After the epidemiological transition: an evaluation of the mortality due to infectious and parasitic diseases in France and Italy using the multiple cause-of-death approach

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According to the theory of the epidemiological transition (Omran 1971), the second phase of the transition (“the age of receding pandemics”) is characterized by a reduction in the mortality related to infectious diseases that are progressively replaced by chronic diseases as primary cause of death. France and Italy, the two countries we are interested in, moved from the second to the third phase of the transition around the middle of the last century. In France (see figure below), the long-term trend toward a decline in mortality rates due to infectious and parasitic diseases have been interrupted only during World War II as well as, in the first midst of the 90s, because of the AIDS epidemics. The slight increase observed in 2000 at ages over 65 is likely to be due to the adoption of the 10th International Classification of Diseases (ICD). It is worth nothing that while mortality rates for infectious and parasitic diseases under the age of 65 are now close to zero (4 p.100,000 in 2007), rates at ages over 65 are not negligible (56 p.100,000). In a 1982 paper, Manton and Stallard suggested that the population aging might result in a fresh upsurge in infectious diseases since degenerative diseases “often progress to a point where the vitality of the organism as a whole is impaired, at which time the organism is susceptible to a lethal infectious complication – usually of the lungs or the blood”.

**Standardized ¹ mortality rates (p. 100,000) due to infectious and parasitic diseases under and over the age of 65 - Metropolitan France, 1925-2007.**

**Data: INED cause-of-death database &Inserm CépiDc mortality database**

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¹ Standardisation based on the WHO European standard population by five-year age groups.
In addition to that, indicators that are commonly used to monitor trends in mortality due to infectious and parasitic diseases tend to underestimate the role played by this group of diseases in the total mortality. First of all, the chapter “certain infectious and parasitic diseases” of the 10th ICD includes only part of these diseases. Many of them (e.g. influenza, pneumonia, acute bronchitis) are classified in other chapters (e.g. with diseases of the respiratory system). Secondly, routine indicators only account for the underlying cause of the death. In a previous study (Désesquelles et al. 2010), we found that septicaemia is very frequently reported on death certificates as contributing cause. In both France and Italy, roughly 3 out of 4 mentions of an infectious or a parasitic disease are not selected as the underlying cause of the death.

For all these reasons, we believe that an analysis of the mortality involving infectious and parasitic diseases that 1) accounts for multiple (underlying or contributing) causes of death 2) does not restrict to the diseases of the chapter “certain infectious and parasitic diseases“, is necessary. The results that we propose to present at the coming IUSSP conference satisfy both of these conditions.

Data we will use for this study are for year 2008. They are based on the information reported on the death certificates by the certifying physicians and coded according to the 10th International Classification of Diseases. A preliminary work will consist in identifying in the entire classification all the diseases that pertain to the group “infectious and parasitic diseases”.

Then, the multiple cause-of-death (MCOD) approach will be applied to these diseases. The method we use is presented in details in a recently published paper (Désesquelles et al. 2012). In order to recalculate mortality levels, we calculate age- and sex-standardized mortality rates 1) for a given disease as the underlying cause of the death, 2) for the same disease reported as multiple cause of the death. The Standardized Ratio of Multiple to Underlying cause (SRMU) is defined as the ratio of the second to the first of these two rates. It measures the underestimation of the role played by a disease in overall mortality when the analysis is performed using the underlying cause only. The SRMU is low for diseases that are usually selected as the underlying cause and high for diseases that are rarely the underlying cause.

The MCOD approach is also used to examine what are the most frequent associations of causes involving a (group of) disease(s). For that specific purpose, we developed an indicator that can be used to compare various underlying causes within a country, or various countries for a given underlying cause. The Cause-of-Death Association Indicator (CDAI) measures the deviation from the mean of the frequency of occurrence of a specific association of causes. It is defined as the ratio between:

- the standardized prevalence at death of a combination between a contributing cause and an underlying cause among all deaths assigned to that underlying cause;
- the standardized prevalence at death of the same contributing cause among all deaths.

If the CDAI is significantly over 100, then the corresponding association is more frequent than expected.

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2 In order to avoid small numbers grouping of diseases will certainly be needed.
3 Standardization is performed in order to remove the effect of the varying age structure of deaths according to the underlying cause. The standard population is the average number of deaths in the two countries under study by five-year age groups.
4 The Cause-of-Death Association Indicator is thus given by following formula:
On the next page we provide an example of the type of graphical tools we use to present our results. The figure is extracted from the paper published in the *European Journal of Population* (Désesquelles et al. 2012). The cells of the table that result from the cross-matching of every site-specific malignant neoplasm as UCD and every contributing cause of death are coloured according to the value of the corresponding CDAI. After computing the standard deviation (σ) of the CDAIs, five classes have been created ([0;100] , [100;100+σ /4], [100+σ /4;100+σ/2], [100+σ /2;100+3σ/4] and [100+3σ /4;∞]). In this analysis that focused on the cancer-related mortality, we found that in both countries septicaemia (Sept), as well as “other infectious diseases” (OInfec) and pneumonia (Pneu) were frequently reported as contributing cause of malignant neoplasms of lymphoid, haematopoietic and related tissue (Haem). Immunosuppression due to the underlying cause - or its treatment – that these associations exemplify is one of the mechanism by which infectious diseases may intervene in the lethal process originated by other causes. But other mechanisms are possible. Infectious diseases may be risk factors for other causes (e.g. chronic viral hepatitis C and liver cancer). The infectious disease and the other causes reported on the death certificate may also have a common cause. Our analysis will shed light on the various ways by which we may witness an upsurge of infectious diseases in the contemporary mortality profile of developed country.

**SELECTED REFERENCES**


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CDAI_{x,c,u} = \frac{\sum x \left( \frac{d_{c,x,u}}{d_x} \bar{d}_x \right)}{\sum x \left( \frac{d_{c,x,u}}{d_x} \bar{d}_x \right) * 100} = \frac{\sum x \left( \frac{d_{c,x,u}}{d_x} \bar{d}_x \right)}{\sum x \left( \frac{d_{c,x}}{d_x} \bar{d}_x \right) * 100}
\]

\[d_{c,x,u} = \text{number of deaths observed at age } x \text{ with underlying cause } u \text{ and contributing cause } c;\]

\[d_x = \text{number of deaths observed at age } x \text{ with cause } u \text{ as underlying cause;}\]

\[d_{c,x} = \text{total number of deaths observed at age } x \text{ with cause } c \text{ as contributing cause (regardless of underlying cause);}\]

\[\bar{d}_x = \text{average number of deaths at age } x \text{ in France and Italy}\]
**CDAIs* - Associations (Vertical axis) with neoplasms as UCD (Horizontal axis) - Italy, 2003**

* Values of the indicator under 100 and/or corresponding to fewer than 50 cases are not shown.

Data: Istat mortality database