

Multi-morbidity at death: what are the most common causes?

Mortality statistics based on the underlying cause of the death (UC) – i.e., the cause that initiated the sequence of events leading to death - have proven to be very powerful for understanding life expectancy trends as well as differences within and between countries. As such, they have been widely used by demographers. At the same time, however, criticism has been raised against selecting one single cause of death from all the information reported on the death certificates, which can include up to 20 different medical causes of death and which, together, are labeled multiple causes (MC). In a 1993 technical report, the US International Institute for Vital Registration and Statistics noted that mortality statistics on causes of death *‘have served well in delineating the major public health problems over the years, and also played an important role in the conduct of epidemiological studies. Yet much can be done to make cause of death statistics more useful, particularly multiple cause of death data’* (IIVRS 1993). As early as 1940, Theodore Janssen, then Chief of the Nosology Section in the Division of Vital Statistics at the US Bureau of the Census, wrote: *‘statistics showing combinations of causes come nearer the truth than do those based on the single cause principle because the majority of deaths actually result from a combination of causes’* (Janssen 1940). Following Janssen, Nam (1986) and Crews (1990) defended the idea that the underlying-cause approach oversimplifies changes in the epidemiological profile and that multiple causes of death are better at capturing the complexity of processes that lead to death in aging societies. In recent decades, a growing number of countries have begun to produce multiple cause-of-death (MCO) data by following the World Health Organization (WHO) coding rules.

Demographers interested in cause-of-death analysis progressively use this material. Because increased life expectancy is due, to a large extent, to better survival from cardiovascular diseases, cancers, and other chronic conditions, an ever-growing share of the population is living with several diseases – a situation referred to as multi-morbidity. From a public health perspective, multi-morbid patients represent a major challenge for caregivers, as interactions between diseases may aggravate the patient’s situation and make clinical care more complex while polypharmacy increases the risk of adverse drug events and non-adherence to treatments. Epidemiologic studies have demonstrated that these patients are at higher risk of dying as showed for instance during the recent COVID-19 pandemic has illustrated (Salive 2013).

Objectives

Because multi-morbidity is an important determinant of mortality, it is important to monitor its contribution to processes leading to death. An algorithm that uses the entire set of causes listed on the death certificates has been developed to classify all death records in a given population according to three main types of morbid process leading to death (simple, multi-morbid and ill-defined) (Grippe et al. 2024). Using the output of this algorithm, Barbieri et al. (2025) assessed the impact of multi-morbidity at death on the mortality gap between the US and three other high-income countries with comparable data, namely France, Italy, and Spain. The results show disproportionately high rates of multi-morbid processes in the US compared with the other three countries. Building on this previous work, we aim at identifying the causes of death (whether underlying or contributing) involved in multi-morbid processes in the hope of uncovering consistent patterns across the four study countries.

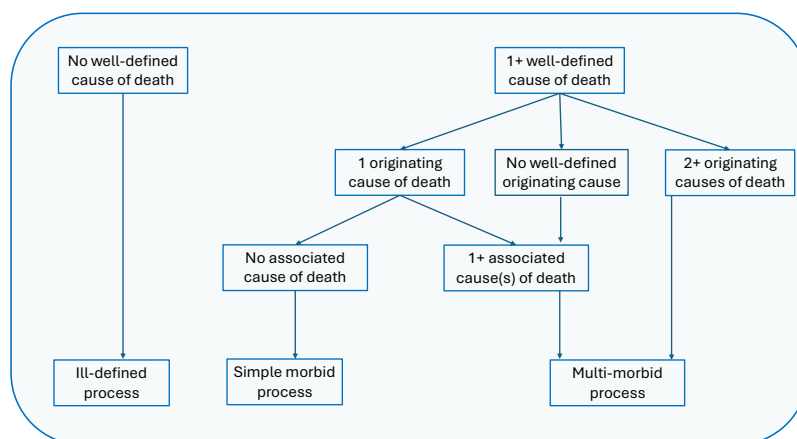
Data and method

We used multiple cause of death information for all deaths at ages 65 and over (when multi-morbidity becomes particularly prevalent) in mainland France, Italy, Spain and the US. The countries have been chosen based on their low levels of mortality, the availability and accessibility of the complete multiple cause-of-death data, the comparability of their data collection and processing systems, similarly aging populations, and high-quality health care systems. The study relies on the processing of multiple cause-of-death information coded to the 10th Revision of the International Classification of Diseases (ICD-10) available in the national vital statistics systems of each of the four countries: the National Center for Health Statistics (NCHS) at the Centers for Disease Control (CDC) in the US, the National Institute for Health and Medical Research (INSERM) in France, the National Institute of Statistics (ISTAT) in Italy, and the National Institute of Statistics (INE) in Spain. All four countries implement automatic coding of the death certificates using similar software. We focused on year 2017 for which data were available in all four countries at the time of this analysis.

The four countries follow the guidelines of the World Health Organization (WHO, 2016) and use the standard death certificate on which reporting physicians, medical examiners, or coroners list all the causes which have directly or indirectly contributed to death. Causes of death are listed on two different sections of the standard certificate form. Part I records the sequence of diseases or conditions which have ended in death, i.e., all medical causes involved in "the sequence of morbid conditions, lesions or poisoning that led directly to death" (WHO, 2015). This section theoretically includes the "underlying cause of death", that is the disease or injury that initiated the chain of events leading to death. Part 2 records all other causes which were not directly responsible for the sequence listed in Part 1 but which nonetheless "contributed significantly to death" (ibid.) by influencing the course of the morbid process, often designated as the associated causes.

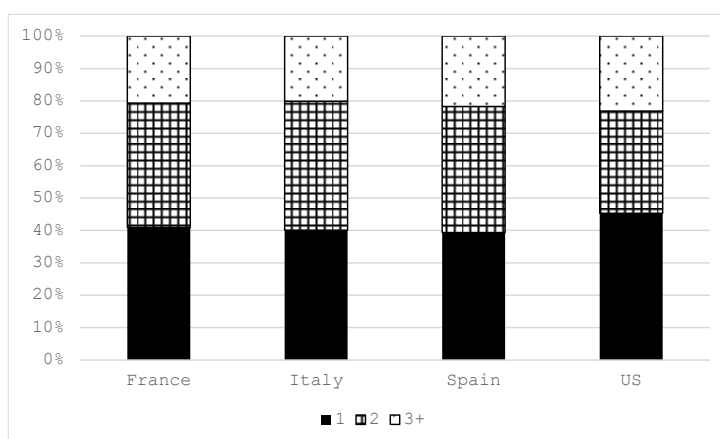
Following the approach developed by Grippo et al. (2024), we classified all death records into one of three types of morbid processes, namely simple causal processes, multi-morbid processes, and ill-defined processes. The algorithm uses the location of the cause on the certificate (Part I or Part II of the death certificate, line number and position on each line) and inter-relation between each pair of causes. In brief, first, the algorithm identifies '*ill-defined*' codes. Second, it uses the decision tables embedded in the IRIS system, a software implemented worldwide to automate coding of all causes of death reported on death certificates into ICD-10 and to identify the underlying cause of death (www.iris-institute.org) to identify one or more '*originating*' causes for any given sequence(s). Originating causes are supposed to be reported alone on the lowest line of Part I, but sometimes they are mistakenly reported elsewhere (e.g. on Part II). All other causes listed Finally, the algorithm classifies the remaining causes in Part I are labeled '*precipitating*' and all (non originating) causes in Part II are labeled '*associated*'. Simple processes characterize deaths with a single originating cause (either a single cause listed on the certificate or a sequence of causes deriving from the same originating condition). Multi-morbid processes characterize deaths with at least two originating causes (where neither one can be the consequence of the other) or with one originating cause and at least one contributing cause in Part II. Ill-defined processes characterize deaths with no well-defined causes listed on the death certificate.

Figure 1. Classifying deaths according to the morbid process



In this research, associated causes and originating causes others than the UC are designated as the contributing causes (CC). On average, 40% of multimorbid deaths include only one CC, 40% include 2 CCs and 20% 3 or more. The average is at 1.9 contributing causes in all four countries.

**Figure 2: Number of contributing causes per death certificate by country
Multimorbid processes in France, Italy, Spain and the US at 65+ in 2017**



Preliminary results

From the tabulation of deaths by underlying cause and morbid process in each country, we examined the distribution of the underlying causes of multimorbid processes (figure 3). They cover the whole range of ICD-10 chapters and the difference with simple processes is not large. They clearly are less frequent for neoplasms, and in compensation more frequent for several causes, in particular for endocrine and metabolic diseases and for diseases of the circulatory system.

Regarding the contributing causes most frequently involved in multimorbid processes (figure 4), diseases of the circulatory system are predominant (around 40% of the multimorbid deaths in France, Spain and the US, 51% in Italy). At a lower level of aggregation of the causes, we find that almost all subgroups of the cardiovascular diseases (including hypertension) are present. The second largest group is generally endocrine and metabolic diseases: around one out of five multimorbid processes include a disease in that group (mainly diabetes) reported as contributing cause. The next most frequent groups are Diseases of the respiratory system and Mental and

behavioral disorders. Dementia is frequently reported on those certificates. The higher prevalence of this group of contributing causes in the US corresponds to a more frequent reporting of “Mental and behavioural disorders due to use of tobacco” (ICD10 code F17.2).

These preliminary results will be discussed and completed by a table of the prevalence of every contributing cause according to the underlying cause in each of the four study countries. We will also examine the specificity of these combinations of causes computing the cause-of-death association indicator (CDAI) (Désequeles et al. 2010).

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Figure 3: Underlying cause (ICD-10 chapters) by type of process and by country – Multimorbid and simple processes in France, Italy, Spain and the US at 65+ in 2017

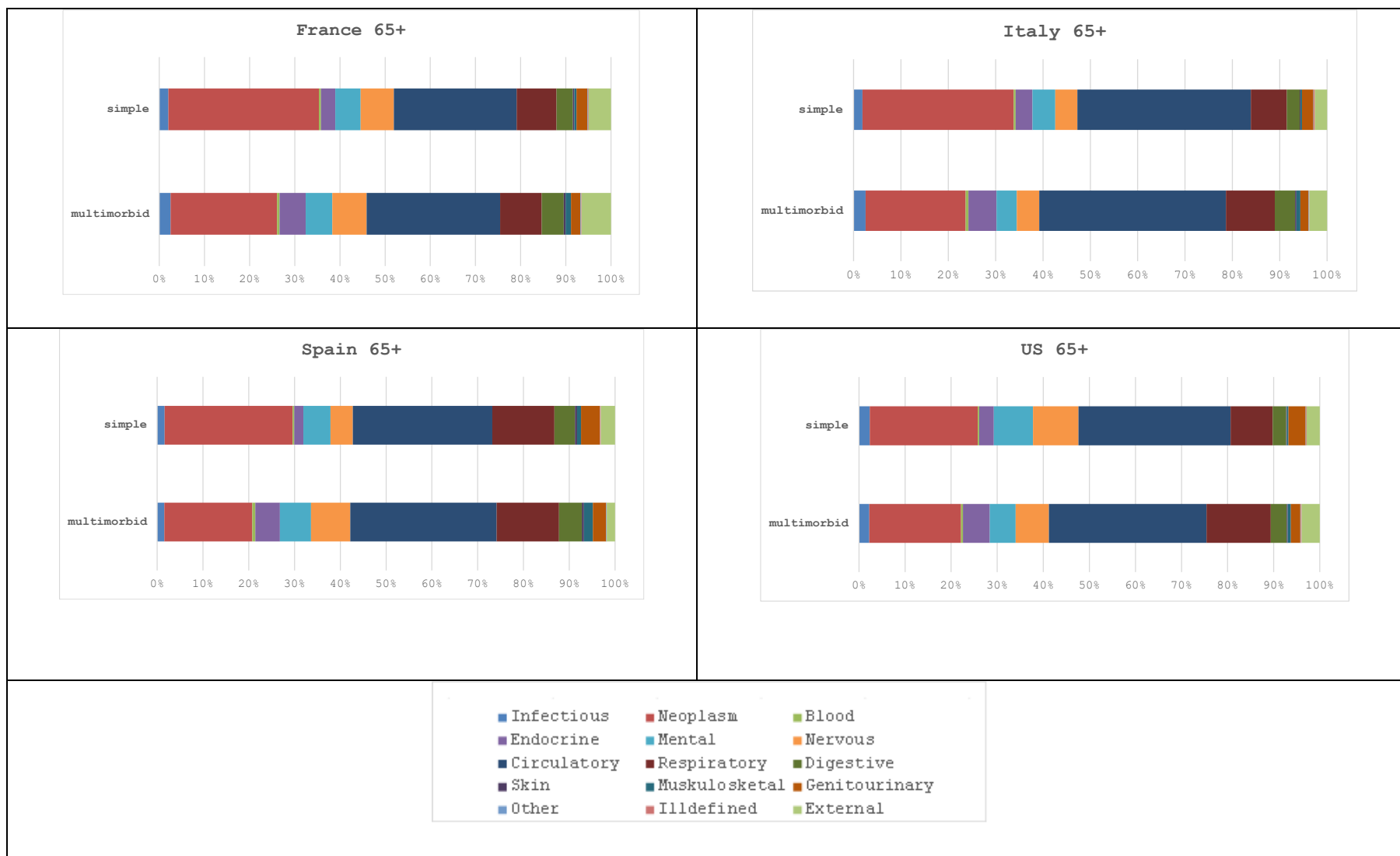


Figure 4: Contributing causes (ICD-10 chapters) by country - Multimorbid processes in France, Italy, Spain and the US at 65+ in 2017

