Changes in the modal age at death of ageing- and behaviour-related diseases in the US: A multiple-cause-of-death approach

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Extended abstract

Even amid the current context of COVID-19, low-mortality countries have largely managed to control infectious diseases that previously led to premature mortality during the initial stages of the epidemiological transition. Consequently, there is little scope for reducing mortality at younger ages today. Instead, the key to further increases in life expectancy primarily relies in reducing mortality at old and very old ages (Leon et al., 2019; Meslé, 2004). Indeed, recent evidence indicates that life expectancy increases at birth have decelerated, particularly in the past decade, in comparison to historical trends, with the majority of life expectancy increases taking place at older ages (Ho & Hendi, 2018; Kallestrup-Lamb et al., 2020; Leon et al., 2019).

Although the current disease burden mainly comes from non-communicable diseases (NCD), advancements in early diagnosis, enhanced medical technologies, treatment methods (including medication), and shifts in behaviour have greatly improved survival chances of individuals afflicted with cardiovascular disease (CVD) and cancer –the two most prevalent NCDs (Faithfull et al., 2017), Consequently, other diseases have become more prevalent as the underlying causes of death (UCoD), especially those related to cognitive decline such as Parkinson's, Alzheimer's and other dementias (European Commission, 2019).

The multiple cause of death framework in the context of increasing comorbidities

Prior to COVID-19, NCD, particularly cancer, CVD, stroke, and neurodegenerative diseases, accounted for about 85% of all deaths (United Nations, 2012). However, the reported UCoD commonly used by demographers in cause-of-death analysis does not offer a comprehensive view of the burden a specific disease carries. This is because, with increasing age, NCDs often occur in the form of comorbidities (Christensen et al., 2009). Consequently, the UCoD becomes less a result of a clearly-defined aetiological (causal) path than the random result of a more generalised deterioration of the capacity for life (Rosenberg, 1999). As mortality shifts towards older ages, the mortality risk therefore becomes more heterogeneous (Engelman et al., 2010; Vaupel, 2010). Assessing mortality related to these key medical factors, such as different cancer types, hypertension, diabetes, and dementia, is not straightforward and has been overlooked in most studies. It is in this context that analysing the age-at-death distribution within a multiple cause-of-death (MCoD) framework offers an excellent opportunity to enhance our understanding of mortality associated with multiple medical conditions.

Studying the modal age at death

In the current context of shifting mortality patterns towards and within older ages and ongoing debates on future (limits to) life expectancy, researchers have increasingly focused on studying the modal age at death (MAD). MAD represents the most common life span in a period, i.e. the age that concentrates the most deaths in a given year. This offers a unique perspective to understand changes in the distribution of deaths, especially in older ages where most deaths occur (Canudas-Romo, 2008; Horiuchi et al., 2013). Unlike life expectancy, which can be influenced by mortality changes at younger ages –making it less indicative for studying old-age mortality–, MAD is solely determined by ages older than itself (Horiuchi, et.al 2013). Thus, the MAD is a good indicator for measuring longevity in a population. Additionally, since it is the most common age at death, the MAD also informs on the shifts of mortality (Bergeron-Boucher, et.al, 2015) and is the indicator to monitor disparities in old-age mortality (Diaconu et.al. 2022).

The MAD is an increasingly used indicator but has limitations in its calculation. Therefore, a lot of the discussion around it has been focused on its estimation (Kannisto, 2001, Canudas-Romo, 2008, 2010, Horiuchi

et.al. 2013, Ouellette & Bourbeau, 2011). There are two studies that have used it to analyse mortality by causes of death. The first one analyses the six leading causes of death for Canadian females and males from 1974 to 2011. This paper concludes with the importance of studying the MAD by cause because although changes can be observed in the general mortality mode, the levels and pace of this differ widely by cause of death (Diaconu et.al. 2016). The second study gives another angle to the advantages of the MAD and displays a comparison among the MAD for leading causes of death in the US and in Canada. The results show that for most diseases levels and trends are very similar, but it is not like that for all, and this inequality needs to be discussed (Diaconu et.al. 2020).

Although the modal age at death has been mainly studied for overall mortality, our contribution here is to

- evaluate the changing modal age at death for ageing-related diseases
- examine the differences in the age-at-death distribution of both the UCoD and MCoD
- consider sex differences therein

Given the availability of long-time series in both UCoD and contributing causes of death, we will analyse this for the US.

Data and method

MCoD and UCoD mortality data for the period 1999-2019 were obtained from the WONDER online database of the Centers for Disease Control and Prevention (https://wonder.cdc.gov). Data are based on death certificates for U.S. residents. Each death certificate contains a single underlying cause of death, up to 20 additional multiple causes and demographic data. 15 cause-of-death mortality categories are analysed, corresponding to the most prevalent NCD and coded according to the 10th revision of the International Classification of Diseases (ICD-10) (Table 1). The population data come from the Human Mortality Database (2023).

To estimate the MAD we first estimated multiple decrement life tables for the UCoD and then used Kannisto's (2001) quadratic approximation to the mode where x is the age with most deaths on the age at death distribution (dx):

$$M = x + \frac{d(x) - d(x-1)}{[d(x) - d(x-1)] + [d(x) - d(x+1)]}$$

Due to a certain flatness in the d(x) curve near its highest point, the mode is sensitive to minor variations in the curve which makes it important that the curve is unimodal and relatively smooth, reason why for visualisation purposes the results were smoothed (loess). For future steps we will compare this with the p-splines approach.

Table 1. Cause-of-death categories used based on the UCOD ICD-10 113 Cause List and sex-specific proportion of deaths according to the UCOD. Ages 50+. 1999, 2009 and 2019.

		Women			Men		
	Cause of death (ICD-10 code)	**1999**	**2009**	**2019**	**19995**	**2009**	**2019**
1	Malignant neoplasms (C00-C97)	21.6	22.3	20.8	26.5	26.5	23.2
1a	of colon, rectum and anus (C18-C21)	2.4	2.1	1.8	2.6	2.4	2.0
1b	of pancreas (C25)	1.3	1.5	1.7	1.3	1.6	1.8
1c	of trachea, bronchus and lung (C33-C34)	5.3	6.0	4.9	8.5	8.1	5.7
1d	of breast (women only) (C50)	3.2	3.2	3.0			
1e	of prostate (men only) (C61)				3.2	2.7	2.4
1f	. of lymphoid, hematopoietic and related tissue (C81-C96)	2.2	2.0	1.8	2.6	2.7	2.4
1g	..Remaining malignant cancers (remainder of C00-C96)	7.2	7.5	7.6	8.2	9.2	9.0
2	Diabetes mellitus (E10-E14)	3.2	2.8	2.8	2.8	3.0	3.5
3	Alzheimer's disease (G30)	2.8	4.9	6.5	1.3	2.3	2.9
4	Heart disease (I00-I09; I11, I13, I20-I52)	32.5	25.2	22.7	32.8	27.2	26.1
5	Cerebrovascular diseases (I60–I69)	8.9	6.6	6.5	6.1	4.7	4.7
6	Influenza and pneumonia (J09-J18)	3.1	2.4	1.9	2.6	2.2	1.8
7	Chronic lower respiratory diseases (J40-J47)	5.4	6.3	6.4	6.1	6.1	5.6
8	Nephritis, nephrotic syndr. & nephrosis (N00-N07,N17-N19,N25-N27)	1.6	2.1	1.9	1.6	2.2	2.0
9	Remaining causes of death	21.0	27.4	30.6	20.1	25.9	30.2
	All deaths (A00-Y98)	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**

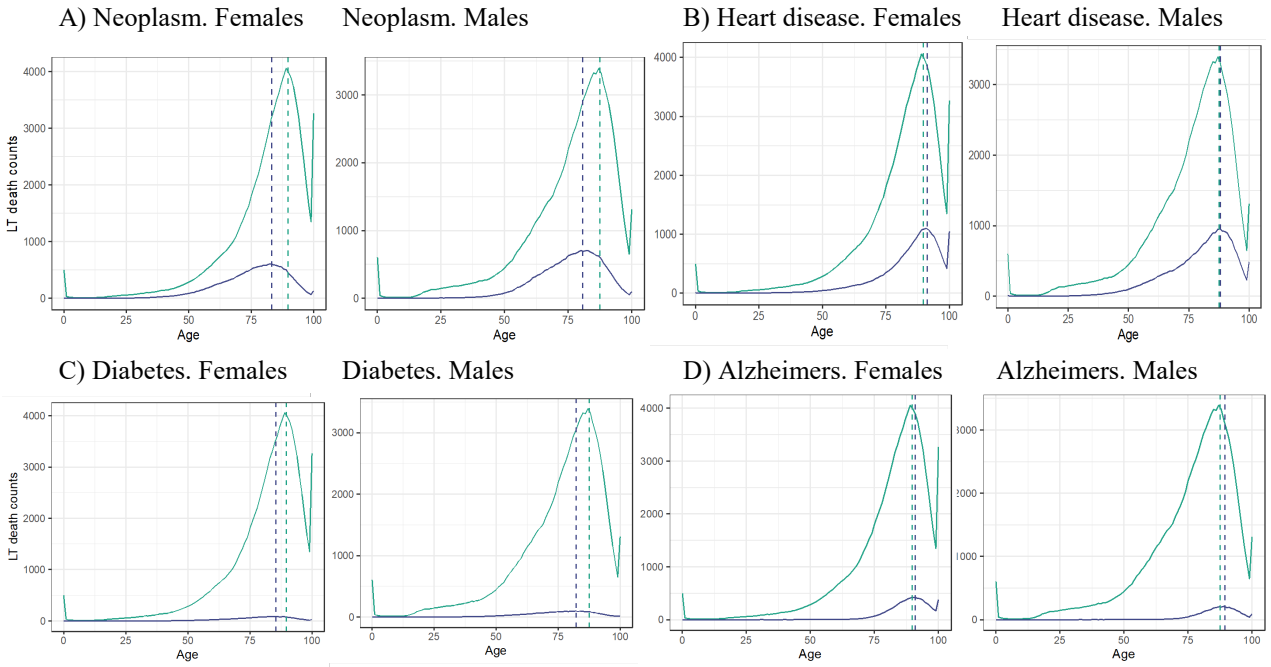
Results

The results of our analysis revealed notable variations in the MAD across different causes and for men and women. For women dying of neoplasms the mode was 83.2 years, whereas the total mortality mode was 89.7. For men, the MAD was, respectively 80.7 and 87.5 years (Figure 1). Furthermore, not all causes exhibited similar patterns; for instance, the mode age for women succumbing to heart disease was 91.2 years, higher than the overall mortality mode. In the case of men, it was 88.2, i.e. just higher than the overall MAD. In both cases, it highlights the significant impact of heart diseases on longevity, considering that about 25% of deaths in the US are attributed to heart diseases (Table 1). Interestingly, diabetes-related deaths were more widely spread out, with a mode lower than the overall mortality, while Alzheimer's-related deaths had a slightly higher mode than the overall mortality.

We then set out to estimate changes in the MAD over time with Loess smoothing (Figure 2). Peaks and troughs can be observed at the same moments for both sexes on most occasions, with a generally upward trend. This gives confidence that the method is adequate, although we do observe the widening sex difference for diabetes. Could it be that women adhere better to improved treatment? - Work still in progress here.

Additionally, we have some results using observed data to estimate MAD using MCoD data and compare them to the results for UCoD (not shown here). For diabetes, we found that the mode of observed deaths is 72 for males for both UCoD and MCoD, but for females it was 72 and 84, respectively, as the age at death appears to be affected by the population's age structure (a cohort effect).

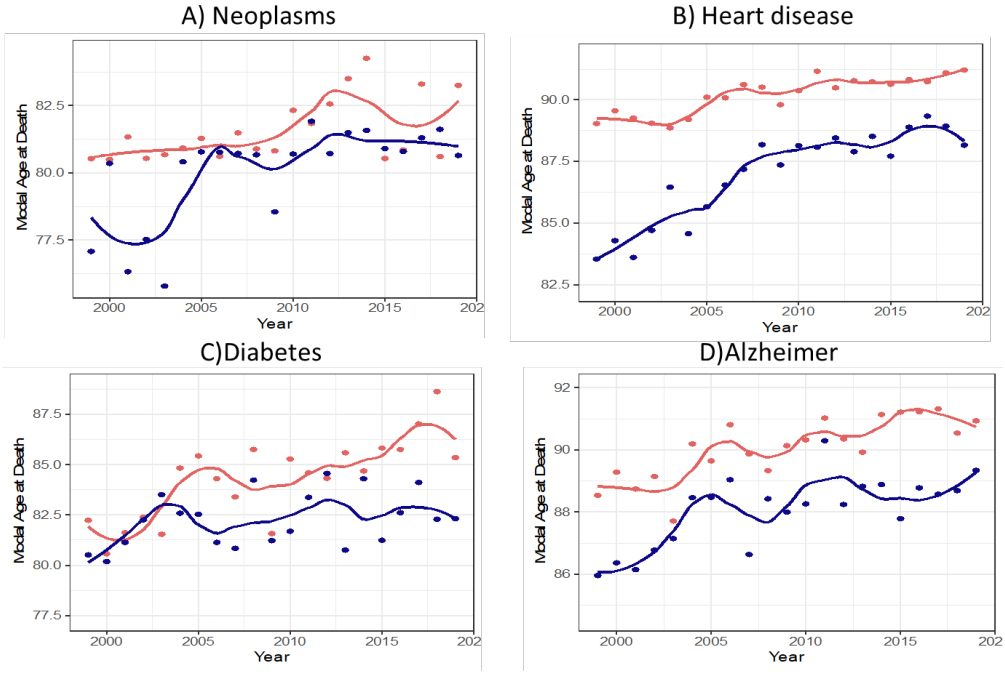
Figure 1. Comparison of the age-at-death distribution (dx) by all causes (green) & selected causes (blue). USA. 2019.



Tentative discussion

Our findings underscore the intricate relationship between specific ageing-related causes of death, gender, and modal age at death, shedding light on the diverse mortality patterns within the studied population. The sex gap at the modal age at death is not the same as the sex gap in other indexes (i.e. life expectancy) as it tends to be smaller because it is not influenced by excess male mortality at younger ages. At the same time, if we want to understand longevity, it is necessary to understand it by causes of death as they have different age patterns (schedules) than general mortality. Likewise, differences in the sex gap of the MAD are driven by sex-specific old age mortality patterns. People only die once but they can die of several causes. We know very little about the distribution of the age at death distribution of the MCoD mortality. In MCoD, a single death can record up to 20 different causes of death and this also has an age pattern. However, methods based on life-table counts or age at death distribution do not work to estimate the Mode of MCoD!

Figure 2 Time series of the MAD by underlying cause. Females (orange), males (blue). USA. 1999- 2019.



References

Canudas-Romo, V. Three measures of longevity: Time trends and record values. Demography 47, 299–312 (2010).

Canudas-Romo V. (2008). The modal age at death and the shifting mortality hypothesis. *Demographic Research, 19*, 1179.

Christensen K.et al (2009). Ageing populations: the challenges ahead. The Lancet, 374(9696), 1196-1208.

Diaconu V., van Raalte A., Martikainen, P. (2022). Why we should monitor disparities in old-age mortality with the modal age at death. Plos one, 17(2), e0263626.

Diaconu V., Ouellette N., Bourbeau, R. (2020). Modal lifespan and disparity at older ages by leading causes of death: a Canada-US comparison. Journal of Population Research, 37, 323-344.

Diaconu V., Ouellette N., Camarda C.G., Bourbeau, R. (2016). Insight on 'typical' longevity: An analysis of the modal lifespan by leading causes of death in Canada. Demographic Research, 35, 471-504.

Engelman M., Canudas-Romo V., Agree E.M. (2010). The implications of increased survivorship for mortality variation in aging populations. *Population and Development Review, 36*(3), 511-539.

European Commission. (2019). Eurostat database. Causes of death - standardised death rate by residence. Retrieved 11/7/2019 http://appsso.eurostat.ec.europa.eu/nui/submitViewTableAction.do

Faithfull S., Burton C., Clarke S., Kirby M., Lyon A., Levitt G., . . . Walter F. (2017). Mitigating risk of cardiovascular disease in people living with and beyond cancer. *Cancer Nursing Practice, 16*(1).

Ho J.Y., Hendi A.S. (2018). Recent trends in life expectancy across high income countries: retrospective observational study. *BMJ, 362*, k2562.

Horiuchi S., Ouellette N., Cheung S.L.K., Robine J.-M. (2013). Modal age at death: lifespan indicator in the era of longevity extension. *Vienna Yearbook of Population Research*, 37-69.

Kallestrup-Lamb M., Kjærgaard S., Rosenskjold C.P.T. (2020). Insight into stagnating adult life expectancy: Analyzing cause of death patterns across socioeconomic groups. *Health economics, 29*(12), 1728-1743.

Kannisto, V. (2001). Mode and dispersion of the length of life. Population: An English Selection, 159-171.

Leon D.A., Jdanov D.A., Shkolnikov V.M. (2019). Trends in life expectancy and age-specific mortality in England & Wales, 1970–2016, in comparison with a set of 22 high-income countries: an analysis of vital statistics data. *The Lancet Public Health, 4*(11), e575-82.

Meslé F. (2004). Gender gap in life expectancy: the reasons for a reduction of female advantage. *Rev Epidemiol Sante Publique, 52*(4), 333-352. doi:10.1016/s0398-7620(04)99063-3

Rosenberg H.M. (1999). Cause of death as a contemporary problem. *Journal of the history of medicine and allied sciences, 54*(2), 133-153.

United Nations. (2012). Population Facts*No. 2012/1*. Retrieved from https://www.un.org/en/development/desa/population/publications/pdf/popfacts/popfacts_2012-1.1.pdf

Vaupel J.W. (2010). Biodemography of human ageing. *Nature, 464*(7288), 536-542.