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causes?**

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We only die once... but from how many causes?

Aline Désesquelles,* Andrea Gamboni,** Elena Demuru** and the MultiCause network♦

When a person dies, the certifying physician records the cause of death on the death certificate. In many cases, several causes are mentioned, as well as the train of events that led to death. Aline Désesquelles and her colleagues explain why this type of information is useful for studying trends in causes of death in a country, and why international comparisons are difficult, notably because of cross-national differences in the ways medical certificates are completed.

Life expectancy in France has increased considerably over recent decades, thanks mainly to a decline in mortality from circulatory diseases and cancers, the two leading causes of death. We know this because statistics on all causes of death are compiled by the CépiDc (Centre d'épidémiologie sur les causes médicales de décès), the French body responsible for producing cause-of-death data from the certificates filled in by physicians when they certify a death (Box 1). Analysing causes of death sheds light on mortality

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Box 1. Determining the cause of death

Renseignements confidentiels et anonymes

Code Postal : Commune de décès : Date de décès : 1. Sexe masculin
Code Postal : Commune de domicile : Date de naissance : 2. Sexe féminin

Causes du décès

PARTIE I Maladie(s) ou affection(s) morbide(s) ayant directement provoqué le décès *
La dernière ligne remplie doit correspondre à la cause initiale.

a) *Septicémie*
due à ou consécutive à : b) *Aplasie*
due à ou consécutive à : c) *Leucémie*
due à ou consécutive à : d) _____

* Il s'agit de la maladie, du traumatisme, de la complication ayant entraîné la mort (et non du mode de décès, ex. : syncope, arrêt cardiaque...)

PARTIE II Autres états morbides, facteurs ou états physiologiques (grossesse...) ayant contribué au décès, mais non mentionnés en Partie I

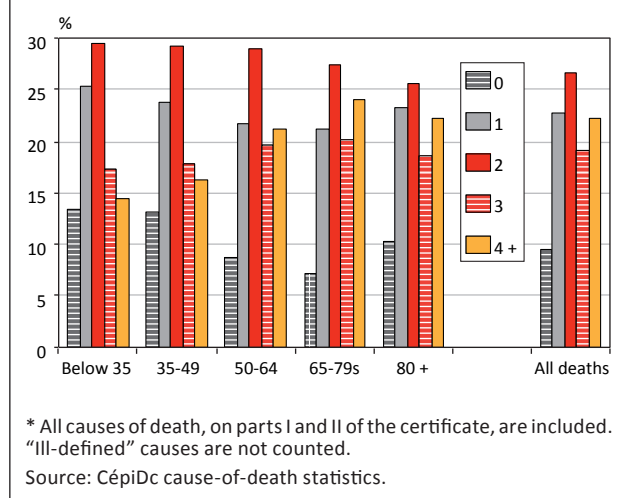
Diabète sucré Hypertension

Informations complémentaires

The medical certificate of death used in France complies with the recommendations of the World Health Organization (WHO). It is in two parts. In part I, the physician describes the train of events that led directly to the death. This first part has four lines, although physicians sometimes mention several causes on a single line. In part II, the physician is asked to indicate any other “morbidity, physiological factor or condition contributing to death but not involved in the process described in part I”. In 2011, three-quarters of the causes mentioned on death certificates were given in part I, but for 30% of deaths, at least one other cause was listed in part II.

The information recorded by the physician is coded by the CépiDc which, again in compliance with WHO recommendations, determines the underlying cause, i.e. the disease or injury that initiated the train of events leading directly to death. In the majority of cases, and if the certificate is filled in correctly, this is the last cause listed in part I. All the other causes mentioned on the certificate, in both part I and part II, are called “contributing causes”.

Figure 1. Number of causes of death mentioned* on death certificates by age group, France, 2011



trends, which may change rapidly or evolve slowly over time. It provides pointers for focusing public health policies on particular targets in order to further reduce mortality or to warn about potential health threats. All causes mentioned on death certificates are recorded and coded by CépiDc, but analyses generally look at just one, the so-called "underlying" cause of death (Box 1). Yet death certificates often mention several causes. Is it useful to take these other causes into account?

From no defined cause... to more than 15 causes!

In France, if ill-defined causes are excluded (Box 2), 2.4 causes of death, on average, are mentioned on the death certificates of persons who died in 2011. For one in ten deaths, the cause is unknown or ill-defined. The proportion is higher for persons who died before age 50, when deaths are more often due to "external causes" (accident, suicide, homicide, etc.). In such cases, if the death is investigated by a coroner, CépiDC does not always receive the death certificate. Almost one-quarter of death certificates in 2011 mentioned just one cause, and a similar proportion mentioned at least four. The record was 20 causes on a single certificate.

The number of causes mentioned increases with age, up to age 80 at least (Figure 1). At ages 65-79, 24% of certificates listed at least four causes, compared with 14% at ages below 35. This rise reflects the increasingly complex disease profiles of the oldest adults, who are often affected by several different illnesses simultaneously. Beyond age 80, the mean number of listed causes drops slightly (2.4 versus 2.6 at ages 65-79) and a much higher proportion of deaths have no recorded cause. For older adults who "die of old age", physicians perhaps find it less useful to give a precise description of the train of events that led to death.

Box 2. Defined and ill-defined causes

The International Classification of Diseases (ICD) of the World Health Organization [1] lists and classifies all diseases, injuries and other health problems. It is used, among other things, to code the causes of death. The latest version of the ICD (10th revision) comprises 21 chapters concerning "special groups" of diseases (infectious diseases, neoplasms, etc.) or the various "body systems" (circulatory system, respiratory system, etc.). In our study, ill-defined causes are those listed in the chapter "Symptoms, signs and abnormal clinical and laboratory findings", as well as certain ill-defined morbid states, such as cardiac arrest, that are classified elsewhere.

Contributing causes are important for medicine and public health policies

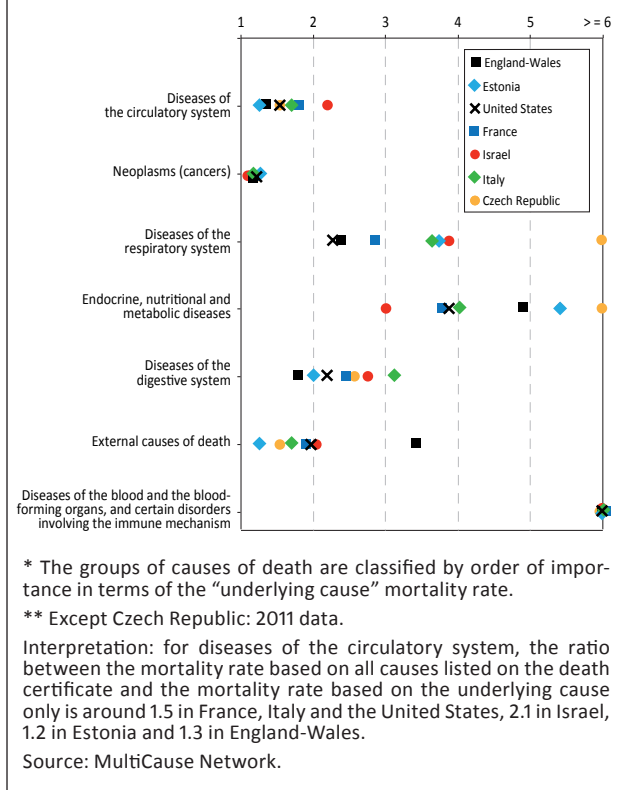
Causes other than the underlying cause are called "contributing causes". They contribute to death in three ways.[2] Most often, they are consequences or complications of the underlying cause or its treatment and, if so, they are mentioned in part I of the death certificate. For example, a haemorrhage due to a gastric ulcer, or septicaemia in a cancer patient whose immune system has been weakened by chemotherapy would come under this category. Contributing causes may also be risk factors for the underlying cause, such as chronic viral hepatitis for liver cancer, for example. Last, they may also interact with the underlying cause by increasing its severity, further weakening the patient or making treatment more complex or less effective. Chronic diseases such as diabetes or hypertension are often involved in this way in the train of events leading to death. Whatever the means by which they contribute to death, there is no doubt that progress in the prevention and treatment of contributing causes will have a positive impact on life expectancy. For this reason, they deserve to be considered more fully in statistical and epidemiological studies.

These causes are underestimated in statistics on underlying causes of death

For seven countries of the MultiCause network (Box 3), Figure 2 shows the ratio between the standardized mortality rates (I) calculated on the basis of all causes mentioned on the death certificates (also called "multiple causes") and the rates based solely on the underlying cause. The calculations concern deaths of persons aged 65 and above. Seven chapters of the International Classification of Diseases (ICD) (Box 2) were selected to illustrate the range of situations encountered. The ratio varies substantially by cause of death and country. The

(1) To ensure comparability, the rates of the different countries are calculated for an identical population age structure.

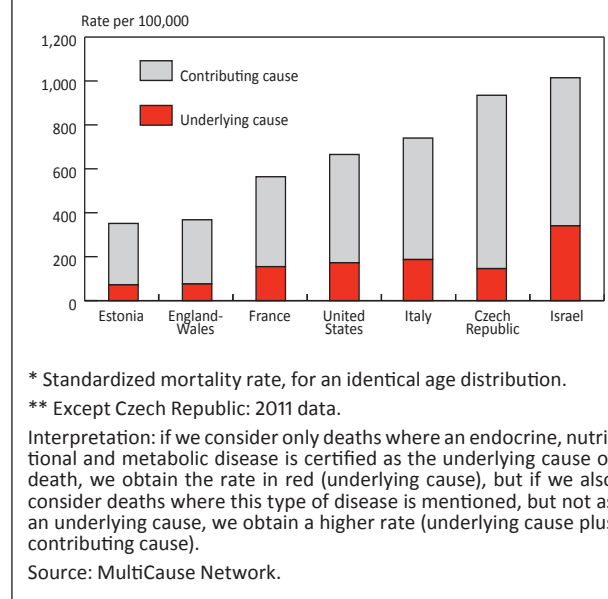
Figure 2. Ratio between “multiple causes” and “underlying cause” mortality rates for 7 groups of causes* and 7 countries, deaths at age 65+, 2009**



higher the ratio, the greater the extent to which the role of the disease or condition in mortality is underestimated if only the underlying cause is considered.

Diseases of the circulatory system and neoplasms (cancers), the two leading underlying causes of death in these seven countries, are largely unaffected when contributing causes are taken into account: when they are recorded on the death certificate, in more than half of cases – and in practically all cases for neoplasms – they are the underlying cause of death. With the exception of England-Wales, this is also the case for external causes of death. By contrast, for diseases of the blood, whose position in the hierarchy of underlying causes of death is very low, the ratio between the “multiple causes” and “underlying cause” mortality rates is often high. While often recorded on death certificates, blood diseases are rarely given as the underlying cause of death. Between these extremes, we find a set of diseases for which the ratio is almost always above 2, but with substantial variability across countries. This is the case for respiratory diseases, for example, which generally rank third or fourth in the list of underlying causes of death, and for which the ratio ranges from 2.2 in the United States to 6.6 in the Czech Republic. This variation probably reflects differences between countries in the way in which pneumonia is certified and coded.[3]

Figure 3. Mortality rate* from endocrine, nutritional and metabolic diseases, deaths at age 65+, 2009**



The example of endocrine, nutritional and metabolic diseases

The contribution of endocrine, nutritional and metabolic diseases to mortality is also severely under-estimated when only their role as the underlying cause is taken into account. Diabetes and obesity, which are included in this group of diseases, often complicate the treatment of patients who are also affected by other diseases. While the standardized “underlying cause” mortality rate is similar in France, Italy, the United States and the Czech Republic, it is half as high in England-Wales and Estonia, and twice as high in Israel (Figure 3). When contributing causes are taken into account, the country rankings are very different. The increase is so spectacular for the Czech Republic that it almost catches up with Israel at the top of the list. Italy, the United States and France, in that order, stand out more clearly. Last, despite a high ratio between the “multiple causes” and “underlying cause” mortality rates, England-Wales and Estonia still have much lower levels than the other countries. Beyond probable differences in the prevalence of these diseases, the ways in which they contribute to death seem to vary across countries, more often as contributing causes in Estonia and the Czech Republic, and as underlying cause in Israel. Differences between countries in the way in which multiple causes are certified and coded, and in the choice of underlying cause may also partly explain these divergences. [4] In Israel, for example, on death certificates where both diabetes and a cardiovascular disease are listed, diabetes is given as the underlying cause more frequently than elsewhere.

Box 3. The MultiCause network

MultiCause is an international research network set up to analyse all causes recorded on death certificates. As well as re-evaluating mortality levels, it is also interested in describing associations between causes. Founded in 2012, MultiCause now brings together researchers from around 20 countries. The indicators used for this study were calculated by network members on the basis of national death statistics produced by the following bodies:

- England - Wales: Office for National Statistics (ONS) Longitudinal Study (0300770). Data from ONS are Crown Copyright. The use of the ONS statistical data in this work does not imply the endorsement of the ONS in relation to the interpretation or analysis of the statistical data
 - United States: National Center for Health Statistics (NCHS)
 - France : CépiDc, National Institute for Health and Medical Research (INSERM)
 - Israel : Ministry of Health
 - Italy : Italian National Institute of Statistics (ISTAT)
 - Czech Republic: Institute for Health Information and Statistics (IHIS)
- All these countries have adopted a medical certificate of death that complies with WHO recommendations and use the 10th revision of the ICD to code causes of death.

Towards greater harmonization in the recording of causes

What did this person die of? While the habit of giving a single cause of death is deeply rooted, the reality is often more complex. The WHO instructions for completing the death certificate are supposed to help the certifying physicians to manage this complexity. Yet countries often still use certificates that deviate slightly from the WHO recommendations. For example, the amount of space and number of lines provided in each part to describe the train of events leading to death may differ. While people in the Czech Republic, in Israel and Italy probably do not die of more causes than in France, the mean number of causes listed on death certificates in these countries is above 3. Moreover, the WHO certificate gives a certain latitude regarding the degree of precision of the description which, of course, also depends on the amount of information available to the physician. So the international research community must pursue its efforts

to standardize and harmonize the recording of causes of death on the death certificate and during the coding stage. Looking at the “multiple” causes of death is useful for determining the one “underlying” cause. This multiple-causes approach is especially important in a context of population ageing, where deaths from a single cause will become increasingly infrequent.

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Abstract

Analysing causes of death provides a better understanding of long-term mortality trends. In France, the death certificates completed by physicians generally mention several causes of death (2.4 on average in 2011). As a general rule, just one of them, the so-called underlying cause, is taken into account. As a result, the contribution of certain diseases – endocrine diseases for example – to mortality is severely underestimated. In a context of rising life expectancy where people increasingly die not from a single cause of death but from several, it is important to also take these contributing causes into account.