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Epidemiology of asthma: ISAAC – International Study of Asthma and Allergies in Childhood

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Despite considerable research efforts, the aetiology of childhood asthma and allergic disease remains poorly understood. Moreover, there is evidence that atopic diseases are on the increase in western countries in recent decades. Epidemiology has the potential to add greatly to our understanding by elucidating risk factors for the development of disease. However, lack of standardisation in case-definition and methodology has so far limited the full potential of epidemiologic studies for temporal and spatial comparisons. ISAAC, the International Study of Asthma and Allergies in Childhood, was founded to maximise the value of epidemiological research into asthma and allergic disease by establishing a standardised methodology and facilitating international collaboration (1, 2). Its specific aims are:

1. Describe the prevalence and severity of asthma, rhinitis and eczema in children living in different centres and to make comparisons within and between countries.
2. Obtain baseline measures for assessment of future trends in the prevalence and severity of these diseases.
3. Provide a framework for further aetiological research into genetic, lifestyle, environmental and medical care factors affecting these diseases.

Relevant themes

Study design

The ISAAC study design comprises three phases. Phase 1 is a compulsory core study to assess the prevalence and severity of asthma and allergic disease in defined populations. Phase 2 is being developed and will involve studies in informative centres of aetiological factors, particularly those suggested by the findings of Phase 1. In addition to questionnaires, Phase 2 will involve objective measures of disease and exposure. Phase 3 will be a repetition of Phase 1 after several years.

In Phase 1, collaborating centres have been recruited from around the world through scientific networks, focusing on locations of particular interest. Participating research centres recruited a random sample of 3,000 children aged 13–14 years. Ascertainment of schoolchildren was through school class registers. Children were then asked to complete the ISAAC core questionnaires on asthma, rhinitis and eczema. Case-definitions and severity were established by asking about cardinal symptoms, not by reference to labels or diagnoses, although these have also been recorded. It was strongly recommended, but not compulsory that the children also complete a video questionnaire on asthma. In addition, it was strongly recommended, but not compulsory, that each centre also recruit a sample of 3,000 children aged 6–7 years. Their parents were asked to complete the ISAAC core questionnaires on asthma, rhinitis, and eczema. The video questionnaire was not administered to this age group.

Questionnaires

For Phase 1, three one-page written ISAAC core questionnaires have been developed by the ISAAC collaborators. They include 8 questions on wheeze, 6 questions on rhinitis and 6 questions on eczema. The wording of questions follows, as far as possible, questions which have been used on published questionnaires and which have found differences between populations. These questions were designed as a minimum set for inclusion in self-completed or interview-administered questionnaires used in population surveys of allergic or skin disease in children.

In response to translation problems with questions on "wheeze" or "whistling from the chest" in written questionnaires, a video questionnaire has been developed and validated in Wellington, New Zealand (3). The video questionnaire involves 5 sequences of asthma symptoms in young persons; three sequences involve various scenes of wheezing (while at rest, after exercise and at night) whereas the final two sequences involve other asthma symptoms (waking at night with cough, a severe attack of asthma). After each sequence, students are asked to write down their answers to questions presented on the video.

In addition to the ISAAC core questionnaires supplementary questionnaires on other respiratory symptoms (cough, phlegm, breathlessness), and on the clinical management of asthma, wheezing, hay fever, rhinitis and eczema have been developed. These should enable investigators to refine case-definition by distinguishing between symptoms due to asthma and other common respiratory disorders, and to examine the distribution of other respiratory conditions in their own right, particularly where the health effects of ambient air pollution are of concern. The questions on disease management focus on medication, management and health care utilisation. They aim at describing patterns of therapy and management of asthma exploring the relationship between treatment and morbidity, and at comparing therapy between countries and over time.

Child contact modules

Several child contact modules on skin tests for atopy, serum IgE tests, blood sampling, storage of dried blood spots for genetic analyses, bronchial responsiveness to hypertonic saline, and examination for flexural dermatitis have been developed for Phase 2 ISAAC. Skin prick tests will be performed using the ALK lancet and 6 "core" allergen extracts, i.e. house dust mites (*Dermatophagoides pteronyssinus* and *farinae*), cat fur, mixed grass pollen, mixed tree pollen and the outdoor mould genus *Alternaria tenuis*. Bronchial provocation tests will use a hypertonic saline challenge according to the ISAAC protocol. Additional modules on blood sampling, serum IgE testing and blood storage have been developed. Furthermore, a module on direct examination of the skin for visible flexural dermatitis offers a potentially useful tool for standardized comparisons of atopic eczema prevalence between centres.

Environmental modules

A protocol for dust collection for aeroallergen analysis has been developed to determine allergen content in dust from homes, day care centres and schools. It involves a description of the equipment, the site and time of collection, the procedure, the extraction and processing of dust, and allergen analysis.

In a pilot survey ISAAC written and video questionnaires have been administered to schoolchildren, aged 12–15 years, in five areas in four countries: in Adelaide (n=1428), Australia; Sidney (n=1519), Australia; West Sussex (n=2097), England; Bochum (n=1928), Germany; and Wellington (n=1863), New Zealand (4). The self-reported prevalence of wheeze during the past 12 months was lower in Germany than in all other centres using results of written and video questionnaires. The one year prevalence of severe speech-limiting wheeze was higher in Wellington (11%), Adelaide (10%) and Sydney (13%) as compared to West Sussex (7%) and Bochum (6%). The self-reported prevalence of frequent attacks, frequent nocturnal wheezing, and doctor-diagnosed asthma during the past 12 months was also higher in the Australasian centres than in the European centres.

In December 1995 more than 120 centres around the world had submitted data of Phase 1 to the ISAAC data coordinating centre in Auckland, New Zealand. Basic descriptive summaries will be compiled and presented for each condition in both age groups in the near future. An ecological analysis will be undertaken using information on the geographical, environmental and ethnic characteristics of each centre. Furthermore, data will also be analysed within each country.

The ISAAC Steering Committee is further proposing a coordinated international study which will follow completion of Phase 1 data analysis. This next study will investigate variations in prevalence which emerge from Phase 1. Comparisons between centres will be undertaken, using objective measures of disease, and assessment of environment, lifestyle, and clinical management. Populations which are potentially informative will be chosen, such as those with contrasting prevalence of disease, environmental exposures, management or genetic factors.

Conclusions

The ISAAC initiative provides a standardized methodology to determine the prevalence and severity of asthma and allergies in childhood. It has attracted worldwide interest and large-scale participation. In the near future, results of Phase 1 worldwide will contribute to a better understanding of disease prevalences around the world.

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