

Investigating Regional Differences in Cardiovascular Outcomes Among Patients
Diagnosed with Hypertrophic Cardiomyopathy

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INTRODUCTION

- Studies examining the associations between geographic region and cardiovascular (CV) outcomes in patients with hypertrophic cardiomyopathy (HCM) are limited in size.¹
- We evaluated these associations in a large, national cohort of patients with HCM.

METHODS

- Study Design
- Retrospective cohort study of adult patients with HCM in Optum’s Market Clarity database from Jan 1, 2013 through Dec 31, 2021 (index date = first HCM diagnosis) in the United States.
 - Patients with ≥2 medical claims with a diagnosis code for HCM (International Classification of Diseases (ICD)-9: 425.1, 425.11 or 425.18; ICD-10: I42. 1 or I42.2) in any position on different dates of service ≥30 days apart.
 - Patients with 6 months of baseline and ≥6 months of follow-up continuous enrollment, and no evidence of Fabry disease or amyloidosis during the study period.

- Study Outcomes
- Clinical characteristics, CV treatments, CV outcomes (AF, stroke, HF, VT, VF, stress cardiomyopathy, SCA, and heart transplant), and mortality.

- Statistical Methods
- Event rates per 100,000 PY to estimate risk of CV outcomes.
 - Kaplan–Meier analysis for all-cause mortality was conducted by US region: Midwest (reference group), Northeast, South, and West; all tests were 2-sided α=0.05.

RESULTS

- Among 24,586 patients with HCM (mean age: 61.3 ± 14.9 years; female: 49%; non-Hispanic White: 74.0%), 42.7% resided in the US Midwest (Northeast 27.1%; South 22.4%; West 7.8%) (**Table 1**; **Figure 1**).
- Patients in the Northeast were less likely to receive beta-blockers, calcium channel blockers, and/or pacemakers, but were more likely to receive disopyramide (*P*<0.001) (**Table 2**).
- Patients in the South were less likely to receive beta-blockers (*P*<0.001) but more likely to receive calcium channel blockers, implantable cardioverter-defibrillators, and/or pacemakers (all *P*<0.05) (**Table 2**).
- Patients in the West were less likely to receive beta-blockers, but more likely to receive disopyramide (all *P*<0.01) (**Table 2**).
- Patients in the Northeast were less likely to experience AF, stroke, HF, and VF (all *P*<0.01) and patients in the West were less likely to experience stroke (*P*=0.020) (**Table 3**).
- Patients in the South were more likely to experience AF and HF (*P*<0.001) (**Table 3**).
- 3-year all-cause mortality rate was lowest in the Northeast (5.2%; *P*<0.001), whereas patients in the South (8.5%), West (8.3%), and Midwest (8.0%) all had similar rates (**Figure 2**).

RESULTS

Table 1. Patient demographics

Demographics	n (%) ^a
Age (continuous), mean (SD)	61.32 (14.93)
Age group, y	
18–39	2176 (8.85)
40–54	4964 (20.19)
55–64	6696 (27.24)
65–74	5509 (22.41)
75+	5241 (21.32)
Sex	
Male	12,537 (50.99)
Insurance type	
Commercial	11,173 (45.44)
Medicare	7737 (31.47)
Medicaid	2207 (8.98)
Other	113 (0.46)
Unknown/missing	3356 (13.65)
US Region	
Northeast	6668 (27.12)
Midwest	10,502 (42.72)
South	5504 (22.39)
West	1912 (7.78)
Race/ethnicity	
White, non-Hispanic	18,181 (73.95)
Black/African American, non-Hispanic	4814 (19.58)
Asian, non-Hispanic	559 (2.27)
Hispanic	1032 (4.20)
Baseline Charlson Comorbidity score (continuous)	1.40 (1.80)

^a Unless otherwise indicated.

Table 2. Incidence rates of cardiovascular outcomes during follow-up

Treatment characteristics	US Region												Incidence Risk Ratio					
	Northeast n=6668			Midwest n=10,502			South n=5504			West n=1912			Northeast vs Midwest		South vs Midwest		West vs Midwest	
	Events	PY	Rate/ 100,000	Events	PY	Rate/ 100,000	Events	PY	Rate/ 100,000	Events	PY	Rate/ 100,000	Ratio	P value	Ratio	P value	Ratio	P value
Pharmacologic treatment																		
BB	3991	12,646	31,560	6358	16,832	37,774	3197	9210	34,714	1117	3237	34,504	0.84	<0.001	0.92	<0.001	0.91	0.005
CCB	2642	17,999	14,679	4356	24,058	18,106	2377	12,213	19,462	760	4514	16,835	0.81	<0.001	1.07	0.005	0.93	0.062
Disopyramide	252	25,768	978	144	36,219	398	91	19,135	476	53	6828	776	2.46	<0.001	1.20	0.183	1.95	<0.001
Antiarrhythmic drugs	1967	20,409	9638	2728	29,373	9287	1558	14,980	10,401	505	5559	9084	1.04	0.211	1.12	<0.001	0.98	0.651
Anticoagulants	2454	19,202	12,780	4769	23,658	20,158	2285	12,947	17,649	763	4877	15,646	0.63	<0.001	0.88	<0.001	0.78	<0.001
Therapeutic procedure																		
SRT	409	25,265	1619	557	35,072	1588	361	18,346	1968	117	6650	1759	–	–	–	–	–	–
SM	307	25,648	1197	448	35,413	1265	284	18,601	1527	86	6735	1277	–	–	–	–	–	–
ASA	164	26,019	630	194	36,000	539	124	18,962	654	44	6825	645	–	–	–	–	–	–
Implantable CD	1160	22,554	5143	1694	31,431	5390	970	16,491	5882	312	6005	5196	0.95	0.219	1.09	0.031	0.96	0.555
Pacemaker	1488	21,590	6892	2301	29,570	7782	1350	15,338	8802	458	5534	8276	0.89	<0.001	1.13	<0.001	1.06	0.230

Figure 1. Patient baseline comorbidities

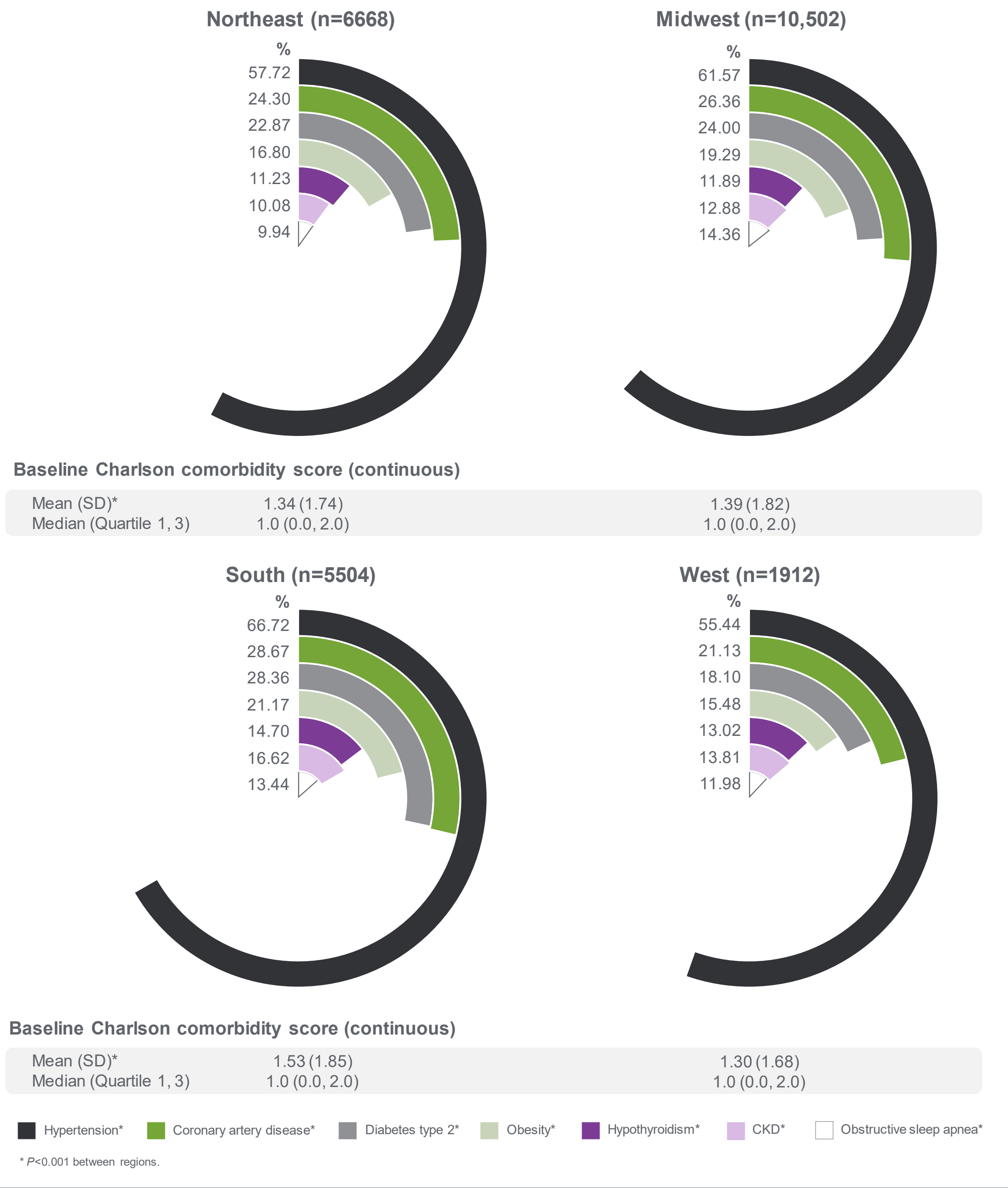
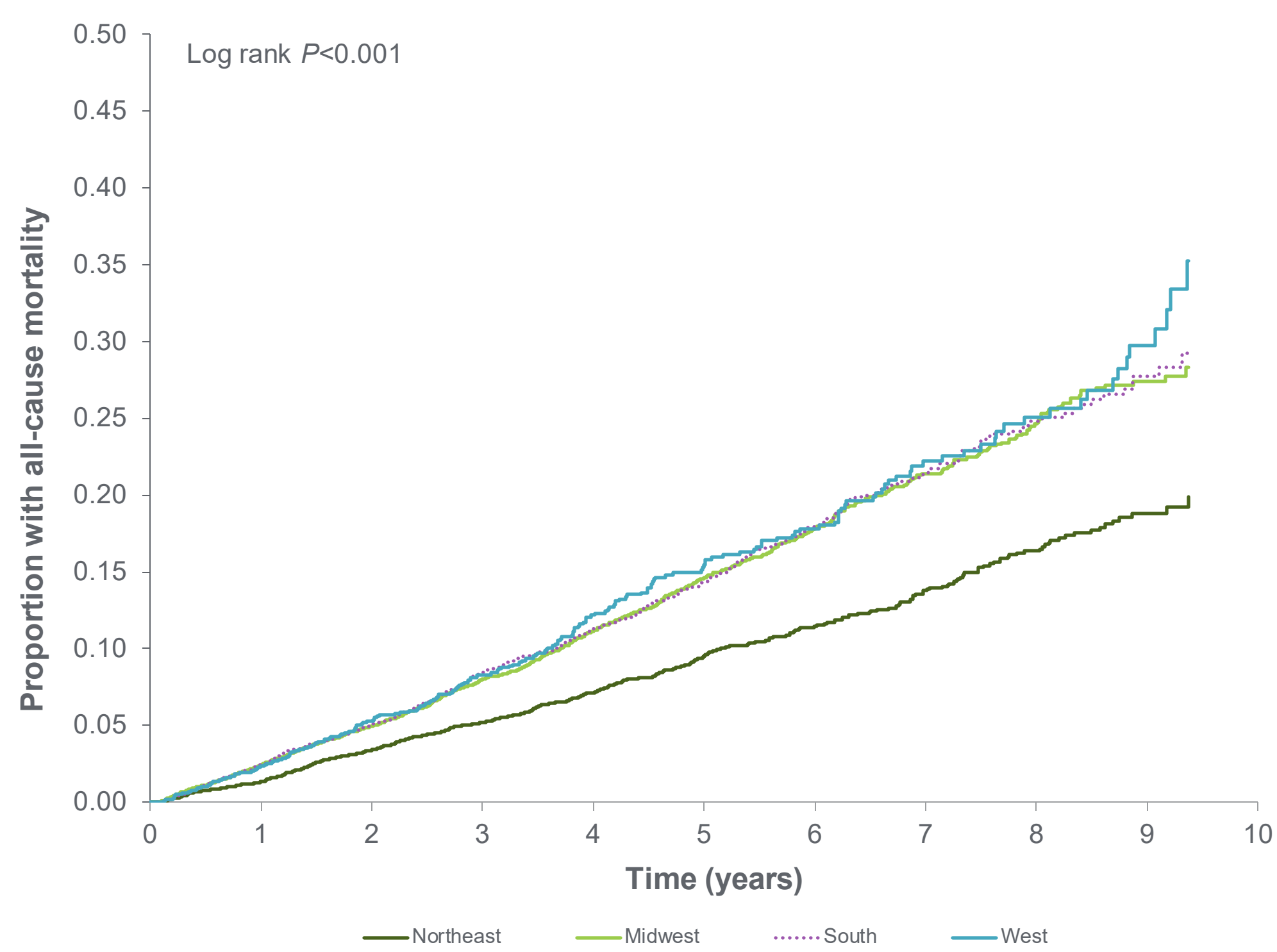


Table 3. Incidence rate of cardiovascular outcomes during follow-up

Clinical outcomes	US Region												Incidence Risk Ratio					
	Northeast n=6668			Midwest n=10,502			South n=5504			West n=1912			Northeast vs Midwest		South vs Midwest		West vs Midwest	
	Events	PY	Rate/ 100,000	Events	PY	Rate/ 100,000	Events	PY	Rate/ 100,000	Events	PY	Rate/ 100,000	Ratio	P value	Ratio	P value	Ratio	P value
AF	2412	18,593	12,972	3632	25,945	13,999	2100	13,111	16,017	715	4856	14,723	0.93	0.004	1.14	<0.001	1.05	0.219
Stroke	1151	23,063	4991	1787	32,121	5563	971	16,871	5755	297	6163	4819	0.90	0.004	1.03	0.394	0.87	0.020
HF	2805	17,491	16,037	4840	23,475	20,618	2741	11,617	23,595	869	4531	19,180	0.78	<0.001	1.14	<0.001	0.93	0.048
VT	1364	4429	30,800	1944	6127	31,726	999	3057	32,680	375	1236	30,338	0.97	0.402	1.03	0.446	0.96	0.429
VF	155	8518	1820	275	10,760	2556	150	5524	2715	52	2135	2436	0.71	<0.001	1.06	0.549	0.95	0.762
SVT	961	6058	15,864	1471	7626	19,290	722	3990	18,094	288	1528	18,854	0.82	<0.001	0.94	0.158	0.98	0.727
Stress CM	50	26,565	188	90	36,427	247	41	19,381	212	15	6941	216	0.76	0.121	0.86	0.413	0.87	0.650
SCA	240	26,273	913	365	36,094	1011	229	19,104	1199	60	6864	874	0.90	0.221	1.19	0.045	0.86	0.295
Heart transplant	63	26,528	237	86	36,463	236	49	19,318	254	18	6910	260	1.01	0.964	1.08	0.680	1.10	0.685

Figure 2. Kaplan–Meier analysis of all-cause mortality during the variable follow-up period



US Region	All-Cause Mortality (time)								
		0 y	0.5 y	1 y	1.5 y	3 y	6 y	9 y	9.5 y
	Proportion	0.0000	0.0078	0.0134	0.0257	0.0518	0.1144	0.1882	0.1985
Northeast	At risk, n	6668	6616	6036	5374	3856	1577	269	67
	Proportion	0.0000	0.0111	0.0242	0.0378	0.0801	0.1777	0.2740	0.2829
Midwest	At risk, n	10,502	10,386	9375	8177	5159	1723	271	69
	Proportion	0.0000	0.0114	0.0247	0.0391	0.0845	0.1795	0.2774	0.2921
South	At risk, n	5504	5442	4887	4277	2753	942	149	33
	Proportion	0.0000	0.0105	0.0236	0.0384	0.0828	0.1781	0.2976	0.3525
West	At risk, n	1912	1892	1678	1474	962	383	72	14

P<0.001, for all regions and times.

LIMITATIONS

- Real-world data in this study utilized ICD-9 and -10 coding for disease identification, patient demographics, and CV outcomes, and may be subject to inconsistencies without patient-level genetic and anatomical confirmation.

CONCLUSIONS

- Incidence of adverse CV outcomes was less frequent in the US Northeast and West.
- All-cause mortality was significantly lower in the Northeast.
- Further research is required to understand and address these regional US differences.

Reference

- Butzner M, et al. *Am Heart J Plus Cardiol Res Pract* 2022;13:100089.

Disclosures

MB and SS: Employees of and own stock in Cytokinetics, Incorporated. **KB, AA, QA, and AB:** Employees of Optum/UHG, who were consultants for Cytokinetics, Incorporated, for this study. **QA, AB, and AA:** Shareholders of UHG stock. **NR:** Consulting/speaking honoraria from Roche Diagnostics and Zoll, and is supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health under Award Number K23HL166961 (the content is solely the responsibility of the author and does not necessarily represent the official views of the National Institutes of Health). **AO:** Consultant/advisor fees from Cytokinetics, Incorporated, Bristol Myers Squibb/ MyoKardia, and Pfizer.

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Abbreviations

AF, atrial fibrillation; ASA, alcohol septal ablation; BB, beta-blocker; CD, cardioverter-defibrillator; CM, cardiomyopathy; CKD, chronic kidney disease; CV, cardiovascular; HCM, hypertrophic cardiomyopathy; HF, heart failure; SCA, sudden cardiac arrest; SM, septal myectomy; SRT, septal reduction therapy; SVT, supraventricular tachycardia; PY, person-years; VF, ventricular fibrillation; VT, ventricular tachycardia.



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