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ORIGINAL RESEARCH

Disparities in Premature Cardiac Death Among US Counties From 1999–2017: Temporal Trends and Key Drivers

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BACKGROUND: Disparities in premature cardiac death (PCD) might stagnate the progress toward the reduction of PCD in the United States and worldwide. We estimated disparities across US counties in PCD rates and investigated county-level factors related to the disparities.

METHODS AND RESULTS: We used US mortality data for cause-of-death and demographic data from death certificates and county-level characteristics data from multiple databases. PCD was defined as any death that occurred at an age between 35 and 74 years with an underlying cause of death caused by cardiac disease based on *International Classification of Diseases, Tenth Revision* (*ICD-10*), codes. Of the 1 598 173 PCDs that occurred during 1999–2017, 60.9% were out of hospital. Although the PCD rates declined from 1999–2017, the proportion of out-of-hospital PCDs among all cardiac deaths increased from 58.3% to 61.5%. The geographic disparities in PCD rates across counties widened from 1999 (Theil index=0.10) to 2017 (Theil index=0.23), and within-state differences accounted for the majority of disparities (57.4% in 2017). The disparities in out-of-hospital PCD rates (and in-hospital PCD rates) associated with demographic composition were 36.51% (and 37.51%), socioeconomic features were 18.64% (and 18.36%), healthcare environment were 18.64% (and 13.90%), and population health status were 23.73% (and 30.23%).

CONCLUSIONS: Disparities in PCD rates exist across US counties, which may be related to the decelerated trend of decline in the rates among middle-aged adults. The slower declines in out-of-hospital rates warrants more precision targeting and sustained efforts to ensure progress at better levels of health (with lower PCD rates) against PCD.

Key Words: county-level disparity ■ factors ■ premature cardiac death ■ trend

Premature cardiac death (PCD) refers to any unexpected or sudden death attributable to cardiac disease that occurred at a younger age and remains a prominent public health issue in the United States and worldwide.[1,2] PCD is a leading cause of global mortality, accounting for 0.2 to 0.3 million deaths annually,[3] with an estimated 15% to 20% of all deaths in the United States.[4] Of these deaths, about 35% occur in middle age (30 to 69 years),[5] and most of occur out of the hospital, eg, before reaching a hospital or in an emergency department.[4,6] Although a number of studies have estimated the incidence of PCD in the United States based on various study designs and populations,[7–9] little is known about the county-level disparities in PCD rates or the factors related to the disparities. In 2012, all countries including the United States committed to achieving a 25% reduction in premature mortality from cardiovascular diseases, cancer, diabetes mellitus, or chronic respiratory diseases by 2025 proposed by World Health Organization (WHO).[10] The Global Cardiovascular Disease Taskforce, comprising the American Heart Association, American

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CLINICAL PERSPECTIVE

What Is New?

- We found increasing proportions of out-of-hospital deaths among patients with premature cardiac death, which appeared to be higher in younger age groups. County-level disparities in mortality were widening during the past 2 decades.

What Are the Clinical Implications?

- Identifying factors that explain disparities in premature cardiac death provides insight into strategies that could help reduce these disparities and achieve more equitable outcomes.

Nonstandard Abbreviations and Acronyms

APC	annual percentage change
ICD-10	*International Classification of Diseases, Tenth Revision*
PCD	premature cardiac death
SCD	sudden cardiac death
WHO	World Health Organization

College of Cardiology Foundation, and other institutions, disseminates information and approaches to reach the WHO 2025 targets by reducing premature deaths from cardiovascular diseases and stroke (The Heart of 25 by 25).[11] Clinical and pathologic findings suggest that atherosclerotic coronary heart disease is the most common pathology underlying PCD, and presence of cardiovascular risk factors is predictive of PCD.[4] Therefore, accurate estimation of the epidemiological trends in PCD in the United States is essential to evaluate progress toward decreasing premature mortality by reducing cardiac disease deaths to achieve the WHO goal.

PCD shows substantial and longstanding geographic variations in terms of incidence and survival in the United States.[7,12,13] Knowledge of county-specific rates of PCD could guide identification of the state-level characteristics, which are relevant to understanding geographic disparities within the United States. Assessment of county-level time trends of PCD could quantify the magnitude of regional contributions to progress toward lowering premature cardiac mortality in the United States. Previous studies reported correlates of PCD rates, including regional-level or system-related factors such as socioeconomic status, demographic composition, healthcare access, and environmental features, providing insight into additional characteristics that may predispose certain regions to PCD rates in disadvantaged areas.[14] Despite recognizing the importance of estimating regional disparities in PCD rates, quantifying their associations in the disparities are limited by lack of standardized and consistent measures of county-level data linked to county-level PCD rates.

Furthermore, sudden out-of-hospital cardiac arrest is the most time-critical medical emergency.[15] Epidemiologic investigation of out-of-hospital cardiac deaths compared with in-hospital deaths is of particular public health importance to better understand the trends and regional disparities in PCD. As a result, the objectives of this study were to: (1) estimate disparities across US counties in PCD rates; and (2) investigate factors related to the disparities in PCD rates. By analyzing the secular trend in PCD rates, this study can present the progress towards achieving the WHO goal and the Heart of 25 by 25.

METHODS

The data that support the findings of this study are available from the corresponding author on request.

Data

This study analyzed US mortality data for 1999–2017 using cause-of-death and demographic data from death certificates from the US National Center for Health Statistics at the Centers for Disease Control and Prevention.[16] This database is available online (https://wonder.cdc.gov/) and includes the following key data elements: age, sex, race, ethnicity, place of death, underlying cause of death, and multiple major contributing causes of death. Places of death include inpatient facilities, outpatient or emergency department setting, dead on arrival, decedent's home, hospice facility, nursing home/long-term care, and unknown and status unknown. Cause of death is assigned according to the *International Classification of Diseases, Tenth Revision* (*ICD-10*), which has been implemented since 1999. Population estimates are provided by the US Census Bureau. All data used in this study are deidentified; thus, institutional review board approval was not required. The data analysis began in April 2019.

This study defined PCD as any unexpected death attributable to cardiac disease that occurred at an age between 35 and 74 years.[6,17] Cardiac disease death was defined as one for which the underlying cause was classified in *ICD-10* codes: ischemic heart disease (I21), dilated cardiomyopathy (I42.0), hypertrophic cardiomyopathy (I42.1 and I42.2), other cardiomyopathies (I42.3-I42.9), arrhythmia (I45.6, I45.8, I46.1, I46.9, I47.2,

Table 1. Trends and County-Level Disparities in Cardiac Death Rates and Place of Death Among US Residents Aged 35 to 74 years, 1999–2017

	Death Rate, Per 100 000*,†,‡	County-Level Disparity in Death Rate Theil Index)			Place of Death, %§						
					Out-of-Hospital						
		Overall	Within-State (Contribution, %)	Between-State (Contribution, %)	Dead on Arrival	Outpatient/ Emergency Department	Decedent's Home	Nursing Home/ Long-Term Care/ Hospice Facility	Total	In-Hospital	Other
Total	55.2	0.11	0.06 (52.9)	0.05 (47.1)	2.6	25.5	27.8	5.0	60.9	34.8	4.3
Sex											
Men	77.3	0.11	0.06 (54.0)	0.05 (46.0)	2.8	27.3	28.3	4.3	62.7	32.2	5.1
Women	34.9	0.13	0.07 (52.8)	0.06 (47.2)	2.1	21.8	26.8	6.6	57.3	39.8	2.9
Age group, y											
35–44	11.4	0.23	0.12 (51.2)	0.11 (48.8)	3.8	32.5	27.9	1.7	66.0	27.3	6.7
45–54	33.8	0.16	0.09 (53.2)	0.08 (46.8)	3.4	30.3	29.7	2.4	65.8	28.3	5.9
55–64	79.2	0.13	0.07 (54.0)	0.06 (46.0)	2.7	26.7	29.2	3.9	62.4	33.0	4.6
65–74	174.9	0.09	0.05 (58.3)	0.04 (41.7)	2.0	22.0	26.1	7.3	57.4	39.4	3.3
Race											
White	53.6	0.10	0.06 (54.7)	0.05 (45.3)	2.6	25.2	29.2	4.9	61.9	33.7	4.4
Black	81.8	0.12	0.07 (60.2)	0.05 (39.8)	2.6	27.0	22.2	5.8	57.6	38.3	4.1
American Indian or Alaska Native	43.2	0.21	0.08 (36.4)	0.13 (63.6)	2.6	23.5	26.1	4.2	56.4	37.9	5.7
Asian or Pacific Islander	23.0	0.09	0.03 (34.7)	0.06 (65.3)	1.8	25.7	16.2	4.4	48.0	48.6	3.4
Year of death											
1999	84.9	0.10	0.06 (57.1)	0.04 (42.9)	4.3	26.7	23.1	4.2	58.3	38.1	3.6
2000	80.2	0.11	0.06 (59.1)	0.05 (40.9)	4.0	26.6	23.5	4.3	58.4	37.9	3.7
2001	75.1	0.12	0.07 (57.7)	0.05 (42.3)	3.7	26.6	24.2	4.6	59.1	37.0	3.9
2002	72.6	0.13	0.07 (56.8)	0.05 (43.2)	3.5	26.2	24.9	4.7	59.4	36.5	4.2
2003	68.2	0.13	0.08 (58.5)	0.05 (41.5)	3.3	26.6	25.8	4.6	60.3	35.8	3.9
2004	62.6	0.14	0.08 (56.9)	0.06 (43.1)	3.0	26.9	26.5	4.7	61.1	34.8	4.1
2005	60.1	0.15	0.08 (56.5)	0.06 (43.5)	3.1	26.9	26.8	4.9	61.7	34.1	4.2
2006	56.8	0.15	0.09 (56.7)	0.07 (43.3)	2.6	26.1	28.0	5.0	61.7	34.2	4.2
2007	54.1	0.16	0.09 (58.1)	0.07 (41.9)	2.6	25.3	28.3	5.3	61.5	34.5	4.1
2008	52.6	0.16	0.09 (56.5)	0.07 (43.5)	2.2	24.1	27.9	4.9	59.1	34.9	6.0
2009	50.3	0.18	0.10 (56.5)	0.08 (43.5)	2.0	25.0	27.8	5.1	59.9	32.6	7.5
2010	49.0	0.19	0.10 (55.0)	0.08 (45.0)	2.0	25.8	29.5	5.2	62.5	33.4	4.1
2011	47.0	0.20	0.12 (58.2)	0.08 (41.8)	2.0	26.1	29.5	5.1	62.7	33.0	4.3

(Continued)

Table 1.Continued

	Death Rate, Per 100 000*,†,‡	County-Level Disparity in Death Rate (Theil Index)			Place of Death, %§						
					Out-of-Hospital						
		Overall	Within-State (Contribution, %)	Between-State (Contribution, %)	Dead on Arrival	Outpatient/ Emergency Department	Decedent's Home	Nursing Home/ Long-Term Care/ Hospice Facility	Total	In-Hospital	Other
2012	45.8	0.21	0.12 (55.4)	0.09 (44.6)	1.8	26.1	29.9	5.3	63.1	32.7	4.2
2013	45.4	0.21	0.12 (58.0)	0.09 (42.0)	1.7	24.9	30.9	5.3	62.8	32.9	4.3
2014	44.5	0.22	0.12 (56.1)	0.10 (43.9)	1.6	24.3	31.0	5.6	62.5	33.2	4.2
2015	44.4	0.23	0.14 (59.0)	0.09 (41.0)	1.4	23.8	31.2	6.0	62.4	33.2	4.4
2016	43.9	0.25	0.15 (58.4)	0.10 (41.6)	1.3	22.9	31.5	5.9	61.6	34.2	4.2
2017	43.0	0.23	0.13 (57.4)	0.10 (42.6)	1.1	22.5	32.2	5.8	61.5	34.3	4.1

Note: *Cardiac disease defined as *International Classification of Diseases, Tenth Revision (ICD-10)* codes I21.0, I21.2, I21.3, I21.4, I21.9, I24.8, I24.9, I25.4, I42, I45.6, I45.8, I46.1, I46.9, I47.2, I49.0, I49.3, I49.5, I49.8, I49.9, R96, Q20, Q21, Q22, Q23, Q24.2, Q24.4, Q24.5, Q24.6, Q24.8, Q24.9, Q87.4, I34.1, I35.0, and I40.

†Age-adjusted to the 2000 projected US population.

‡The trend of the death rate was tested by interrupted time series analysis. Mortality decreased by 3.51 (95% CI, −3.97 to −3.05; *P*<0.01) deaths per 100 000 people annually from 1999–2010, and decreased annually at a rate of 0.75 (95% CI, −0.97 to −0.52; *P*<0.01) from 2010–2017.

§Out-of-hospital cardiac death defined as any cardiac death occurring in outpatient or emergency department settings, dead on arrival, in the decedent's home, or in a hospice facility or nursing home/long-term care. Other includes place of death unknown.

I49.0, I49.3, I49.5, I49.8, I49.9, and R96), congenital heart disease (Q20, Q21, Q22, Q23, Q24.2, Q24.4, Q24.5, Q24.6, Q24.8, Q24.9, Q87.4, I34.1, and I35.0), myocarditis (I40), and others (I25.4). Based on a majority of studies,[6–8,11,12,18] we defined out-of-hospital cardiac death as any cardiac death occurring in outpatient or emergency department settings, dead on arrival, or pretransport location, including decedent's home, hospice facility, nursing home, and long-term care home. We defined in-hospital cardiac death as a cardiac death occurring in inpatient facilities. All analyses were restricted to individuals aged 35 to 74 years to focus on PCD.

Statistical Analysis

We assessed the age-adjusted PCD rates and proportions of PCDs by place of death for groups defined by sex (men and women), race (white, black, American Indian/Alaska Native, and Asian/Pacific Islander), age group (35–44, 45–54, 55–64, and 65–74 years), and year. To assess the geographic disparity and decompose the disparities, we conducted the Theil index of county-level mortality. The advantage of Theil index is that it can decompose the disparity into within- and between-state disparities.[19,20] To examine the trends in the PCD rates from 1999–2017, we assessed the annual percentage change (APC), which was calculated by using age-adjusted logistic regression and orthogonal polynomial contrasts.[21] Furthermore, to assess the progress towards achieving the Heart of 25 by 25, we estimated the state-specific age-adjusted rates in 1999, 2010, and 2017, and relative changes during 1999–2010, 2010–2017, and 1999–2017 for each state. The trends of the PCD rates were tested by interrupted time series analysis, for identifying whether the mortality varied significantly by year.[22] Age-adjusted PCD rates were standardized by the direct method to the 2000 US population.[23]

Hierarchical linear mixed models were used to estimate the associations of factors with state-specific PCD rates. Based on literature review, we included 4 sets of state-specific characteristics that could potentially be associated with PCD rates, including demographic composition, socioeconomic features, healthcare environment, and population health status. Demographic composition included population size, rural, sex, age, racial/ethnic, and foreign born. Socioeconomic features included median household income, unemployment, school enrollment, and violent crime rate. Healthcare/environment included density of primary care physicians, diabetic Medicare enrollees with glycated hemoglobin test, access to places for physical activity, and access to healthy foods. Population health status included cardiovascular

Table 2. County-Level Cardiac Death Rate and Relative Change From 1999 to 2017, by Sex, Age, and Race

	Out-of-Hospital									In-Hospital								
	Men			Women			Total			Men			Women			Total		
Characteristics	Death Rate in 1999	APC	95% CI	Death Rate in 1999	APC	95% CI	Death Rate in 1999	APC	95% CI	Death Rate in 1999	APC	95% CI	Death Rate in 1999	APC	95% CI	Death Rate in 1999	APC	95% CI
Age-specific rate (per 100 000 population)																		
35 to 44 y	13.6	−0.4*	−0.4 to −0.3	4.9	−0.08*	−0.1 to −0.06	9.2	−0.2*	−0.2 to −0.2	4.8	−0.05*	−0.07 to −0.03	2.8	−0.04*	−0.05 to −0.03	3.8	−0.04*	−0.06 to −0.03
45 to 54 y	44.4	−1.1*	−1.2 to −1.0	13.3	−0.2*	−0.2 to −0.1	28.6	−0.6*	−0.7 to −0.6	16.9	−0.3*	−0.4 to −0.2	8.5	−0.2*	−0.2 to −0.1	12.6	−0.2*	−0.3 to −0.2
55 to 64 y	109.1	−2.6*	−3.1 to −2.1	39.2	−0.8*	−1.0 to −0.6	72.7	−1.7*	−2.0 to −1.3	57.9	−1.5*	−1.8 to −1.1	31.6	−1.0*	−1.2 to −0.7	44.2	−1.2*	−1.5 to −0.9
65 to 74 y	227.5	−6.3*	−7.5 to −5.1	105.9	−3.0*	−3.5 to −2.5	160.7	−4.5*	−5.3 to −3.6	164.3	−5.6*	−6.6 to −4.5	96.9	−3.5*	−4.1 to −2.9	127.2	−4.4*	−5.2 to −3.6
Age-adjusted rate† (per 100 000 population)																		
White	71.3	−1.3*	−1.6 to −0.9	29.0	−0.4*	−0.6 to −0.3	49.7	−0.8*	−1.1 to −0.6	39.7	−0.9*	−1.1 to −0.6	23.9	−0.6*	−0.8 to −0.4	31.6	−0.7*	−0.9 to −0.5
Black	82.9	−0.4*	−0.7 to −0.1	45.6	−1.0*	−1.2 to −0.8	62.6	−1.3*	−1.6 to −1.0	55.0	−1.1*	−1.4 to −0.8	36.8	−1.0*	−1.3 to −0.8	45.1	−1.1*	−1.3 to −0.8
American Indian or Alaska Native	42.8	−1.0*	−1.2 to −0.8	17.3	−0.3*	−0.4 to −0.1	29.6	−0.6*	−0.8 to −0.5	29.6	−0.6*	−0.8 to −0.4	19.6	−0.5*	−0.6 to −0.3	24.4	−0.5*	−0.7 to −0.3
Asian or Pacific Islander	21.2	−0.4*	−0.5 to −0.2	7.7	−0.2*	−0.2 to −0.1	14.0	−0.3*	−0.3 to −0.2	20.9	−0.4*	−0.6 to −0.3	12.4	−0.4*	−0.5 to −0.3	16.4	−0.4*	−0.5 to −0.3
Total	70.5	−1.3*	−1.6 to −1.0	30.0	−0.5*	−0.7 to −0.4	49.6	−0.9*	−1.1 to −0.7	40.5	−0.9*	−1.1 to −0.6	25.0	−0.7*	−0.8 to −0.5	32.5	−0.8*	−1.0 to −0.5

APC indicates annual percentage change.
*P<0.01.
†Age-adjusted to the 2000 projected US population.

disease risk index, self-rated poor/fair health, and total Medicare reimbursements per enrollee (a measure of healthcare utilization as a proxy for illness). These data were obtained from multiple databases from 2011–2017 that had been introduced in our previous study.[14] The data sources are outlined in Table S1. To quantify the extent to which the 4 sets of factors associated with the county-level disparities in PCD rates, we conducted dominance analysis for decomposition by examining the relative importance of these variables in contributing to the R^2 of the regression.[24] Counties were combined as needed to create stable units of analysis for each of the various statistical methods. All analyses were conducted in Stata 14.1 (StataCorp LP). The data analysis began in April 2019.

RESULTS

Disparities in PCD rates

Table 1 shows the disparities in the age-adjusted rates of PCD and the place of PCDs by sex, race, and age. Between 1999 and 2017, a total of 1 598 173 cardiac disease deaths occurred between the ages of 35 to 74 years in the United States (age-standardized rate 55.2 per 100 000 people-years), of which 60.9% occurred out of hospital and 34.8% occurred in hospital. The age-adjusted PCD rates were twice as high in men as in women (77.3 versus 34.9), and 3.5 times as high in blacks as in Asians or Pacific Islanders (81.8 versus 23.0). Age-specific cardiac death rates increased with age and the rates among adults aged 65 to 74 years were 15.3 times as high as those aged 35 to 44 years. For the geographic disparities, Theil index increased from 0.10 in 1999 to 0.23 in 2017, indicating a widened county-level mortality disparity. The geographic disparities were decomposed by between-state and within-state, and within-state differences accounted for the majority of disparity (57.4% in 2017). From 1999 to 2017, although the age-adjusted rates of PCD decreased, the overall proportion of out-of-hospital rates among PCDs increased slightly from 58.3% to 61.5%. PCDs that occurred in outpatient or emergency department settings declined from 26.7% to 22.5%, while those that occurred in the decedent's home increased from 23.1% to 32.2%. The results of interrupted time series analysis demonstrated that the PCD rates decreased by 3.51 (95% CI, −3.97 to −3.05; $P<0.01$) deaths per 100 000 people annually from 1999 to 2010, and decreased annually at a rate of 0.75 (95% CI, −0.97 to −0.52; $P<0.01$) from 2010 to 2017.

Table 2 and Figure 1 show that although all of the rates of PCD decreased from 1999 to 2017, the magnitude of decline varied across age, sex, and race. The decline rates (deaths per 100 000 people annually)

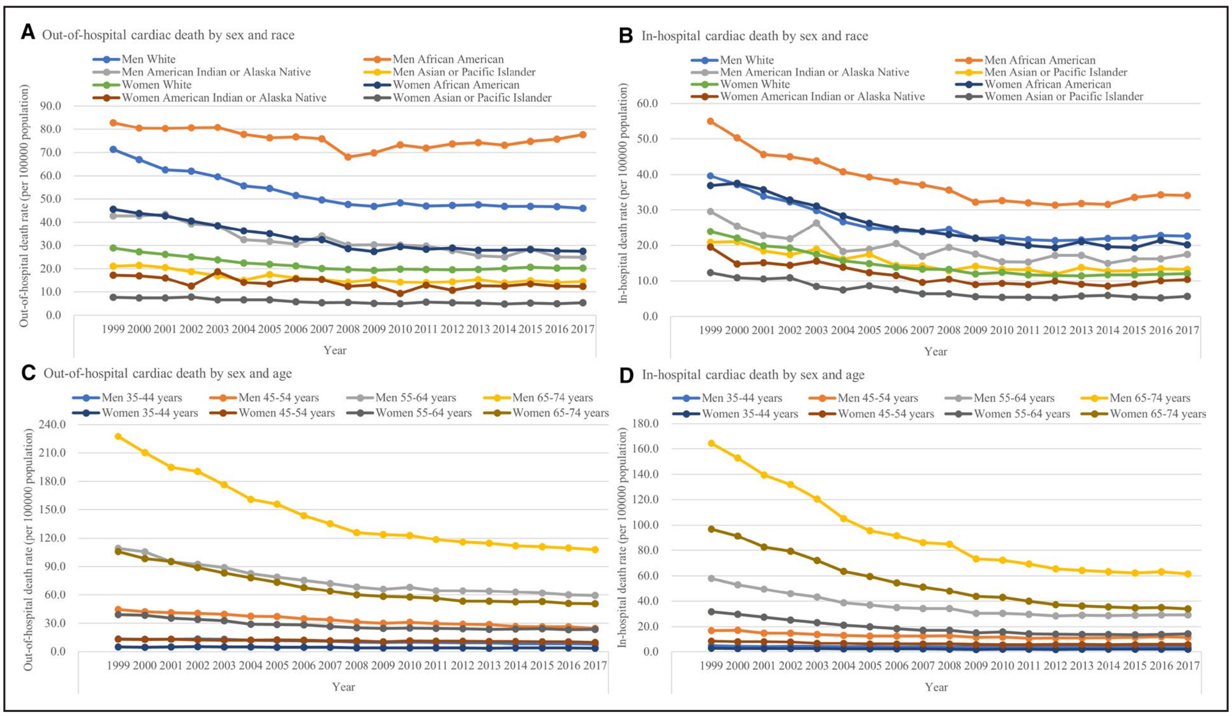

Figure 1. Age-adjusted rates of out-of-hospital and in-hospital cardiac death (per 100 000 population) in US residents aged 35 to 74 years, by sex, race, and age, from 1999 to 2017.
A, Out-of-hospital cardiac death by sex and race. **B**, In-hospital cardiac death by sex and race. **C**, Out-of-hospital cardiac death by sex and age. **D**, In-hospital cardiac death by sex and age.

were particularly lower among those in the 35- to 44-year age group (APC=−0.2 out of hospital and −0.04 in hospital), compared with those in the 65- to 74-year age group (APC=−4.5 out of hospital and −4.4 in hospital). Within each age group, the PCDs among men showed higher decline rate (deaths per 100 000 people annually) than women, particularly for out-of-hospital PCDs (APC=−1.5 out of hospital and −0.5 in hospital). Blacks had the highest age-adjusted rates of out-of-hospital and in-hospital cardiac death both in men and women from 1999 to 2017. Nevertheless, the out-of-hospital PCD rates among men had the lowest decline rate (deaths per 100 000 people annually) for blacks (APC=−0.3; 95% CI, −0.7 to −0.1 [*P*<0.01]) than that for whites (APC=−1.3; 95% CI, −1.6 to −0.9 [*P*<0.01]), American Indian or Alaska Native (APC=−1.0; 95% CI, −1.2 to −0.8 [*P*<0.01]), and Asian or Pacific Islander (APC=−0.4; 95% CI, −0.5 to −0.2 [*P*<0.01]). Results of interrupted time series analysis on trends in the PCD rates by sex, race, and age are shown in Table S2. Moreover, the distribution of underlying causes for both out-of-hospital and in-hospital PCDs varied by age and sex (Table S3). In general, ischemic heart disease was more common in the older group, and cardiomyopathy was more frequent in the younger group. In each age subgroup, men had a higher proportion of ischemic heart disease but lower proportions of arrhythmia and congenital heart disease (Table S3). Overall, the magnitude of decline from 1999 to 2017 for PCD other than ischemic heart disease was much slower than that from ischemic heart disease (Figure S1).

Factors Related to Disparities in PCDs

State-specific mortality from cardiac death and relative changes during 1999 to 2010 and 2010 to 2017 were calculated to describe state-level disparities in PCDs (Figure 2). In 2017, Arkansas had the highest rate of PCD at 113.9 (per 100 000 population), while Minnesota had the lowest rate at 22.6, showing a large disparity of PCD across states. The PCD rate in each state declined from 1999 to 2017, although the relative changes during 2010 to 2017 were much smaller than those during 1999 to 2010 in the majority of states. Notably, 3 states had increasing rates of PCD from 2010 to 2017. For example, South Dakota experienced a 47.9% decrease in its death rate during 1999 to 2010 but a 27.8% increase in its death rate during 2010 to 2017. At the same time, 2 states including Rhode Island and Wyoming had a larger decline in

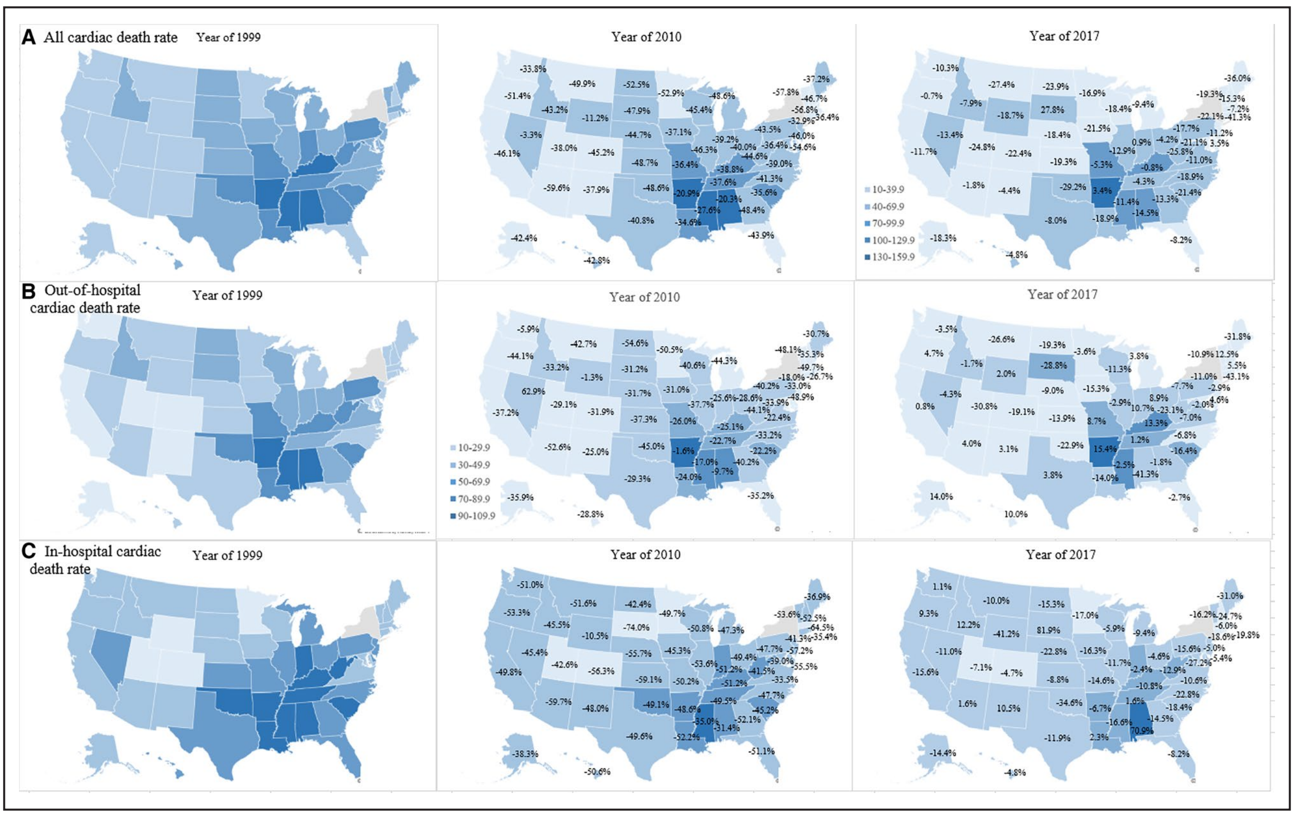

Figure 2. Age-adjusted rate (per 100 000 population) of all cardiac death and out-of-hospital and in-hospital cardiac death in patients aged 35 to 74 years across states in the United States, 1999, 2010, and 2017.
A, All cardiac death rate. **B**, Out-of-hospital cardiac death rate. **C**, In-hospital cardiac death rate.

their PCD rates during 2010 to 2017 in comparison with the earlier period from 1999 to 2010. Notably, 19 states had increasing rates of out-of-hospital cardiac death from 2010 to 2017, while having previously had decreasing rates from 1999 to 2010. In addition, 9 states had similarly worsening trends for in-hospital cardiac death. For example, in South Dakota, in-hospital PCD rate declined 74% between 1999 to 2010, but increased 81.9% from 2010 to 2017. However, 5 states (Alabama, Maine, Nevada, Rhode Island, and Utah) had larger declines in their out-of-hospital cardiac death rates during 2010 to 2017 compared with the earlier period from 1999 to 2010. Between-county disparity and the results of interrupted time series analysis on trends in the state-level PCD rates (per 100 000 population) are shown in Table S4. The majority of states showed increasing between-county disparity during 2010 to 2017, in comparison with that during 1999 to 2010.

Dominance analysis showed that demographic composition was 36.51% associated with the regional disparities in out-of-hospital PCD rates; socioeconomic features, 20.85%, healthcare environment, 18.64%; and population health status, 23.73%. Demographic composition had a 37.51% rate associated with the disparities in in-hospital PCD rates; socioeconomic features, 18.36%; healthcare environment, 13.90%; and population health status, 30.23% (Table 3).

For out-of-hospital PCD rates, each 1-point increase in the percentage of black residents, mortality was higher by 0.078 (95% CI, 0.030–0.125) deaths per 100 000 people-years; and for each 1-point increase in the percentage of Asian residents, mortality was higher by 0.605 (95% CI, 0.403–0.807) deaths per 100 000 people-years. For each 1-point increase

Table 3. County-Level Factors Associated With Age-Adjusted PCDs (Deaths Per 100 000 Population)

County Characteristics	Out-of-Hospital			In-Hospital		
	Standard Dominance Statistic, %	Coefficient	95% CI	Standard Dominance Statistic, %	Coefficient	95% CI
Demographic composition						
Rural, %	36.78%	0.381***	(0.351, 0.411)	37.51%	0.140***	(0.127, 0.154)
Female, %		−0.431**	(−0.819, −0.043)		0.060	(−0.130, 0.250)
Aged ≥65 y, %		0.482***	(0.296, 0.668)		0.123***	(0.059, 0.187)
African American, %		0.078***	(0.030, 0.125)		0.074***	(0.055, 0.093)
American Indian/Alaskan Native, %		−0.627***	(−0.797, −0.456)		−0.158***	(−0.223, −0.094)
Asian, %		0.605***	(0.403, 0.807)		0.167***	(0.111, 0.223)
Hispanic, %		−0.061*	(−0.132, 0.010)		0.004	(−0.020, 0.028)
Foreign born, %		−0.253***	(−0.422, −0.084)		−0.096***	(−0.147, −0.046)
Economic and social features						
Median household income, $1000	20.85%	−0.190***	(−0.250, −0.130)	18.36%	−0.030***	(−0.050, −0.009)
Unemployed, %		−0.565***	(−0.781, −0.349)		−0.110***	(−0.187, −0.033)
Enrolled in school, %		−0.219**	(−0.404, −0.033)		−0.141***	(−0.213, −0.069)
No. of violent crime per 100 000 population		0.001	(−0.002, 0.003)		−0.002***	(−0.003, −0.001)
Health care and features of the environment						
No. of primary care physicians per 100 000 population	18.64%	0.010	(−0.008, 0.027)	13.90%	0.011***	(0.005, 0.018)
Medicare enrollees age 65 to 75 with diabetes undergoing HbA_{1c} test, %		−0.475***	(−0.617, −0.334)		−0.171***	(−0.230, −0.112)
Access to exercise opportunities, %		−0.105***	(−0.139, −0.070)		−0.006	(−0.019, 0.007)
Food environment index		−1.026***	(−1.687, −0.364)		−0.171	(−0.415, 0.073)
Population health indicators						
CVD risk index	23.73%	1.295***	(0.712, 1.877)	30.23%	0.835***	(0.637, 1.033)
Poor/fair health, %		0.811***	(0.644, 0.978)		0.296***	(0.226, 0.367)
Total Medicare reimbursements per enrollee, $1000		1.196***	(0.733, 1.658)		0.212**	(0.046, 0.379)
R^2		49.94%			55.20%	

CVD indicates cardiovascular disease; and PCD, premature cardiac death.
*P<0.05, **P<0.01; ***P<0.001.

in the percentage of foreign-born residents, mortality was lower by 0.253 (95% CI, −0.422 to −0.084) deaths per 100 000 people-years. Mortality associations for median household income (thousands of dollars) was −0.190 (95% CI −0.250 to −0.130) deaths per 100 000 people-years; for percentage of unemployment, −0.565 (95% CI, −0.781 to −0.349) deaths per 100 000 people-years; and for percentage of school enrollment, −0.219 (95% CI, −0.404 to −0.033) deaths per 100 000 people-years. For healthcare/environment, the percentage of Medicare enrollees with diabetes mellitus who underwent glycated hemoglobin testing was inversely associated with mortality at −0.475 (95% CI, −0.617 to 0.334) deaths per 100 000 people-years, access to exercise opportunities was negatively associated with mortality at −0.105 (95% CI, −0.139, −0.070) deaths per 100 000 people-years, and the food environment index was negatively associated with mortality at −1.026 (95% CI, −1.687 to −0.364) deaths per 100 000 people-years. For the population health status, the cardiovascular disease risk index was positively associated with mortality at 1.295 (95% CI, 0.712–1.877) deaths per 100 000 people-years; percentage of poor/fair health population, 0.811 (95% CI, 0.644–0.978) deaths per 100 000 people-years; and total Medicare reimbursements per enrollee, 1.196 (95% CI, 0.733–1.658) deaths per 100 000 people-years. For in-hospital PCD, number of primary care physicians per 100 000 population was negatively associated with mortality at −0.011 (95% CI, −0.005 to −0.018). The number of violent crimes per 100 000 population was positively associated with mortality at 0.002 (95% CI, 0.001–0.003). The proportion of women, Hispanics, access to exercise opportunities, and food environment index showed no significance with the in-hospital PCD rates (Table 3).

DISCUSSIONS

This is one of the first national analyses on factors related to disparities in PCD rates among US counties. Taking advantage of vital statistics from the entire United States, we found increasing proportions of out-of-hospital death among all PCDs, which appeared to be higher in younger age groups, and the county-level disparities in PCD rates were widening during the past 2 decades, and were associated with demographic composition, socioeconomic features, healthcare environment, and population health status.

The rate of PCD in our study at 55.2 per 100 000 population in 2017 was consistent with those reported by recent prospective studies.[25] Although the American Heart Association has set a strategic goal of reducing PCDs of all Americans by 20% from 2010 to 2020,[26] our findings suggest that a deceleration in the decline of PCD rates has occurred since 2011, and, if this trend continues, strategic goals may not be reached.

Approximately 60% of PCDs occurred out of the hospital, suggestive of either sudden and unexpected nature, such as sudden cardiac death (SCD), or continuing problems of delays in seeking care, particularly in younger age and nonwhite subgroups. Sudden death from primary cardiac arrests or ST-segment–elevation myocardial infarction is more likely to occur before the patient reaches the hospital.[27] It is estimated that in the United States, almost 60% of SCD cases are managed by prehospital emergency medical services. Only about 5% of the patients with cardiac arrest survive and are discharged from the hospital.[25] Low population awareness of signs and symptoms of a heart attack and calling 9-1-1, and lack of appropriate emergency medical service responses could result in this low survival rate. Therefore, there is a need to implement comprehensive strategies at the system level for managing out-of-hospital PCD.[28] In addition, SCDs at a younger age have devastating economic and social impact, and can lead to more lost productivity than those occurring later in life. Unlike other countries, including Japan, Italy, and Israel, there is no national program in the United States for early screening of potential underlying diseases that may cause SCD in the young, largely because of a lack of agreement on the screening methods that could provide optimal predictive values and effectiveness. Our findings suggest a need for a potential program that can identify high-risk young populations prone to SCD.[29] Our findings also serve to emphasize that we should compare the factors related to disparities in out-of-hospital PCD with those in in-hospital PCD, and target specific strategies for each of them.

Black individuals continued to have the highest PCD rates during the period from 1999 to 2017. Nevertheless, the out-of-hospital PCD rates among men had the lowest decline rate for blacks than that for whites, American Indians or Alaska Natives, and Asians or Pacific Islanders. There were several reasons. Blacks have a higher prevalence of traditional cardiac risk factors including hypertension, left ventricular hypertrophy, diabetes mellitus, coronary heart disease, and heart failure.[30] There are also significant disparities in healthcare delivery, and blacks generally have less access to health care.[31] The US national representative survey reported that 90% of black individuals with cardiac arrest had never been told of their risk for cardiac death, and 60% had not sought medical care for heart disease symptoms.[32] Additional observational analysis pointed out that blacks underutilized lifesaving therapies such as implantable cardioverter-defibrillators[33] and had lower rates of bystander cardiopulmonary resuscitation than those of high neighborhood socioeconomic status.[34] In addition, genomic analysis indicated that genetic variants predisposing to cardiac death might be more prevalent in black individuals.[35,36] These findings suggest that the investments in prevention and treatment will need to account for large existing racial and ethnic disparities in PCD, with priorities focusing on disadvantaged populations.

Furthermore, we found that county-specific PCD rates varied considerably across the United States, and the disparities among the US counties were widening. Beyond describing the regional disparities in PCD, identifying potentially pathogenic factors that could explain county disparities would provide insight into how to reduce disparities and achieve more equitable health outcomes.[37–40] The understanding of these factors can be useful in designing targeted evidence-based public health interventions and policies for the neediest clusters of counties and populations. Therefore, effective strategies should address specific drivers that underlie the disparities and be tailored to local context before implementing interventions. Since socioeconomic status (eg, income) might be related to the disparities in PCD rates, our findings quantified that socioeconomic features could explain larger disparities in out-of-hospital PCD than those in in-hospital PCD, while population health status could add more information for explaining the disparities in in-hospital PCD than those in out-of-hospital PCD. For both out-of-hospital and in-hospital PCD, disparities were largely associated with demographic composition and socioeconomic circumstances beyond the scope of healthcare environment, implying that reducing regional disparities might likely require policies aiming at improving the socioeconomic circumstances of disadvantaged states. For in-hospital PCD, access to health care may not influence the disparities as much as poor health status in the first place, making primordial prevention of risk factors a primary health-related goal for reducing the geographic disparities. We also found that the within-state differences accounted for a majority of disparity across US counties. Thus, it is a necessary to analyze how such pathogenic factors that underlie the disparities in PCD rates vary within counties.

In addition, we found that the majority of states with a relatively higher between-county disparity had worse trends in PCD rates. This finding is consistent with our previous study showing that the inequitable distribution of health resources might be an important determinant of bad health outcomes.[18] The finding also accords with previous studies concluding that relative inequalities in premature cardiovascular deaths are projected to widen further, reflecting slower mortality declines.[41] These findings provide solid evidence that improving socioeconomic conditions of disadvantaged populations could help improve their health outcomes. More detailed analyses should be focused on the relationship between the geographic disparities and temporal trends in PCD rates. Moreover, case studies of the states with the lowest rates of PCD, especially those with lower between-county disparity during 2010 to 2017 than that during 1999 to 2010, are warranted to identify the factors and interventions that may be leading to their better PCD rates, and that could be disseminated to the other states.

Study Limitations

This study had several limitations. First, our study was based on county-level data, and all of the explained factors are county-level, so as an ecological study, ecological fallacy cannot be avoided. Second, the accuracy of the underlying cause of death data depends on the certifier of each death and the state and national nosologists who determine the *ICD-10* codes and the underlying cause. The cause-of-death information on the death certificate is not always validated by medical record or autopsy verification. Thus, misclassification of cases may occur; it cannot be determined whether the direction of misclassification results in under-reporting or over-reporting of the incidence of PCD. The specificity of national mortality codes in identifying cardiovascular disease has been reported to be as high as 97%, but the sensitivity has been found to be lower, resulting in the potential underestimation of the PCD rate.[42] One prospective study showed that the death certificate–based method results in a significantly higher number of cases compared with prospective adjudication of SCD cases.[25] Whether the use of death certificate–based methods and the use of *ICD* codes is an accurate method for identifying the absolute number of SCD cases is unknown; however, annual trends and comparisons between age, sex, and race groups should not be affected.

Third, the time of onset of disease symptoms and exact time of death are not available for analyses, which limited our ability to identify SCD and non-SCD. Clinically, SCD is the unexpected death from a cardiac cause a short time (often within 1 hour) after the onset of symptoms with no other probable cause of death suggested from the medical record or interview of relatives.[43] Unfortunately, such a definition is difficult to apply in public health surveillance because information on the time of onset is often not available from death certificate data sets. However, studies involving retrospective physician review have reported that the validity of the underlying cause of death on the death certificate for both PCD that occurred out of the hospital and SCD is reasonably high.[44,45] Furthermore, our inclusion criterion was based on *ICD-10* codes identified on the basis of a literature review, in which researchers targeted SCD in young and middle-aged adults.[6–8,12,18]

CONCLUSIONS

Disparities in PCD rates existed across US counties, which may be related to the decelerated trend of decline in the rates among middle-aged adults. The slower declines in out-of-hospital rates is alarming and warrants more precision targeting and sustained efforts to ensure progress at better levels of health (with lower PCD rates) against PCD.

ARTICLE INFORMATION

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Author contributions: design of the study: Jin and Zheng; collection, management, analysis, and interpretation of the data: Jin and Song; preparation, review, or approval of the article: Jin, Song, Zhang, Trisolini, Labresh, Smith, Jr, and Zheng; decision to submit the article for publication: Jin, Song, Zhang, Trisolini, Labresh, Smith, Jr, and Zheng.

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Disclosures

None.

Supplementary Materials

Tables S1–S4
Figure S1

REFERENCES

1. Kaltman JR, Thompson PD, Lantos J, Berul CI, Botkin J, Cohen JT, Cook NR, Corrado D, Drezner J, Frick KD, et al. Screening for sudden cardiac death in the young: report from a National Heart, Lung, and Blood Institute Working Group. *Circulation*. 2011;123:1911–1918.
2. Stecker EC, Reinier K, Marijon E, Narayanan K, Teodorescu C, Uy-Evanado A, Gunson K, Jui J, Chugh SS. Public health burden of sudden cardiac death in the United States. *Circ Arrhythm Electrophysiol*. 2014;7:212–217.
3. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, Simone GD, Ferguson TB, Ford E, Furie K, Gillespie C, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics–2010 update: a report from the American Heart Association. *Circulation*. 2010;121:e46–e215.
4. Hayashi M, Shimizu W, Albert CM. The spectrum of epidemiology underlying sudden cardiac death. *Circ Res*. 2015;116:1887–1906.
5. World Health Organization. *Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000–2016*. Geneva: WHO; 2016. Available at: http://terrance.who.int/mediacentre/data/ghe/GlobalCOD_method_2000_2016.pdf?ua=1. Published 2018. Accessed May 31, 2018.
6. Zheng ZJ, Croft JB, Giles WH, Mensah GA. Sudden cardiac death in the United States, 1989 to 1998. *Circulation*. 2001;104:2158–2163.
7. Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP, Rea T, Lowe R, Brown T, Dreyer J, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. *JAMA*. 2008;300:1423–1431.
8. Rea TD, Eisenberg MS, Sinibaldi G, White RD. Incidence of EMS-treated out-of-hospital cardiac arrest in the United States. *Resuscitation*. 2004;63:17–24.
9. Kong MH, Fonarow GC, Peterson ED, Curtis AB, Hernandez AF, Sanders GD, Thomas KL, Hayes DL, Al-Khatib SM. Systematic review of the incidence of sudden cardiac death in the United States. *J Am Coll Cardiol*. 2011;57:794–801.
10. World Health Organization. Set of 9 voluntary global NCD targets for 2025. Available at: https://www.who.int/nmh/ncd-tools/definition-targets/en/. Accessed March 16, 2019.
11. Sacco RL, Roth GA, Reddy KS, Arnett DK, Bonita R, Gaziano TA, Heidenreich PA, Huffman MD, Mayosi BM, Mendis S, et al. The heart of 25 by 25: achieving the goal of reducing global and regional premature deaths from cardiovascular diseases and stroke: a modeling study from the American Heart Association and World Heart Federation. *Circulation*. 2016;133:e674–e690.
12. Girotra S, van Diepen S, Nallamothu BK, Carrel M, Vellano K, Anderson ML, McNally B, Abella BS, Sasson C, Chan PS, et al. Regional variation in out-of-hospital cardiac arrest survival in the United States. *Circulation*. 2016;133:2159–2168.
13. Kolte D, Khera S, Aronow WS, Palaniswamy C, Mujib M, Ahn C, Iwai S, Jain D, Sule S, Ahmed A, et al. Regional variation in the incidence and outcomes of in-hospital cardiac arrest in the United States. *Circulation*. 2015;131:1415–1425.
14. Song S, Michael GT, Kenneth AL, Sidney CS, Jin Y, Zheng ZJ. Factors associated with county-level variation in premature mortality due to noncommunicable chronic disease in the United States, 1999–2017. *JAMA Netw Open*. 2020;3:e200241.
15. Myat A, Song KJ, Rea T. Out-of-hospital cardiac arrest: current concepts. *Lancet*. 2018;391:970–979.
16. National Center for Health Statistics. Compressed Mortality File 1999-2017 on CDC WONDER, released October 2014. Atlanta, GA: Centers for Disease Control and Prevention; 2014. Available at: http://wonder.cdc.gov/cmf-icd10.html. Published 2019.Accessed April 20, 2019.
17. Lopez AD, Adair T. Is the long-term decline in cardiovascular-disease mortality in high-income countries over? Evidence from national vital statistics. *Int J Epidemiol*. 2019;48:1815–1823.
18. Zheng ZJ, Croft JB, Giles WH, Mensah GA. Out-of-hospital cardiac deaths in adolescents and young adults in the United States, 1989 to 1998. *Am J Prev Med*. 2005;29:36–41.
19. Song S, Hou Z, Zhang L, Meng Q, Kawachi I. Can equitable distribution of health resources reduce under-five mortality rate? A cross-sectional study with multilevel analysis of rural counties in China. *Lancet*. 2018;392:S58.
20. Rossen LM, Schoendorf KC. Trends in racial and ethnic disparities in infant mortality rates in the United States, 1989–2006. *Am J Public Health*. 2014;104:1549–1556.
21. Whitfield GP, Carlson SA, Ussery EN, Fulton JE, Galuska DA, Petersen R. Trends in meeting physical activity guidelines among urban and rural dwelling adults—United States, 2008–2017. *MMWR Morb Mortal Wkly Rep*. 2019;68:513–518.
22. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int J Epidemiol*. 2017;46:348–355.
23. Klein RJ, Schoenborn CA. Age adjustment using the 2000 Projected U.S. population. *Healthy People 2010 Stat Notes*. No. 20. Hyattsville, MD: National Center for Health Statistics; 2001. DHHS Publication no.(PHS) 2001-1237.

24. Budescu DV. Dominance analysis: a new approach to the problem of relative importance of predictors in multiple regression. *Psychol Bull*. 1993;114:542.
25. Shiels MS, Chernyavskiy P, Anderson WF, Best AF, Haozous EA, Hartge P, Rosenberg PS, Thomas D, Freedman ND, de Gonzalez AB. Trends in premature mortality in the USA by sex, race, and ethnicity from 1999 to 2014: an analysis of death certificate data. *Lancet*. 2017;389: 1043–1054.
26. Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Horn LV, Greenlund K, Daniels S, Nichol G, Tomaselli GF, et al; American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and setting national goals for cardiovascular health promotion and disease reduction: the AHA's strategic Impact Goal through 2020 and beyond. *Circulation*. 2010;121:586–613.
27. Escobedo LG, Zack MM. Comparison of sudden and nonsudden coronary deaths in the United States. *Circulation*. 1996;93:2033–2036.
28. Graham R, McCoy MA, Schultz AM. *Strategies to Improve Cardiac Arrest Survival: a Time to Act*. Washington, DC: National Academies Press; 2015.
29. Idriss SF, Berger S, Harmon KG, Kindman A, Kleiman R, Lopez-Anderson M, Molossi S, Saarel TE, Strnadova C, Todaro T, et al. Prevention of sudden cardiac death in the young: developing a rational, reliable, and sustainable national health care resource. *Am Heart J*. 2017;190:123–131.
30. Carnethon MR, Pu J, Howard G, Albert MA, Anderson CAM, Bertoni AG, Mujahid MS, Palaniappan L, Taylor HA Jr, Willis M, et al. Cardiovascular health in African Americans: a scientific statement from the American Heart Association. *Circulation*. 2017;136:e393–e423.
31. Chen J, Vargas-Bustamante A, Mortensen K, Ortega AN. Racial and ethnic disparities in health care access and utilization under the Affordable Care Act. *Med Care*. 2016;54:140–146.
32. Groeneveld PW, Heidenreich PA, Garber AM. Racial disparity in cardiac procedures and mortality among long-term survivors of cardiac arrest. *Circulation*. 2003;108:286–291.
33. Hernandez AF, Fonarow GC, Liang L, Al-Khatib SM, Curtis LH, LaBresh KA, Yancy CW, Albert NM, Peterson ED. Sex and racial differences in the use of implantable cardioverter-defibrillators among patients hospitalized with heart failure. *JAMA*. 2007;298:1525–1532.
34. Starks MA, Schmicker RH, Peterson ED, May S, Buick JE, Kudenchuk PJ, Drennan IR, Herren H, Jasti J, Sayre M, et al. Association of neighborhood demographics with out-of-hospital cardiac arrest treatment and outcomes: where you live may matter. *JAMA Cardiol*. 2017;2:1110–1118.
35. Kao WHL, Arking DE, Post W, Rea TD, Sotoodehnia N, Prineas RJ, Bishe B, Doan BQ, Boerwinkle E, Psaty BM, et al. Genetic variations in NOS1AP are associated with sudden cardiac death in US white community based populations. *Circulation*. 2009;119:940.
36. Deo R, Albert CM. Epidemiology and genetics of sudden cardiac death. *Circulation*. 2012;125:620–637.
37. Patel SA, Ali MK, Narayan KMV, Mehta NK. County-level variation in cardiovascular disease mortality in the United States in 2009–2013: comparative assessment of contributing factors. *Am J Epidemiol*. 2016;184:933–942.
38. Patel SA, Narayan KMV, Ali MK, Mehta NK. Interstate variation in modifiable risk factors and cardiovascular mortality in the United States. *PLoS One*. 2014;9:e101531.
39. Strömsöe A, Svensson L, Claesson A, Lindkvist J, Lundström A, Herlitz J. Association between population density and reported incidence, characteristics and outcome after out-of-hospital cardiac arrest in Sweden. *Resuscitation*. 2011;82:1307–1313.
40. Dwyer-Lindgren L, Bertozzi-Villa A, Stubbs RW, Morozoff C, Machenbach JP, van Lenthe FJ, Mokdad AH, Murray CJL. Inequalities in life expectancy among US counties, 1980 to 2014. *JAMA Intern Med*. 2017;177:1003–1011.
41. Keaver L, Pérez-Ferrer C, Jaccard A, Webber L. Future trends in social inequalities in obesity in England, Wales and Scotland. *J Public Health*. 2020;42:e51–e57.
42. Harriss LR, Ajani AE, Hunt D, Shaw J, Chambers B, Dewey H, Frayne J, Beauchamp A, Duvé K, Giles GG, et al. Accuracy of national mortality codes in identifying adjudicated cardiovascular deaths. *Aust N Z J Public Health*. 2011;35:466–476.
43. Zipes DP, Wellens HJJ. Sudden cardiac death. *Circulation*. 1998;98: 2334–2351.
44. Folsom AR, Gomez-Marin O, Gillum RF, Kottke TE, Lohman W, Jacobs DR. Out-of-hospital coronary death in an urban population—validation of death certificate diagnosis: the Minnesota Heart Survey. *Am J Epidemiol*. 1987;125:1012–1018.
45. Iribarren C, Crow RS, Mstat PJH, Jacobs D Jr, Luepker R. Validation of death certificate diagnosis of out-of-hospital sudden cardiac death. *Am J Cardiol*. 1998;82:50–53.

SUPPLEMENTAL MATERIAL

Table S1. Variables included in the regression analysis with data source and summary statistics.

County Characteristics	Data source	Median	Interquartile ranges	Max	Min
Demographic composition					
Population, 2011–2017, thousands	CPE[I]	42.41	83.73	10170.29	4.44
% Rural, 2011-2017	CHRR[II]	50.56	45.61	100.00	0.00
% Female, 2011–2017	CPE[I]	50.58	1.34	56.84	34.05
% Aged ≥65 years, 2011–2017	CPE[I]	16.49	4.63	56.94	5.10
% African American, 2011–2017	CPE[I]	3.81	13.13	85.33	0.05
% American Indian/Alaskan Native, 2011–2017	CPE[I]	0.51	0.69	93.80	0.04
% Asian, 2011–2017	CPE[I]	0.76	1.12	43.90	0.04
% Hispanic, 2011–2017	CPE[I]	4.02	6.96	96.32	0.27
% Foreign born, 2011–2017	ACS[III]	2.90	4.47	52.00	0.00
Economic and social features					
Median household income, 2011-2017, thousands of dollars	SAIPE[IV]	40.77	14.02	136.19	15.33
% Unemployed, 2011–2017	Bureau of Labor Statistics[V]	6.39	3.31	29.70	0.82
% Enrolled in school, 2011-2017	ACS[III]	24.88	4.74	55.16	7.86
Numbers of violent crime per 100,000 person-years, 2011–2017	CHRR[II]	240.65	245.46	2349.64	0.00
Health care and features of the environment					
Primary care physicians per 100,000 population, 2011-2017	CHRR[II]	52.63	37.97	631.94	0.00
% Medicare enrollees age 65-75 with diabetes undergoing HbA1c test, 2011-2015※	DAHC[VI]	85.62	2.95	100.00	12.28
% People with access to places for physical activity, 2014-2019※	CHRR[VII]	61.7	24.88	100.00	0.00
Food environment index, 2014-2019† ※	CHRR[VIII]	7.41	1.02	10.00	0.50
Population health indicators					
NCD risk index, 2011-2017* ※	CHRR[II]	-0.01	2.56	5.67	-7.04
% poor/fair health, 2011-2017	CHRR[II]	16.90	7.50	50.80	3.60
Total Medicare reimbursements per enrollee, 2011-2016, thousands of dollars	DAHC[VI]	9.92	1.48	17.72	4.52

Sources: [I] Census Population Estimates (CPE).

[II] University of Wisconsin Population Health Institute. County Health Rankings & Roadmaps (CHRR) provides a model to help communities understand the factors influencing healthy residents. It summaries many health outcome and health factors from other databases each year.

[III] American Community Survey (ACS).

[IV] Small Area Income and Poverty Estimates (SAIPE).

[V] Bureau of Labor Statistics.

[VI] Dartmouth Atlas of Health Care (DAHC). DAHC is a publicly available source of data providing county-level Medicare spending and mortality rates, selected measures of primary care access and quality and hospital and physician capacity measures.

[VII] 2014-2019 CHRR databases summarized this variable from OneSource Global Business Browser (Avention, Concord, Massachusetts), DeLorme map data (DeLorme, Yarmouth, Maine), Esri (Redlands, California), and Census Bureau TIGER/Line files from 2012-2018.

[VIII] 2014-2019 CHRR databases summarized this variable from US Department of Agriculture Food Environment Atlas, Map the Meal Gap (DAFEA) from 2011-2016.

※ For those variables restricted to year range, we conducted ordinary least square regression model to predict the missing value.
† Food environment index is a composite score, ranging from 1 to 10, describing limits on access to healthy foods, with 1 indicating the lowest access to healthy foods, and 10 indicating the highest access to healthy foods.
* NCD risk index was calculated by principal components analysis on county-level prevalence of diabetic, tobacco smoking, excessive drinking, obesity and physical inactivity.

Table S2. Results of ITS on trends in age-adjusted rates of cardiac death (per 100000 population) in US residents aged 35-74 years, by sex, race and age, 1999-2017.

Group	Out-of-hospital cardiac death				In-hospital cardiac death			
	Trend prior to 2010		Trend post 2010		Trend prior to 2010		Trend post 2010	
	Coefficient	p-value	Coefficient	p-value	Coefficient	p-value	Coefficient	p-value
By sex and race								
Men White	-2.4	<0.01	-0.2	<0.01	-1.7	<0.01	0.1	0.05
Men African American	-1.3	<0.01	0.6	<0.01	-2.0	<0.01	0.3	0.02
Men American Indian or Alaska Native	-1.5	<0.01	-0.7	<0.01	-1.0	<0.01	0.2	0.10
Men Asian or Pacific Islander	-0.7	<0.01	0.03	0.5	-0.8	<0.01	0.04	0.50
Women White	-1.0	<0.01	0.1	0.01	-1.2	<0.01	-0.004	0.96
Women African American	-1.8	<0.01	-0.2	<0.01	-1.7	<0.01	0.01	0.90
Women American Indian or Alaska Native	-0.4	<0.01	0.3	0.1	-0.9	<0.01	0.1	0.20
Women Asian or Pacific Islander	-0.3	<0.01	-0.02	0.7	-0.7	<0.01	0.02	0.50
By sex and age								
Men 35-44 years	-0.4	<0.01	-0.3	<0.01	-0.07	<0.01	0.02	0.20
Men 45-54 years	-1.4	<0.01	-0.9	<0.01	-0.5	<0.01	0.07	0.40
Men 55-64 years	-4.3	<0.01	-1.1	<0.01	-2.6	<0.01	-0.1	0.20
Men 65-74 years	-10.0	<0.01	-2.0	<0.01	-9.0	<0.01	-1.4	<0.01
Women 35-44 years	-0.09	<0.01	-0.06	0.05	-0.07	<0.01	0.01	0.14
Women 45-54 years	-0.2	<0.01	-0.2	<0.01	-0.3	<0.01	0.03	0.07
Women 55-64 years	-1.5	<0.01	-0.2	<0.01	-1.6	<0.01	-0.2	0.20
Women 65-74 years	-4.9	<0.01	-0.9	<0.01	-5.4	<0.01	-1.1	<0.01
Total	-1.7	<0.01	-0.1	0.01	-1.4	<0.01	0.07	0.30

Table S3. Distribution (%) of underlying cause among PCDs, by age and sex, 1999-2017.

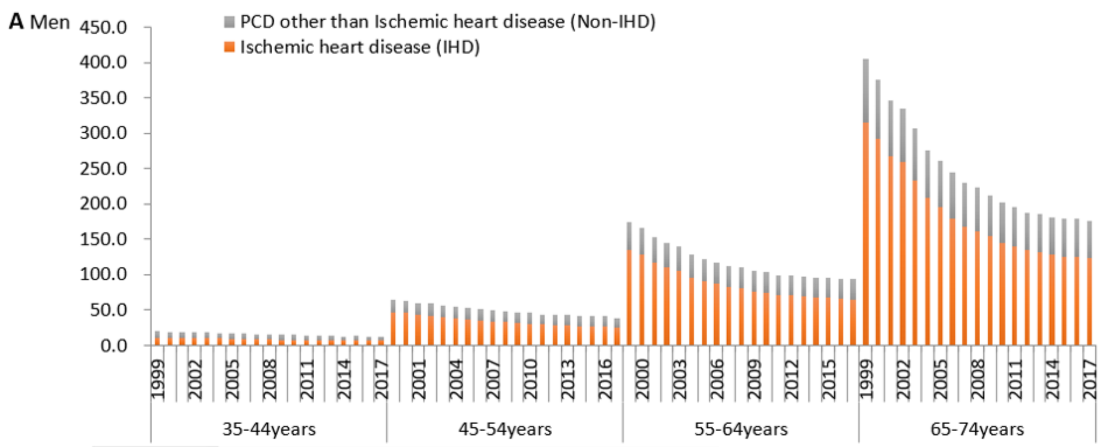
Type of cardiac disease (ICD 10)	Total		35-44 years		45-54 years		55-64 years		65-74 years	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
Out-of-hospital										
Ischemic heart disease	73.8	68.8	58.2	46.5	71.7	62.3	75.6	70.4	75.9	72.5
Dilated cardiomyopathy	3.0	2.8	9.0	8.6	4.6	5.2	2.5	2.5	1.7	1.5
hypertrophic cardiomyopathy	0.9	0.8	4.3	3.2	1.6	1.7	0.6	0.7	0.2	0.4
Other cardiomyopathies	7.3	7.6	10.2	11.6	7.3	8.5	6.6	7.2	7.4	7.0
Arrhythmia	13.4	17.2	13.7	21.1	13.0	18.6	13.6	17.3	13.4	16.3
Congenital heart disease	1.5	2.6	4.0	7.7	1.6	3.2	1.1	1.8	1.4	2.3
Myocarditis	0.1	0.2	0.6	1.1	0.2	0.5	0.1	0.2	0.0	0.1
Other	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0
In-hospital										
Ischemic heart disease	67.6	65.7	46.4	42.5	62.0	56.1	68.8	64.8	70.4	70.2
Dilated cardiomyopathy	3.3	2.5	8.9	5.8	4.9	4.1	3.1	2.7	2.4	1.9
hypertrophic cardiomyopathy	0.4	0.6	1.6	1.6	0.7	0.9	0.4	0.6	0.2	0.5
Other cardiomyopathies	13.6	11.8	21.9	18.7	16.5	15.2	13.2	12.4	12.3	10.2
Arrhythmia	11.5	14.2	13.7	20.4	12.5	18.5	11.6	15.4	10.8	12.2
Congenital heart disease	3.5	4.9	6.8	9.8	3.1	4.7	2.8	3.9	3.8	5.0
Myocarditis	0.1	0.2	0.6	1.2	0.2	0.4	0.1	0.1	0.1	0.1
Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table S4. Results of ITS on trends in age-adjusted rates of cardiac death (per 100000 population) in US residents aged 35-74 years, by state, 1999-2017.

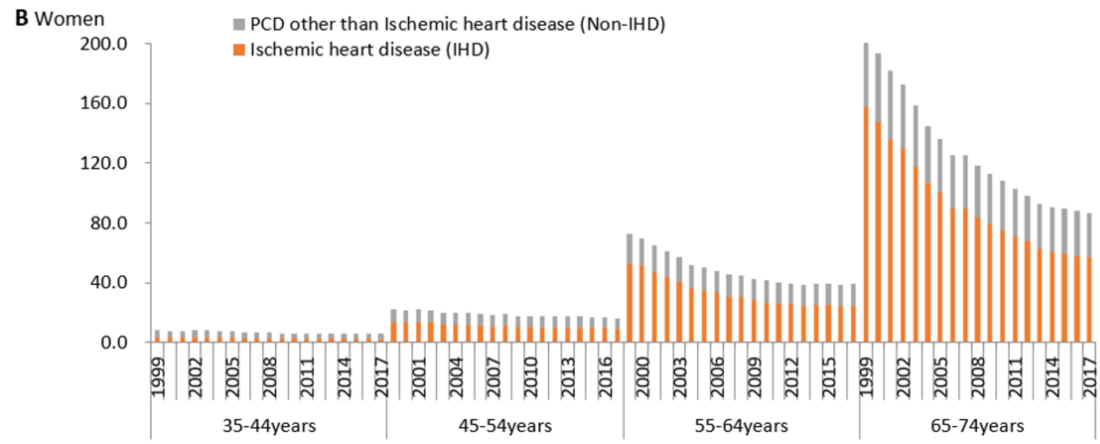
State	Between-county Inequality		Out-of-hospital cardiac death				In-hospital cardiac death			
	prior to 2010	post 2010	Trend prior to 2010		Trend post 2010		Trend prior to 2010		Trend post 2010	
	Theil Index	Theil Index	Coefficient	p-value	Coefficient	p-value	Coefficient	p-value	Coefficient	p-value
Alabama	0.06	0.10	-1.3	<0.01	-4.5	<0.01	-1.5	<0.01	3.8	0.01
Alaska	0.02	0.07	-0.8	0.05	0.8	0.07	-0.5	0.02	0.2	0.28
Arizona	0.07	0.04	-2.1	<0.01	0.1	0.10	-1.5	<0.01	0.3	<0.01
Arkansas	0.04	0.06	0.02	0.90	2.3	<0.01	-2.4	<0.01	0.1	0.58
California	0.05	0.11	-0.9	<0.01	-0.009	0.79	-1.1	<0.01	-0.02	0.67
Colorado	0.14	0.17	-0.8	<0.01	-0.4	<0.01	-0.7	<0.01	0.1	0.03
Connecticut	0.01	0.01	-0.4	<0.01	-0.8	<0.01	-0.9	<0.01	-0.2	0.11
Delaware	0.02	0.01	-1.7	<0.01	-0.1	0.73	-1.6	<0.01	0.02	0.97
District of Columbia	NA	NA	-0.6	0.03	0.23	0.54	-1.0	0.02	0.6	0.26
Florida	0.04	0.05	-1.5	<0.01	-0.05	0.49	-1.9	<0.01	0.06	0.27
Georgia	0.07	0.15	-5.3	<0.01	0.01	0.90	-2.8	<0.01	0.1	0.43
Hawaii	0.02	0.02	-0.9	<0.01	-0.4	0.48	-2	<0.01	-0.1	0.58
Idaho	0.05	0.05	-1.2	0.03	0.5	0.18	-1.1	<0.01	0.2	0.31
Illinois	0.06	0.10	-2	<0.01	-0.2	0.06	-1.3	<0.01	-0.01	0.67
Indiana	0.03	0.05	-1.4	<0.01	0.6	<0.01	-1.8	<0.01	0.2	0.10
Iowa	0.05	0.07	-1.5	<0.01	-0.7	<0.01	-1.4	<0.01	-0.03	0.85
Kansas	0.06	0.09	-2.1	<0.01	-0.6	0.02	-1.8	<0.01	0.06	0.52
Kentucky	0.06	0.10	-1.1	0.02	1.4	<0.01	-2.2	<0.01	-0.07	0.54
Louisiana	0.08	0.20	-1.4	<0.01	-0.8	0.03	-1.9	<0.01	0.5	0.03
Maine	0.02	0.02	-1	<0.01	-1.2	<0.01	-1	<0.01	-0.1	0.67
Maryland	0.04	0.04	-1.3	<0.01	-0.1	0.47	-0.9	<0.01	-0.1	0.61
Massachusetts	0.02	0.02	-2.2	<0.01	0.5	0.01	-1.7	<0.01	0.1	<0.01
Michigan	0.06	0.13	-2	<0.01	0.4	0.03	-1.4	<0.01	0.04	0.57
Minnesota	0.07	0.14	-1.5	<0.01	-0.2	0.06	-0.7	<0.01	0.04	0.67
Mississippi	0.05	0.06	-2.6	<0.01	-0.4	0.09	-2.1	<0.01	-0.07	0.84
Missouri	0.06	0.10	-1.9	<0.01	0.4	0.23	-1.8	<0.01	-0.06	0.54
Montana	0.06	0.12	-2	<0.01	-0.9	<0.01	-1	<0.01	-0.2	0.46
Nebraska	0.05	0.13	-1.3	<0.01	-0.3	0.18	-1.5	<0.01	0.003	0.99
Nevada	0.03	0.11	0.9	0.20	-0.8	0.07	-1.2	<0.01	0.28	0.25
New Hampshire	0.02	0.01	-0.9	<0.01	0.2	0.58	-1.1	<0.01	-0.05	0.64
New Jersey	0.02	0.03	-1.7	<0.01	-0.004	0.98	-2.2	<0.01	0.1	0.25
New Mexico	0.06	0.05	-0.4	0.05	0.02	0.93	-0.7	<0.01	0.5	0.10
New York	0.04	0.06	-1.8	<0.01	0.02	0.71	-1.3	<0.01	-0.2	0.13
North Carolina	0.03	0.04	-1.7	<0.01	-0.2	0.17	-1.5	<0.01	-0.3	<0.01

North Dakota	0.03	0.10	-3.4	<0.01	-0.3	0.31	-1.2	0.01	-0.1	0.33
Ohio	0.04	0.06	-1.9	<0.01	0.6	<0.01	-1.8	<0.01	0.4	<0.01
Oklahoma	0.03	0.05	-2.7	<0.01	-1.1	0.16	-2	<0.01	-0.9	0.04
Oregon	0.02	0.04	-1.1	<0.01	0.1	0.02	-0.7	<0.01	0.3	0.04
Pennsylvania	0.03	0.06	-2.6	<0.01	-0.2	0.51	-1.6	<0.01	0.2	0.68
Rhode Island	0.01	0.01	-1.7	<0.01	-1.8	<0.01	-0.7	<0.01	-0.1	0.23
South Carolina	0.06	0.13	-2.2	<0.01	-1.1	<0.01	-1.8	<0.01	-0.4	0.15
South Dakota	0.08	0.10	-2.3	<0.01	1.2	0.19	-2	<0.01	0.7	0.16
Tennessee	0.05	0.09	-1.7	<0.01	0.4	0.29	-1.8	<0.01	0.3	0.03
Texas	0.06	0.11	-1.8	<0.01	0.1	0.24	-1.1	<0.01	-0.1	0.36
Utah	0.04	0.06	-1.1	<0.01	-0.7	<0.01	-0.6	<0.01	-0.04	0.73
Vermont	0.01	0.02	-2.3	<0.01	-0.97	0.07	-1.2	<0.01	-0.04	0.87
Virginia	0.05	0.08	-1.1	<0.01	-0.34	0.11	-0.5	<0.01	-0.05	0.70
Washington	0.06	0.07	-0.2	0.10	-0.2	<0.01	-1	<0.01	0.2	<0.01
West Virginia	0.02	0.02	-3.4	<0.01	-1.2	<0.01	-1.6	<0.01	-0.1	0.50
Wisconsin	0.05	0.07	-2.3	<0.01	-0.7	<0.01	-1.1	<0.01	0.1	0.01
Wyoming	0.04	0.05	0.2	0.70	-0.2	0.77	-0.4	0.10	-0.5	0.13
Total	0.04	0.07	-1.7	<0.01	-0.1	0.01	-1.4	<0.01	0.07	0.30

Figure S1. Trend in death rates from the ischemic heart disease vs. PCD other than ischemic heart disease by sex and age, 1999-2017.



	Year of 2009	Relative change	Year of 2009	Relative change	Year of 2009	Relative change	Year of 2009	Relative change
IHD	11.3	-41.0%	47.2	-45.8%	134.6	-51.5%	314.9	-61.0%
Non-IHD	8.6	-29.8%	17.9	-25.7%	40.4	-29.9%	89.6	-40.6%



	Year of 2009	Relative change	Year of 2009	Relative change	Year of 2009	Relative change	Year of 2009	Relative change
IHD	3.4	-25.7%	13.9	-34.5%	52.6	-53.4%	158.0	-64.1%
Non-IHD	4.4	-27.3%	8.4	-16.1%	20.1	-27.4%	48.8	-38.7%