



International Trends in Asthma Mortality Rates in the 5- to 34-Year Age Group*

A Call for Closer Surveillance

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Background: International time trends in asthma mortality have played an important sentinel role in the identification of two epidemics of asthma mortality in some countries in the 1960s and the 1970s and 1980s. Since then, little attention has been paid to the ongoing international time trends.

Methods: Country-specific data on asthma mortality rates since 1960 in the 5- to 34-year-old age group were collated. To be included in the analysis, countries were required to have data available prior to 1980. A scatter plot smoothing technique was used to model the change in asthma mortality rates with time.

Results: Asthma mortality rates from 20 countries were included in the analysis. An increase in asthma mortality rates was found in the 1960s, with a mean increase of 53% from 0.55 per 100,000 in 1960 and 1961 to a peak of 0.84 in 1966 and 1967. This trend was followed by a progressive decline to a nadir of 0.45 per 100,000 in 1974 and 1975. A gradual increase was then found in asthma mortality rates to a peak of 0.62 per 100,000 in 1985 and 1986, with a mean increase of 38% during this period. Since the late 1980s, there has been a widespread and progressive reduction in mortality rates to a level of 0.23 per 100,000 in 2004 and 2005, with a mean reduction of 63% during this period.

Conclusions: The widespread increase in asthma mortality in the 1980s and the subsequent, even greater reduction has largely gone unrecognized. We propose that awareness of such trends and their causes is important and that they are investigated contemporaneously.

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Key words: asthma; international; mortality; pharmacovigilance

Abbreviations: ICD = International Classification of Diseases; ICS = inhaled corticosteroid

International time trends in asthma mortality are inherently difficult to interpret because of the many factors that may change in different countries over time. Despite these difficulties, they have

played an important sentinel role in the identification of two epidemics of asthma mortality in some countries in the 1960s and the 1970s and 1980s.^{1,2} Investigation of these epidemics identified that the major causes were the overuse of high-dose, potent, poorly selective β -agonists isoprenaline and fenoterol, respectively^{3–6}; the consequent regulatory restriction of their use and other improvements in management led to a resolution of the epidemics.^{4,6,7} However, since then little attention has been paid to the ongoing international time trends despite continued concerns that have been expressed about the safety of β -agonist drugs, including the novel long-acting preparations^{8–10} and the evidence that the widespread use of inhaled corticosteroids (ICSs) has the potential to reduce asthma mortality.^{11–13} For these reasons,

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we have collated available data on asthma mortality rates for 20 countries since 1960.

MATERIALS AND METHODS

To be included in the analysis, countries had to have data available prior to 1980 to ensure that long-term trends in mortality could be determined. In accordance with standard practice, asthma mortality rates have been confined to the 5- to 34-year age group because the correct assignment of asthma mortality is firmly established in this group.¹⁴ Although most deaths occur in the older age group, the accuracy of asthma as the cause of death progressively declines with increasing age because of confounding with other respiratory disorders, such as COPD, or the presence of intercurrent medical conditions.

Asthma mortality data were obtained from the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research (or WONDER) Web site (<http://wonder.cdc.gov>), the Eurostat Web site (<http://epp.eurostat.ec.europa.eu>), and personal correspondence with representatives of the remaining countries. Deaths for asthma were certified according to the *International Classification of Diseases* (ICD) in use during that time period (codes 7 to 10), with the revisions having a minimal effect in the coding of the 5- to 34-year age group. For each country, the asthma mortality rates were expressed as the number of deaths due to asthma per 100,000 persons. A scatter plot smoothing technique suitable for noisy data was used to model the trends of asthma mortality rates with time. This technique, implemented using PROC LOESS (SAS Institute; Cary, NC),¹⁵ is a procedure that provides information on the form of a relationship between variables where it may not be easily described by conventional regression. The LOESS technique uses locally weighted regression across the range of the predictor variable (time) to generate a smooth fit to the data that is robust to the effect of outlying values.¹⁵ The degree of smoothing of the curve is determined by the width of the window determining the weighted average, with a wider window of data resulting in greater smoothness and a smaller window resulting in less.

RESULTS

Figure 1 shows asthma mortality rates for the 20 countries included in the analysis and the smoothed fit with 90% confidence intervals. The data set of the asthma mortality rates for the individual countries

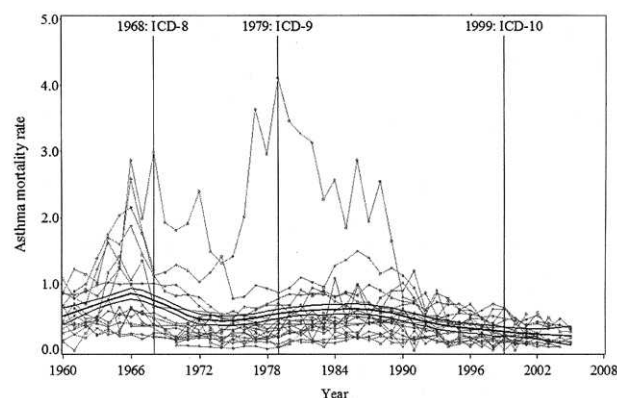


FIGURE 1. Asthma mortality rates (deaths per 100,000 persons 5 to 34 years of age) in 20 countries since 1960 (gray circles and interpolation) and the smoothed fit with 90% confidence intervals (black lines). The countries included are Australia, Austria, Belgium, Canada, Denmark, England and Wales, Finland, France, Germany, Hong Kong, Italy, Japan, the Netherlands, New Zealand, Norway, Republic of Ireland, Scotland, Spain, Sweden, and the United States. The ICD codes introduced during this period were ICD, 8th revision, in 1968, ICD, 9th revision, in 1979, and ICD, 10th revision, in 1999.

per year is shown in Table 1. There was a mean 53% increase in asthma mortality rates from 0.55 per 100,000 in 1960 and 1961 to a peak of 0.84 per 100,000 in 1966 and 1967 (see Table E1 in online supplementary material). This trend was followed by a progressive decline to a nadir of 0.45 per 100,000 in 1974 and 1975. A gradual increase in rates was found to peak at 0.62 per 100,000 in 1985 and 1986, with a mean increase of 38% during this period.

Since the late 1980s, there has been a widespread and progressive reduction in mortality rates to a level of 0.23 per 100,000 in 2004 and 2005. The magnitude of the reduction has been substantial, with a mean reduction of 63% in the countries included in this analysis. Although the reduction in mortality rates generally was consistent among countries, there was variation in the timing of its onset. For example, in England and Wales, mortality rates peaked at 0.99 in 1987, with a progressive decline to 0.33 in 2005, whereas in the United States, mortality did not peak until 1995, with a subsequent decline from 0.56 to 0.35 in 2005.

The smooth fit for the time trends in asthma mortality was very similar, with the exclusion of New Zealand, which experienced epidemics of asthma mortality in the 1960s and the 1970s and 1980s, and Australia, which experienced an epidemic of asthma mortality in the 1960s and had the highest rate of asthma mortality, after New Zealand, in the 1970s and 1980s (see Fig E1 in online supplementary material). This finding can be attributed to the regression technique used, which is robust to the effect of outlying values.

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