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## Journal of Asthma

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597262>

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Claire Fuhrman <sup>a</sup>; Eric Jouglu <sup>b</sup>; Zoé Uhry <sup>a</sup>; Marie-Christine Delmas <sup>a</sup>

<sup>a</sup> Institut de veille sanitaire, Saint-Maurice Cedex, France <sup>b</sup> Centre d'épidémiologie sur les causes médicales de décès (CépiDC-INSERM), Le Vésinet Cedex, France

Online Publication Date: 01 May 2009

**To cite this Article** Fuhrman, Claire, Jouglu, Eric, Uhry, Zoé and Delmas, Marie-Christine(2009)'Deaths with Asthma in France, 2000-2005: A Multiple-Cause Analysis',*Journal of Asthma*,46:4,402 — 406

**To link to this Article:** DOI: 10.1080/02770900902795553

**URL:** <http://dx.doi.org/10.1080/02770900902795553>

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ORIGINAL ARTICLE

# Deaths with Asthma in France, 2000–2005: A Multiple-Cause Analysis

CLAIRE FUHRMAN,<sup>1,\*</sup> ERIC JOUGLA,<sup>2</sup> ZOÉ UHRY,<sup>1</sup> AND MARIE-CHRISTINE DELMAS<sup>1</sup>

<sup>1</sup>*Institut de veille sanitaire, Saint-Maurice Cedex, France*

<sup>2</sup>*Centre d'épidémiologie sur les causes médicales de décès (CépiDc-INSERM), Le Vésinet Cedex, France*

Mortality from asthma has decreased in many countries since the 1990s. Mortality statistics are usually based only on the underlying cause of death. The objectives of this study were to describe the characteristics of deaths and the trends in asthma-related mortality using multiple-cause analysis.

Data were obtained from the French Centre of Epidemiology on Medical Causes of Death. Because ICD-10 was implemented in 2000, the analysis covers the period 2000–2005.

In 2004–2005, asthma was the underlying cause of 42% of deaths with certificates mentioning asthma. The age-standardised rates of death from asthma decreased from 2000 through 2005 (–12% and –11%/year in the 1–44 and 45–64 age groups, respectively). The decline for all deaths with asthma was less pronounced (–9%/year in the 1–44 age group and –8%/year in the 45–64). Among adults aged 65 or older, the decrease in asthma-related mortality was higher in men (–12%/year for underlying cause, –9% for multiple-cause) than women (–5% and –3%, respectively). Since 2002, age-standardised rates of asthma-related mortality have been higher in women than men. In people aged 1–44 years, in-hospital deaths have declined between 2000 and 2005 while the proportion of non-hospital deaths increased from 53% to 67%.

Regardless of the definition used, the age-standardised rate of asthma-related deaths decreased from 2000 to 2005, and the faster decline for underlying cause than for multiple-cause mortality argues for a real decline in mortality attributable to asthma. Using multiple cause-of-death analysis provides additional information for asthma mortality surveillance.

## INTRODUCTION

Mortality from asthma has decreased since the 1980s in France as in other countries (1–4). This decline can be attributed to better disease management and wide use of inhaled controller medications (5, 6). Nonetheless, about 1,000 deaths from asthma still occur each year in France, and most of them are preventable with appropriate disease management (7, 8).

Most studies investigating asthma mortality are based on underlying cause-of-death data only; multiple-cause analyses are sparse (9, 10). However, taking into account all conditions listed on the death certificate provides a better estimation of the global burden of the disease on mortality. It also documents comorbid conditions that lead to death and can help to interpret changes in trends induced by revisions of the International Classification of Diseases (ICD) (9, 11). The contribution of multiple-cause analysis varies according to the type of diseases considered (12). This approach is particularly warranted for such chronic diseases as diabetes or obstructive pulmonary disease (11, 13, 14). In the US and in the UK, asthma was listed as the underlying cause of death in 40% to 50% of all death certificates that mentioned asthma (9, 10).

The objectives of this study were to describe the characteristics of deaths for which asthma was mentioned as either the underlying cause or anywhere on the death certificate (multiple-cause analysis) and to describe trends in asthma-related mortality between 2000 and 2005.

## METHODS

Mortality data were obtained from the Centre of Epidemiology for Medical Causes of Death (CépiDc-INSERM). Medical death certificates contain two sections in which physicians can enter the medical conditions of the deceased. Part I asks for the underlying cause of death (that is, the disease that initiated the chain of events resulting in death) and for the sequence leading directly to death (intermediate and direct causes). Part II allows the physician to list additional conditions that contributed to the death but were not part of the direct causal sequence. The coding rules of the ICD select the underlying cause of death. Associated causes of death are all other significant conditions that contributed to the death. Until 1999, CépiDc used ICD-9 to code causes of death for entry in the national death statistics database and recorded a maximum of two contributing causes (in addition to the immediate and the underlying causes) for each death. Since 2000, when ICD-10 was implemented and manual coding was replaced by an automated coding system, all causes mentioned by the certifying physician have been recorded.

The analyses were conducted for cases with asthma (ICD-10: J45 or J46) recorded as the underlying cause (death from asthma) or mentioned anywhere on the certificate (death with asthma). Analyses here concern deaths from 2000 to the end of 2005 of people who were living and died in France. Because of the difficulties in diagnosing asthma in infants, the analysis considers only the population 1 year of age or older.

Population figures provided by the French National Institute for Statistics and Economic Studies (INSEE) were used to calculate the 5-year age-specific mortality rates for each calendar year. Age-standardized rates (direct method) were calculated by applying the age-specific mortality rates to the 1976 European standard population (15).

\*Corresponding author: Claire FUHRMAN, Institut de veille sanitaire, 12 rue du Val d'Osne, 94415 Saint-Maurice Cedex France; E-mail: c.fuhrman@invs.sante.fr

The annual percent change in asthma mortality rates was estimated for three age groups (1–44, 45–64, and 65 and older) with Poisson regression models. In each age group, the model included a linear time trend and an interaction between sex and a qualitative age effect. An interaction term between sex and year was also introduced in the model to test the time trends according to gender.

Data about the place of death, recorded on the death certificate, were also studied. A death was considered as an out-of-hospital death when it did not occur in hospital (public or private, including emergency room) or in a nursing home.

## RESULTS

### Number of Deaths

The mean annual number of deaths from asthma (asthma as underlying cause) decreased from 1,567 in 2000–2001 to 1,166 in 2004–2005 in France (Table 1). In 2000–2005, asthma was listed as the underlying cause on 44% of the death certificates that mentioned asthma (deaths with asthma). This proportion decreased slightly from 2000 to 2005. Deaths from asthma accounted for more than 70% of all deaths with asthma among people 1 to 34 years of age and only 40% among those 75 years of age or more.

### Mortality Rates and Time Trends

The 2004–2005 mean annual standardized rates were 1.3/100,000 for mortality from asthma and 3.0/100,000 for mortality with asthma (Table 2). They were similar for men and women, and slightly higher for women among people over 65 years of age. Regardless of the definition used (underlying cause or any mention), the specific mortality rates increased with age, especially among those older than 65 years (Figure 1).

The standardized death rates from asthma decreased between 2000 and 2005. Among people younger than 65, the decrease was similar for men and women ( $p = 0.48$  in the 1- to 44-year age group and  $p = 0.95$  in the 45- to 64-year age

TABLE 2.—Trends in age-standardized rates of mortality from asthma and mortality with asthma by sex and age group in France, between 2000 and 2005.

|                          | Observed age-standardized <sup>a</sup><br>rates by period and EAPC <sup>b</sup> |           |           |                              |
|--------------------------|---------------------------------------------------------------------------------|-----------|-----------|------------------------------|
|                          | 2000–2001                                                                       | 2002–2003 | 2004–2005 | EAPC [CI 95%] <sup>c</sup>   |
| <b>Death from asthma</b> |                                                                                 |           |           |                              |
| All ages                 |                                                                                 |           |           |                              |
| Men                      | 2.0                                                                             | 1.6       | 1.2       |                              |
| Women                    | 1.8                                                                             | 1.6       | 1.3       |                              |
| Overall                  | 1.9                                                                             | 1.6       | 1.3       |                              |
| 1–44 years               |                                                                                 |           |           |                              |
| Men                      | 0.4                                                                             | 0.3       | 0.2       |                              |
| Women                    | 0.3                                                                             | 0.2       | 0.2       |                              |
| Overall                  | 0.3                                                                             | 0.2       | 0.2       | –11.9 [–16.0; –7.6] <i>d</i> |
| 45–64 years              |                                                                                 |           |           |                              |
| Men                      | 2.3                                                                             | 1.6       | 1.4       |                              |
| Women                    | 1.8                                                                             | 1.4       | 1.1       |                              |
| Overall                  | 2.0                                                                             | 1.5       | 1.3       | –10.8 [–13.5; –8.0] <i>d</i> |
| 65 years or older        |                                                                                 |           |           |                              |
| Men                      | 10.7                                                                            | 8.8       | 6.3       | –12.3 [–14.9; –9.6] <i>d</i> |
| Women                    | 10.1                                                                            | 9.8       | 8.1       | –4.6 [–6.6; –2.6] <i>d</i>   |
| Overall                  | 10.4                                                                            | 9.5       | 7.5       |                              |
| <b>Death with asthma</b> |                                                                                 |           |           |                              |
| All ages                 |                                                                                 |           |           |                              |
| Men                      | 4.3                                                                             | 3.8       | 3.0       |                              |
| Women                    | 3.6                                                                             | 3.4       | 2.9       |                              |
| Overall                  | 3.9                                                                             | 3.6       | 3.0       |                              |
| 1–44 years               |                                                                                 |           |           |                              |
| Men                      | 0.5                                                                             | 0.5       | 0.3       |                              |
| Women                    | 0.4                                                                             | 0.3       | 0.3       |                              |
| Overall                  | 0.5                                                                             | 0.4       | 0.3       | –8.6 [–12.1; –5.0] <i>d</i>  |
| 45–64 years              |                                                                                 |           |           |                              |
| Men                      | 4.1                                                                             | 3.3       | 2.8       |                              |
| Women                    | 3.0                                                                             | 2.5       | 2.2       |                              |
| Overall                  | 3.5                                                                             | 2.9       | 2.5       | –8.2 [–10.3; –6.1] <i>d</i>  |
| 65 years or older        |                                                                                 |           |           |                              |
| Men                      | 26.3                                                                            | 23.6      | 18.1      | –8.7 [–10.5; –6.8] <i>d</i>  |
| Women                    | 22.5                                                                            | 22.6      | 19.1      | –3.4 [–4.9; –1.9] <i>d</i>   |
| Overall                  | 24.0                                                                            | 23.1      | 18.9      |                              |

<sup>a</sup>Rates (per 100 000), standardized to the European population.

<sup>b</sup>EAPC=estimated annual percent change.

<sup>c</sup>Confidence intervals are corrected for over-dispersion when necessary.

<sup>d</sup> $p < 0.001$ .

group). The estimated annual percent change (EAPC) was –11.9% in people 1 to 44 years of age and –10.8% in those 45 to 64 years of age (Table 2). Among adults 65 years of age and over, mortality from asthma decreased more for men than for women ( $p < 0.001$ ), with an EAPC of –12.3% in men and –4.6% in women. The sex ratio (male/female) for mortality from asthma among those 65 years of age or older was 1.1 in 2000–2001 and 0.8 in 2004–2005.

The decline in mortality was less pronounced when including all deaths with asthma (Table 2). For people under 65, time trends did not differ significantly according to sex ( $p = 0.43$  and  $p = 0.47$  in the 1- to 44-year and 45- to 64-year age groups, respectively); the EAPC was –8.6% among those 1 to 44 years of age and –8.2% among those 45 to 64 years of age. Among adults over 65 years of age, the EAPC was –8.7% in men and –3.4% in women (significant gender difference:  $p < 0.001$ ).

### Conditions Associated with Asthma on the Death Certificate

When asthma was mentioned as the underlying cause of death, the most frequently associated causes were cardiovascular diseases. This association increased with age, from 19% among those 1 to 24 years of age to 48% of those 65 years of age or older (Table 3). Neither chronic obstructive pulmonary disease (COPD) nor chronic respiratory failure was mentioned often for people younger than 45 years, but at least one was found on about 10% of the death certificates

TABLE 1.—Number of deaths with asthma as underlying or as associated cause, according to period, sex, and age in France, 2000–2005.

|             | Deaths with asthma, 2000–2005<br>Asthma as the underlying cause |       |      |
|-------------|-----------------------------------------------------------------|-------|------|
|             | N                                                               | N     | %    |
| Period      |                                                                 |       |      |
| 2000–2001   | 6,762                                                           | 3,134 | 46.4 |
| 2002–2003   | 6,565                                                           | 2,817 | 42.9 |
| 2004–2005   | 5,613                                                           | 2,335 | 41.6 |
| Sex         |                                                                 |       |      |
| Men         | 7,602                                                           | 3,204 | 42.2 |
| Women       | 11,338                                                          | 5,082 | 44.8 |
| Age (years) |                                                                 |       |      |
| 1–4         | 24                                                              | 17    | 70.8 |
| 5–14        | 53                                                              | 38    | 71.7 |
| 15–24       | 124                                                             | 92    | 74.2 |
| 25–34       | 190                                                             | 142   | 74.7 |
| 35–44       | 496                                                             | 296   | 59.7 |
| 45–54       | 1,077                                                           | 622   | 57.8 |
| 55–64       | 1,489                                                           | 755   | 50.7 |
| 65–74       | 3,317                                                           | 1,483 | 44.7 |
| 75–84       | 6,237                                                           | 2,505 | 40.2 |
| 85+         | 5,929                                                           | 2,334 | 39.4 |
| Overall     | 18,936                                                          | 8,284 | 43.8 |

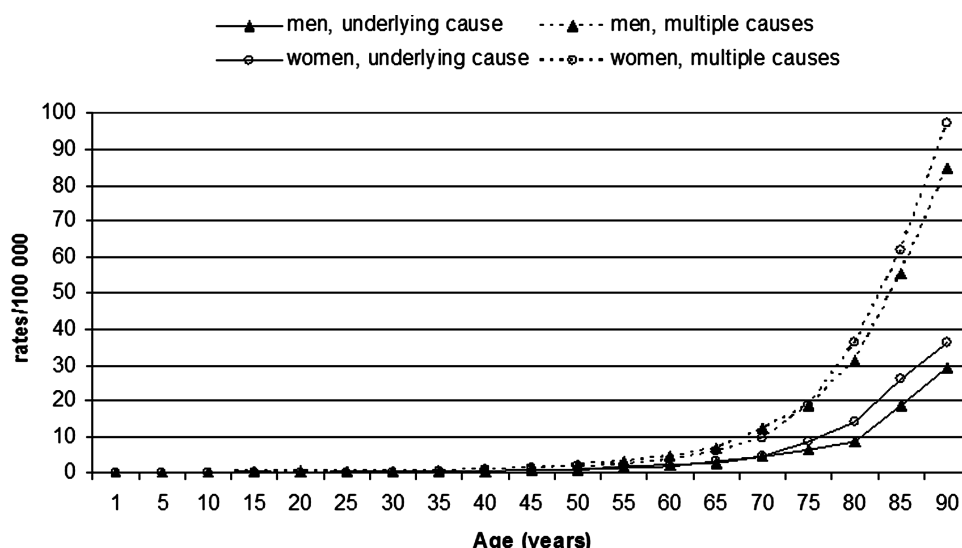


FIGURE 1.—Age-specific mortality rates from asthma (underlying cause) and with asthma (multiple causes), France, mean annual rates 2004–2005.

for people 45 to 64 years of age and 22% for those over 65. Lower respiratory infections were mentioned on 4% of the death certificates for those 1 to 24 years of age and in 16% of certificates for those 65 years of age or older. Tobacco use disorder was listed on 6.8% of the certificates of death from asthma for adults 25 to 64 years of age.

When asthma was listed as a contributing (but not the underlying) cause, the most frequent underlying causes of death in the youngest age group were external causes of mortality (injury, suicide, accidents) (28% in people younger than 25 years of age) (Table 4). Among adults, the most frequent underlying causes were cardiovascular diseases: 27% among people 25 to 44 years of age and 44% among those 65 years of age or more, followed by neoplasms (6% and 14%). COPD was the underlying cause of death in about 11% of the adults 45 years of age or older.

### Place of Death

More than half (55%) of all deaths from asthma occurred outside the hospital (66% for men and 49% for women). The overall proportion of out-of-hospital deaths remained steady

between 2000 and 2005. However, among people younger than 45 years, the number of in-hospital deaths decreased by 56% and the number of out-of-hospital deaths by only 26%, resulting in an overall increase in the proportion of out-of-hospital deaths (Table 5). Overall, out-of-hospital deaths accounted for half of all deaths mentioning asthma anywhere in the certificate.

TABLE 4.—Underlying causes of death when asthma was mentioned as an associated cause of death but not the underlying cause, France, 2000–2005.

| Underlying cause <sup>a</sup>                 | Age group (years) |       |       |       |       |       |            |       |
|-----------------------------------------------|-------------------|-------|-------|-------|-------|-------|------------|-------|
|                                               | 1–24              |       | 25–44 |       | 45–64 |       | 65 or more |       |
|                                               | n                 | %     | n     | %     | n     | %     | n          | %     |
| Cardiovascular diseases                       | 7                 | 13.0% | 66    | 26.6% | 411   | 34.6% | 4067       | 44.4% |
| Ischemic heart disease                        | 0                 | 0%    | 17    | 6.9%  | 173   | 14.6% | 1319       | 14.4% |
| COPD                                          | 1                 | 1.9%  | 9     | 3.6%  | 133   | 11.2% | 969        | 10.6% |
| CRF                                           | 0                 | 0%    | 1     | 0.4%  | 8     | 0.7%  | 57         | 0.6%  |
| Lower respiratory infections                  | 1                 | 1.9%  | 6     | 2.4%  | 30    | 2.5%  | 339        | 3.7%  |
| External causes                               | 15                | 27.8% | 48    | 19.4% | 94    | 7.9%  | 539        | 5.9%  |
| Infectious and parasitic diseases             | 1                 | 1.9%  | 16    | 6.5%  | 23    | 2.0%  | 184        | 2.0%  |
| Neoplasms                                     | 3                 | 5.6%  | 17    | 6.9%  | 191   | 16.1% | 1282       | 14.0% |
| Lung cancer                                   | 0                 | 0%    | 3     | 1.2%  | 53    | 4.5%  | 173        | 1.9%  |
| Endocrine, nutritional and metabolic diseases | 3                 | 5.6%  | 18    | 7.3%  | 74    | 6.2%  | 506        | 5.5%  |
| Mental and behavioural disorders              | 4                 | 7.4%  | 24    | 9.7%  | 73    | 6.1%  | 176        | 1.9%  |
| Diseases of the nervous system                | 5                 | 9.3%  | 14    | 5.6%  | 30    | 2.5%  | 307        | 3.4%  |
| Diseases of the digestive system              | 2                 | 3.7%  | 20    | 8.1%  | 74    | 6.2%  | 360        | 3.9%  |
| Congenital malformations                      | 5                 | 9.3%  | 2     | 0.8%  | 0     | 0     | 5          | 0.05% |
| Others                                        | 7                 | 13.0% | 7     | 2.8%  | 48    | 4.0%  | 370        | 4.0%  |

<sup>a</sup> Cardiovascular diseases: I00–I99; ischaemic heart diseases: I20–I25; COPD: J40–J44; CRF: J961; lower respiratory infections: J10–J18 J20–J22; external causes: V01–Y89; infectious and parasitic diseases: A00–B99; neoplasms: C00–D48; lung cancer: C33 C34; endocrine, nutritional and metabolic diseases: E00–E90; mental and behavioural disorders: F00–F99; diseases of the nervous system: G00–G99; diseases of the digestive system: K00–K93; congenital malformations: Q00–Q99  
COPD = chronic obstructive pulmonary disease;  
CRF = chronic respiratory failure.

TABLE 3.—Main associated causes of death when asthma was the underlying cause, France, 2000–2005.

| Associated causes <sup>a</sup> | Age group (years) |       |       |       |       |       |            |       |
|--------------------------------|-------------------|-------|-------|-------|-------|-------|------------|-------|
|                                | 1–24              |       | 25–44 |       | 45–64 |       | 65 or more |       |
|                                | n                 | %     | n     | %     | n     | %     | n          | %     |
| Cardiovascular diseases        | 28                | 19.0% | 115   | 26.3% | 504   | 36.6% | 3052       | 48.3% |
| Ischemic heart disease         | 0                 | 0     | 9     | 2.1%  | 59    | 4.3%  | 564        | 8.9%  |
| COPD or CRF                    | 2                 | 1.4%  | 13    | 3.0%  | 140   | 10.2% | 1375       | 21.7% |
| COPD                           | 1                 | 0.7%  | 6     | 1.4%  | 79    | 5.7%  | 665        | 10.5% |
| CRF                            | 1                 | 0.7%  | 7     | 1.6%  | 72    | 5.2%  | 788        | 12.5% |
| Lower respiratory infections   | 6                 | 4.1%  | 22    | 5.0%  | 77    | 5.6%  | 1009       | 16.0% |
| Tobacco use disorder           | 1                 | 0.7%  | 29    | 6.6%  | 94    | 6.8%  | 98         | 1.6%  |

<sup>a</sup> Cardiovascular diseases: I00–I99; ischemic heart disease I20–I25; COPD: J40–J44; CRF: J961; lower respiratory infections: J10–J18 J20–J22; tobacco use disorder: F17.  
COPD = chronic obstructive pulmonary disease;  
CRF = chronic respiratory failure.

TABLE 5.—Place of death according to year, sex, and age group among people 1 to 44 years of age with asthma as the underlying cause of death, France, 2000–2005.

|             | N   | Out-of-hospital deaths <sup>a</sup> |      |
|-------------|-----|-------------------------------------|------|
|             |     | n                                   | %    |
| Sex         |     |                                     |      |
| Men         | 335 | 221                                 | 66.0 |
| Women       | 250 | 139                                 | 55.6 |
| Age (years) |     |                                     |      |
| 1–4         | 17  | 9                                   | 52.9 |
| 5–14        | 39  | 19                                  | 50.0 |
| 15–24       | 92  | 51                                  | 55.4 |
| 25–34       | 142 | 79                                  | 55.6 |
| 35–44       | 396 | 202                                 | 68.2 |
| Period      |     |                                     |      |
| 2000–01     | 253 | 135                                 | 53.4 |
| 2002–03     | 182 | 125                                 | 68.7 |
| 2004–05     | 150 | 100                                 | 66.7 |
| Total       | 585 | 360                                 | 61.5 |

<sup>a</sup>Deaths occurred outside hospital (including emergency room), medical setting, or nursing home.

## DISCUSSION

In 2000–2005, asthma was listed as the underlying cause of death for 44% of death certificates that mentioned asthma (70% among children and young adults). Considering all conditions listed on the death certificate permits a better assessment of the overall burden of chronic diseases. The interest of a multiple-cause-of-death analysis has been highlighted for COPD that affects especially older adults with comorbidities (11, 13, 16).

Several studies have shown that mortality among older asthma patients is greater than among their counterparts without asthma, even when asthma is not the direct cause of death (17, 18). Chronic respiratory failure and other significant comorbidities are frequent among older adults with asthma and this disorder may contribute to death without being its underlying cause. Cause-of-death reporting may be less accurate among older people, and thus some deaths assigned to asthma may actually be due to COPD (19). Multiple-cause analysis thus provides additional information for adults over 45 years of age. For example, our study found for this age group that 20% of the death certificates reporting asthma as the underlying cause mentioned COPD or chronic respiratory failure and 46% mentioned cardiovascular disease. Conversely, COPD was the underlying cause of death for 11% and cardiovascular disease for 43% of deaths with asthma listed as an associated cause.

In children and young adults, several studies have shown the validity of death certificates reporting asthma as the underlying cause of death (20, 21). Asthma-related deaths in these groups mainly follow severe attacks in patients with poor preventative practices who delayed seeking medical attention (7, 22). Using the underlying cause of death alone thus seems satisfactory for describing asthma-related mortality rates and trends among young people.

Regardless of the definition used (underlying or multiple-cause), the age-standardized rates of asthma-related deaths in our study decreased from 2000 to 2005. The decline was more pronounced for underlying than for multiple-cause mortality. This may suggest that mortality directly attributable to asthma has in fact declined.

Another useful aspect of multiple-cause analysis is that it helps to interpret mortality trends when the rules for assigning the underlying cause have changed during the study period (9). In France, ICD-10 was implemented at the same time as an automated coding system that made it possible to record all causes mentioned on the death certificate. Because this major change in the number of causes registered in the database affected the trends of multiple-cause death rates for asthma between 1999 and 2000, we limited our analysis to the more recent period.

A decline in asthma mortality since the 1990s has been reported in several countries including France (1–4). One explanation is that asthma management improved substantially after the implementation of guidelines that include wide use of inhaled corticosteroids (5, 6, 23). Better diagnosis of COPD followed by more accurate cause-of-death certification may also partially explain the decrease in asthma-related mortality among older adults.

We described different patterns according to sex and age. Among people 1 to 64 years of age, mortality rates were slightly higher for men than women and the decrease over time was similar for both sexes. By contrast, among adults 65 years of age or older, the decline in mortality rates was less marked among women than men (respectively,  $-3.4\%$  and  $-8.7\%$  per year for underlying cause and  $-8.7\%$  and  $-11.1\%$  for multiple causes). Mortality rates in this age group have been higher in women than men since 2002. These various trends according to sex have been reported in several countries since the end of the 1980s (1, 3). In the US, standardized asthma mortality rates are higher for women than for men (10). The increase in women's smoking may explain in part the slower decline of asthma-related mortality rates among women. Tobacco exposure results in worse asthma attacks and is harmful to ventilatory function.

Our study highlighted the decline of in-hospital deaths, while the proportion of non-hospital deaths increased among younger decedents. In the past decade, mortality from severe asthma requiring admission to an intensive care unit has decreased in Australia (24). In France, the death rate among patients admitted for asthma decreased from 1998 through 2002 (25). Many factors may have played a role in improving the outcome of severe asthma episodes that require hospitalization, including better management in emergency care units (26) and the improvement of mechanical ventilation techniques.

More than half the deaths occurred outside a medical setting. These out-of-hospital deaths did not include those registered in the hospital after cardiorespiratory arrest at home with attempted resuscitation. Although out-of-hospital deaths from asthma are infrequent events, they suggest a major failure in the use of controller therapy and in appropriate seeking of medical care during exacerbations. They are particularly preventable (22, 27); indeed, they represent the ultimate measure of management failure. Their surveillance is not only relevant but also important.

In summary, the surveillance of asthma-related mortality based solely on the underlying cause of death is probably sufficient for children and young adults. Conversely, multiple-cause analysis provides additional information for characterizing the global burden of asthma-related mortality

among older adults. Regardless of the definition used (underlying or multiple cause of death), the age-standardized rates of asthma-related deaths decreased from 2000 to 2005 and the faster decline in mortality from asthma than in mortality with asthma demonstrates a real decline in mortality due to asthma.

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