Disentangling the Roles of Disease Incidence and Case Fatality in the US Cardiovascular Mortality Stagnation

Authors: Marcus Ebeling* (1,2,3), Neil Mehta (4), Leah Abrams (5), Mikko Myrskylä (1,3,5)

*presenting author

1 – Max Planck Institute for Demographic Research, Rostock, Germany

2 – Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden

3 – Max Planck – University of Helsinki Center for Social Inequalities in Population Health, Rostock, Germany

4 – Department of Epidemiology, University of Texas Medical Branch, Galveston (TX), USA

5 – Department of Community Health, Tufts University, Medford (MA), USA

6 – Population Research Unit, University of Helsinki, Helsinki, Finland

Abstract

Improvements in US mortality have slowed markedly since around 2010, with stagnation in cardiovascular disease (CVD) mortality emerging as one of the key factors. Most evidence to date has relied on cause-of-death data, which capture overall mortality trends but cannot disentangle the mechanisms driving changes in cause-specific death rates. Such rates can shift because more people develop disease (changing incidence) and/or because more people with disease die from it (changing case fatality). Each mechanism implies distinct underlying processes and points to different public health interventions. To clarify the drivers of CVD mortality stagnation, we examine how changes in incidence and case fatality have shaped mortality from myocardial infarction (MI) and stroke between 1988 and 2021. Using multiple cause-of-death data, the National Inpatient Sample - a nationally representative database of hospital admissions - and the Human Mortality Database, we estimate age-, sex-, and race/ethnicity-specific incidence, case fatality, and death rates. Counterfactual analyses will quantify the contributions of incidence and case fatality to overall mortality change and assess prospects for future improvements. The analysis will identify the periods and population groups in which each mechanism has dominated. Cross-national comparisons using Swedish registry data will provide additional context and validation. Beyond helping to disentangle the drivers of US mortality stagnation, this analysis will also provide methodological insights into the caveats and dynamics underlying changes in cause-of-death-specific mortality more generally. Understanding these mechanisms is crucial for developing effective prevention policies and for returning to mortality improvements in the future.

Background

US mortality improvements slowed in the early 2000s and have largely stalled over the past decade.[1,2] This stagnation is evident among both working-age adults and older individuals.[3,4] One major contributor to this trend is the stagnation in cardiovascular disease (CVD) mortality, particularly among older populations.[5,6] Although numerous studies have examined population-level CVD mortality trends, most analyses have relied solely on cause-of-death data. While informative about overall mortality patterns, such data provide

limited insight into the mechanisms driving changes in cause-specific death rates. To address this gap, we link national cause-of-death records with hospitalization data from the U.S. and use myocardial infarction (MI) and stroke - two major CVD conditions - to assess how changes in disease incidence and case fatality have contributed to CVD mortality trends over the past three decades.

Cause-specific death rates can shift due to changes in either disease incidence or case fatality, each carrying distinct implications for prevention and intervention. Rising incidence implies that more individuals are developing the disease. If case fatality remains constant, higher incidence alone will increase cause-specific death rates because there are more individuals with the disease. Such patterns point to upstream health problems and highlight the need for primary (preventing disease occurrence) prevention. In contrast, increasing case fatality indicates that more individuals with the disease are dying, even if incidence is stable. In this scenario, the attention is shifted to secondary prevention (early detection) and tertiary prevention (reducing disease impact after diagnosis). Distinguishing between these mechanisms is therefore essential for understanding recent CVD mortality trends in the US and guiding effective public health responses.

Myocardial infarction (MI) and stroke are still two of the leading causes of death in the United States.[7] Over the past few decades, the incidence and case fatality of both conditions have changed substantially, though the patterns differ depending on the condition and the population group. The incidence of MI declined until the early 2000s, likely reflecting improvements in prevention, risk factor control and treatment.[8] The incidence of stroke has also declined, though the decrease has been more gradual and less uniform across demographic groups.[9] For both diseases, however, there is little evidence from the most recent years, particularly since the stagnation of CVD mortality began in 2010.

In this study, we will address two main research questions:

(1) How have death rates, incidence and case fatality of stroke and MI changed from three decades ago until now?

(2) How have incidence and case fatality contributed to changes in death rates, and what are the prospects for future improvements in MI and stroke mortality?

Data

Data on causes of death comes from the annual datasets on multiple cause of death data published by the Center of Disease Control (CDC).[10] From this data, we will use information on the year of death, age at death, place of death, sex, race/ethnicity as well as the underlying and the contributing causes of death. Information in hospitalization is derived from the National Inpatient Sample (NIS).[11] The NIS is the largest

publicly available all-payer inpatient healthcare database in the US. It is maintained by the Healthcare Cost and Utilization Project (HCUP) and contains a stratified sample of hospital discharge records from community hospitals nationwide. The NIS includes information on patient demographics, diagnoses, procedures, hospital characteristics, and outcomes, making it a valuable resource for tracking national trends in hospitalizations and disease incidence over time. Data on the person-years of exposure comes from the Human Mortality Database[12] and for person-years of exposure by race-ethnicity, from the US Census bureau. All data is available for the time period 1988 to 2021. The analysis will be restricted to ages 40 and older.

Identifying incident and deceased cases

The ideal dataset for this task would enable us to track individuals over time, as is possible with the population registers available in the Nordic countries. In the US, however, such datasets are rarely accessible and often only cover specific states or regions. Our approach is therefore designed to accurately approximate incident and deceased cases with the available data, based on several assumptions. To assess the robustness of these assumptions, we conduct a series of sensitivity analyses examining how alternative definitions affect our results.

We define the total number of incident cases as the sum of those who reach hospital and those who die before admission. In our main analysis, hospital cases are identified in the NIS as patients with MI or stroke recorded as the primary diagnosis. Cases that do not reach hospital are defined as deaths in which MI or stroke is listed as the underlying cause of death and the place of death is outside of hospital. Case fatality is typically measured over specific time periods, such as 28 days or 365 days.[13] However, since our data does not permit measurement at such a fine temporal resolution, we rely on one-year case fatality. Accordingly, we define deceased cases as all deaths with MI or stroke listed as the underlying (or contributing) cause, regardless of place of death in our main analysis.

Statistical Analysis

In the first step, we will calculate disease-specific mortality, incidence, and case fatality rates for myocardial infarction (MI) and stroke by five-year age group, sex, race/ethnicity, and year. We will then examine temporal trends and differences across racial and ethnic groups. In the second step, we will exploit the mathematical relationship between population, incidence, and case fatality (Deaths = Population x Incidence x Case Fatality) to conduct counterfactual analyses assessing how changes in incidence and case fatality have shaped population-level death rates over time. This approach will also allow us to explore hypothetical scenarios illustrating how future reductions in incidence or case fatality could influence CVD

mortality trends. In this context, we will also analyze how the disease composition within the CVDs has changed over time and might continue to change in the future given the importance of MI and stroke for the overall category. Recognizing potential limitations in U.S. data coverage and comparability, we will replicate the analyses using Swedish and Finnish register data to strengthen the robustness and interpretability of our findings.

Preliminary Results

We only recently gained access to the NIS data, so we cannot present any concrete results at this stage. However, we can outline the starting point of the analysis. We have calculated the age-standardized total cardiovascular disease (CVD) death rate (left panel) and the myocardial infarction (MI)-specific death rate (right panel) for the years 1999 to 2020. The all-CVD death rate shows the stagnation that occurred around 2010, as described. This stagnation is visible for both women and men. The MI-specific death rate also shows a slowdown since around 2010, but death rates continue to decline, albeit at a slower rate. As cause-specific death rates are only the consequence of changes in the underlying processes of developing and dying from the disease, the results suggest once more that stagnation or a slowdown in improvements must be accompanied by changes to one or both of these processes. We will shed light on these complex dynamics at the conference.

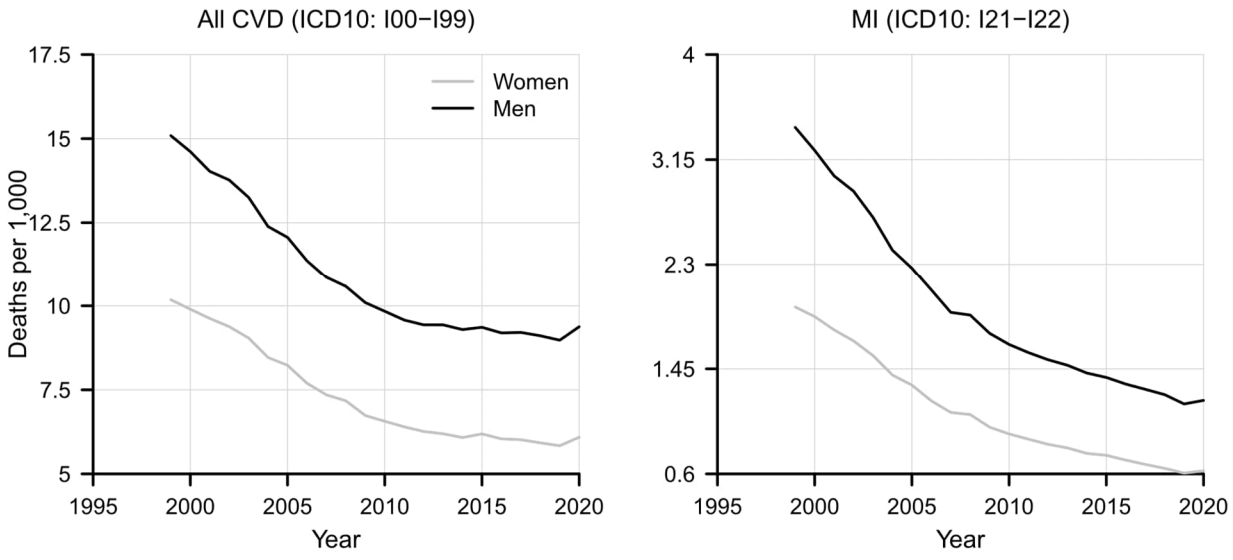

Figure 1 All-CVD and MI-specific age-standardized death rate, Women and Men, Years 1999 to 2021. *Notes: We used the total population of 1999 as standard. For this analysis, cause-specific counts have been derived from CDC Wonder, while person-years from the Human Mortality Database are used.*

Future Steps

Access to all the datasets listed in this abstract has now been granted. However, there was not enough time to present preliminary results in the abstract. The next step will therefore be to conduct the analysis outlined above.

References

1. Woolf SH. Falling Behind: The Growing Gap in Life Expectancy Between the United States and Other Countries, 1933–2021. *Am J Public Health*. 2023;113(9):970-980. doi:10.2105/AJPH.2023.307310

2. Preston SH, Vierboom YC. Excess mortality in the United States in the 21st century. *Proc Natl Acad Sci*. 2021;118(16):e2024850118. doi:10.1073/pnas.2024850118

3. Polizzi A, Dowd JB. Working-age mortality is still an important driver of stagnating life expectancy in the United States. *Proc Natl Acad Sci*. 2024;121(4):e2318276121. doi:10.1073/pnas.2318276121

4. Abrams LR, Myrskylä M, Mehta NK. The “double jeopardy” of midlife and old age mortality trends in the United States. *Proc Natl Acad Sci*. 2023;120(42):e2308360120. doi:10.1073/pnas.2308360120

5. Aron, L, Woolf, Steven H. *U.S. Health in International Perspective: Shorter Lives, Poorer Health*. National Academies Press; 2013.

6. Mehta NK, Abrams LR, Myrskylä M. US life expectancy stalls due to cardiovascular disease, not drug deaths. *Proc Natl Acad Sci*. 2020;117(13):6998-7000. doi:10.1073/pnas.1920391117

7. Products - Data Briefs - Number 521 - December 2024. doi:10.15620/cdc/170564

8. Salari N, Morddarvanjoghi F, Abdolmaleki A, et al. The global prevalence of myocardial infarction: a systematic review and meta-analysis. *BMC Cardiovasc Disord*. 2023;23(1):206. doi:10.1186/s12872-023-03231-w

9. Koton S, Schneider ALC, Rosamond WD, et al. Stroke Incidence and Mortality Trends in US Communities, 1987 to 2011. *JAMA*. 2014;312(3):259-268. doi:10.1001/jama.2014.7692

10. National Center for Health Statistics (NCHS). Mortality Data – Vital Statistics NCHS’s Multiple Cause of Death Data, 1960–2015. Published online 2016.

11. Healthcare Cost and Utilization Project (HCUP). HCUP National Inpatient Sample (NIS) 1988-2021. Published online 2025. www.hcup-us.ahrq.gov/nisoverview.jsp

12. University of California, Berkeley (USA), and Max Planck Institute for Demographic Research (Germany). Human Mortality Database. Published online 2024.

13. Modig K, Berglund A, Talbäck M, Ljung R, Ahlbom A. Estimating incidence and prevalence from population registers: example from myocardial infarction. *Scand J Public Health*. 2017;45(17_suppl):5-13. doi:10.1177/1403494817702327