Understanding end-of-life multimorbidity: An analysis of Multiple Causes of Death in Denmark

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Background

The process leading to death is often complex, involving numerous health risks and diseases that individuals face throughout their lifespan. Death is ultimately attributed to a single underlying cause—defined as the condition that initiated the sequence of events leading to death. A large body of research has focused on analysing the underlying cause to identify the main health threats in populations. While this approach has proven valuable, it does not provide a full picture of the mortality risks within a population. Focusing solely on the underlying cause can obscure the broader morbidity process leading to death, particularly when multiple conditions interact.

The average number of contributing causes to death has been increasing over time and varies by sex and age group, with older individuals typically presenting a more complex combination of causes (Cheng et al., 2012; Jetté et al., 2010). Due to the complexity of determining a single cause when multiple health conditions are involved, misreporting or misclassification of the underlying cause of death has been a persistent issue in mortality studies (Bishop et al., 2023).

To offer a clearer picture of the morbid conditions leading to death, researchers have started investigating Multiple Causes of Death (MCoD) data, which provide a more comprehensive view by recording all conditions that contributed to an individual's death (Janssen, 1940). This approach offers deeper insights into the complexity of mortality risks and the interactions between competing causes of death. MCoD data are especially valuable in highlighting conditions that may not be the primary cause but significantly contribute to the mortality process, such as chronic diseases that are often relegated to secondary or contributory roles on death certificates. For this reason, one could think that MCoD data are a valuable proxy of the health conditions of individuals at the end of their lives.

Building on the MCoD literature and using high-quality Danish registry data, we investigate the reliability of MCoD data and whether they accurately reflect health conditions near death. By combining the Danish Population and Death registers with the Chronic Diseases register and Cancer register, we trace diagnoses from specific diseases (COPD, dementia, diabetes, and various cancers including lung, breast, prostate, colorectal, and pancreatic) and examine their appearance on death certificates. We conduct four analyses: (1) descriptive statistics examining frequency and placement of diagnosed diseases on death certificates; (2) logistic regression modelling factors influencing disease recording (age at diagnosis, time between diagnosis and death, educational attainment); (3) multiple decrement life tables comparing cause-specific mortality patterns for populations with chronic diseases; and (4) a Cause of Death Association Indicator (CDAI) to quantify co-occurrence patterns between conditions. Through this comprehensive approach, we aim to determine whether MCoD data are representative of actual morbidities present at the end of life or rather capture the chain of events leading to death, while also evaluating the quality of death registration in Denmark.

Data and Methods

In our study, we use multiple high-quality Danish registers. The core data sources include the Danish Population Register, the Cause of Death Register, the Chronic Diseases and Severe Mental Disorders Register, and the Cancer Register. We also link the Danish Education Register to assess socioeconomic gradients in death certificate reporting. Using personal identifiers, we are

able to link records from different registries for the same individual, enabling us to connect demographic information with detailed health diagnoses, educational attainment, and cause-of-death data. We analyse data from 2010 onwards, as the quality of the Chronic Diseases Register is highest from this period, through 2019, thus excluding the COVID-19 pandemic to avoid its effects on mortality and death registration patterns in Denmark.

Our study population includes all Danish residents aged 50 and older who have been diagnosed with COPD, dementia, diabetes, or cancer. For cancer, we focus on five major types: lung, breast, prostate, colorectal, and pancreatic cancers, selected for their high incidence and varying mortality patterns. These diseases were selected because they frequently appear in different positions on the death certificate due to their nature, making them ideal for analysing the reliability of MCoD data. For each individual, we have information on age at diagnosis, sex, date of birth, date of death, causes of death in different positions on the death certificate, and highest educational attainment.

The analysis employs four complementary approaches: (1) and (2) assess whether MCoD data are representative of morbid conditions present at the end of life; (3) and (4) assess whether MCoD data capture the chain of events leading to death. These analyses also evaluate the quality and consistency of death registration in Denmark across different population groups and disease categories.

(1) As a first exploration of the Danish MCoD data, we conduct descriptive analyses investigating the number of times and percentage each diagnosed disease appears on the death certificate (in any position) and, for those who have the disease reported on the death certificate, the frequency of appearance in Part 1 or Part 2 of the death certificate.

(2) To assess what factors influence whether a diagnosed disease appears on the death certificate, we employ logistic regression models. The dependent variable is a binary indicator of whether the diagnosed disease appears anywhere on the death certificate. Key independent variables include: sex, educational attainment (up to secondary education, tertiary education), age at diagnosis (50-64, 65-79, 80+), and time between diagnosis and death (<1 year, 1-2 years, 2-3 years, 3+ years). We run separate models for each disease to capture disease-specific reporting patterns.

(3) We construct multiple decrement life tables to compare cause-specific mortality patterns between populations with and without their chronic diseases reported on the death certificates. We calculate the probability of dying from specific causes ${}_nq_x^i$, the number of cause-specific deaths ${}_nd_x^i$, and cause-specific death ratios for each chronic disease cohort $ratio_x^i = \frac{\sum_x nd_x^i}{\sum_i \sum_x nd_x^i}$, where *x* represents age and *i* the cause of death. Analyses are stratified by sex, time period (2-year intervals from 2010-2011 to 2018-2019), diagnoses disease, and whether the diagnosed disease appears on the death certificate. Causes of death are classified according to the 17 categories of the Human Cause of Death Data. This approach enables us to quantify differences in mortality profiles and identify whether individuals with unreported chronic conditions have distinct patterns of recorded causes of death.

(4) Finally, we compute the Cause of Death Association Indicator (CDAI) to quantify co-occurrence patterns between chronic diseases and the 17 HCD cause categories (Désesquelles et al., 2010). The CDAI is calculated as: the standardised difference between observed and expected co-occurrences:

$CDAI = \frac{\sum_x \frac{d_{uc,x}}{d_{u,x}} \cdot \frac{\overline{d_x}}{\sum_x \overline{d_x}}}{\sum_x \frac{d_{c,x}}{d_x} \cdot \frac{\overline{d_x}}{\sum_x \overline{d_x}}}$, where x represents age, c is the diagnosed disease, and u is the underlying cause of death. Deaths with bar pertain to the total Danish population. This analysis helps determine whether MCoD data capture meaningful disease interactions in the mortality process rather than random co-occurrences, providing insight into whether the data reflect actual causal pathways to death.

Confidence intervals for analyses (3) and (4) are obtained using bootstrapping techniques.

Preliminary results

In the population with COPD, the appearance rate of the diagnosed disease on the death certificate is 35%. Among those with the disease reported on the death certificate, slightly less than half of the time the disease appears in Part 1 of the certificate (Table 1).

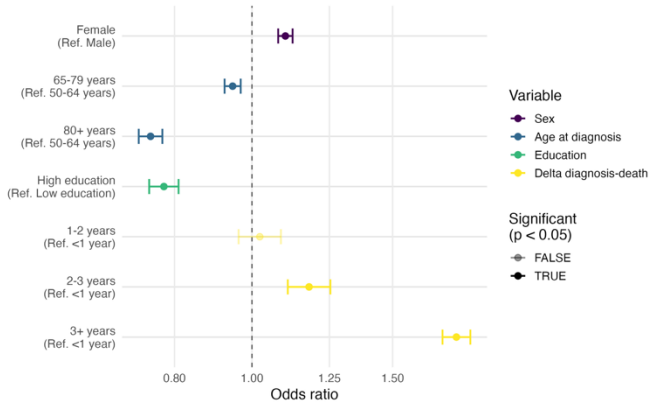
Table 1. Frequency of reporting and placement on the death certificate of the diagnosed disease (COPD). Denmark, 2010-2019

Population with COPD		
Disease reported on death certificate	**n**	**%**
No	15739	64,9
Yes	**8496**	**35,1**

Placement on death certificate	**n**	**%**
1.a	645	7,6
1.b	1347	15,9
1.c	518	6,1
1.d	1488	17,5
2.1	2929	34,5
2.2	1075	12,7
2.3	356	4,2
2.4	133	1,6

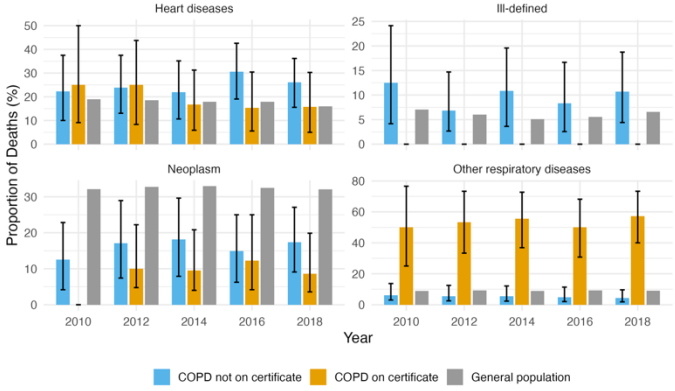
(2) We then assess the odds ratio of having the disease reported on the death certificate for the subpopulation with diagnosed COPD (Figure 1). Women have higher odds of having COPD reported on their death certificate. Older age at diagnosis and higher educational attainment are associated with lower odds of COPD reporting. Finally, the longer the time since diagnosis, the higher the odds of having the disease reported on the death certificate.

Figure 1. Odds ratios (OR) for COPD being reported on the death certificate. Denmark, 2010-2019



(3) In Figure 2, we present the proportion of deaths among men with COPD by four leading causes of death and year, resulting from the multiple decrement life tables computed for the subpopulations with COPD reported (in orange) and not reported (in blue) on the death certificate. Women's results are not presented but are in line with those observed for men. The main difference between the two subpopulations arises when looking at deaths from other respiratory diseases, which exceed 50% for those with the disease reported on the death certificate and are less than 5% for their counterpart. On the other hand, for the

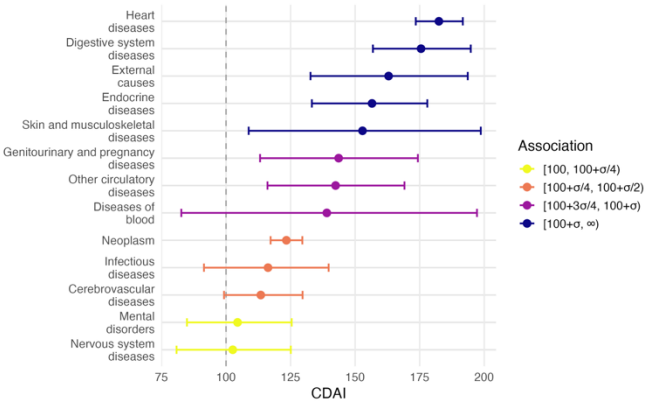
Figure 2. Cause-specific mortality by COPD reporting status on death certificate. Denmark, men, 2010-2019



COPD not on certificate subpopulation, the proportion of ill-defined deaths is significantly higher than for their counterpart. Heart diseases and neoplasms are in both cases the other leading causes of death, with the latter being much less prevalent than in the overall Danish population (shown in grey).

(4) In Figure 3, we present the CDAI indicator to assess the association between underlying causes of death being reported while COPD is also reported on the death certificate. Values above 100 represent association, with higher values representing stronger associations. The confidence intervals capture the uncertainty of the estimates, given the size of some groups, where combinations of diseases on the death certificate are less frequent than others. Heart and digestive system diseases together with external causes are the top three causes of death associated with COPD.

Figure 3. CDAI values for cause of death associations with COPD. Denmark, 2010-2019



Preliminary conclusion and next steps

We have obtained results for all diseases under study and are currently synthetising findings across conditions. Our findings indicate that while MCoD data cannot reliably represent the true burden of multimorbidity at death, however, they do provide valuable insights into the perceived causal pathways and disease interactions in the dying process. Our next steps include: (a) visualizing all results to compare reporting patterns and disease associations across all diseases and over time; (b) assess whether to extend the analysis to the COVID-19 pandemic period. This will depend on whether pre-pandemic trends remain stable. If substantial changes are observed, we will address pandemic effects in a separate paper.

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