ORIGINAL ARTICLE

The decrease in asthma-related mortality in France

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Available online 24 April 2010

KEYWORDS
Asthma;
Mortality;
Trend;
Regional disparities;
France

Summary
Background. — Asthma-related morbidity, mortality and socioeconomic cost represent significant public health problems. Despite efficient therapies, in 1999 asthma still killed around 2000 people in France.

Methods. — This study investigated the changes in asthma-related mortality in metropolitan France between 1980 and 2005 and examined its regional disparities. Annual age- and gender-specific mortality rates for asthma were calculated, as well as age-standardized rates. The change in asthma-related mortality was estimated by the annual average rate of change fitted using a log-linear regression model. Lastly, regional disparities were mapped.

Results. — After having levelled off between 1990 and 1995, asthma-related mortality significantly decreased. From 2000 onwards the drop was more rapid in men than in women. The observed decrease was significant only in people over 35. In 2005, there were 1129 deaths due to asthma. Moreover, regional disparities could be seen.

Conclusions. — The decline of asthma-related mortality that started in 1986 continued until 2005. Possible explanations could be better patient care, including the use of inhaled corticosteroids and therapeutic education, and improvement in the recording of deaths.

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Introduction

Asthma is a major public health problem because of its high prevalence, particularly in children, often preventable deaths, and the economic burden it causes. The World Health Organization estimates the number of asthmatics worldwide at 300 million, with 30 million in Europe [1]. The prevalence of this disease in France is approximately 3.5 million, including a third of children [2]. Asthma affects 5 to 7% of adults in France, 10 to 15% of young adults (aged 20–24 years) and adolescents, and 8% of school age children [3,4]. The total medical and societal cost of asthma was estimated at 1.5 billion Euros in 2001 in France [5]. As regards mortality, asthma causes around 250,000 deaths a year worldwide; most of these deaths are preventable with earlier diagnosis, better patient care and the development of therapeutic education [1,5]. Despite advances in these fields, asthma is still an underlying cause of death in France. The study by Delmas et al., integrating the most recent data on asthma mortality in metropolitan France, found that asthma still caused around 2000 deaths in 1999 [6]. Asthma mortality had, however, decreased in the past few decades in several countries that had shown different prior trends.

Since 1970–1980, an increase in asthma mortality had been recorded in several countries such as the United States, Australia, New Zealand, Italy, England and Wales, followed by a decrease from 1985–1990 with gender- and age-related variations [7–13]. Mortality started to decrease in the United States from 1995 until 2002 and in Australia from 1989 until 2003; the trend was less marked in Australians aged between 5 and 34 years [7–9]. In New Zealand, a period of high asthma mortality until 1989 was followed by a sudden fall in rates [10]. The trends in Italy, England and Wales were marked by decreases recorded from 1987 to 1996 and 1985–1990 to 2005, respectively, depending on the age group [11–13]. Spain and the Netherlands also saw a reduction in asthma mortality from 1980 until the mid-1990s, mainly in the over 35 years age group, [11,14] and Finland from 1981 to 2003 [15]. The factors explaining this reduction in mortality observed since the 1990s include the impact of international recommendations for asthma management, national programmes such as in Finland, and improvements in specific treatments for severe asthma, in particular the use of oral and inhaled corticosteroids (ICS) [15–18].

In metropolitan France, analysis of trends in asthma mortality between 1970 and 1990 showed an increase until the mid-1980s, followed by a decrease, in particular in the 5–34 years age group [19]. These results were confirmed by the study carried out by Delmas et al. describing the subsequent trend in asthma mortality between 1980 and 1999 [6]. After an increase between 1980 and 1986, with a rise in crude death rates to 4.0/100,000 in males and 4.5/100,000 in females in 1986, asthma mortality decreased until 1999, with a more progressive decrease in females than males. The same downward trend was also observed in children and young adults. In 1999, crude asthma-related death rates were 2.8/100,000 in males and 3.9/100,000 in females [6].

The present study provides a more comprehensive analysis than the study recently published in Allergy [20]. We describe the trends in asthma mortality in metropolitan France between 1980 and 2005, with particular emphasis on the analysis of gender- and age-related trends since 2000, the year the International Classification of Diseases (ICD) was revised and changes were made in the statistical coding of causes of death. Finally, we present gender-related regional disparities, and propose a more detailed discussion, in particular on the different factors that could possibly explain the observed results.

Material and methods

Data relating to cause of death were supplied by the Centre d’épidémiologie sur les causes médicales de décès (CépiDc—Epidemiological Centre on Medical Causes of Death), a French National Institute for Health and Medical Research (Inserm) laboratory, that monitors the medical causes mentioned on death certificates in France. The analysis involved all deaths in metropolitan France between 1st January 1980 and 31st December 2005, for which asthma was mentioned as the underlying cause of death (ICD-9 code 493 and ICD-10 J45–J46). For each death, we used information on age, gender and region of death.

We describe the trend in asthma mortality for males and females, for the period 1980–2005, using age-standardized mortality rates. The direct standardization method was applied using 10-year age classes with for reference population the mean population of metropolitan France in 1980. The trend was measured as the percentage of average annual change, on the hypothesis that this percentage was constant over time. This indicator was calculated applying a linear model derived from the natural logarithm of the standardized asthma mortality rate for the year. Average Annual Percent Change (AAPC) was defined as follows:

\[
AAPC = (\exp(\beta) - 1) \times 100
\]

where \( \beta \) is the logarithmic increase in mortality per year.

Interaction terms were introduced into the model to test whether rate trends differed with gender. When interaction was not significant, the trend was measured using the age-and gender-standardized AAPC. In the period 2000–2005, the specific annual rates by age and gender were calculated as well as their annual average trend.

To analyse regional disparities, we mapped, by gender, the regional variations in average age-standardized asthma mortality rates over the period 2003–2004, compared with the national rates. The reference population was the average population of metropolitan France in 2003 by gender. Data on deaths registered in 2005 could not be integrated because these data were not available by gender and age at regional level for that year.

Demographic data were provided by the French National Institute for Statistics and Economical Studies and were supplied by region of residence.

The threshold of statistical significance was fixed at 5%. Analyses were performed using SAS version 9.1 software and Cartes&Bases version 5.5.

Results

In metropolitan France, the asthma mortality curve showed a peak in 1986, in males and females, followed by a sig-
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Between 2000 and 2005, asthma was mentioned as the underlying cause of death on a total of 7966 death certificates with 58% of deaths occurring after 75 years and 7% before 45 years. The number of asthma-related deaths decreased by 1586 in 2000 to 1129 in 2005; the crude death rate decreased from 2.7 to 1.9/100,000. The standardized rates for asthma mortality had decreased in males and females, from 2.0 to 1.1/100,000 and 1.9 to 1.3/100,000, respectively; i.e. a significant fall of −12.1 and −7.6% per year (Table 1).

There was an age-related mortality gradient; the oldest individuals showed the highest rates (Table 2). Between 2000 and 2005, asthma mortality decreased considerably in individuals over 35 years with a significant log-linear decrease in males over 75 years, not observed in females of the same age.

The regions the most affected by asthma mortality in males were Auvergne, Picardy and Poitou-Charentes and in females in Brittany; the least affected, in both males and females, were the East and South-West regions (Fig. 2).

Discussion

This study noted the peak in asthma mortality in 1986, previously identified by Delmas et al., which can be partly explained by winter influenza epidemics in 1985 and 1986

Table 1  Number of asthma-related deaths and standardized mortality rates in metropolitan France (per 100,000 population), by year, 2000–2005 (data from CépiDc, Inserm).

<table>
<thead>
<tr>
<th>Year</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of deaths</td>
<td>1586</td>
<td>1440</td>
<td>1359</td>
<td>1353</td>
<td>1099</td>
<td>1129</td>
</tr>
<tr>
<td>Standardized rates</td>
<td>2.0</td>
<td>1.8</td>
<td>1.5</td>
<td>1.4</td>
<td>1.0</td>
<td>1.1</td>
</tr>
<tr>
<td>Males</td>
<td>1.9</td>
<td>1.7</td>
<td>1.6</td>
<td>1.6</td>
<td>1.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CépiDc: centre d’épidémiologie sur les causes médicales de décès (Epidemiological Centre on Medical Causes of Death).

*: p < 0.05.

Table 2  Trends in age- and gender-specific asthma mortality rates (per 100,000 population), 2000–2005 (data from CépiDc, Inserm).

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Gender</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>Average annual change (in %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>Male</td>
<td>0.2</td>
<td>0.2</td>
<td>0.1</td>
<td>0.1</td>
<td>0.0</td>
<td>0.1</td>
<td>−27.4*</td>
</tr>
<tr>
<td>Female</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.0</td>
<td>0.0</td>
<td>0.1</td>
<td>−5.5</td>
<td></td>
</tr>
<tr>
<td>15–24</td>
<td>Male</td>
<td>0.2</td>
<td>0.3</td>
<td>0.2</td>
<td>0.1</td>
<td>0.1</td>
<td>0.2</td>
<td>−11.2</td>
</tr>
<tr>
<td>Female</td>
<td>0.3</td>
<td>0.4</td>
<td>0.3</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>−11.7</td>
<td></td>
</tr>
<tr>
<td>25–34</td>
<td>Male</td>
<td>0.3</td>
<td>0.3</td>
<td>0.6</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
<td>−11.2***</td>
</tr>
<tr>
<td>Female</td>
<td>0.3</td>
<td>0.5</td>
<td>0.6</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
<td>−11.4**</td>
<td></td>
</tr>
<tr>
<td>35–44</td>
<td>Male</td>
<td>1.6</td>
<td>1.6</td>
<td>1.3</td>
<td>1.0</td>
<td>1.0</td>
<td>0.9</td>
<td>−11.4***</td>
</tr>
<tr>
<td>Female</td>
<td>1.8</td>
<td>2.0</td>
<td>1.5</td>
<td>1.4</td>
<td>1.3</td>
<td>1.4</td>
<td>−10.7**</td>
<td></td>
</tr>
<tr>
<td>45–54</td>
<td>Male</td>
<td>2.7</td>
<td>2.6</td>
<td>1.9</td>
<td>1.8</td>
<td>1.8</td>
<td>1.5</td>
<td>−10.7**</td>
</tr>
<tr>
<td>Female</td>
<td>3.0</td>
<td>3.2</td>
<td>2.7</td>
<td>2.6</td>
<td>2.4</td>
<td>2.5</td>
<td>−10.7**</td>
<td></td>
</tr>
<tr>
<td>55–64</td>
<td>Male</td>
<td>6.4</td>
<td>6.4</td>
<td>4.7</td>
<td>4.6</td>
<td>3.8</td>
<td>3.4</td>
<td>−10.7**</td>
</tr>
<tr>
<td>Female</td>
<td>9.0</td>
<td>9.0</td>
<td>8.0</td>
<td>7.0</td>
<td>6.0</td>
<td>6.0</td>
<td>−10.7**</td>
<td></td>
</tr>
<tr>
<td>65–74</td>
<td>Male</td>
<td>19.1</td>
<td>17.3</td>
<td>14.2</td>
<td>14.0</td>
<td>9.0</td>
<td>9.6</td>
<td>−14.4**</td>
</tr>
<tr>
<td>Female</td>
<td>20.5</td>
<td>18.0</td>
<td>19.3</td>
<td>20.4</td>
<td>15.6</td>
<td>16.9</td>
<td>−3.7</td>
<td></td>
</tr>
</tbody>
</table>

*: p < 0.05; **: p < 0.01; ***: p < 0.0001.
The methods used for both studies show similarities, not found in other studies on this subject [21]. Following the peak in 1986, asthma mortality significantly decreased until 1990, levelled off from 1990 to 1995, then decreased until 1999. The trends in that period did not show significant gender differences. From 2000, the rates became lower than those observed in the early 1980s in both males and females. Age structure being equal, the decrease in asthma mortality was significantly higher in males than in females, $-12.1$ and $-7.6\%$, respectively per year. This decrease was recorded in individuals over 35 years. In addition, from 2002 onwards, asthma mortality that had been higher in males until then has become higher in females.

Though the trend showed a fall, 1129 individuals died from asthma in metropolitan France in 2005, i.e. a crude mortality rate of $1.9/100,000$. There were also geographical disparities in 2003–2004. In males, the regions most affected were Auvergne, Picardy and Poitou-Charentes, and in females, Brittany. The least affected were the East and South-West regions in both males and females.

Several changes occurred in 2000, which make interpretation of asthma mortality trends between 1999 and 2000 difficult. In the context of implementation of the 10th revision of the ICD, new diseases were coded, others were clarified, and the coding algorithm for causes of death was modified. For asthma, only the modifications in the coding algorithm could have had an effect on trends. Furthermore, formerly manual, the coding of causes of death became an electronic process in 2000 at CépiDc. For this reason, the period 2000–2005 was analysed separately.

Several transverse studies have been carried out in France to estimate the prevalence of asthma in both adults and children, and according to severity level, but there is little knowledge available on trends in prevalence and severity, making interpretation of mortality trends difficult [2–4,22]. However, a significant decrease in hospitalization rates for asthma was recorded in adolescents and adults between 1998 and 2002 [23]. This decrease in hospitalization rates, accompanied by the fall in asthma mortality rates since the mid-1980s, could indicate an improvement in care management for asthmatic patients. Factors explaining this could include the impact of the Global Initiative for Asthma (GINA) recommendations, initially implemented in 1995 and regularly updated since then; these recommendations mainly concern asthma management and dose adjustment according to the level of severity [16]. The long-term treatment advised for persistent mild, moderate and severe asthma was ICS, associated with long-acting beta2-agonists (LABA) for moderate to severe asthma. Since 2006, the recommendations advise adaptation of treatment to asthma control rather than severity level. Studies have shown that single inhaler therapy associating an ICS and an LABA provides better asthma control compared with ICS therapy alone [24,25]. These drugs, marketed since 2001, can contribute towards better compliance and avoid interruption of ICS therapy in patients treated with LABA. It is, however, difficult to determine the specific role of these drugs in reducing asthma mortality. Furthermore, it would be interesting to study trends in tobacco smoking in asthmatic patients compared with non-asthmatics. The decreases observed since 2000, particularly in elderly men, could also be the result of better diagnosis and statistical coding of chronic obstructive pulmonary disease, which is seen more frequently in males [26].

Our study underestimates the real impact of asthma on mortality as it is only based on the underlying cause of death. As a chronic disorder, asthma can contribute to the disease process without being the underlying cause of death. It would thus be pertinent to complete this study with an analysis of deaths where asthma was the underlying or associated cause. Moreover, some studies show excess mortality, all causes taken into account, in asthmatic patients compared with non-asthmatics [22].

This study requires completion with an analysis of socioeconomic disparities, with the inclusion of tobacco smoking status; however this information, though sometimes mentioned on the death certificate, is of questionable quality and not generally available. The procedures followed by physicians when certifying deaths are crucial in the anal-
ysis of mortality based on underlying and associated causes of death. It is thus essential that each physician retraces as accurately as possible the disease process leading to death by systematically indicating, when appropriate, the history of tobacco smoking in the associated morbid conditions.

The regional disparities in asthma mortality do not correspond to those observed for hospitalizations [23]. They could represent socioeconomic inequalities between populations in different regions, inequalities in the care of asthmatic patients, in health care structures and access to care; the interpretation of such differences would require the implementation of further studies at regional level. To date, no available data enable us to explain the gender-related geographic disparities.

Conclusions

The decline in asthma mortality that started in 1986 continued until 2005. Possible explanations could be better patient care, including the use of ICS, therapeutic education, and improvements in the recording of deaths. However, there were still 1129 deaths due to asthma in 2005. Most of these deaths were preventable. Further efforts are required to reduce this mortality with better understanding of regional disparities and clear identification of the causes.

Conflict of interest

This study did not involve any conflict of interest.

Acknowledgements

We would like to express our gratitude to the Société de pneumologie de langue française (SPLF – French-language Society of Pneumonology) for funding this study. We also thank the Centre d’épidémiologie sur les causes médicales de décès (CépiDc – Epidemiological Centre on Medical Causes of Death) for providing data and invaluable advice on this data source.

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