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Improving the identification of multiple causes of death in the absence of death certificates

How to use probabilistic cause-of-death estimation methods in low- and middle-income countries to improve prevention

Health developments represent a challenge for healthcare systems and public policy alike. High-income countries developed the multiple-causes-of-death approach, which takes into account all the causes entered on the death certificate, as a way to capture the high prevalence of multimorbidity in adult mortality. This approach has shown that health statistics based on the main cause of death underestimate the contribution of infectious diseases to the mortality of the elderly. What is the situation then in low- and middle-income countries without death certificates? A study[1] conducted by the French National Institute for Demographic Studies (INED), with AFD funding, sets out to answer this question.

In low- and middle-income countries, population ageing is behind a change in causes of death and an increase in multimorbidity to which public health policies need to respond ((Barjenee *et al.*, 2020). The fact that health data are still often patchy, if not non-existent, means that the challenge of identification and analysis methods is key. Drawing on a database of probable causes of adult death among some 20 populations surveyed in Sub-Saharan Africa and Asia, we present here a new approach to identify the multiple causes of death.

Demographic transition and increase in age at death

A great deal of health progress has been made in the low- and middle-income countries since the 1950s. Life expectancy, of less than 50 years at that time, stands today at more than 70 in Latin America, Asia and North Africa. In Sub-Saharan Africa where it is the lowest, life expectancy now stands at 60. This progress has benefited first and foremost young children due to the rollback of what are known as diseases "of poverty" (infectious and parasitic diseases, malnutrition and maternal mortality). In addition, it has come in tandem with a drop in the fertility rate, which has altered the age structure by reducing the proportion of children in the population. The share of adult deaths in the total number of deaths has logically grown over time.

[1] SESSEGO A. (2021), "Studying multiple causes of death in LMICs in the absence of death certificates: taking advantage of probabilistic cause-of-death estimation methods (InterVA-4)", Document de Travail 268. Aubervilliers: INED.

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Multimorbidity: A public health challenge for ageing populations

The share of non-communicable diseases (cardiovascular diseases, cancers, respiratory diseases, diabetes, etc.) occurring mainly in adulthood has risen. Whereas respiratory infections and tuberculosis were the leading cause of death across all ages in the 1990s, cardiovascular diseases are reported to have become predominant in Sub-Saharan Africa and South Asia (IHME, 2019). Most of these diseases are chronic and susceptible to comorbidities, especially with age. These multimorbidities complicate patient care and now form a key element of healthcare policies in high-income countries where life expectancy is over 80. Yet in low- and middle-income countries today, this adjustment represents a challenge to healthcare structures unaccustomed to treating certain non-communicable diseases (such as cancer) or chronic diseases (such as diabetes, Martini and Figgs, 2010).

Various approaches have been developed to study these multimorbidities, including the approach that consists of analysing all the causes of death entered on the death certificate rather than just the main cause of death given (Désesquelles *et al.*, 2016).

When health statistics fall short: the verbal autopsy method

In poor countries, civil registration and vital statistics systems, where they exist and work, only rarely collect causes of death (see Map 1). A real "scandal of invisibility" (Setel *et al.*, 2007), this lack of health statistics prevents any detailed measurement of the weight of the different burdens of disease at work in mortality.

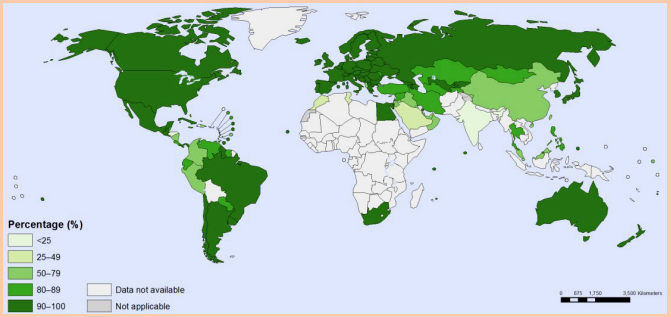
At local level, however, health and demographic surveillance systems (HDSS) can supply such statistics from multi-round surveys of a geographically delimited population (from 10,000 to 200,000 individuals for the largest sites). When a death occurs in the population, information is collected from final caregivers about the signs and symptoms leading up to death. These "verbal autopsies" are traditionally interpreted by doctors to determine, as far as possible, a cause of death, but they are now increasingly interpreted by algorithms that automatically determine the causes of death.

Today, the most frequently used algorithm is called InterVA: promoted by the INDEPTH HDSS network[2] to harmonise the method, it is used by the majority of these health and demographic surveillance systems. InterVA is based on the probabilities, estimated by a panel of experts, of presenting a particular symptom given a particular cause of death (Byass *et al.*, 2012). Taking the symptoms declared by final caregivers in a standardised questionnaire[3] , InterVA estimates a probability associated with each cause. If the most probable cause presents a probability of less than 40%, then the cause of death is considered to be unknown. Otherwise, the algorithm selects the cause with the highest probability and up to two additional causes. These elements are used to determine, where information is available, one to three probable causes of each death.

[2] A network of nearly 50 health and demographic surveillance systems in 19 countries across Africa, Asia and the Pacific region covering a total of 3.8 million individuals (http://www.indepth-network.org).

[3] Proposed by the WHO: https://www.who.int/healthinfo/statistics/verbalautopsystandards/en/

Map 1 — Civil registration coverage of causes of death by country, 2007-2016 period



Source: World Health Organization, 2018.

Using cause-of-death estimation methods to identify multiple causes of death

These probabilistic methods were developed to study mortality by cause at aggregate population level (the weight of a cause in general mortality is estimated by the sum of its probabilities), but the question is whether they can also be used to estimate multiple causes of death. We propose using them here in a new and original way to identify multiple pathologies that have led to death at individual level. In a context of imperfect and incomplete data, if a number of causes are attributed to a death, it does not necessarily mean that they are multiple causes. This multiplicity of reported factors might result more from uncertain diagnosis, especially when these causes have similar symptomology (as in the case of pneumonia and malaria, for example). To exclude this uncertainty, we formulate the hypothesis that the causes with sufficiently different symptomology may be considered as multiple causes, unlike causes with similar symptoms. Taking this principle, we have developed an indicator of similarity between two causes of death.

Studying multiple causes in African and Asian countries

We applied this approach to data on 72,330 adult deaths from around 20 health and demographic surveillance systems located in Sub-Saharan Africa and Asia (Box 1). Of this total, 7,734 deaths (nearly 11%) were attributed more than one probable cause by the InterVA algorithm.[4]

Observing the distribution of the similarity index for these deaths, rounded out by the medical literature on the risk of confusion between different causes (such as malaria and pneumonia), we fixed a threshold for the selection of deaths with sufficiently different causes, based on their symptomatology, to consider them as co-occurring. We found that 1,591 deaths presented probable multiple causes (Figure 1), accounting for 2.2% of adult deaths.

This is a very low proportion compared with the information available on death certificates in Northern countries (Désesquelles *et al.*, 2016). Yet this observation comes as no surprise in that the data collected here are much more incomplete and that the identification of multiple causes of death was not central to the design of the tool used to diagnose the causes of death. Yet the fact remains that these identified multiple causes shine new light on mortality by cause in Southern countries.

[4] Just 0.5% of deaths (345 deaths) were attributed three causes of death. To simplify the analysis, we have not taken these third causes into account.

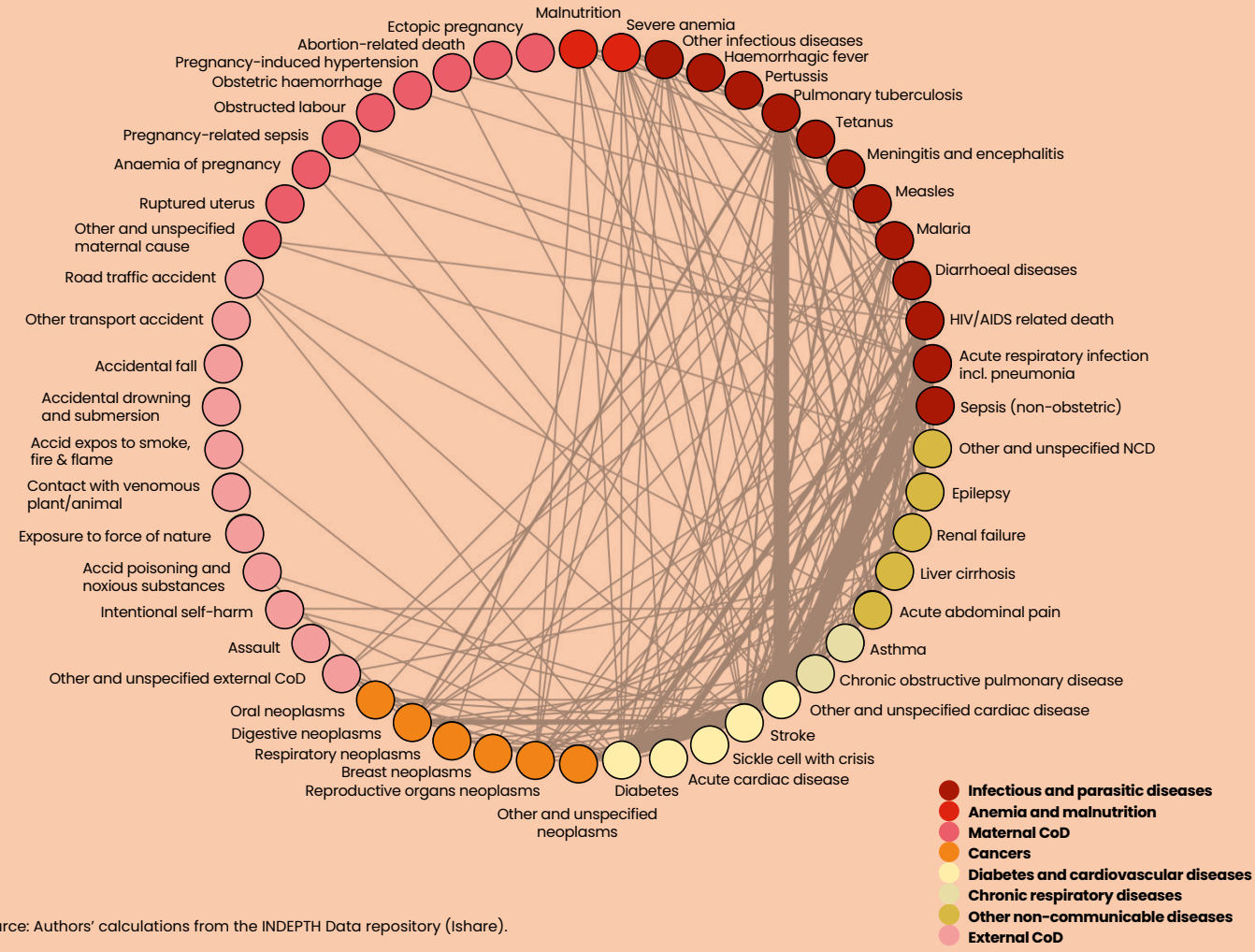
Box 1 – Data used: over 70,000 adult deaths in Sub-Saharan Africa and Asia

The INDEPTH network makes available a database of deaths by cause collected from 22 Health and Demographic Surveillance System sites in nine Sub-Saharan African countries and four Asian countries. These data provide the age bracket, gender, site and cause(s) of death as well as their probability estimated by the InterVA-4 software. Virtually all of the deaths occurred in rural areas over the 2003-2012 period.
On this basis, we selected all the 72,330 deaths occurring aged 15 and over. At aggregate level, diseases of poverty, non-communicable diseases, and injuries and violent deaths represent respectively 42%, 39% and 6% of the causes of death. However, the sum of the probabilities totals just 87% and 13% of mortality is indeterminate.

Among the multiple causes identified, diabetes and cardiovascular diseases represent a large weight of multimorbidity (nearly 70%), due in part to the association of these chronic diseases with acute infectious diseases and the high level of associations of diabetes and cardiovascular diseases with other non-communicable diseases. At the more detailed level of causes of death, the most frequent multimorbidity is found to be the association of diabetes and stroke (9.3%), a well-known multimorbidity where the former is a risk factor for the latter.

Among the most common associations, acute diseases co-occur with chronic diseases, top of the list of which are acute pulmonary infections and pulmonary tuberculosis in addition to non-acute cardiac diseases (17% of associations). Chronic diseases, whether infectious or not, are hence frequently associated with acute opportunistic diseases. Chronic bronchitis represents, in association with an acute respiratory infection, 4% of the probable associated causes, which is one of the most common associations of cause.

Figure 1 — Associations among the multiple causes identified



Source: Authors' calculations from the INDEPTH Data repository (Ishare).

Interpretation — Each circle represents a cause of death in the InterVA classification. Each line represents associations of two causes of death: the thicker the line, the more frequent the association. The most frequent associations are: diabetes and stroke (9.3% of deaths from multiple causes), pneumonia and other cardiac diseases (9%), tuberculosis and other cardiac diseases (8%), chronic bronchitis and acute respiratory infection (4%).

Coverage: 1,591 deaths presenting multiple causes among the 72,330 deaths aged 15 years and over occurring from 1992 to 2012 in 22 INDEPTH network Health and Demographic Surveillance Systems.

A total of 66% of these multiple causes involve an association between a disease of poverty – primarily infectious and parasitic diseases – and a non-communicable disease. Infectious diseases can cause particularly fast deterioration of an individual's state of health in that it is weakened by a non-communicable disease. Yet these two groups of diseases are often addressed separately by public health systems.

Conclusion

The proposed multiple-causes-of-death approach to understanding multimorbidity has its limitations. The estimated proportion of deaths from multiple causes is low compared with similar studies conducted in Northern countries. However, this observation calls for some qualification for three reasons:

1. The information collected remains imperfect and incomplete, since death was not certified by a doctor since it is not possible to rely on a death certificate.
2. The tool at our disposal is very different, with information collected from the deceased's final caregivers, while the INterVA algorithm was not designed to identify multiple causes especially since, for certain causes, the symptoms taken into account include the occurrence of other diseases. This is especially the case with AIDS and associated opportunistic diseases (such as tuberculosis in particular);
3. Our approach is extremely cautious since we exclude, by definition, all causes with similar symptomatology to prevent any risk of confusion. Yet some of these causes probably co-occur without our being able to single them out at this point.

However, this approach does show that the weight of diabetes and circulatory diseases would probably be much greater if all the causes associated with a death were to be taken into account. It also reveals the complexity of the occurrences of certain deaths: associations between diseases of poverty and non-communicable diseases – two groups generally addressed separately. Yet non-communicable diseases represent a high risk factor for opportunistic infectious diseases. A good illustration of this is the recent example of the Covid-19 pandemic, whereby the risk of complications increases with multiple non-communicable diseases (high blood pressure, diabetes, chronic respiratory diseases, etc.).

Likewise, infectious diseases are risk factors for non-communicable diseases. Such is the case, for example, with sexually transmitted diseases, which are susceptible to cervical cancer. In the same way, our approach provides insights into the associations between acute diseases and chronic diseases.

Although children's health must definitely remain a public health priority, the vast majority of deaths now occur in adulthood. Today, for example, over 8 in 10 deaths in low- and middle-income countries occur at the age of 15 and over. Public health policies need to take on board this new fact and put in place prevention and treatment measures geared to the more complex needs of adults. Adults suffer from chronic diseases (diabetes, high blood pressure, cancers, HIV, chronic obstructive pulmonary disease, etc.), which call for routine monitoring and expensive treatments. They also require equipment and special training for health workers, which poor countries' health systems find hard to meet (Martini and Figg, 2010). Considering the dual human and health cost, prevention should be the first pillar of action to reduce adult mortality and the study of multiple causes could help to better identify the risk factors associated with the main causes of death.

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