

**Speizer F E, Doll R & Heaf P.** Observations on recent increase in mortality from asthma. *Brit. Med. J.* 1:335-9, 1968. [Medical Res. Council of Great Britain, Statistical Res. Unit, and Univ. Coll. Hosp. Medical Sch., London, England]  
See also companion reference #3.

A dramatic increase in mortality in young people in England and Wales during the early 1960s was documented. In children ages 10-14, there was an eight-fold increase over seven years, and in 1966 asthma accounted for 7 percent of all deaths. [The SCJ® indicates that this paper has been cited in over 265 publications since 1968.]

Frank E. Speizer  
Department of Medicine  
Harvard Medical School  
Boston, MA 02115

March 4, 1985

As part of a postdoctoral fellowship in chronic disease epidemiology with Sir Richard Doll, I wanted to learn about the natural history and methods of treatment of asthma in Great Britain. In my search of the recent literature, I found a letter to *Lancet* written by a pediatrician that cited crude mortality statistics at all ages for asthma in England and Wales for the years 1950-1964.<sup>1</sup> There were very sharp changes that occurred at different times, and it was apparent that because of diagnostic uncertainty there was no way to use total mortality data to assess change in death rates. We therefore reasoned that there must be an age group in which no other disease that looked like asthma would either dilute or inflate the reporting rate. We rather arbitrarily settled on the age group of 5 to 34. (At about the same time, Gandevia in Australia had settled on 5 to 54 and was seeing a very similar phenomenon.<sup>2</sup>)

I spent several days with the modern-day equivalent of the "Bills of Mortality" to obtain the basic data by age and sex. At this point, the competence, effectiveness, and efficiency of British civil servants must be mentioned. We needed current data, and, with a phone call and meeting with the Registrar General, we had it. Within weeks, we were provided with copies of all the death certificates over several years that mentioned asthma.

From these we were able to document a very significant increase of coroner cases, i.e., sudden, unexpected deaths. From the Committee on Safety and Drugs, we received information on frequency of reported adverse drug reactions. From the College of General Practitioners, we obtained data on outpatient morbidity rates over several years.

In an attempt to identify potential risk factors, we set up a follow-up study of incident deaths from asthma. The results of that study were published as a companion to the paper being discussed and indicated an association between excessive use of pressurized spray containers of isoproterenol and excess mortality.<sup>3</sup>

There are probably three reasons this paper has been frequently cited. First, for teaching purposes the paper is an exposition on how one must be aware of the pitfalls in using death-certificate data over any extended period of time. Second, and far more importantly from a health perspective, this paper and its companion investigation led to immediate action. Because of these results, the Committee on Safety and Drugs, in 1967, aware of our preliminary findings, issued a warning to all physicians in Great Britain on the potential hazards of pressurized aerosol sympathomimetic preparations. In addition, certain preparations that formerly had been available "over the counter" were changed to prescription only, and a more potent preparation was removed from the market. Although cause and effect were never proven, in Great Britain, coincident with a fall in sales of the pressurized sympathomimetic preparations, there was a fall in mortality.<sup>4</sup> Finally, with a single telephone call to the Medical Research Council headquarters, Doll was able to arrange for approximately a dozen of the brightest and ablest workers in the country to be brought together for a day to discuss issues that ranged from clinical pharmacology, toxicology, cell physiology, and epidemiology to the treatment of asthma. These investigators went their own ways and have greatly improved our understanding of the mechanism of action of airway responsiveness to pharmacologic agents.<sup>5</sup> Unfortunately, "sudden and unexpected deaths from asthma" continue to occur,<sup>6</sup> and in general, the reason appears to be that neither patient, family, nor physician appreciates the potential dangers when usual forms of therapy do not provide appropriate relief.

1. Smith J M. Death from asthma. *Lancet* 1:1042, 1966. (Cited 35 times.)
2. Gandevia B. The changing pattern of mortality from asthma in Australia: 2. Mortality and modern therapy. *Med. J. Aust.* 1:884-91, 1968.
3. Speizer F E, Doll R, Heaf P & Strang L B. Investigation into use of drugs preceding death from asthma. *Brit. Med. J.* 1:339-43, 1968. (Cited 255 times.)
4. Inman W H W & Adelstein A M. Rise and fall of asthma mortality in England and Wales in relation to use of pressurized aerosols. *Lancet* 2:279-85, 1969. (Cited 195 times.)
5. Patterson J W. *Clinical pharmacology of inhaled isoproterenol*. Paper read at the 12th meeting of the European Society for the Study of Drug Toxicity, June 1970. Uppsala, Sweden.
6. British Thoracic Association. Deaths from asthma in two regions in England. *Brit. Med. J.* 285:1251-5, 1982.