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# Cause-of-Death Diversity From a Multiple-Cause Perspective in the United States

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**ABSTRACT** Cause-of-death diversity captures the variability of deaths across causes and is an important marker of heterogeneity in a population's health. We contribute to the debate of cause-of-death diversity dynamics by following a novel multiple causes of death (MCOD) approach and applying it to the U.S. context between 2003 and 2018 and across education groups. Results show that cause-of-death diversity increased over this period, especially up to 2012. These trends were mainly driven by increases in the groups aged 65 years or more. The inclusion of MCOD resulted in higher increases in cause-of-death diversity over time compared with merely using underlying causes of death, except for the 85 or more age group, where no difference was observed for males and a reverted gradient was observed for females. Results by educational attainment reveal lower diversity among the highest educated groups and widening differences across groups from around 2012 onward. The clear educational gradient observed at ages 30–64 diminished at older ages. The observed increases in cause-of-death diversity should be monitored to better understand mortality dynamics in aging populations. Our new MCOD diversity measures suggest that traditional approaches relying on single causes of death might be underestimating cause-of-death diversity dynamics, particularly for males.

**KEYWORDS** Multiple causes of death • Diversity • Inequalities • Health • Multimorbidity

## Introduction

Patterns in causes of death are known to be key indicators of population health. Much is known about leading causes of death and how they have shifted over time (e.g., from a majority of deaths caused by infections and communicable diseases to a majority of deaths caused by noncommunicable diseases; Omran 1998). However, much less is known about the dispersion of deaths across causes—*cause-of-death diversity*—and how it has evolved over time. Cause-of-death diversity refers to the extent to which some populations die from more similar or dissimilar causes compared with other populations. The diversity in causes of death is unarguably an important marker of population health heterogeneity, with higher values suggesting higher

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disparities across causes of death, and therefore more difficulties in diagnosis and treatment (i.e., micro-level effects) and health planning (i.e., macro-level effects). The study of cause-of-death diversity has received very little attention from academia (Bergeron-Boucher et al. 2020) despite its important practical implications—especially in the swift aging process that is sweeping the world. In this article, we propose a new approach to measure cause-of-death diversity that has been adapted to the specificities prevailing in low-mortality settings and therefore that is able to account for multiple causes of death (MCOD).

Cogent indicators aiming to measure cause-of-death diversity in low-mortality settings should ideally be sensitive to (1) the increasingly high prevalence of comorbidity and (2) the differences in health outcomes across population groups. On the one hand, as mortality shifts toward older ages, the presence of comorbidities becomes progressively more prevalent, thus complicating the assignation of a single cause of death—which is commonly referred to as "the underlying cause of death" (Alpérovitch et al. 2009; Tinetti et al. 2012). This is nowadays more important than ever before as mortality has shifted toward older ages (e.g., Brown et al. 2012), and managing comorbidities at old age has become a major challenge for health care and public health management (Barnett et al. 2012; McPhail 2016). In this context, some researchers have raised concerns about the oversimplification of underlying cause-of-death approaches given the complexity and quality of cause-of-death assignation (Flagg and Anderson 2021). This suggests the need to go beyond the single-cause-of-death approach, for example, by exploring MCOD, to achieve a better understanding of current mortality dynamics (Désesquelles et al. 2014). On the other hand, in a context of persisting and widening health inequalities across socioeconomic groups (e.g., Chetty et al. 2016; Mackenbach et al. 2018; Montez et al. 2019; Permanyer et al. 2018; Sasson 2016), it would be desirable if cause-of-death diversity measures could be broken down in such a way that informs the extent of diversity occurring within and between socioeconomic groups. Such decomposition could be extremely useful in potentially identifying the main locus of cause-of-death diversity (i.e., unveiling whether diversity comes from differences occurring within or between groups) and pinpointing the key drivers of changes over time. In this study, we examine cause-of-death diversity in the United States by age group, sex, and educational attainment in a context of changing mortality dynamics (2003–2018) by developing and applying a new approach based on the analysis of multiple causes of death. Focusing on the United States is particularly relevant given the disrupting mortality trends experienced over the last decade.

## Background

### Mortality Dynamics in the United States

Mortality and life expectancy have stagnated in the United States over the last decade after a longer period of consistent mortality declines. These dynamics have positioned the country in a disadvantaged mortality situation as compared with other low-mortality countries (Ho and Hendi 2018; Woolf and Schoomaker 2019). Understanding mortality patterns and distribution by causes of death is crucial to revert stagnated trends and, therefore, to further contribute to life expectancy improvements. Several risk factors and underlying causes of death, including the so-called "deaths of despair," diabetes, and obesity, have grown over the last decade and contribute to explaining the observed mortality stagnation trends (Barbieri 2019; Case and Deaton 2017; Janssen et al. 2020; Preston et al. 2018). For example, drug-related mortality trends between 2010 and 2017 had a negative impact on life expectancy of 0.1 and 0.4 years for females and males, respectively (Mehta et al. 2020), while obesity-related mortality trends had an estimated negative impact between 2000 and 2012 of 0.3 and 0.5 years for females and males, respectively (Vidra et al. 2019). These causes of death are particularly relevant among working-age individuals, and despite their growing importance, these risk factors are not the only drivers of all-cause mortality among such groups. Conversely, small variations in leading and relatively important causes of death, for example, cardiovascular causes or cancers, also impact mortality dynamics. Indeed, the observed slowdown in the decline of cardiovascular mortality over the last decade has been shown to be a key factor for the observed all-cause mortality stagnation (Sidney et al. 2019) and is estimated to account for a 1.1-year decline in life expectancy between 2010 and 2017.

In the United States, as well as in all other low-mortality countries, mortality is mainly concentrated at old ages. In this population aging context, the small mortality improvement from cardiovascular causes that occurred at ages 65 and older in the United States (Sidney et al. 2019) may be worrisome for the future prospects of mortality decline. The higher survival at older ages has contributed to increasing frailty and health vulnerability of individuals and populations. As a consequence, the variability in age at death—or life span variation—among older individuals (60+) has been increasing over the last decades (Engelman et al. 2010; Permanyer and Scholl 2019). This is particularly important in the United States and in other low-mortality contexts given the elevated number of old-age deaths and the rising prevalence of both comorbidities (King et al. 2018) and life expectancy with morbidities (Payne 2022). These increases in health heterogeneity (e.g., coexistence of chronic morbidities) represent increased competing risks, and as the number of competing causes increases, the assignation of the underlying cause of death may become challenging.

## Multiple Causes of Death

Death certificates allow the possibility to include multiple causes of death. The vast majority of studies investigating cause-of-death patterns have relied on the so-called "underlying cause of death"—that is, "(a) the disease or injury which initiated the train of events leading directly to death, or (b) the circumstances of the accident or violence which produced the fatal injury" (World Health Organization 2016:1067). The importance of listing all causes in death certificates, or MCOD, for better understanding mortality has been stressed for many decades (Janssen 1940). However, the majority of studies on mortality issues have neglected the non-underlying causes of death listed in the certificates, potentially because most cause-of-death mortality data sets include data only on the underlying cause of death (e.g., the WHO Mortality Database). This (over)simplification may be particularly limiting when aiming to study specific causes of death, given that some broad groups of causes are more likely to be left as contributory causes when multiple causes are listed, as is the case for endocrine diseases (Redelings et al. 2006).

The reasons for using these more detailed data to improve our understanding of cause-specific mortality are becoming increasingly clear in a context of rising (multi) morbidity and shifting mortality toward older ages. The value of MCOD is illustrated by the observation that the number of causes of death listed on death certificates tends to increase with age, at least up to about age 85 (Désesquelles et al. 2016; Grundy and Stuchbury 2022), and the number of different causal morbidity patterns (multi-morbidity at death) also increases with age until about age 90 (Grippo et al. 2020). Additionally, important concerns have been raised regarding the oversimplification of underlying cause-of-death approaches given the complexity of cause-of-death assignation (Flagg and Anderson 2021; Trias-Llimós and Permanyer 2020). Concurrently, a growing body of literature using MCOD in mortality studies has emerged, and several methodologies dealing with MCOD have been developed in the last decade (e.g., Désesquelles et al. 2010, 2012; Grippo et al. 2020; Moreno-Betancur et al. 2017; Piffaretti et al. 2016).

## Previous Studies on Cause-of-Death Diversity

The current dynamics of aging populations, as well as the observed stagnation in U.S. mortality over recent years, demand a comprehensive assessment of mortality dynamics from different angles. A promising area of research explores the extent to which individuals die from a narrower or wider variety of causes of death—that is, cause-of-death diversity. Such diversity and how it has changed over time have the potential to provide a new perspective that could improve the understanding of mortality dynamics. While this idea was first proposed in the 1980s (Izsak 1986), cause-of-death diversity remained largely unexplored until recently. To the best of our knowledge, only one publication made use of cause-of-death variability indicators by using underlying cause-of-death mortality data from 15 low-mortality countries for the last couple of decades (Bergeron-Boucher et al. 2020). The main findings of this research pointed toward an increasing cause-of-death diversity, driven particularly by individuals aged 50 or more. This seemed to be explained by the faster decline of cardiovascular causes of death as compared with other causes (e.g., mental or nervous), which are gaining importance in the cause-of-death mortality composition (Bergeron-Boucher et al. 2020). Therefore, in a context of growing comorbidities and difficulties assigning underlying causes of death, assessments of cause-of-death diversity can be greatly enhanced by incorporating the MCOD perspective.

## Growing Educational Inequalities in Mortality

Socioeconomic gradients in health and mortality exist and persist worldwide, and they are particularly striking in the U.S. context (e.g., Brown et al. 2012; Montez et al. 2019; Sasson 2016). Inequalities in mortality have been rapidly rising over the last couple of decades (Olshansky et al. 2012; Sasson 2016). Importantly, this can be seen in increasing educational inequalities in mortality in two dimensions. On the one hand, looking at the means, we know that life expectancy gaps increased in favor of highly educated groups. On the other hand, when looking at the dispersion of ages at death (life span inequalities), we observe that low-educated groups experience more uncertainty in the timing of death, with a persistent or even increasing gap across educational groups over the last decades (Sasson 2016). Improving this worrisome situation regarding socioeconomic inequalities in health and mortality represents one of the main principles and goals of the U.S. Department of Health and Human Services' Healthy People 2030 (Office of Disease Prevention and Health Promotion n.d.).

Education has been the most widely used indicator in studying socioeconomic health inequalities. Education captures "the transition from parents' socioeconomic position to own socioeconomic position and it is also a strong determinant of future employment and income" (Galobardes et al. 2006:8). Furthermore, education has been commonly used as an important marker of individual lifestyles, social relationships, and health care use (Hayward et al. 2015; Zajacova and Lawrence 2018). So far, educational inequalities in mortality have been widely analyzed in terms of life expectancy and life span variation, but not regarding cause-of-death diversity. A series of questions regarding socioeconomic inequalities in cause-of-death diversity remain unanswered and are particularly interesting in the U.S. context, which has been characterized by disrupting mortality dynamics over the last decade. For example, are less advantaged educational groups dying from more dissimilar sets of causes of death or from more similar sets of causes of death compared with the most advantaged educational groups?

## Data and Methods

### Data

We use individual-level multiple causes of death mortality data for the period 2003–2018 from the Centers for Disease Control and Prevention covering the entire U.S. population (Centers for Disease Control and Prevention 2021). We restrict our data to adult deaths at age 30 or more and assume that education is completed by age 30. Cause-of-death mortality data are classified into 13 groups, following the standards of the International Classification of Diseases revision 10 (ICD-10) main (groups of) chapters. We select the more commonly used chapters as underlying causes of death: Infectious (ICD-10 codes: A00–B99), Neoplasms (C00–D48), Metabolic (E00–E88), Mental (F01–F99), Nervous (G00–G98), Cardiovascular (I00–I99), Respiratory (J00–J98), Digestive (K00–K92), Musculoskeletal (M00–M99), Genitourinary (N00–N98), and Ill-defined (R00–R99); we group all External causes within one category (S00–Y89), and we group the remaining chapters under the label of Other Causes (blood (D50–D89), eye and ear (H00–H93), skin (L00–L98), pregnancy (O00–O99), perinatal (P00–P96), and congenital (Q00–Q99)). This implies that, for example, a death certificate with several causes belonging to the same group (e.g., ischemic heart diseases and hypertensive diseases) is assumed to have only one cause of death (a cardiovascular

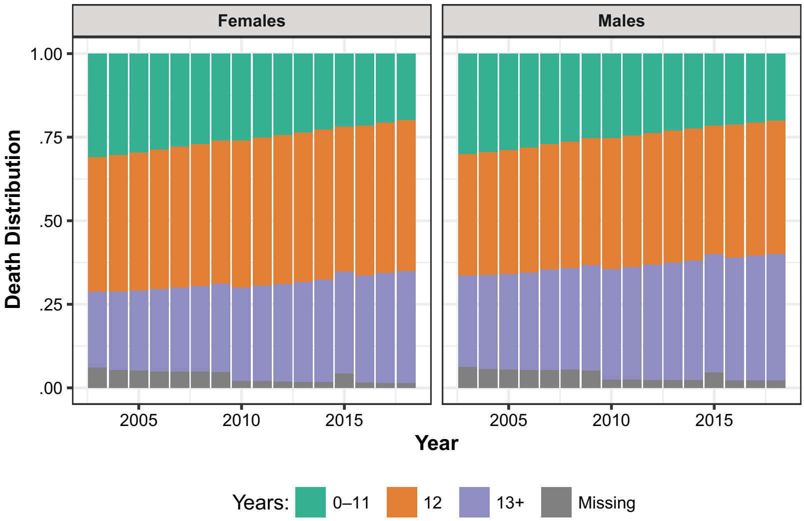


**Fig. 1** Death distribution by sex, year, and highest educational level (years of education) at ages 30 and over in the United States, 2003–2018

cause, in this example). These 13 groups of causes are labeled as $C_i$, and the set of all possible causes of death considered in this study is denoted as $C = \{C_1, \ldots, C_{13}\}$. As for the non-underlying causes of death, we use in all analyses the record axis codes variables in the original data (i.e., those codes that have been completely data-processed and that reflect "cleaned" data).

Mortality in the United States in the period 2003–2018 reached an absolute figure of nearly 41 million deaths, representing more than one million deaths per sex and year. Educational attainment was used as a proxy of socioeconomic status. Education was categorized according to either the 1989 or the 2003 revision depending on the year and state. The 1989 revision classified education according to the completed number of years of schooling, whereas the 2003 revision classified education according to the highest level of education completed (e.g., bachelor's degree) (Rostron et al. 2010). We harmonized education into three categories according to completed years of education: 0–11 years (low education), 12 years (high), and 13+ years (at least some college). The educational distribution of deaths in the pooled data was the following: 23.9% of deaths with low education, 41.5% with high education, 31.1% with at least some college, and 3.5% were missing information. This last group was excluded from the analyses. Figure 1 depicts the composition of deaths by educational attainment over time. This composition has been changing over time, as reflected in the increasing share of deaths with higher educational levels.

All analyses are performed separately by sex and time period for the adult population (aged 30 or more), as well as for the age-specific subsamples of 30–64, 65–84, and 85+. Specific analyses by educational attainment and stratifying by the variables mentioned are also presented. All analyses were conducted using R version 4.0.5 in RStudio 1.3.959.

## Methods

In the MCOD setting, we use the notation $(\mathbf{v};i)$ to formally indicate that a given death has been attributed to an underlying cause *and* potentially other causes, where $\mathbf{v}=(v_1,\ldots,v_{13})\in\{0,1\}^{13}\setminus\mathbf{0}$ is a 13-dimensional vector of zeros and ones (with a "1" in position *j* to indicate that cause-of-death *j* has contributed to that specific death, and "0" for the opposite), and $i\in\{1,\ldots,13\}$ indicates which of the 13 elements of $C$ (causes of death) is *the* underlying cause of death.[1] To illustrate: the vector $(\mathbf{a};2)=((1,1,1,0,\ldots,0);2)$ will be used for those death certificates indicating that $C_2$ is the underlying cause of death and $C_1$ and $C_3$ are contributing causes of death. The generic elements $(\mathbf{v};i)$ will be referred to as "sets of causes of death." We restricted our sample to the 500 most prevalent sets of causes of death in 2018, which turn out to represent 95% of the total deaths across the analyzed period (ranging between 95.5% in 2003 and 93.9 in 2018).

Our approach to measuring cause-of-death diversity in an MCOD setting requires making assessments of the extent of similarity or dissimilarity among any two sets of causes of death (e.g., $(\mathbf{a};i)$ vs. $(\mathbf{b};k)$; see below). To make this comparison, one must first decide the degree to which underlying causes of death are more important or relevant than the other causes listed in the death certificate. Since this is a highly context-specific issue that is likely to vary considerably across individual deaths, we make some simplifying assumptions. First, we assign a weight $W>0$ to the underlying cause of death and another weight $\omega\geq 0$ to all the remaining causes of death listed in the death certificate, with the restriction that $W\geq\omega$. Second, we further assume that in a hypothetical death certificate listing all 13 causes of death as contributing causes, the sum of the corresponding "importance weights" must equal 1 (a standard normalization procedure). Since there is only one underlying cause of death and potentially 12 contributory causes in our approach, the following restriction must hold:

$$W+12\omega=1.$$

Thus, fixing $W$, one must have that

$$\omega=\frac{1-W}{12}.$$

Imposing these mild restrictions, we conclude that the values of $W$ are allowed to move between 1/13 and 1. While the choice of $W$ is arbitrary, the meaning of its extreme values is clear. If we choose $W=1$, then $\omega=0$ and we are in the standard single-cause-of-death setting where the causes in the death certificate other than the underlying cause of death are ignored. At the other extreme, when $W=1/13$, then $\omega=1/13$, so we are in a setting where the underlying cause of death is only as important as, and not more important than, the other causes included in the death certificate. For all other intermediate values of $W$, the underlying cause of death is more important than the other causes of death included in the list in varying degrees. In the empirical section of the article, we

[1] Observe that at least one of the $v_i$ included in $\mathbf{v}$ must be a 1 (i.e., there must be at least one cause of death).

present all our findings for different values of $W$ (1/13, 0.2, 0.5, and 1), and we present the results for the intermediate value of $W = 0.5$ in the results by educational attainment, leaving the results derived from using other $W$ values in the robustness checks shown in the online supplementary materials.

### *Measuring Cause-of-Death Diversity in an MCOD Setting*

The approach we follow to measure cause-of-death diversity is simple: take two death certificates at random and measure how similar or dissimilar the corresponding sets of causes of death are. In this way, we obtain an estimate of the extent of (dis)similarity among deaths occurring in the population. The suggested approach has two steps. First, we measure the extent of (dis)similarity between any two sets of causes of death (i.e., distances). Second, we average such measures across all possible pairs.

#### Step 1: Define Distances

Given any two sets of causes of death $(\mathbf{a};i) = ((a_1,\ldots,a_{13});i)$ and $(\mathbf{b};j) = ((b_1,\ldots,b_{13});j)$, we define the distance between them as

$$d((\mathbf{a};i),(\mathbf{b};j)) = \sum_{k=1}^{13} \left| w_{i,k}a_k - w_{j,k}b_k \right|, \tag{1}$$

where $w_{i,k}$ (respectively, $w_{j,k}$) equals $W$ whenever $i = k$ (respectively, $j = k$) and equals $\omega$ otherwise. This distance function compares the similarity between the two causes-of-death vectors. The function is sensitive to the degree of overlap between the vectors $\mathbf{a}$ and $\mathbf{b}$ (i.e., it increases when the different causes of death in the two vectors do not coincide) and to the corresponding underlying causes of death $(i, j)$. Implicitly, it assumes that the distance between any two single underlying, but different, causes of death is the same (see Example 2 below). We illustrate how this measure behaves in examples provided in Box 1.

#### Step 2: Average Across Pairs

After defining how to measure the extent of (dis)similarity between any two sets of causes of death, we then average the results across all possible pairs. Following this approach, we obtain the following measure of MCOD diversity:

$$D = \sum_{(\mathbf{a};i)\in\Omega} \sum_{(\mathbf{b};j)\in\Omega} p^*_{(\mathbf{a},i)} p^*_{(\mathbf{b},j)} d((\mathbf{a};i),(\mathbf{b};j)), \tag{2}$$

where $\Omega = (\{0,1\}^{13} \setminus \mathbf{0}) \times \{1,\ldots,13\}$ is the set of all possible sets of causes of death, and $p^*_{(\mathbf{a},i)}$ is the life table–adjusted share of death certificates having $(\mathbf{a};i)$ as the corresponding set of causes of death. The use of life table–adjusted shares of death certificates facilitates an accurate comparison of our cause-of-death diversity across educational groups and over time. This adjustment was done by multiplying the share of deaths by

**Box 1** Basic examples to represent the estimation of distances between sets of causes of death

*Example 1*

Let $(\mathbf{a};1) = \big((1,1,0,\dots,0);1\big)$ represent a death certificate indicating the presence of two causes of death (Infectious ($C_1$) and Neoplasms ($C_2$)), with the first one being the underlying cause of death. Likewise, $(\mathbf{a};2) = \big((1,1,0,\dots,0);2\big)$ indicates the presence of the same two causes, but with the second one being the underlying cause of death; and let $(\mathbf{b};3) = ((0,0,1,1,0,\dots,0);3)$ represent a death certificate indicating the presence of Metabolic ($C_3$) and Mental ($C_4$) as causes of death, with the former being the underlying cause. The degree of (dis)similarity among these sets of causes of death according to the abovementioned distance function can be calculated as follows:

$$d\big((\mathbf{a};1),(\mathbf{a};2)\big) = |W\cdot 1 - \omega\cdot 1| + |\omega\cdot 1 - W\cdot 1| = 2(W-\omega)$$

$$d\big((\mathbf{a};1),(\mathbf{b};3)\big) = |W\cdot 1 - \omega\cdot 0| + |\omega\cdot 1 - \omega\cdot 0| + |\omega\cdot 0 - W\cdot 1| + |\omega\cdot 0 - \omega\cdot 1| = 2(W+\omega)$$

$$d\big((\mathbf{a};2),(\mathbf{b};3)\big) = |\omega\cdot 1 - \omega\cdot 0| + |W\cdot 1 - \omega\cdot 0| + |\omega\cdot 0 - W\cdot 1| + |\omega\cdot 0 - \omega\cdot 1| = 2(W+\omega).$$

Thus, for all admissible values of $W \geq \omega > 0$, the distance between $(\mathbf{a};1)$ and $(\mathbf{a};2)$ is smaller than the distance between $(\mathbf{a};1)$ and $(\mathbf{b};3)$. This coheres with the fact that $(\mathbf{a};1)$ and $(\mathbf{a};2)$ share the same set of causes of death, while $(\mathbf{a};1)$ and $(\mathbf{b};3)$ do not have in common any cause.

*Example 2*

How does the distance function behave when comparing death certificates indicating the presence of a different single cause of death? In that case, it is easy to show that the distance function equals $|W\cdot 1 - \omega\cdot 0| + |\omega\cdot 0 - W\cdot 1| = 2W$. Comparing this distance with respect to the distances obtained in the previous example, we have that $2(W-\omega) < 2W < 2(W+\omega)$. Again, this coheres with the intuition that (i) $(\mathbf{a};1)$ and $(\mathbf{a};2)$ should be closer between them than the single-cause-of death profiles $((1,0,\dots,0);1)$ and $((0,1,0,\dots,0);2)$ because the former share the same sets of causes of death; and (ii) $(\mathbf{a};1)$ and $(\mathbf{b};3)$ should be further away between them than is the case for the single-cause-of death profiles $((1,0,\dots,0);1)$and $((0,0,1,0,\dots,0);3)$, because the former profiles have less in common than the latter.

the corresponding $d_x$ proportion from life tables. This procedure is equivalent to using multiple-decrement life table data. To be able to compute life tables, population data from the Human Mortality Database and the education distribution of the population from the Current Population Survey were used (see online appendix A for further details).

The cause-of-death diversity indicator $D$ can be interpreted as the mean distance between sets of causes of death, or in other words, as the expected distance between two randomly chosen deaths. In a hypothetical society where everyone died from the exact same set of causes (the lowest level of diversity), the distance function would always be 0, so $D$ would also be equal to 0. At the other extreme, when individuals tend to die from a more variegated set of causes, the distance function tends to increase, and so does the corresponding diversity indicator $D$.[2] To compare our results across different $W$ values and over time, we normalized the results using 2003 as the baseline ($D_{2003} = 1$) for any given $W$. The diversity indicator $D$ belongs to a widely used class of social indicators designed to measure "diversity" in different forms. For instance, very similar indices have been used to assess cultural, ethnic, or religious diversity in various settings (Bossert et al. 2011). In all cases, the indices are defined as the mean level of dissimilarity that exists among the elements being compared. Indeed, the well-known Gini coefficient for income inequality has a very similar functional form and can be interpreted exactly in this way: it is the mean income difference between all pairs of individuals.

If the suggested MCOD diversity indicator is applied to a distribution of "single causes of death" (i.e., assuming the only information we take into consideration is the underlying cause of death, so $W=1$), we end up with a (multiple of a) well-known measure of diversity: the index of fractionalization (henceforth denoted as $F$). Under the aforementioned assumptions, $D$ can be written as

$$D = 2\sum_{i=1}^{13} \sum_{j \neq i} p_i^* p_j^* = 2\left(1 - \sum_{i=1}^{13} p_i^{*2}\right) = 2F, \quad (3)$$

where $p_i^*$ is the adjusted share of deaths attributable to cause $C_i$ (the derivation of this formula is shown in the online appendix B). The fractionalization index applied in a "single causes of death" setting simply can be understood as the probability that two randomly chosen deaths are attributable to different causes. Thus, the MCOD diversity indicator proposed in this study can be seen as a generalization of the $F$ index to a broader and richer setting.

*Decomposing Cause-of-Death Diversity by Educational Groups*

Another attractive characteristic of our diversity index $D$ is that it admits decompositions that are easy to interpret. Assume the population under study is partitioned across $G$ groups. In the appendix we show that $D$ can be decomposed into within- and between-group components, as

[2] Our diversity indicator $D$ is maximized whenever all deaths are evenly distributed across the different "single-cause-of-death profiles" (i.e., those sets of causes of death where there is only one underlying cause of death). When this happens, the maximum of $D$ equals $2W(k-1)/k$, where $k$ is the number of causes of death. In our setting (where $k=13$), this maximum is approximately equal to $1.85 \cdot W$.

$$D = \underbrace{\sum_{g=1}^{G} p_g^2 D_g}_{\text{Within-component}} + \underbrace{\sum_{g=1}^{G-1} \sum_{h=g+1}^{G} 2 p_g p_h D_{gh}}_{\text{Between-component}}, \tag{4}$$

where $p_g$ is the population share of group $g$, $D_g$ is the diversity index applied within group $g$, and $D_{gh}$ is the diversity between groups $g$ and $h$—that is, the expected distance between a randomly chosen individual from group $g$ and a randomly chosen individual from group $h$. The derivation of this formula is shown in the online appendix C. This decomposition will be applied to assess the extent to which the observed changes in cause-of-death diversity between 2003 and 2018 are attributable to the contribution of between educational groups cause-of-death diversity and within educational groups cause-of-death diversity.

*The Role of the Changing Composition of the Population*

As shown in Figure 1, the education composition of the deaths distribution has been shifting over time for the period we analyzed. We perform a sensitivity analysis aiming to assess the extent to which the observed changes in cause-of-death diversity between 2003 and 2018 are due to: (1) changes in the composition of the population by educational level and (2) changes in the diversity between and within educational groups.

Our cause-of-death diversity indicator can be written in time $t$ as $D_t = f\left(\mathbf{p}_t, \mathbf{D}_t\right)$; that is, $D$ is a function of the vector of population shares (i.e., the different $p_g$) and the vector containing the within-group ($D_g$) and between-group ($D_{gh}$) diversity levels, all measured in year $t$ (see Eq. (4)). The diversity changes over time can be decomposed as

$$\Delta D = D_2 - D_1 = f\left(\mathbf{p}_2, \boldsymbol{D}_2\right) - f\left(\boldsymbol{p}_1, \boldsymbol{D}_1\right) = \Delta_p + \Delta_D, \tag{5}$$

where $\Delta_p$ can be interpreted as the contribution of compositional changes to changes in diversity, while $\Delta_D$ measures the contribution of the within- and between-group diversity changes to changes in overall diversity. Following Kitagawa's decomposition (Kitagawa 1964; Shkolnikov et al. 2012),

$$\Delta_p = \frac{\left[\left(f\left(\mathbf{p}_2, \mathbf{D}_2\right) - f\left(\mathbf{p}_1, \mathbf{D}_2\right)\right) + \left(f\left(\mathbf{p}_2, \mathbf{D}_1\right) - f\left(\mathbf{p}_1, \mathbf{D}_1\right)\right)\right]}{2}, \tag{6}$$

$$\Delta_D = \frac{\left[\left(f\left(\mathbf{p}_2, \mathbf{D}_2\right) - f\left(\mathbf{p}_2, \mathbf{D}_1\right)\right) + \left(f\left(\mathbf{p}_1, \mathbf{D}_2\right) - f\left(\mathbf{p}_1, \mathbf{D}_1\right)\right)\right]}{2}. \tag{7}$$

## Results

### Number of Causes Listed in Death Certificates

Figure 2 depicts the mean number of different causes listed in the death certificates by age group and sex. For males, the number of listed causes increased from 1.99 in 2003

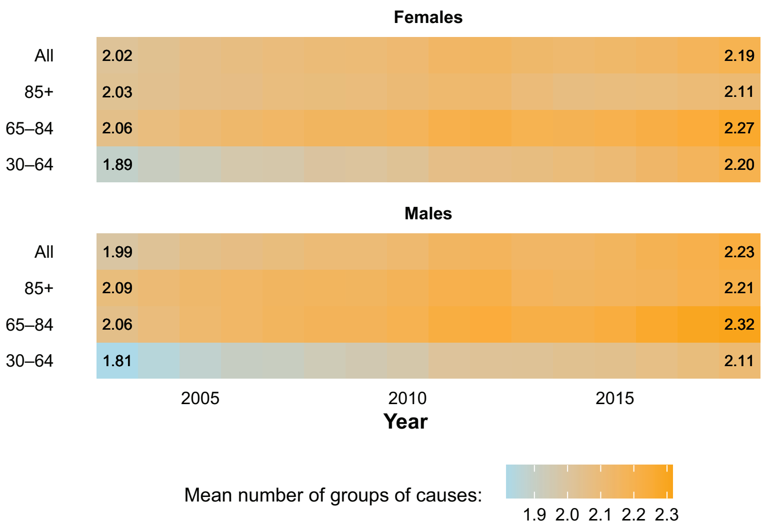


**Fig. 2** Mean number of groups of causes listed in death certificates by age and sex in the United States, 2003–2018

to 2.23 in 2018, while for females the corresponding numbers were 2.02 and 2.19. These increases were observed across all age groups, but they tended to be larger for the working-age group and at comparable levels across educational groups (online Figure S2).

## Shares (Sets of Causes of Death)

In 2018, the most prevalent groups of causes of death were cardiovascular, respiratory, neoplasms, mental, metabolic, and ill-defined (Figure 3). For example, for males, more than 180,000 deaths—12.6% of the total number deaths—had only cardiovascular cause/s listed in their death certificates. The first combination of two or more major causes of death was that of metabolic and cardiovascular causes, which summed to around 55,000 deaths (3.8%). The horizontal lines on the lower left side of the Figure 3 plots show the total number of cases for each individual cause. For example, about 800,000 males died with a cardiovascular cause listed in the death certificate (54.7%). For females, cardiovascular causes were also present in around 760,000 death certificates (54.9%), and they were also the first group of causes with more than 180,000 deaths (13.2%). Among females, the first combination of multiple major causes of death was that of respiratory and cardiovascular causes, which summed to more than 45,000 deaths (3.3%).

## Cause-of-Death Diversity

Cause-of-death diversity trends are presented in Figure 4. The different values of $W$ represent the importance of the underlying versus other causes of death listed in the death certificate. When $W$ equals 1, we are in the underlying cause of death setting. When $W$

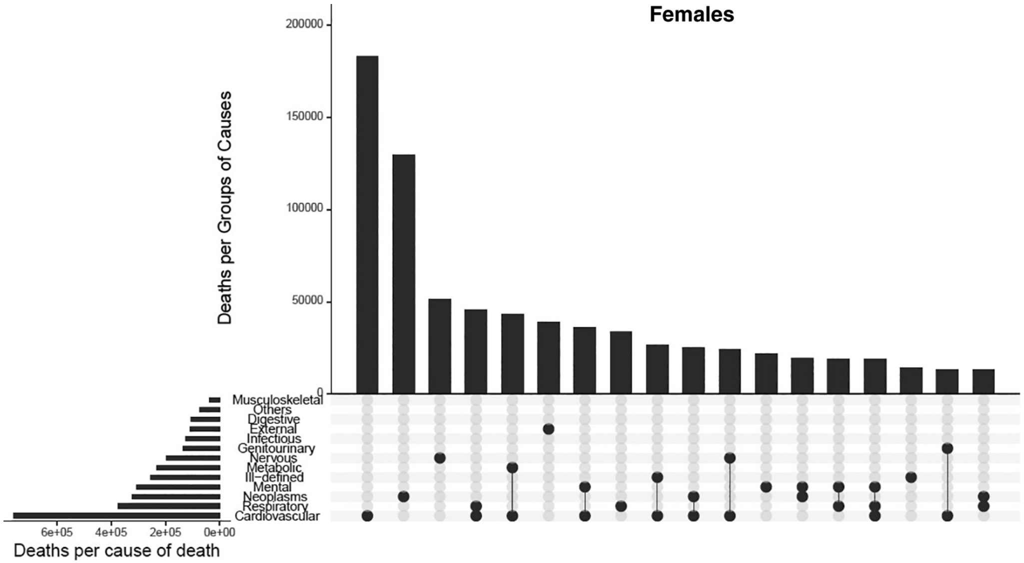


**Fig. 3** Combinations of causes of death (selection of 30 major combinations of causes, vertical bars) and number of deaths with each single cause listed in the death certificate (horizontal bars) at ages 30 and over, United States, 2018

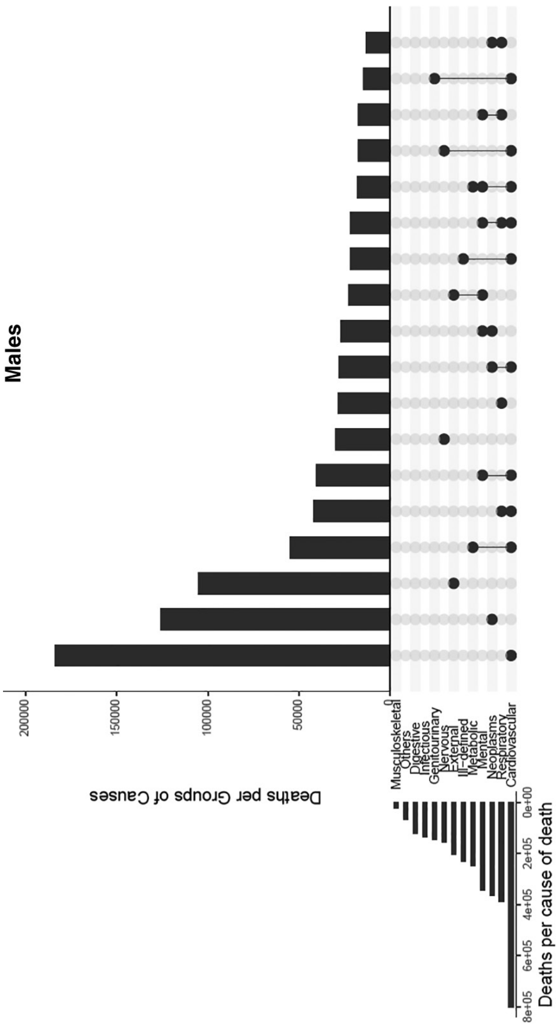


**Fig. 3** (continued)

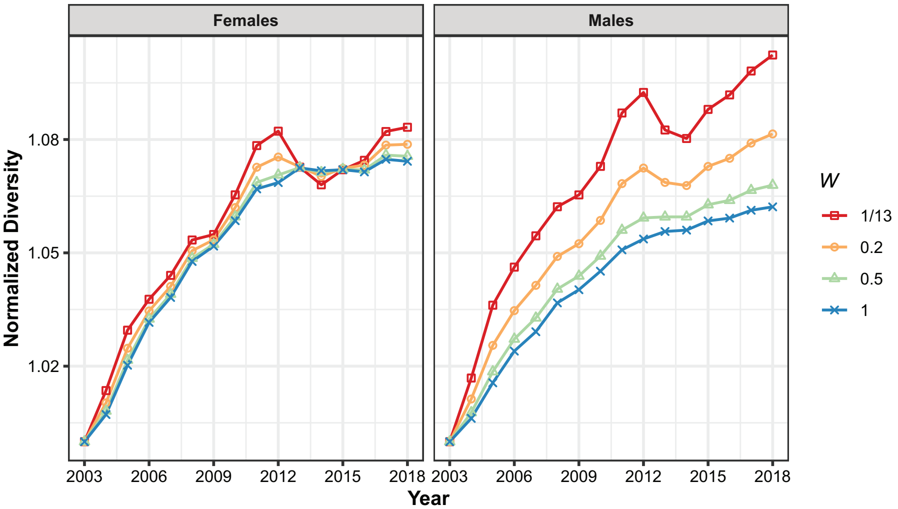


**Fig. 4** Trends in normalized ($D_{2003} = 1$) cause-of-death diversity according to the importance of the underlying versus other causes of death ($W$), United States, 2003–2018. When $W = 1$, we are in a single/underlying cause-of-death setting where the causes in the death certificate other than the underlying cause of death are ignored. At the other extreme, when $W = 1/13$, we are in a setting where the underlying cause of death is only equally important and not more important than the other causes included in the death certificate. For all other intermediate values of $W$, the underlying cause of death is more important than the other causes of death included in the list in varying degrees.

equals 1/13, we are in an MCOD setting in which each group of cause listed in the death certificate has the same importance, irrespective of its position. For $W$ values ranging between 1/13 and 1, the underlying cause is assumed to be more important than the other causes included in the death certificate. For any given $W$, we observe increases in cause-of-death diversity trends. These increases are more pronounced in the first half of the analyzed period (2003–2010) and are more remarkable as $W$ declines (e.g., with growing importance of MCOD). In the second half of the period (2010–2018), increases in cause-of-death diversity slowed down, particularly for females, and in the scenario when uniquely underlying causes of death are considered ($W = 1$) for males.

Trends in cause-of-death diversity have increased across all age groups (Figure 5). These increases were rather constant over the time span for ages 30–84, whereas for the older age group they stagnated from around 2012 onward. Furthermore, increases in cause-of-death diversity were found to have clear age-specific patterns regarding the relative importance of the underlying cause of death versus the other causes listed in the death certificate. That is, at working ages (30–64), cause-of-death diversity over the period 2003–2018 increased by 11% and 14% for males and females, respectively, when all causes in the death certificate were accounted to be equally important ($W = 1/13$), whereas diversity was much smaller in a context of underlying causes of death ($W = 1$): 2% for males and 6% for females. At ages 65–84, differences in the cause-of-death diversity increased as $W$ values decreased. Specifically, increases ranged between 6–7% ($W = 1$) and 11–12% ($W = 1/13$) for both males and females. Finally, at older ages, differences in the trends by $W$ were nonexistent for males and were found to be in the opposite direction for females—with greater increases within

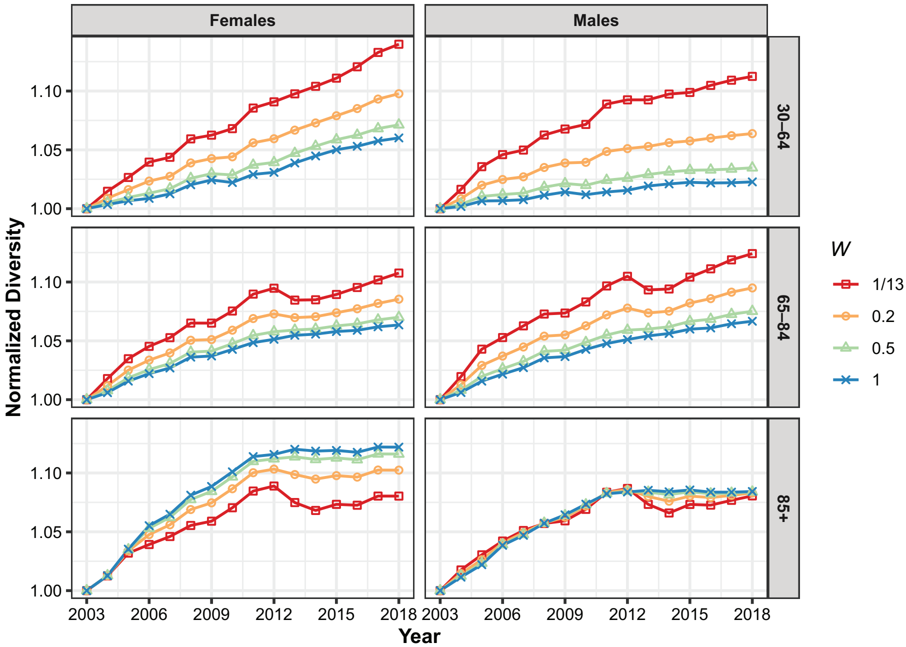


**Fig. 5** Trends in normalized ($D_{2003}$ = 1) cause-of-death diversity according to the importance of the underlying versus other causes of death ($W$) by age groups, United States, 2003–2018. When $W = 1$, we are in a single/underlying cause-of-death setting where the causes in the death certificate other than the underlying cause of death are ignored. At the other extreme, when $W = 1/13$, we are in a setting where the underlying cause of death is only equally important and not more important than the other causes included in the death certificate. For all other intermediate values of $W$, the underlying cause of death is more important than the other causes of death included in the list in varying degrees.

the underlying cause of death approach. That is, the use of underlying causes of death results in a 12% increase in cause-of-death diversity between 2003 and 2018 for females and an 8% increase for males, whereas considering all causes listed in the death certificate to be equally important results in reduced increases of around 8% for both females and males ($W$ = 1/13). These results were robust when certificates with missing education were included in the analyses (see online Figures S3 and S4).

## Diversity by Educational Groups

Cause-of-death diversity trends by educational group are presented for a scenario considering multiple causes of death that gives a high importance to the underlying cause ($W = 0.5$) (Figure 6). In general, diversity is slightly higher for females than for males. For both sexes and educational groups, cause-of-death diversity increased over the analyzed period, and levels were lower among higher educated groups and higher among the lowest educated groups. A visual inspection of trends over time suggests that cause-of-death diversity increases slow down after 2012 for the highest educated group as compared with the period 2003–2012. From 2012 onward, higher educated groups presented overall smaller increases over time as compared with lower educated groups.

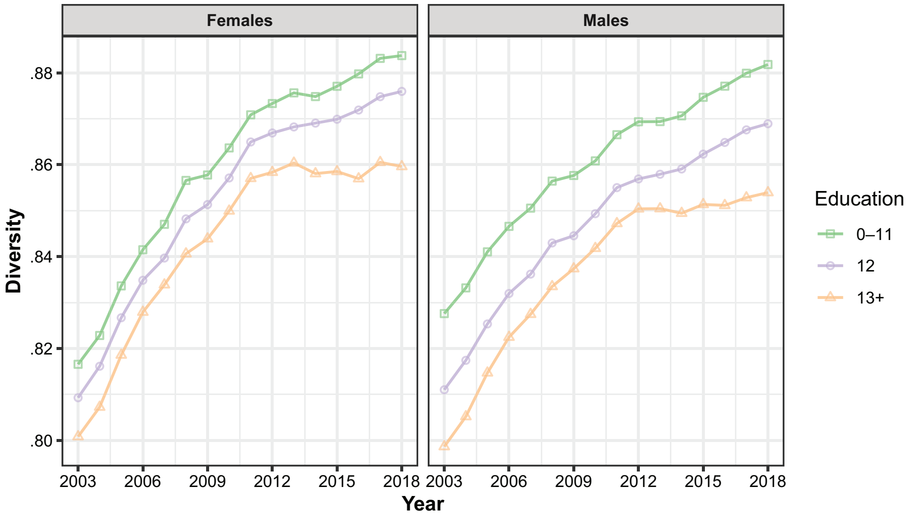


**Fig. 6** Trends in cause-of-death diversity by sex and educational level at ages 30 and over, $W=0.5$, United States, 2003–2018

Results for other levels of *W* are generally in line with those presented, but for lower values of *W*, a clearer educational gradient (lower cause-of-death diversity among higher educated groups) for females was clearly observed (see online Figure S5).

When broken down by age groups, the results suggest a clear educational gradient at working ages, particularly for females (Figure 7). This gradient diminished at ages 65 and over. For females, the educational gradients were minimal at ages 85 and over, except for the latest years. For males aged 65–84, a visual inspection of trends suggests educational differences when comparing the low-educated group with the middle- and high-educated group, but not when comparing the last two. Furthermore, time trends do not suggest important differences in cause-of-death diversity across educational groups, that is, increases were comparable across all age groups. Estimates for other levels of *W* are in line with these results and can be found in online Figure S6.

## Contribution of Between Versus Within Educational Groups to Cause-of-Death Diversity

The observed changes in cause-of-death diversity between 2003 and 2018 by age group, sex, and *W* are attributable to different extents of (1) changes between educational groups and (2) changes in the contribution of cause-of-death diversity within educational groups, as presented in Figure 8. In all subpopulations, and for the different values of *W*, the increases in diversity were mostly driven by increases in diversity within educational groups, which accounted for at least 75% of the total increases in diversity—except for females aged 85+. The dynamics of diversities between educational groups played a smaller and almost residual role.

Finally, we have quantified the extent to which changes in the educational composition of deaths could explain the observed cause-of-death diversity dynamics between 2003 and 2018 (online Figure S7). For all age groups, sex, and *W* values, the

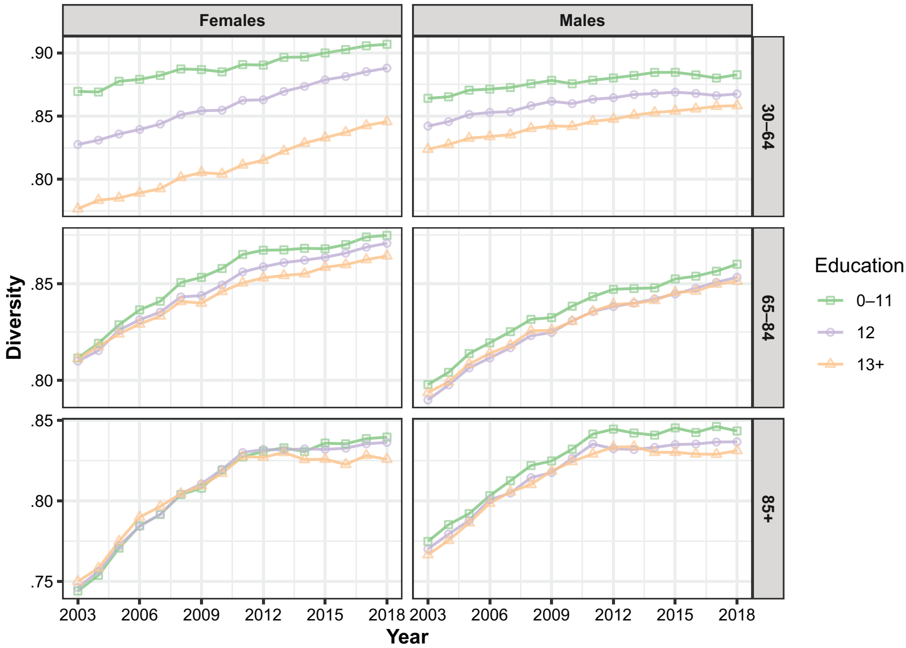


**Fig. 7** Trends in cause-of-death diversity by sex, age group, and educational level at ages 30 and over, $W=0.5$, United States, 2003–2018

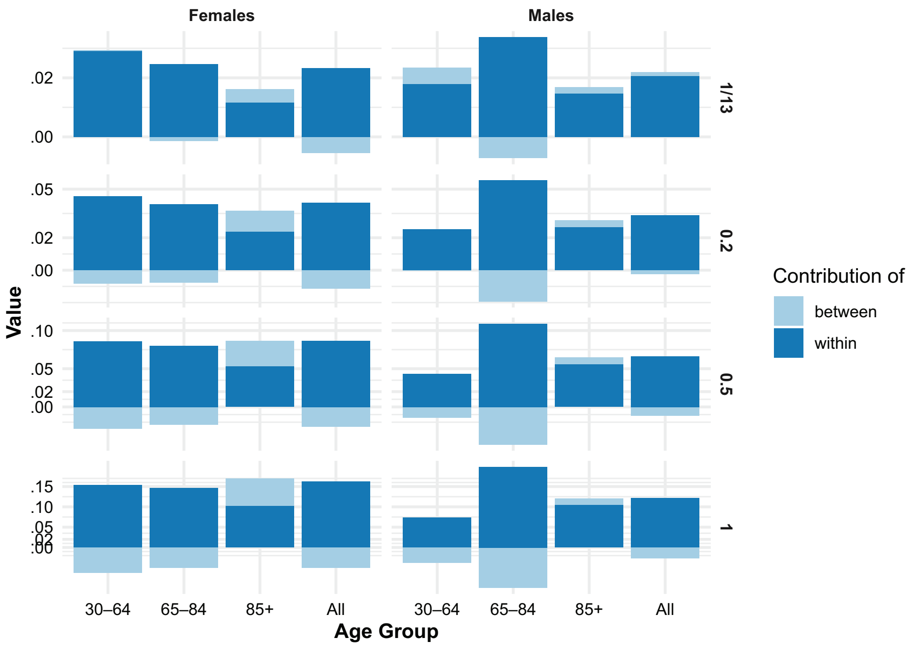


**Fig. 8** Decomposition of cause-of-death diversity increases between 2003 and 2018 between dynamics of between and within educational group contributions at ages 30 and over, United States

observed changes in cause-of-death diversity are almost entirely explained (at least 99%) by changes in the dynamics between and within educational group cause-of-death diversity, and not by changes in the composition of deaths by education.

## Discussion

Using detailed multiple causes of death, we have shown that cause-of-death diversity has been increasing in the United States from 2003 onward, when analyzing deaths from both the "underlying cause" and an MCOD perspective. The latter suggested faster increases in cause-of-death diversity compared with merely considering underlying causes of death, especially for males. These trends were particularly pronounced until around 2012, and decelerated thereafter owing to the stagnation observed in the age group of 85 and over. Our results by educational attainment show an important and widening educational gradient as lower educated groups presented higher cause-of-death diversity, mainly at working ages, but with notable differences across age groups.

### Evaluation of Data and Methods

We relied on the use of multiple causes of death rather than merely focusing on underlying causes of death, as typically done in most mortality studies that use cause-of-death data. In our view, this is particularly relevant in aging societies because of the shift in mortality toward older ages and the increase in comorbidities (King et al. 2018). Given the recognized challenges in determining the underlying cause of death at old ages (Alpérovitch et al. 2009; Flagg and Anderson 2021), the use of MCOD may lessen coding issues and improve our understanding of mortality dynamics. Of course, this does not imply that MCOD are perfectly recorded, and it is possible that social, biomedical, and coding factors may bias both underlying cause and MCOD assignment. These factors may change over time, and therefore when looking at time trends we cannot rule out the possibility that coding practices may influence cause-of-death diversity dynamics. Coming up with a reasonable approach to control for the effect of such factors would at least require having data to reliably measure those concepts—an interesting line of research that is well beyond the scope of this study. Yet, MCOD data are still highly relevant for complementing underlying cause-of-death analyses.

To make good use of the data, we used a broad and well-defined cause-of-death grouping (e.g., cardiovascular, respiratory), which was convenient because no changes in the International Classification of Diseases have occurred over the analyzed period, and therefore potential minor changes in coding practices are unlikely to have played a major role in our estimated results. This grouping was also convenient in terms of keeping the analytical strategy relatively manageable in computational terms. The downside of using such a broad classification is that it becomes more difficult to assess the role of specific causes of death on cause-of-death diversity. Finally, we acknowledge that diversity is dependent on the number of causes of death used, and therefore studying the effect that more granular classifications can have on cause-of-death diversity measures would be of great added value in future research.

Our estimates were based on different assumptions regarding the relative importance of the underlying cause of death. At one extreme, we considered scenarios where only the underlying cause of death was relevant ($W=1$), and at the other extreme, we considered scenarios where all causes listed in the death certificate were equally important ($W = 1/13$ in this study). The latter can be seen as a strong assumption, but it is sufficiently informative to be included. However, a plausible good solution may lie with values within this range. To facilitate the reading of the results by education, we presented the results for a middle scenario ($W=0.5$), and we placed the results for other $W$ values in the supplementary material.

Our methodological approach on the estimation of cause-of-death diversity is an adaptation of popular approaches commonly applied to assess heterogeneity in human societies or animal ecosystems (Alesina et al. 2003; Bossert et al. 2011; Mouchet et al. 2010). While the number of indices measuring the concept of "diversity" is very large, they tend to be highly correlated (Davydov and Weber 2016). The choice of one measure or another is often guided by the properties it satisfies. The advantage of our proposed diversity measure is that it can be broken down into clearly interpretable within-group and between-group components when the population under study is partitioned across socially relevant groups. However, our methodology is subject to certain assumptions that deserve some discussion. First, a critical part of our approach is the measurement of distances between groups of causes of death. For the sake of parsimony, we assumed that all different causes are equally distant from one another. However, we allowed the underlying cause of death to play a more prominent role than the other causes listed in the death certificate, as detailed in the Methods section and in Box 1. We acknowledge that the assumption of equal distance between causes may be arguable. For example, cardiovascular causes may be etiologically closer when compared to respiratory causes than, for example, external causes of death. However, the objective of this study was to estimate diversity across a broad group of causes of death and not across etiological factors. Therefore, an objective and etiological measurement of cause-of-death distances needs to be addressed by future studies on this topic.

Second, one might argue that our findings could be affected by the mean number of causes listed in the death certificates, which tends to gradually increase over time (see Figure 2 and online Figure S2). Yet, the fact that those mean values are higher does not imply that cause-of-death diversity must be necessarily higher (an increasing number of causes repeating across most individuals would decrease diversity). Our approach is not based merely on counting the *number* of causes listed in death certificates, but rather on comparing the similarities or dissimilarities that might exist among them, while accounting for the potentially different role of the underlying cause of death.

Third, a challenge to be addressed in all education-specific time trends population health studies relates to changes in the population composition by educational attainment, which is postulated to partly account for life expectancy dynamics (e.g., Hendi, 2015, 2017; Montez and Zajacova 2014). The results of our sensitivity analysis suggest that the changing education composition in the United States has played a negligible role on cause-of-death diversity trends (see online Figure S7).

### Comparison and Explanation of Results

Our all-age and age-specific results when considering "underlying causes of death" only ($W=1$) are in line with those from a recent study using underlying cause of death data and the Shannon index of entropy as a measure of diversity (Bergeron-Boucher et al. 2020). Our results for MCOD suggested faster increases in cause-of-death diversity over time as compared with merely using underlying causes of death, especially for males. This implies that the previously estimated cause-of-death diversity increases may be conservative (Bergeron-Boucher et al. 2020). A notable exception is that for the oldest age group, differences in the time trends for different given importance of MCOD were not found in males and were found to be in the opposite direction for females. This result seems to be supported by the growing comorbidity prevalence among older women (King et al. 2018), given that older individuals with comorbidities may tend to die from more similar causes of death when MCOD are taken into the analysis than when using underlying causes of death. Consider the following hypothetical example: the cause-of-death diversity $D$ among three women dying from three different underlying causes of death (e.g., cardiovascular, respiratory, and mental), but from overall identical multiple causes of death (e.g., cardiovascular, respiratory, and mental), would be larger when only the underlying cause is considered ($W=1$) than when MCOD were taken into consideration.

According to Bergeron-Boucher et al. (2020), the main driver of the recent increases in cause-of-death diversity over time in low-mortality countries was the decline of the most prevalent cause of death: cardiovascular deaths. Our findings on the deceleration of cause-of-death diversity increases around the early 2010s coincide with the stagnation of cardiovascular mortality (Glynn et al. 2019; Mehta et al. 2020; Sidney et al. 2019), so cardiovascular causes may be an important determinant of our results. However, in an MCOD framework, cardiovascular causes of death may be less important, given that the deceleration of diversity increases is not evident among males. Nonetheless, explaining the role of specific causes of death given their positions in death certificates to the observed cause-of-death diversity trends was beyond the scope of this study. A better understanding of the mechanism behind the observed increases in cause-of-death diversity remains to be elucidated.

### Educational Gradients

Our results by educational groups highlight important age-specific patterns that raise new questions in population health inequality studies in the United States. Our findings pointed toward a clear educational gradient in cause-of-death diversity, with the lowest educated groups presenting the highest cause-of-death diversity (i.e., more heterogeneity in their cause of death patterns), and vice versa. These results could be related to the disadvantages of low socioeconomic class in terms of low-paid and more physically demanding occupations, worse living conditions, limited access to health services or networks, or unhealthier lifestyles (e.g., Case and Deaton 2021; Davey Smith et al. 1998; Hayward et al. 2015). That is, our results are generally in line with previous results on education-specific life expectancy and life span variation estimates, as the lowest educated groups also showed lower life expectancy and higher life span variation compared with their more educated counterparts (Case and Deaton 2021; Sasson 2016). It seems, therefore, that the higher the life span variation, the higher the cause-of-death diversity, which coheres with the fact that deaths at more dissimilar ages are likely to be caused by a more variegated set of factors than deaths occurring at more similar ages.[3] Additionally, important and changing components of the mortality composition in the United States are the growing role of obesity, alcohol, drug-related mortality, and overall deaths of despair (Case and Deaton 2017; Janssen et al. 2020; Sasson and Hayward 2019; White et al. 2020), which tend to have a larger impact on low-socioeconomic groups (Richardson et al. 2015; Siddiqi et al. 2015).

Nonetheless, cause-of-death diversity has increased across all educational groups, but these differentials seem to have widened since the 2010s. These findings are not surprising given the well-documented increases in socioeconomic inequalities in mortality in the United States over recent years (Leive and Ruhm 2022; Sasson and Hayward 2019). Clear educational gradients were observed across the analyzed period for working-age populations, but time trends at higher age groups showed lower differences across educational groups. For example, at ages 65 and over the educational gradients seemed smaller, which is in line with well-documented declines in mortality inequalities across educational groups at older ages (Elo and Preston 1996). This common pattern of declining inequalities with age could be partly explained by selection. That is, those from low-educational groups that reach old age are more selected compared with those from high-educational groups. In addition, we should consider that education is a strong socioeconomic proxy at working ages and for recent generations, but that for older groups and birth cohorts, other socioeconomic indicators (e.g., household income) might more accurately reflect individuals' socioeconomic position (Galobardes et al. 2006). Unfortunately, other socioeconomic variables that would better reflect wealth were not available in the data.

## Final Reflections

Assessing cause-of-death diversity trends from an MCOD perspective yields valuable information on the variability of groups of causes to be tackled in order to contribute to all-cause mortality reduction. Because individuals tend to die from increasingly heterogeneous sets of causes, the effort toward reducing mortality should be divided within a larger group of causes. This implies that mortality improvements may have a higher cost as mortality from more causes of death would need to be addressed to further contribute to reducing all-cause mortality. In other words, a higher diversification

[3] A positive relationship between the levels of life span variation and cause-of-death diversity can also be identified in the findings reported in Bergeron-Boucher et al. (2020). While in that paper one can see that, when life span variation decreases in a given country, the corresponding level of cause-of-death diversity tends to increase, when one compares these two variables across countries for a fixed moment in time, the relationship is seemingly positive (see panel B in their Figures 4 and E1). That is, at a fixed moment in time, in those countries where life span variation is larger, cause of death variation tends to be larger as well. This is precisely the pattern we observe in the United States when comparing educational groups rather than countries.

of causes of death might require a wider variety of specific treatments, therefore potentially reducing the effectiveness of health policies.

The current COVID-19 pandemic represents an additional challenge for health systems and may drive important changes in the distribution of deaths across causes that may be reflected in cause-of-death diversity increases. This is especially important in the United States, which has been lagging behind other low-mortality countries over the last decade. In addition, the rise of socioeconomic inequalities in health and mortality over recent decades calls for increased investment in public health for the lower socioeconomic classes as well as for overall population health. Given the well-known mortality differences across U.S. states (Montez et al. 2019), further studies on the topic should examine the role of geography in improving our understanding of the most recent mortality dynamics. In conclusion, cause-of-death diversity has increased in the United States, these increases were higher for males when multiple causes of death were accounted for, and the socioeconomic gap increased over the last decade. Given the large and increasing prevalence of comorbidity in low-mortality populations, cause-of-death studies based on single causes of death alone might be missing the mark. Monitoring cause-of-death diversity can be seen as a complement to currently existing approaches that measure heterogeneity in population health. Future cause-of-death diversity studies should further disentangle the role of different sets of causes of death in cause-of-death diversity and assess differences across socioeconomic groups to best guide equitable public health interventions. ■

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