



## The contemporary trends and geographic variation in premature mortality due to heart failure from 1999 to 2018 in the United States



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### ABSTRACT

**Objectives:** We aimed to examine the contemporary trends and regional variations in premature mortality due to heart failure across the U.S. from 1999 to 2018.

**Background:** For most U.S. census regions, it is unknown whether premature mortality (deaths among persons under age 65) due to heart failure is increasing -or decreasing.

**Methods:** In this descriptive study, the death certificate data were retrieved from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (WONDER) database and examined from 1999 to 2018 for the underlying cause of death. Age-adjusted mortality rates (AAMR) per 100,000 persons and annual percent change (APC) in rates stratified by census region were calculated using Joinpoint trend analysis software.

**Results:** There were 118,116 premature deaths due to heart failure from 1999 to 2018 across the U.S. Of these 52.40% of deaths were reported in the South, 20.30% in the Midwest, 15.10% in the West, and 12.20% in the Northeast. The AAMRs were the highest in the South region (range: 3.1–4.9) and the lowest in the Northeast region (range: 1.5–1.9). There was an overall decline in mortality across all regions from 1999 till 2011–2012. However, mortality has an upward trajectory throughout all the census regions after 2012.

**Conclusions:** This study on nationwide data showed that overall premature mortality due to heart failure declined from 1999 to 2011–2012 followed by an upward trajectory from 2012 to 2018; the explanation for this merits further discovery.

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### 1. Introduction

Cardiovascular disease-related death (CVD) remains the leading cause of mortality and morbidity in the United States. Age-adjusted all CVD related mortality decreased significantly in the first decade of the 21st century, however, premature death (deaths among persons under age 65) due to heart disease (HD) increased 4% among middle-aged adults (45–64 years) from 2011 to 2017 [1]. Heart failure was mentioned on 378,800 (13.4%) death certificates in 2018 alone [2]. The previous decline in in-hospital mortality due to HF-related deaths first stagnated and more shockingly reversed in certain demographic groups. Largely, the perpetually increasing prevalence of coronary artery disease, and diabetes mel-

litus (DM) is responsible for the growing heart failure population. In addition, obesity, smoking, an aging population, socioeconomic risk factors (poverty), increasing awareness, and early diagnosis of heart failure might have contributed to the escalating prevalence of heart failure (6.2 million) across the U.S. It is known that the prevalence of heart failure mortality in the U.S. shows demographic and regional variations that are significantly associated with variation in the prevalence of risk factors (DM, obesity) [3]. Data are limited regarding the contemporary trends of premature mortality (age 25–64 years) due to HF-related deaths and regional variations of these trends across the United States. We aimed to investigate contemporary trends of heart failure related premature mortality, and patterns of geographic distribution across the U.S.

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**Table 1**

Table 1 shows regional annual percent change (APC)

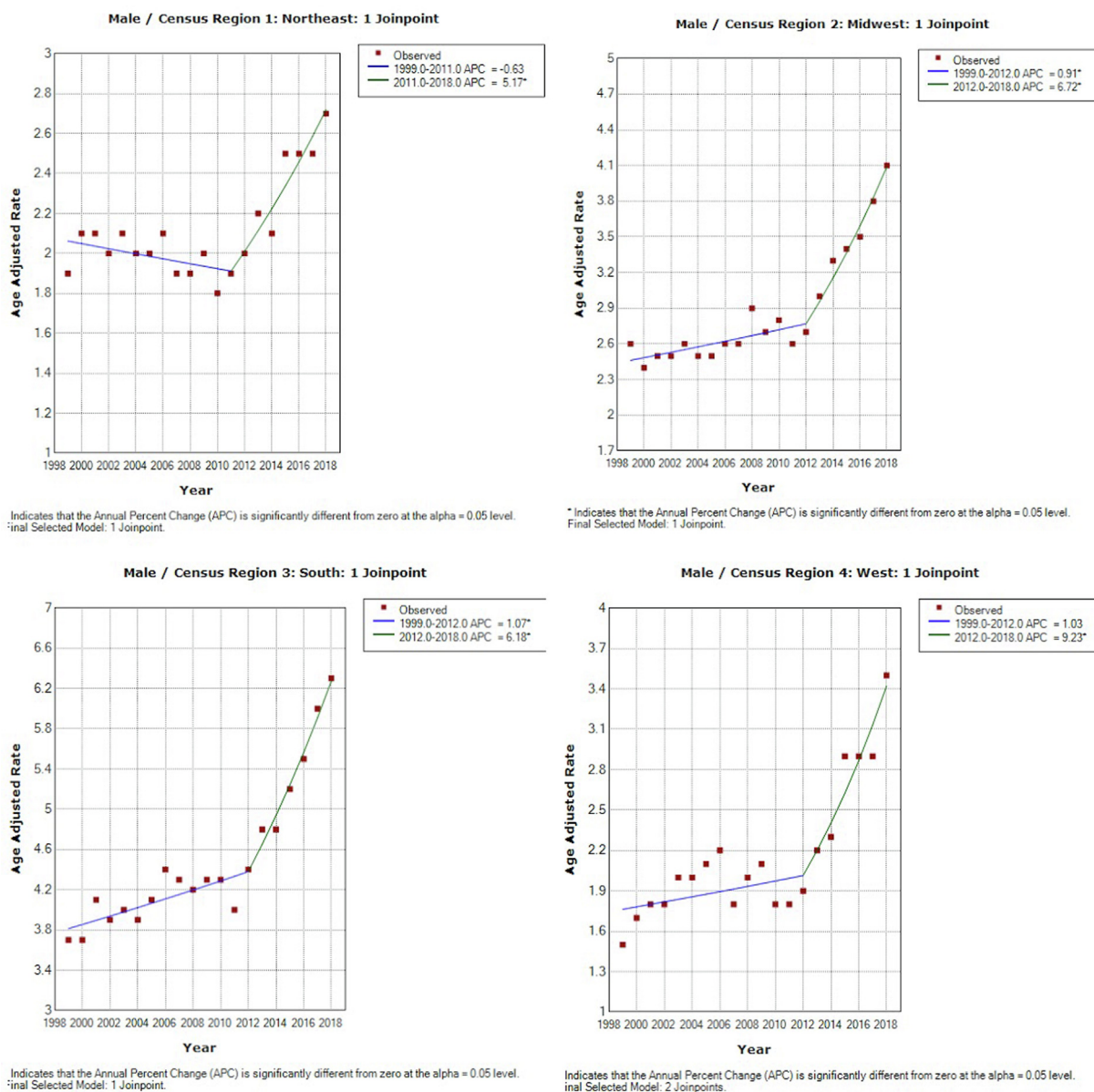
Census region	Gender	Annual percent change (year)	Annual percent change (year)
Northeast	Female	-2.24* (1999–2011)	5.66* (2011–2018)
Northeast	Male	-0.63 (1999–2011)	5.17* (2011–2018)
Midwest	Female	-0.34 (1999–2012)	6.54* (2012–2018)
Midwest	Male	0.91* (1999–2012)	6.72* (2012–2018)
South	Female	-0.42 (1999–2011)	4.54* (2011–2018)
South	Male	1.07* (1999–2012)	6.18* (2012–2018)
West	Female	-0.97 (1999–2012)	6.40* (2012–2018)
West	Male	1.03 (1999–2012)	9.23* (2012–2018)

\*Indicates Annual Percentage Change (APC) is significantly different from zero at the alpha = 0.05 level.

**2. Methods**

In this descriptive study, the death certificate data were retrieved from the Centers for Disease Control and Prevention Wide-Ranging

Online Data for Epidemiologic Research (WONDER) database and examined from 1999 to 2018 for the underlying cause of death. WONDER database was queried for the underlying cause of death (heart failure I50) using ICD-10 113 cause list in four census regions, CENS-R1 (Census Region 1: Northeast) CENS-R2 (Census Region 2: Midwest) CENS-R3 (Census Region 3: South) CENS-R4 (Census Region 4: West) from 1999 to 2018. The crude death rate, and age-adjusted mortality rate (AAMR) for all races, all genders with age <65 years were calculated with 95% confidence interval (CI) and standard error (SE). AAMRs were further stratified by gender (male, female in four census regions). Age-adjusted mortality rates (AAMR) per 100,000 persons and annual percent change (APC) in rates stratified by census region were calculated using Joinpoint trend analysis software. CDC WONDER is an integrated information and communication system developed by the Centers for Disease Control and Prevention (CDC) for public health. It provides access to a wide array of public health information including mortality (death), cancer incidence, and many other health-related topics. Data analyses were done from April 2020 to December 2020.



**Fig. 1.** Annual Percent Change (APC) among male (Northeast, South, West, Midwest regions).

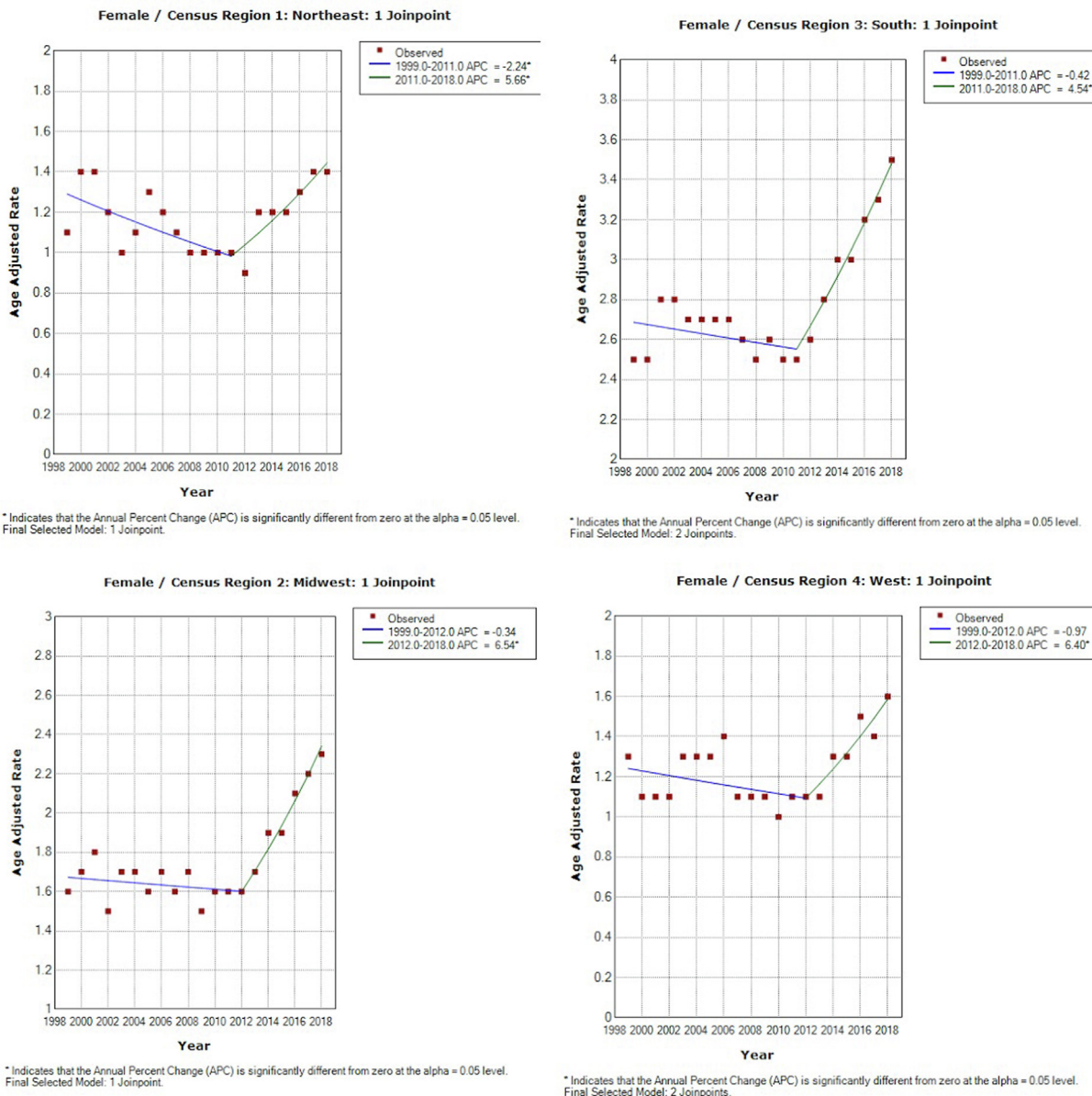


Fig. 2. Annual Percent Change (APC) among female (Northeast, South, West, Midwest regions).

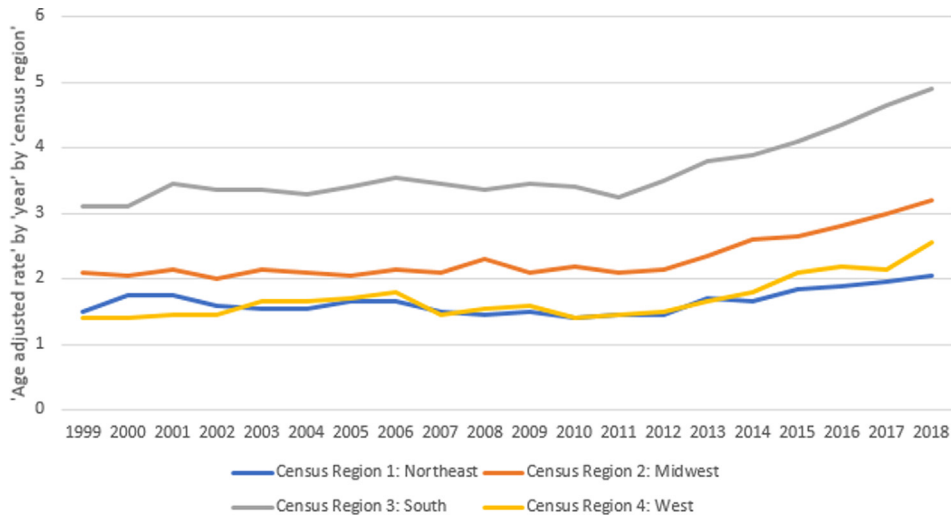


Fig. 3. Age-adjusted mortality rate by year and by census region.

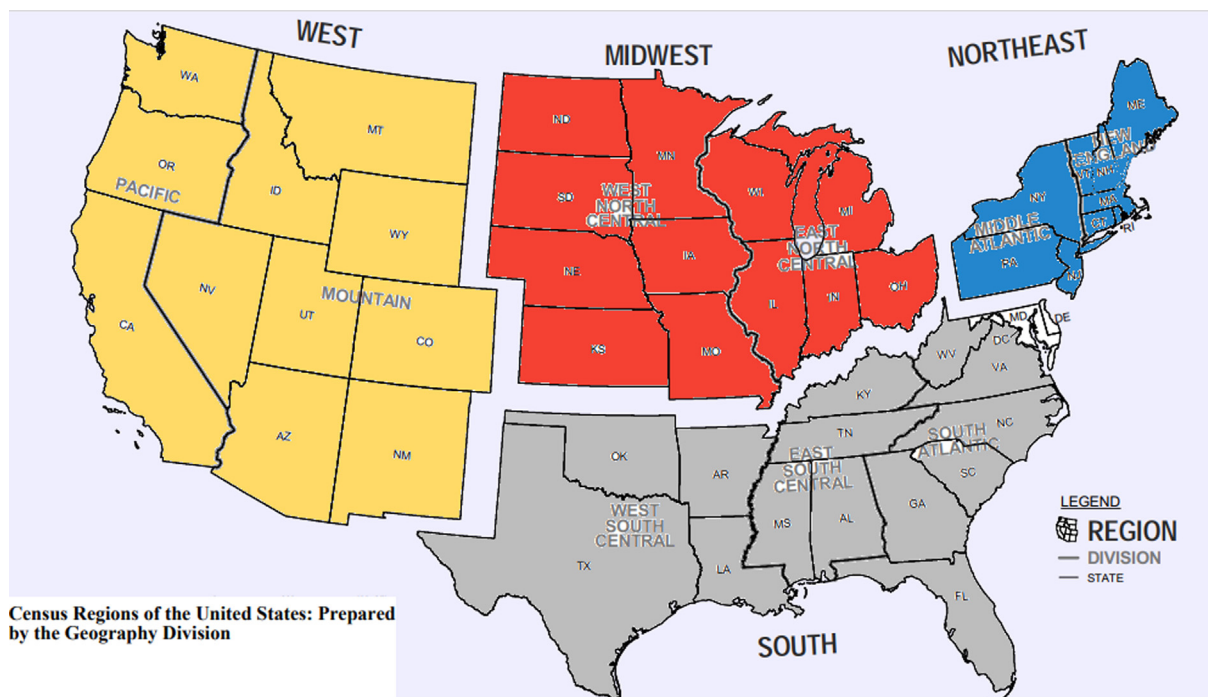


Fig. 4. Census regions of the United States, prepare by the Geography division.

### 3. Results

There were 118,116 premature deaths due to heart failure from 1999 to 2018 across the U.S. Of these 52.40% of deaths were reported in the South, 20.30% in the Midwest, 15.10% in the West, and 12.20% in the Northeast. The age-adjusted mortality rate for the Northeast region with 95% CI was 1.61 (1.6–1.7), for Midwest 2.3 (2.3–2.4), for the South 3.6 (3.6–3.7), and for the West was 1.7 (1.7–1.7). The AAMRs were highest in the South (range: 3.1–4.9) and lowest in the Northeast (range: 1.5–2.0). There was an overall reduction in mortality (APC) across all regions till 2011 and 2012 (Table 1). However, age-adjusted mortality has an upward trajectory throughout all the census regions after 2012 (Figs. 1, 2, 3). Statistically significant APC across U.S census regions are marked in table 1 (alpha = 0.05 level) (see Fig. 4).

### 4. Discussion

During the study period from 1999 to 2018 different trends were observed in premature mortality due to heart failure. There were significant geographic differences in age-adjusted mortality rates; a downward trajectory of overall HF-related premature mortality was observed till 2011–2012 followed by a substantial rise till 2018. These downward trends are illustrated in AAMR for females in all census regions (Northeast, Midwest, West, South) and AAMR for males in the Northeast region (Figs. 1, 2). Our findings of the highest AAMR (3.6) of the South region are consistent with spatial shifts of high-risk CVD distribution from the Northeast and the Midwest counties to the South in the last few decades [4]. Increasing premature mortality due to HF may elucidate an overall increase in premature CVD mortality. Conversely, there is data suggestive of a substantial decline in overall premature cardiovascular disease mortality from 2000 to 2015 [5]. Despite the evidence-based practices, public health interventions, strategic goals, community awareness/participation (Million heart project), new drugs, and clinical innovations the death toll is rising, and CVD mortality is expected to account for >23.6 million deaths/year globally by

2030 [6]. AHA projected an increasing prevalence of HF from 2.42% in 2012 to 2.97% by 2030 in the U.S. [7]. However, cancer-related deaths are the second leading cause of death in the USA, and the death rate declined by 19% from 1999 to 2017. Non-ischemic cardiomyopathy (CM) contributes to HF-related premature mortality, and up to 50% are idiopathic CM with no disease specifying therapy available resulting in poor prognosis [8]. In addition, innovation and new cardiovascular products are facing challenges like negative spending growth recently due to considerable developmental cost and low prices and sales. Our study has many limitations including the utilization of the WONDER database that may misreport the HF-related mortality. Hypertensive heart disease, CAD, smoking, obesity, DM, racial-socioeconomic disparities are well-recognized risk factors for HF which are not accounted for in our study. These risk factors might have played a significant role in the geographical variation observed in our study. Our study highlights an imperative need to identify the obstacles in continued improvements in HF management, to decrease premature mortality and reverse the trajectory. Further, premature mortality due to HF is a multifaceted problem. Utilization of clinical and focussed public health interventions, ensuring cost-effective, sustainable, and high-quality care to optimize the treatment of known and modifiable risk factors for HF can help reinstate HF trends.

### 5. Conclusion

This comprehensive analysis on nationally representative data elucidates that geographic and gender-based disparities exist in premature death due to heart failure; the explanation for this merits further discovery. Despite adherence to the evidence-based practices, age-adjusted mortality has an upward trajectory throughout all the census regions after 2012. This study suggests an imperative need of public health interventions to navigate premature mortality due to heart failure towards declining trends. Future studies are needed to validate the clinical implications of our findings.

### 5.1. Clinical perspectives

This study illustrates alarming trends in premature mortality due to heart failure. Our findings may help clinicians and policy-makers to understand the gravity of the problem and navigate public health interventions to reverse the current trajectory. A special focus on preventive intervention and prioritizing utilization of health resources can help decrease the burden of premature mortality due to heart failure.

### 5.2. Translational outlook

Although our findings indicate worsening trends of premature mortality due to heart failure throughout the U.S., additional research is imperative to delineate the trends of premature mortality due to heart failure stratified by race, county level, and income. Similar studies from other countries can be performed to corroborate our findings and provide insight into premature mortality from heart failure globally.

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None.

### CRediT authorship contribution statement

Drs. Ali Raza Ghani, and Mohsin Sheraz Mughal have full access to all the data in the study, share first authorship and take responsibility for the integrity and the accuracy of the data analysis. Concept and design: Ali Raza Ghani, Mohsin Sheraz Mughal, Sundeep Kumar. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Mohsin S Mughal, Ali Raza Ghani, Sundeep Kumar. Critical revision of the manuscript for important intellectual content: Mahboob Alam, Haris M. Usman, Deanna

Mikhalkova. Statistical analysis: Ali Raza Ghani, Mohsin Sheraz Mughal. Administrative, technical, or material support: Deanna Mikhalkova. Supervision: Haris M Usman, Mahboob Alam, Deanna Mikhalkova.

### Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

### References

- [1] S.C. Curtin, Trends in cancer and heart disease death rates among adults aged 45–64: United States, 1999–2017, *Natl. Vital Stat. Rep.* 68(5) (2019) 1. [https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68\\_05-508.pdf](https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_05-508.pdf). Accessed December 25, 2019 Google Scholar.
- [2] S.S. Virani, A. Alonso, E.J. Benjamin, M.S. Bittencourt, C.W. Callaway, A.P. Carson, A.M. Chamberlain, et al., Heart disease and stroke statistics—2020 update: a report from the American Heart Association, *Circulation* 141 (9) (2020) e139–e596, <https://doi.org/10.1161/cir.0000000000000757>.
- [3] L. Liu, X. Yin, M. Chen, H. Jia, H.J. Eisen, A. Hofman, Geographic variation in heart failure mortality and its association with hypertension, diabetes, and behavioral-related risk factors in 1,723 counties of the United States, *Front. Public Health* 6 (2018), <https://doi.org/10.3389/fpubh.2018.00132>.
- [4] M. Casper, M.R. Kramer, H. Quick, L.J. Schieb, A.S. Vaughan, S. Greer, Changes in the geographic patterns of heart disease mortality in the United States, *Circulation* 133 (12) (2016) 1171–1180, <https://doi.org/10.1161/circulationaha.115.018663>.
- [5] Y. Chen, N.D. Freedman, P.S. Albert, et al., Association of cardiovascular disease with premature mortality in the United States, *JAMACardiol.* 4 (12) (2019) 1230–1238, <https://doi.org/10.1001/jamacardio.2019.3891>.
- [6] Global Status Report on Noncommunicable Diseases 2014, World Health Organization, Geneva, Switzerland, 2014. [http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854_eng.pdf). Accessed December 2, 2016, Google Scholar.
- [7] E.J. Benjamin, P. Muntner, A. Alonso, et al., Heart Disease and Stroke Statistics—2019 Update: A Report From the American Heart Association, *Circulation* 139 (2019) e56–e528 [Crossref] [PubMed].
- [8] A.H. Wu, Management of patients with non-ischaemic cardiomyopathy, *Heart* 93 (3) (2007) 403–408, <https://doi.org/10.1136/hrt.2005.085761>.