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This work was supported by the Intramural Research Program of the National Institute of Allergy and Infectious Diseases and the National Cancer Institute, National Institutes of Health. This project has been funded in whole or in part with federal funds from the National Cancer Institute, National Institutes of Health, under contract no. HHSN261200800001E. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US government.

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interests.

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Available online April 6, 2016.

<http://dx.doi.org/10.1016/j.jaci.2016.03.016>

Adult but no pediatric anaphylaxis-related deaths in the Finnish population from 1996 to 2013



To the Editor:

The incidence of anaphylaxis-related deaths is estimated at 0.5 to 5.5 per million.¹ This corresponds to 0.65% to 2% of

anaphylaxis-related deaths among patients experiencing severe reactions.² We previously reported an increasing incidence of pediatric anaphylaxis-related hospitalizations in Sweden and Finland.³ However, the number of anaphylaxis-related deaths in these countries is not known.

To this end, we now aimed to investigate the epidemiology of anaphylaxis-related deaths in the Finnish population between 1996 and 2013 and to describe the causes of fatal anaphylaxis and the substances involved.

This study is based on the death certificates that form the basis of the Finnish Official Cause-of-Death Database. In Finland, the determination of the cause-of-death is based on medical or forensic evidence. The Finnish Official Cause-of-Death statistics are, in practice, 100% complete, as each death, its certificate, and the corresponding personal information in the Finnish computerized population register are cross-checked. The accuracy of the death certificates and their cause-of-death codes are further verified by autopsies, which are performed in 94% to 97% of accidental deaths.⁴ The cause-of-death codes used are based on the International Classification of Diseases. Herein, we included death certificates during the time period of version International Classification of Diseases, Tenth Revision (ICD-10), which was introduced in 1996.

From Statistics Finland, we obtained copies of the death certificates of all Finnish people who died between 1996 and 2013 because of anaphylaxis and/or allergic reactions (ICD-10 codes: T78.0-T78.4, T63, T88.6, and T88.7). The information in the death certificates was retrospectively analyzed to ascertain the proportion of the cases that fulfill the anaphylaxis criteria created by Sampson et al.⁵

The annual age-specific populations were obtained from Official Statistics of Finland. The incidence of anaphylaxis-related deaths (per 1,000,000 persons) was based on the results of the entire population of children and adults in Finland, rather than cohort- or sample-based estimates. As pediatricians in Finland treat mainly patients younger than age 16 years, herein, the term “child” refers to people younger than 16 years. Incidence rates of anaphylaxis deaths were estimated per 1,000,000 person-years along with 95% CIs by dividing the number of anaphylaxis deaths by the total number of person-years. Poisson regression was used to calculate statistical differences in incidences. Sex differences were compared using the chi-square test. The level of statistical difference was set at *P* less than .05. Statistical analysis was performed using SPSS 21.0 for Windows software (SPSS Inc, Chicago, Ill).

During the 18-year study period, 56 Finnish adults and no children died from anaphylaxis. The annual number of anaphylaxis-related deaths among the Finnish population ranged from 1 to 7 and the incidence of deaths ranged from 0.19 to 1.28 per million person-years (Fig 1). There was a secular trend toward an increased incidence of anaphylaxis-related deaths during the period (*P* < .04). The analysis of data in 3-year periods indicated a trend toward an increased incidence of anaphylaxis deaths in the latter years of the study (2005-2013) (Fig 1). The cumulative incidence of anaphylaxis deaths was 0.59 per million person-years.

In total, the proportion of anaphylaxis-related deaths was 61% in men and 39% in women, most of which occurred at health care units (29%), homes (25%), and summer cottages (13%). The mean age at the time of death was 59.0 years (range, 17-83 years). Only 1 patient was younger than 20 years (a 17-year-old Finnish girl who died while abroad as a result of a food-induced

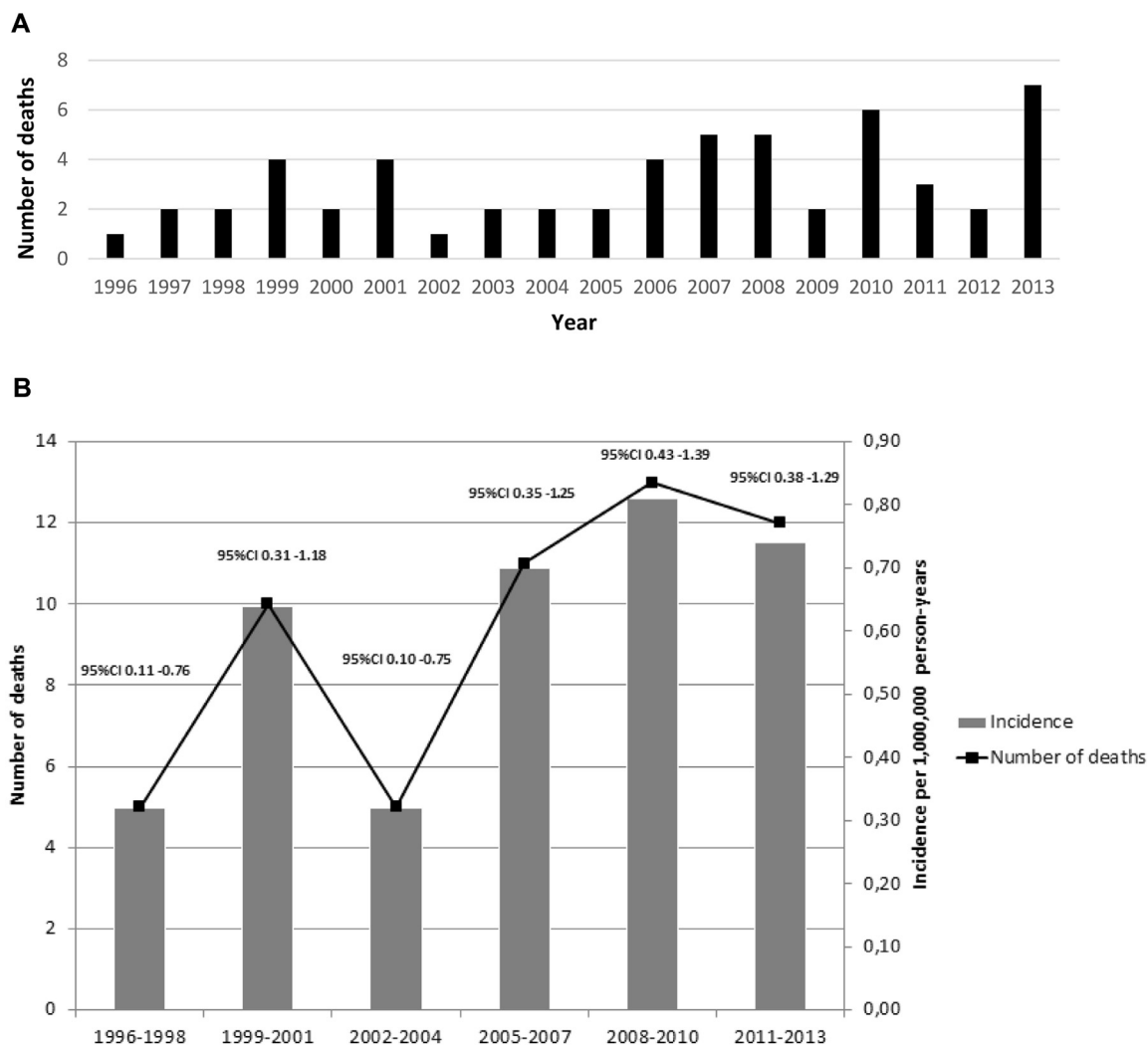


FIG 1. Annual number of anaphylaxis-related deaths (A) and the number, incidence (per 1,000,000 person-years), and 95% CIs of anaphylaxis-related deaths in the Finnish population between 1996 and 2013, in 3-year periods (B).

TABLE I. The causes of anaphylaxis-related deaths and distribution by age in the Finnish population from 1996 to 2013

Agents	Age < 16 y, n (%)	Age 16-64 y, n (%)	Age ≥ 65 y, n (%)	Total, n (%)
Pharmaceuticals	0 (0.0)	14 (37.8)	8 (42.1)	22 (39.3)
Analgesics	—	2 (5.4)	—	2 (3.6)
Anesthetics	—	4 (10.8)	—	4 (7.1)
Antibiotics	—	1 (2.7)	3 (15.8)	4 (7.1)
Antineoplastic and immunomodulating agents	—	1 (2.7)	—	1 (1.8)
Cardiovascular system	—	1 (2.7)	—	1 (1.8)
Contrast agents	—	2 (5.4)	2 (10.5)	4 (7.1)
Blood and blood-forming organs	—	—	1 (5.3)	1 (1.8)
Local anesthetic	—	2 (5.4)	—	2 (3.6)
Other pharmaceutical	—	1 (2.7)	2 (10.5)	3 (5.4)
Nonpharmaceuticals	0 (0.0)	23 (62.1)	11 (57.9)	34 (60.7)
Insect stings	—	16 (43.2)	7 (36.8)	23 (41.1)
Food	—	3 (8.1)	2 (10.5)	5 (8.9)
Snake bite	—	—	1 (5.3)	1 (1.8)
Plant	—	—	1 (5.3)	1 (1.8)
Unknown	—	4 (10.8)	—	4 (7.1)
Total	0 (0.0)	37 (66.1)	19 (33.9)	56 (100.0)

Pharmaceutical agents were classified according to the Anatomical Therapeutic Chemical Classification System.

anaphylaxis). The most common cause of anaphylaxis-related deaths was insect stings (41%). Other common causes were food (9%), antibiotics (7%), and contrast agents used in radiology (7%) (Table 1). Anaphylaxis-related deaths resulting from wasp stings were more common among men (53%) than among women (18%) ($P = .03$).

Most patients had sudden loss of consciousness (89%) after allergen exposure and suffered from respiratory compromise (70%). Persistent gastrointestinal symptoms were present in 55% of the patients. In total, 93% of the patients fulfilled the anaphylaxis criteria created by Sampson et al.⁵

The present study shows low, but slightly increasing incidence of anaphylaxis and an absence of anaphylaxis-related pediatric deaths in Finland between 1996 and 2013. In a previous study of pediatric out-of-hospital cardiac arrests in Finland between 1985 and 1994, none of these deaths was attributable to anaphylaxis,⁶ thereby providing further evidence that anaphylaxis-related deaths in the Finnish pediatric population are very rare. Likewise, asthma mortality in Finnish children is also rare.⁷ The reason for the absence of fatal anaphylaxis among children is unclear, but it is tempting to speculate that this is partly attributable to good asthma care among pediatric population.⁸ The slightly increasing trend of anaphylaxis-related deaths may relate to the increasing burden of allergic diseases among Finnish adults.⁹

This study also provides important information on the trends in anaphylaxis-related deaths in a well-defined population. Comparable studies from other countries investigating the secular trends of anaphylaxis-related deaths are scarce.¹ One major strength of our study is that 93% of the patients fulfilled the anaphylaxis criteria created by Sampson et al,⁵ despite the fact that our study period predates these criteria by a decade. Furthermore, the internationally recognized Anatomical Therapeutic Chemical classification system was used to classify the pharmaceutical agents. Moreover, our study is based on nationwide data because the death certificates for anaphylaxis-related deaths were extracted from a registry that covers virtually all deaths in Finland.

The present study also has some limitations. Anaphylaxis is often an unclear event. We acknowledge that ICD-10 coding may not have identified all cases. Similarly, it has been estimated that even Sampson et al's criteria will not capture all cases of anaphylaxis.⁵ Moreover, severe anaphylaxis events may not always be witnessed and/or the causing substance may be unidentified. Furthermore, because data were based on death certificates, information on the circumstances surrounding anaphylaxis-related deaths was somewhat limited.

In conclusion, a total of 56 Finnish adults, but no children, died from anaphylaxis between 1996 and 2013. This corresponds to a total incidence of 0.59 per million person-years. There was evidence of slightly increasing trend over time. Slightly more

Finnish men than women died from anaphylaxis during this time. Medications and insect stings caused 80% of anaphylaxis deaths. Most anaphylaxis-related deaths occurred at home or a health care unit.

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The project has received funding from Tampere Tuberculosis Foundation, Väinö and Laina Kivi Foundation, and the Karin and Sten Mörtstedt Initiative on Anaphylaxis. Disclosure of potential conflict of interest: J. E. Kivistö receives research support from Tampere Tuberculosis Foundation and Väinö and Laina Kivi Foundation. J. Karjalainen serves as a consultant for GlaxoSmithKline, Novartis, and Teva; receives payments for lectures from Boehringer Ingelheim, GlaxoSmithKline, Mundipharma, Novartis, Orion, Takeda, and Teva; and receives travel support from Boehringer Ingelheim and Teva. The rest of the authors declare that they have no relevant conflicts of interest.

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Available online June 21, 2016.
<http://dx.doi.org/10.1016/j.jaci.2016.05.015>