this work in her honor.

FUNDING INFORMATION

This work was originally supported by the National Heart, Lung, and Blood Institute (NHLBI) (K23HL142835 to Lauren Gilstrap). This funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication. After Dr. Gilstrap's death and the closure of this award, the continuation and completion of this work was performed without funding.

CONFLICT OF INTEREST STATEMENT

Dr. Skinner is a consultant for Sutter Health, an investor in Dorsata, Inc., and was a consultant for the Eurasia Group. Dr. Zeitler reports consulting for Sanofi, Medtronic, and Biosense Webster; research support from the National Institutes of Health, Biosense Webster, and Sanofi; travel and speaking for Medtronic, Abbott, and Sanofi. The remaining authors have no relationships with the industry to report.

ORCID

Emily P. Zeitler MD, MHS  <https://orcid.org/0000-0002-4848-4775>

REFERENCES

- Harrington RA, Califf RM, Balamurugan A, Brown N, Benjamin RM, Braund WE, Hipp J, Konig M, Sanchez E, Joynt Maddox KE. Call to Action: Rural Health: A Presidential Advisory From the American Heart Association and American Stroke Association. *Circulation*. 2020 Mar 10;141(10):e615-e644. doi: 10.1161/CIR.0000000000000753. Epub 2020 Feb 10. PMID: 32078375.
- Agunwamba AA, Kawachi I, Williams DR, Finney Rutten LJ, Wilson PM, Viswanath K. Mental health, racial discrimination, and tobacco use differences across rural-urban California. *J Rural Health*. 2017;33:180-189.
- Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in obesity among adults in the United States, 2005 to 2014. *JAMA*. 2016;315:2284-2291.
- Callaghan T, Ferdinand AO, Akinlotan MA, Towne SD, Jr., Bolin J. The changing landscape of diabetes mortality in the United States across region and rurality, 1999–2016. *J Rural Health*. 2020;36:410-415.
- Sun LY, Tu JV, Sherrard H, et al. Sex-specific trends in incidence and mortality for urban and rural ambulatory patients with heart failure in eastern Ontario from 1994 to 2013. *J Card Fail*. 2018;24:568-574.
- Cosby AG, McDoom-Echebiri MM, James W, Khandekar H, Brown W, Hanna HL. Growth and persistence of place-based mortality in the United States: the rural mortality penalty. *Am J Public Health*. 2019;109:155-162.
- Kulshreshtha A, Goyal A, Dabhadkar K, Veledar E, Vaccarino V. Urban-rural differences in coronary heart disease mortality in the United States: 1999–2009. *Public Health Rep*. 2014;129:19-29.
- Cross SH, Mehra MR, Bhatt DL, et al. Rural-urban differences in cardiovascular mortality in the US, 1999–2017. *JAMA*. 2020;323:1852-1854.
- Manemann SM, St Sauver J, Henning-Smith C, et al. Rurality, death, and healthcare utilization in heart failure in the community. *J Am Heart Assoc*. 2021;10:e018026.

10. Pierce JB, Shah NS, Petito LC, et al. Trends in heart failure-related cardiovascular mortality in rural versus urban United States counties, 2011–2018: a cross-sectional study. *PLoS One*. 2021;16:e0246813.
11. Moscovice I, Rosenblatt R. Quality-of-care challenges for rural health. *J Rural Health*. 2000;16:168-176.
12. Douthit N, Kiv S, Dwolatzky T, Biswas S. Exposing some important barriers to health care access in the rural USA. *Public Health*. 2015;129:611-620.
13. Goins RT, Williams KA, Carter MW, Spencer M, Solovieva T. Perceived barriers to health care access among rural older adults: a qualitative study. *J Rural Health*. 2005;21:206-213.
14. Henning-Smith C, Evenson A, Corbett A, Kozhimannil K, Moscovice I. Rural Transportation: Challenges and Opportunities. <https://rhrc.umn.edu/publication/rural-transportation-challenges-and-opportunities/>
15. Ezekowitz JA, Bakal JA, Kaul P, Westerhout CM, Armstrong PW. Acute heart failure in the emergency department: short and long-term outcomes of elderly patients with heart failure. *Eur J Heart Fail*. 2008;10:308-314.
16. Lee DS, Schull MJ, Alter DA, et al. Early deaths in patients with heart failure discharged from the emergency department: a population-based analysis. *Circ Heart Fail*. 2010;3:228-235.
17. Setoguchi S, Stevenson LW, Schneeweiss S. Repeated hospitalizations predict mortality in the community population with heart failure. *Am Heart J*. 2007;154:260-266.
18. Solomon SD, Dobson J, Pocock S, et al. Influence of nonfatal hospitalization for heart failure on subsequent mortality in patients with chronic heart failure. *Circulation*. 2007;116:1482-1487.
19. Loccoh EC, Joynt Maddox KE, Wang Y, Kazi DS, Yeh RW, Wadhwa RK. Rural-urban disparities in outcomes of myocardial infarction, heart failure, and stroke in the United States. *J Am Coll Cardiol*. 2022;79:267-279.
20. Gilstrap L, Austin AM, Gladders B, et al. The association between neurohormonal therapy and mortality in older adults with heart failure with reduced ejection fraction. *J Am Geriatr Soc*. 2021;69:2811-2820.
21. Gilstrap L, Austin AM, O'Malley AJ, et al. Association between beta-blockers and mortality and readmission in older patients with heart failure: an instrumental variable analysis. *J Gen Intern Med*. 2021;36:2361-2369.
22. ACS. American Community Survey. 2018. Accessed September 7, 2018. <https://www.census.gov/programs-surveys/acs/>
23. CDC. Census Regions and Divisions in the United States. 2017. Accessed July 1, 2018. https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf
24. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998;36:8-27.
25. Singh GK. Area deprivation and widening inequalities in US mortality, 1969–1998. *Am J Public Health*. 2003;93:1137-1143.
26. Hall SA, Kaufman JS, Ricketts TC. Defining urban and rural areas in U.S. epidemiologic studies. *J Urban Health*. 2006;83:162-175.
27. Greenwood-Ericksen MB, Kocher K. Trends in emergency department use by rural and urban populations in the United States. *JAMA Netw Open*. 2019;2:e191919.
28. Harrington RA, Califf RM, Balamurugan A, et al. Call to Action: Rural Health: a Presidential Advisory from the American Heart Association and American Stroke Association. *Circulation*. 2020;141:e615-e644.
29. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med*. 2005;352:225-237.
30. Parkash R, Wightman H, Miles G, et al. Primary prevention of sudden cardiac death with device therapy in urban and rural populations. *Can J Cardiol*. 2017;33:437-442.
31. Writing Committee M, Yancy CW, Jessup M, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;128:e240-327.
32. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145.
33. White-Williams C, Rossi LP, Bittner VA, et al. Addressing social determinants of health in the care of patients with heart failure: a scientific statement from the American Heart Association. *Circulation*. 2020;141:e841-e863.
34. Social Determinants of Health. <https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/rural/2017-social-determinants.pdf>
35. Social Determinants of Health. 2021. https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1
36. Lutfiyya MN, McCullough JE, Haller IV, Waring SC, Bianco JA, Lipsky MS. Rurality as a root or fundamental social determinant of health. *Dis Mon*. 2012;58:620-628.
37. CDC/ATSDR Social Vulnerability Index. 2021. <https://www.atsdr.cdc.gov/placeandhealth/svi/index.html>
38. Rural America at a Glance. Washington, DC. <https://www.ers.usda.gov/webdocs/publications/90556/eib-200.pdf>
39. *Older Population in Rural America*. Washington, DC.
40. Sterling MR, Ringel JB, Pinheiro LC, et al. Social determinants of health and 90-day mortality after hospitalization for heart failure in the REGARDS study. *J Am Heart Assoc*. 2020;9:e014836.
41. Maroko AR, Doan TM, Arno PS, Hubel M, Yi S, Viola D. Integrating social determinants of health with treatment and prevention: a new tool to assess local area deprivation. *Prev Chronic Dis*. 2016;13:E128.
42. Kaufman BG, Thomas SR, Randolph RK, et al. The rising rate of rural hospital closures. *J Rural Health*. 2016;32:35-43.
43. Primm K, Ferdinand AO, Callaghan T, Akinlotan MA, Towne SD, Jr., Bolin J. Congestive heart failure-related hospital deaths across the urban-rural continuum in the United States. *Prev Med Rep*. 2019;16:101007.
44. Chen HF, Carlson E, Popoola T, Suzuki S. The impact of rurality on 30-day preventable readmission, illness severity, and risk of mortality for heart failure Medicare home health beneficiaries. *J Rural Health*. 2016;32:176-187.

SUPPORTING INFORMATION

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

How to cite this article: Zeitler EP, Joly J, Leggett C, et al. The role of comorbidities, medications, and social determinants of health in understanding urban-rural outcome differences among patients with heart failure. *J Rural Health*. 2023;1-8. <https://doi.org/10.1111/jrh.12803>