

## **A comparison of the mortality due to Parkinson's disease, Alzheimer's disease, and other senile dementias of France and Italy using the multiple cause-of-death approach**

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The multiple cause-of-death (MCO) approach is emerging as a promising tool in order to study the mortality profile of ageing populations. At old ages, death is indeed often the final stage of a long morbid process that involves several conditions. We use this approach to compare the mortality of Italy and France for a set of conditions that are emblematic of the increased life expectancy: Parkinson's disease, Alzheimer's disease, and other senile dementias. How do the certifying physicians report these diseases on the death certificates? What are the other conditions frequently mentioned on those certificates? When one of these conditions is mentioned as contributory cause, what is the underlying cause? These are some of the questions we want to address.

Data for the two countries are based on the information reported on the death certificates by the certifying physicians and coded according to the 10<sup>th</sup> International classification of diseases (ICD-10). The list of causes we use comprises 15 large groups and 69 sub-groups. We first calculate age- and sex-standardized mortality rates for 1) a given cause reported as the underlying cause of the death, 2) the same cause reported as multiple (underlying or contributory) 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 given condition in overall mortality when the analysis is performed using the underlying cause only. The SRMU is low for conditions that are usually selected as the underlying cause and high for conditions that are rarely the underlying cause.

We developed an indicator of the frequency of the combinations of causes that can be used to compare various underlying causes within a country, or various countries for a given underlying cause (Désesquelles et al, 2010). The **Cause-of-Death Association Indicator (CDAI)** is the ratio between:

- the standardized prevalence at death of a combination between a contributory cause  $c$  and an underlying cause  $u$  among all deaths assigned to that underlying cause ( $SP_{c/u}$ );
- the standardized prevalence at death of the same contributory cause among all deaths ( $SP_c$ ). It represents the prevalence that would be observed for underlying cause  $u$  and contributory cause  $c$  if these two causes were independent.

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Standardization<sup>1</sup> is performed in order to remove the effect of the varying age structure of deaths according to the underlying cause. The Cause-of-Death Association Indicator is thus given by following formula:

$$CDAI_{u,c} = \frac{SP_{c/u}}{SP_c} = \frac{\frac{\sum_x \left( \frac{{}_u d_{c,x}}{{}_u d_x} \cdot \bar{d}_x \right)}{\sum_x \bar{d}_x}}{\frac{\sum_x \left( \frac{d_{c,x}}{d_x} \cdot \bar{d}_x \right)}{\sum_x \bar{d}_x}} * 100 = \frac{\sum_x \frac{{}_u d_{c,x}}{{}_u d_x} \cdot \bar{d}_x}{\sum_x \frac{d_{c,x}}{d_x} \cdot \bar{d}_x} * 100$$

${}_u d_{c,x}$  = number of deaths observed at age  $x$  with underlying cause  $u$  and contributory cause  $c$ ;

${}_u d_x$  = number of deaths observed at age  $x$  with cause  $u$  as underlying cause;

$d_{c,x}$  = total number of deaths observed at age  $x$  with cause  $c$  as contributory cause (regardless of underlying cause);

$d_x$  = total number of deaths observed at age  $x$  (regardless of underlying cause);

$\bar{d}_x$  = average number of deaths at age  $x$  in France and Italy

The results we present here are preliminary. Indicators have been computed for year 2003, and they are partial for Italy. These computations will be replicated for a more recent year (2008) and for the two countries. Studies that use multiple causes of death in order to compare a set of countries are very scarce. This situation may be partly due to the quite widely shared skepticism about the quality and, consequently, about the comparability of the multiple-cause-of-death data. We believe, on the contrary, that it argues in favor of this line of research. Both the similarities and dissimilarities that emerge from the comparison of a set of countries must be interpreted with caution, but they are a potentially fruitful source of information. Unless a clear bias can be identified, similar findings usually reinforce each other's credibility. Dissimilarities may correspond to country-specific certifying and coding practices, but they may also reflect real differences in the morbid processes prevailing in the countries.

Table 1 shows that the standardized mortality rates for the three conditions under study are higher in France than in Italy. The difference is especially high for Alzheimer's disease (10.2 in France vs. 5.9 per 100,000 in Italy) and for other dementias (10.8 vs. 6.9 per 100,000). It is reduced for Parkinson's disease (4.4 in France vs. 3.2 per 100,000 in Italy). We cannot conclude from this that Alzheimer's disease and other dementias are more prevalent in France. The diagnosis of

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<sup>1</sup> the standard population is the average number of deaths in the two countries by five-year age groups.

Alzheimer's disease is known to be problematic. Doubts about the accuracy of the diagnosis may lead to different reporting practices in the two countries.

**Table 1 – Standardized mortality rates (per 100,000) for each cause reported as underlying cause (1) or multiple cause (2) and Standardized Ratio of Multiple to Underlying cause (2/1). Deaths over the age of one, France and Italy, 2003**

CAUSE OF DEATH	ITALY			FRANCE		
	Underlying cause (1)	Multiple cause (2)	SRMU	Underlying cause (1)	Multiple cause (2)	SRMU
Dementia (excluding Alzheimer's Disease)	6,9	21,0	3,1	10,8	20,8	1,9
Alzheimer's disease	5,9	9,5	1,6	10,2	15,6	1,5
Parkinson's disease	3,2	8,5	2,6	4,4	8,2	1,9
<b>All causes of deaths</b>	<b>562</b>	<b>1370</b>	<b>2,4</b>	<b>551</b>	<b>1119</b>	<b>2,0</b>

*Data: France: Inserm CépiDc mortality database / Italy: ISTAT mortality database*

Interestingly, the SRMU for Alzheimer's disease is almost equal in the two countries (1.6 in Italy and 1.5 in France), and the impact of the MCO approach for that disease is very moderate. When reported on the death certificate, Alzheimer's disease is frequently selected as the underlying cause of the death. Finally, when accounting for contributory causes, the mortality rate for Alzheimer's disease remains higher in France than in Italy (15.6 vs 9.5 per 100,000). Regarding dementias, the MCO approach makes equal the situation of the two countries (21 per 100,000). The SRMU for dementias is indeed higher in Italy (3.1) than in France (1.9), suggesting that dementia is more frequently reported as contributory cause of the death in Italy than in France. The situation is very similar for Parkinson's diseases. The SRMU is higher in Italy (2.6) than in France (1.9). When accounting for the mentions as contributory cause of the death, mortality for rates Parkinson's diseases are very close in the two countries (8.5 in Italy and 8.2 per 100,000 in France).

Over the age of 65, when one of the three conditions under study is reported as contributory cause of the death, the most frequent underlying cause of the death is a disease of the circulatory system. There however may be more specific combinations of causes involving these conditions. Figures 1 and 2 (resp. 3 and 4) display the CDAs for female deaths (resp. male deaths) occurring in France over the age of 65 in 2003. The size of the circle is proportional to the value of the CDAs. Figures 1 and 3 are for deaths where Alzheimer's disease, dementia or Parkinson's disease is the underlying cause of the death. Figures 2 and 4 are for cases where these conditions are reported as contributory cause of the death.

Results are very similar for the three conditions and for the two sexes. "Lung diseases due to external agents" (which in most cases correspond to "pneumonitis due to food and vomit"), "malnutrition and other nutritional deficiencies", "diseases of the skin and subcutaneous tissue", "external causes" as well as "pneumonia" and "acute lower respiratory diseases" are very

frequently involved in the process leading to death. Clearly, all these causes reflect the circumstances surrounding the final stage of death at old age that are often characterized by bed confinement, loss of autonomy, and frailty. More specifically to Alzheimer's disease and other dementias, we find a frequent combination with epilepsy. Dementia, which is a possible complication of Parkinson's disease, often contributes to the deaths due to that disease. The three conditions also frequently contribute to deaths attributed to an infectious disease (e.g. septicaemia and intestinal infectious diseases) or to a genitourinary disease.

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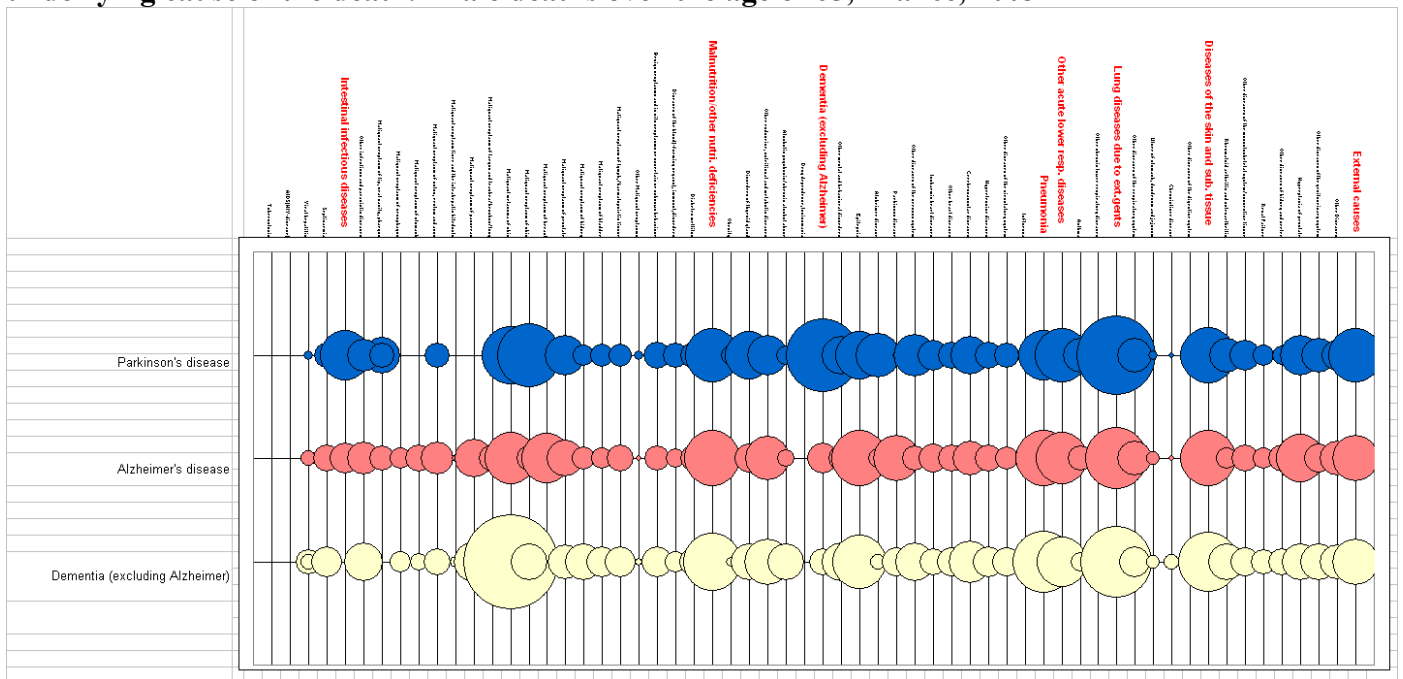
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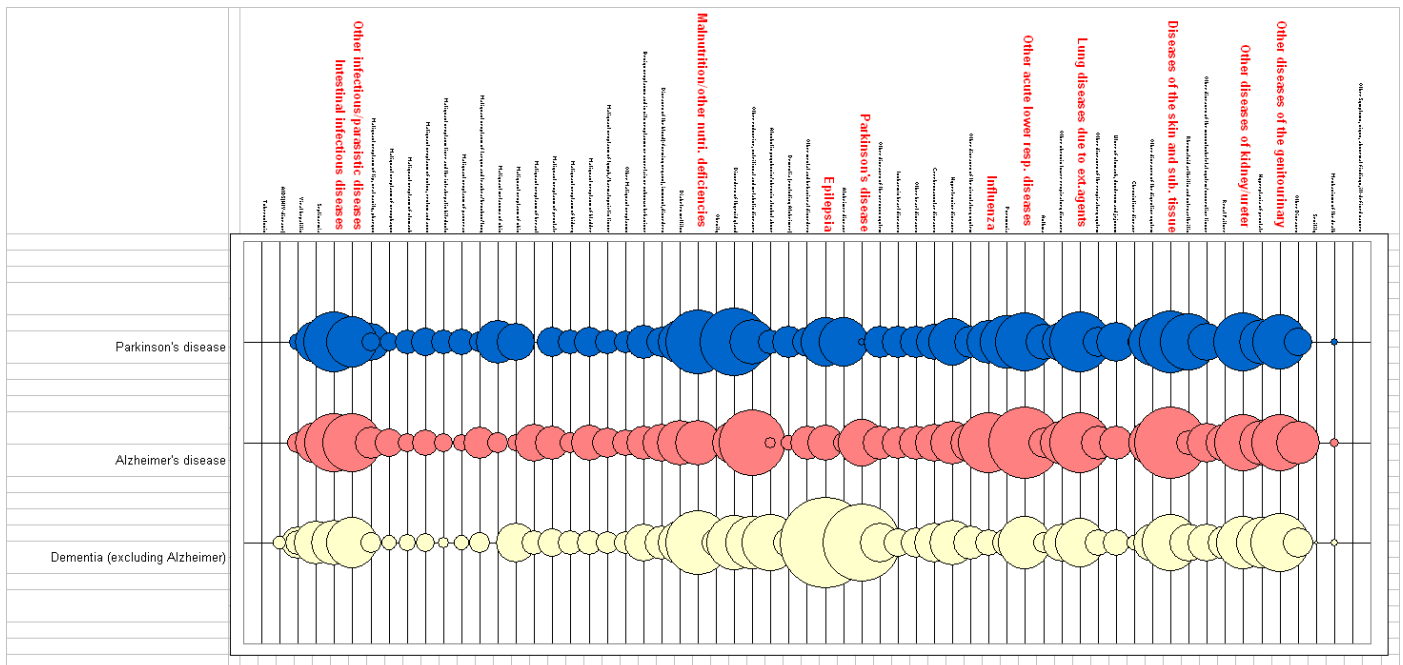
**Figure 3 – CDAsI – Parkinson’s disease, Alzheimer’s disease, and other senile dementias as underlying cause of the death. Male deaths over the age of 65, France, 2003**



Horizontal axis: contributory cause

Data: France: Inserm CépiDc mortality database / Italy: ISTAT mortality database

**Figure 4 – CDAsI – Parkinson’s disease, Alzheimer’s disease, and other senile dementias as contributory cause of the death. Male deaths over the age of 65, France, 2003**



Horizontal axis: underlying cause

Data: France: Inserm CépiDc mortality database / Italy: ISTAT mortality database