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INTERNATIONAL

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STUDY OF

A

ASTHMA AND

Manual

S

ALLERGIES IN

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CHILDHOOD

Auckland (NZ) / Münster (FRG)

December 1993 (2nd edition)

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1.0 What is ISAAC?

1.1 Purpose

The aetiology of asthma and allergic disease remains poorly understood despite considerable research. Epidemiology has the potential to add greatly to our understanding by elucidating the risk factors for asthma and allergic disease and thereby suggesting productive avenues for research into causation. Epidemiological studies have so far failed to reach their full potential because of lack of standardisation in case-definition and methodology which limits the value of spatial and temporal 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. Its specific aims are to:

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.

1.2 Overview of study design

The ISAAC study design comprises three phases. Phase I is a compulsory core study designed to assess the prevalence and severity of asthma and allergic disease in defined populations. Phase II, which has yet to be developed, will investigate possible aetiological factors, particularly those suggested by the findings of Phase I. Phase III will be a repetition of Phase I after a period of three years.

This document is primarily concerned with Phase I. In this Phase each research centre should recruit a random sample of 3000 children aged 13-14 years. Children will be ascertained through school class registers and asked to complete the ISAAC core questionnaires on asthma, rhinitis and eczema. Case-definitions and severity are established by asking about cardinal

symptoms, not by reference to labels or diagnoses (although these will be recorded). It is strongly recommended, but not compulsory, that the children also complete a video questionnaire on asthma. The video questionnaire was developed in response to translation problems with written questionnaires and obviated the need to describe symptoms verbally. The validity of the research instruments has been investigated.

It is strongly recommended, but not compulsory, that each centre also recruit an additional sample of 3000 children aged 6-7 years. Children will be identified through school class registers and their parents asked to complete the core questionnaires on asthma, rhinitis, and eczema. The video questionnaire will not be administered to this age group.

It is envisaged that certain research centres may wish to incorporate the ISAAC core protocol into a larger or more focused investigation of asthma and allergy. The ISAAC core protocol has therefore been designed to accommodate additional questionnaire material and supplementary investigations.

A detailed description of the scientific background, protocol, and development of instruments is provided below.

1.3 Requirements for participants

1. Prospective research centres must produce a detailed research protocol showing how the ISAAC Phase I protocol will be implemented locally. Key issues to be addressed include: the method for sampling schools; the geographical definition of the centre; the approach to ethnic group comparisons if these are being made; the season of data collection; if appropriate, method of translating ISAAC core questionnaire into other language(s); evidence that ethical and other necessary permissions have been granted.
2. Each research centre is responsible for obtaining its own funding.
3. Each centre is responsible for coding and entering its own data. A copy of the data required for international and inter-regional comparisons must be made available in suitable electronic form to the ISAAC executive for analysis at the designated data centre.
4. Each centre may publish its own data without the approval of ISAAC. All publications and communications arising from

comparisons of more than five international centres require the approval of ISAAC and will be authored by ISAAC whose participants will be identified.

We invite the widest possible participation in ISAAC, and welcome interested investigators to participate in the development of further studies. Investigators with research experience in the epidemiology of asthma and/or allergic diseases are particularly encouraged to join ISAAC. Research centres able to access distinctive populations (by virtue of their geography, race and/or ethnic characteristics) are similarly welcome.

2.0 Development and administration of the project

2.1 History

ISAAC emerged from pre-existing multinational collaborations regarding childhood asthma epidemiology including:

- October 1989 – Development of standardised questionnaire for measuring asthma prevalence in the UK (London), New Zealand (Auckland), and Australia (Melbourne).
- May 1990 – Investigators in Auckland, New Zealand, approached experienced investigators in five countries to establish a collaborative group interested in conducting international comparative studies of asthma severity in children.
- December 1990 – An international workshop on monitoring trends and determinants of asthma and allergies was convened in Bochum, Germany. Interested researchers from Germany, UK (London), New Zealand (Wellington), and the USA established a collaborative group to develop a standardised protocol.
- March 1991 – Merging of the Auckland and Bochum initiatives.
- June 1991 – Formation of a steering committee for the organisation of international collaborative studies of childhood asthma and allergies. The countries represented included New Zealand (Auckland, Wellington), UK (London), and Germany (Bochum).
- December 1991 – Second international workshop on monitoring trends and determinants of asthma and allergies was convened in

Bochum, Germany, to finalise a standard protocol for research. Presentation of the pilot study involving Wellington, Bochum, London, Sydney and Adelaide. Steering Committee was extended to include USA (Tucson).

- December 1992 – Third International Workshop on International Study of Asthma and Allergies in Childhood in London.

2.2 Organisational structure

General approach

The organisation of ISAAC consists of four levels:

- the Steering Committee (including the Executive)
- regional coordinators
- national coordinators
- collaborating centres

The general approach is that, in a particular region, a regional coordinator is appointed by the steering committee, who then recruits national coordinators. A regional meeting of national coordinators is held to organise the implementation of Phase I in the region. The national coordinators then complete the recruitment of collaborating centres in their own countries and a national meeting is held prior to the start of data collection. This general approach is flexible. For example, many European centres have already started data collection, or are about to start, and some instances a national meeting has already been held.

Collaborating centres

The responsibilities of the collaborating centres are to:

- complete the registration form
- liaise with the national coordinator
- carry out Phase I according to the protocol in the manual
- forward a “clean” data set to the national coordinator

National coordinators

The national coordinators are generally responsible for a single country. However, in some instances they may be responsible for several small neighbouring countries, particularly if these only have one collaborating centre and/or if no suitable national coordinators are available.

The responsibilities of the national coordinators are to:

- recruit and register collaborating centres
- organise translation and production of the Phase I manual and questionnaires
- organise a national meeting of collaborating centres to organise the implementation of Phase I
- liaise with the collaborating centres and provide assistance when required, including “cleaning” of the data
- liaise with the regional coordinators
- check and forward the “clean” national data sets to the regional coordinators
- organise a further national meeting of collaborating centres to discuss the results of Phase I

Regional coordinators

The regional coordinators are responsible for a broad region of the world. The regions will generally be based on the six WHO regions of the world, since these are widely used and logically organised. However, in some instances a WHO region may be split into sub-regions, if the number of collaborating centres or countries is large.

The ISAAC regions are currently as follows:

| WHO region | ISAAC region |
|-----------------------|--|
| Europe | Western Europe Eastern Europe/Baltics |
| Americas | North America Latin America |
| Africa | Africa |
| South East Asia | South East Asia |
| Western Pacific | Asia-Pacific Oceania |
| Eastern Mediterranean | Eastern Mediterranean |

The responsibilities of the regional coordinators are to:

- recruit national coordinators
- help national coordinators with translation and production of the Phase I manual and questionnaires, and approval of the final version before use
- organise a meeting of national coordinators to organise the implementation of Phase I (prior to the national meetings specified above)
- assist with national meetings
- liaise with national coordinators and provide assistance when required, including official feedback from the Steering Committee, and checking of national data sets
- liaise with the Steering Committee, and participate in meetings of the Extended Steering Committee
- organise a further meeting of national coordinators to discuss the results of Phase I and to plan Phase II

The Steering Committee

The Steering Committee has recently been expanded and now includes the Regional Coordinators, and the Module Leaders (of the various Phase II

modules that are under development), in addition to the original members of the Steering Committee.

The responsibilities of the Steering Committee are:

- recruit regional coordinators
- assist with the regional meetings
- liaise with regional coordinators and provide assistance when required
- coordinate the implementation and conduct of Phase I
- organise the further development of modules and methods for Phase II
- coordinate the analyses and publications of data
- organise future international ISAAC meetings

The full Steering Committee will meet annually.

The Executive

The ISAAC study is coordinated on a day-to-day basis by a three-member executive. The current executive consists of:

- Dr. Innes Asher (Data Coordination)
- Prof. Richard Beasley (Implementation of Phase I)
- Dr. David Strachan (Methods Development)

The Executive is chaired by Dr. Asher.

2.3 Funding

Each research centre is responsible for obtaining its own funding. At the time of writing, funding has been successfully obtained from the Health Research Council of New Zealand for three New Zealand centres, from the Locally Organised Research Fund of the Department of Health in England for one English centre, and from the Ministry for Work, Health and Social Affairs of the German State of North Rhine-Westphalia for one German centre. In France three centres obtained complete and another three centres obtained partial funding. In Italy two centres are funded and in Spain

funding has been obtained for four centres. Funding support is expected to be obtained in the near future for a number of other centres.

3.0 Scientific background

There is considerable concern regarding a possible increase in the prevalence and incidence of asthma and allergies in Western countries.

3.1 Asthma

Asthma is one of the most important diseases of childhood in developed countries. Estimates of the 12 month period prevalence of parent reported wheezing illness vary greatly but range from 10-15% in the UK to 30% in Australasia and amongst these, the proportion with a diagnosis of asthma ranges from 30-70%. About one third of those affected by asthma experience restriction of activities and loss of school. Anti-asthmatic drugs are the most frequently used prescribed therapy in childhood. There is evidence that the prevalence and severity of asthma is increasing. Hospital admissions have increased to a greater degree in many countries and this has been attributed both to changes in medical practice and changes in prevalence. A number of countries experienced epidemics of mortality in the 1960's and subsequently a further epidemic occurred in New Zealand.

At national and to a lesser extent sub-national level there are geographical variations in prevalence, mortality and hospital admissions. The cause of these regional variations is unknown. It is known that genetic factors predispose to asthma and other atopic disorders but migrant studies indicate that the reasons for regional variations are environmental rather than genetic. An environmental factor might act either by "inducing" the asthmatic tendency in a genetically susceptible individual or by "inciting" attacks in individuals who have become asthmatic. Little is known about inducing factors and while something is known about inciting factors (infection, allergens, inhaled irritants, emotion, exercise), their role in explaining regional differences is obscure. There is general concern that factors associated with modern lifestyle and environment (e.g. air pollution or diet) may be responsible but evidence is meagre. A further complication is the possibility that some forms of treatment might themselves be increasing mortality and morbidity.

3.2 Rhinitis

There are no widely agreed criteria for the diagnosis or classification of non-infectious rhinitis. The principle symptoms of non-infectious rhinitis are sneezing, running nose (rhinorrhea), and/or nasal blockage. Patients are generally classified according to the suspected aetiology of their condition into allergic and non-allergic types. Rhinitis is labelled “allergic” when a causative allergen can be identified. Otherwise it is labelled “non-allergic”. This approach to classification is problematic in that it is impossible to be certain that a non-allergic subject would not prove reactive to some allergen yet to be examined.

Surprisingly little is known about the prevalence or distribution of rhinitis. Very few studies have used standardised case definitions and the majority have focused on hayfever (seasonal allergic rhinitis) leaving other forms of the condition unstudied. The estimated prevalence of hay fever among school children in different countries has been reported to vary between 0.5 and 28%. There is also evidence the prevalence of hay fever may vary between different geographical regions within countries. Britain, Sweden and the United States have reported increases in the prevalence of diagnosed hay fever in recent decades. Possible explanations for differences in prevalence over time and between places, include differences in the diagnostic criteria of doctors, differences in patients' consulting behaviour, and differences in putative environmental provoking factors (e.g. aeroallergen burden, air pollution).

3.3 Eczema

Little is known about the epidemiology of eczema or atopic dermatitis. However, geographical variations in prevalence have been described in Britain and these closely match regional variations in hayfever. This suggests within-country variation in the underlying atopic tendency. Comparisons over time in Britain and Denmark have suggested that eczema (as reported by parents) is more common among more recent generations of children.

In theory, eczema is more readily confirmed by objective tests than either asthma or rhinitis. However, there are currently no internationally accepted criteria for definition of atopic dermatitis. A list of major and

minor criteria proposed by Hanifin and Rajka in the 1970s have been further evaluated and widely applied in clinical studies but have not been defined and standardised in a manner suitable for epidemiological studies. A team of British dermatologists are currently developing and validating definitions of atopic dermatitis based on questionnaire data with or without clinical signs. The former, which correspond closely to the major criteria proposed by Hanifin and Rajka, have been incorporated into the initial phase of the present study.

3.4 Significance of the proposed study

Much research has been conducted into the reasons why some individuals rather than others develop asthma and other atopic diseases such as rhinitis and eczema. The main finding has been that a family history of atopic disease is a major risk factor. Environmental factors nevertheless remain important in the expression of disease but studies at an individual level have had rather limited value in identifying what those factors are. Another approach is to investigate why the level of disease varies from population to population. Factors affecting the prevalence of disease at a population level may be different. Indeed there are some factors which can only be studied in this way because whole populations may be fairly evenly exposed to the factor, thus precluding epidemiological study within the population. There is little firm evidence concerning the reasons for trends in atopic disease (and of atopic status per se) within populations. One obstacle to the investigation of population differences (and of trends) has been the lack of a suitable and generally accepted method of measuring the prevalence and severity of asthma and other atopic diseases in children. The other obstacle has been the absence of a coordinated research programme to obtain and analyse comparative data. The ISAAC study has been developed to address these questions.

4.0 Aims and Objectives

1. To 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. To obtain baseline measures for assessment of future trends in the prevalence and severity of these diseases.

3. To provide a framework for further aetiological research into lifestyle, environmental, genetic and medical care factors affecting these diseases.

5.0 Methods

5.1 Overview

The collaborative studies will be conducted in three phases. Phase I is the core study described in detail here. Phase II involves more detailed studies of aetiological factors and clinical examination of subgroups of children. Phase III will be a repetition of Phase I after three years.

5.2 Collaborating centres

5.2.1 Countries

This will be a multicentre study, involving as many centres and countries as wish to collaborate who can meet the requirements of the study protocol. It is hoped that many countries will have at least two centres participating to enable a within country comparison as well as between country comparisons.

5.2.2 Research centres

An ISAAC research centre is a distinctive population in terms of its geography, race and/or ethnic characteristics, where one or more named investigators have agreed to follow the ISAAC study protocol described in this manual. Where existing data suggest regional differences in asthma or allergic diseases, participation of these centres will be of particular value. The sample of children taking part in ISAAC should not previously have been recruited systematically for research into asthma or allergies (although individual children may have been so involved). However, investigators may wish to use ISAAC as the first stage in new local research about these conditions.

5.2.3 Investigators

Investigators who have experience with asthma or its epidemiology, especially in children, are particularly encouraged to join ISAAC.

5.3 Subjects

5.3.1 Selection

The population of interest is school children within a given geographical area. A random sample of two age groups of children will be studied: 13-14 year olds and 6-7 year olds. The sampling unit will be a school for each age group. Each school in the centre which would contain the age group of interest will be allocated a number, and the schools will be selected using a table of random numbers. Sampling of each age group will be separate. Once a school has been chosen, two school years will be chosen which include those with the greatest proportion of 13 year olds and 14 year olds; those with the greatest proportion of 6 year olds, and 7 year olds. It is recognised that there will be some children outside the specified age ranges in each class chosen. These children may be included in the data collection, but will be excluded from analysis for the international comparison.

The younger age group has been chosen to give a reflection of the early childhood years, when asthma is common, and admission rates are particularly high. However some centres may not have the resources to proceed with the younger age group. The older age group has been chosen to reflect the period when mortality from asthma is more common. School children are the most accessible people of any age group.

A minimum of 10 schools (or all the schools) per centre are needed to obtain a representative sample. If a selected school refuses participation, then the school will be replaced by another chosen at random. No eligible children will be excluded from the sample.

If a school for disabled children (e.g. blind, intellectually handicapped) is chosen, they will be studied. However it is acknowledged that there may be a disproportionate number of children of the 13-14 year age group who are unable to participate in such a school. This would be one reason for non-participation.

5.3.2 Ethnic group and gender

Where comparisons between ethnic groups are planned, the question on ethnicity should preferably follow that used in the most recent Census of

Populations in the individual centre. There will be a question to identify the gender of the child.

5.3.3 Sample size

The aim is to detect differences, if they exist, which are meaningful clinically, epidemiologically, economically and for health service delivery. The sample size required to detect differences in severity of asthma is higher than that required to detect the same magnitude in differences in prevalence of asthma because severe asthma is less common. The sample size estimates are stringent because of the number of hypotheses being tested and the need to be certain of the results in such a major study. A sample size of 3000 has been chosen, which gives the following power:

1. Prevalence of wheezing

If the true one year prevalence of wheezing is 30% in one centre and 25% in another centre, with a sample size of 3000, the study power to detect this difference will be 99% at the 1% level of significance.

2. Severity of wheezing

If the true one year prevalence of severe asthma is 5% in one centre and 3% in another centre with a sample size of 3000 the study power to detect this difference will be 90% at the 1% level of significance.

It is recognised that some centres may have limited resources or populations but it is nevertheless desirable for them to be included in the prevalence comparisons. Centres with sample sizes in the range of 1000-2999 will only be included in the prevalence comparisons but not the severity comparisons. This summary table of sample size and power considerations shows the effect of changing sample size on the power of detecting differences in the prevalence of asthma:

Sample size and power considerations

Table 1a

| Prevalence of troublesome asthma | | | | |
|--------------------------------------|-------------------------|-----------|---------|---------|
| POWER (%) (significance level 1%) | Difference being tested | | | |
| Sample size | 5% v 3% | 5.5% v 3% | 6% v 3% | 6% v 4% |
| 3000 | 90 | 98 | 99 | 82 |
| 2500 | 83 | 95 | 99 | 72 |
| 2000 | 71 | 89 | 97 | 60 |
| 1500 | 55 | 70 | 90 | 44 |
| 1000 | 34 | 53 | 71 | 26 |

Table 1b

| Severity of sleep disturbance due to wheezing | | | |
|---|--|------|------|
| Sample size (significance level 1%) | Difference being tested (% population who are in a different response category, e.g. never woken with wheeze, woken less than one night per week) | | |
| Power (%) | 20% | 25% | 30% |
| 90 | 3000 | 2100 | 1500 |
| 80 | 2500 | 1700 | 1200 |
| 70 | 2150 | 1400 | 1000 |
| 60 | 1800 | 1200 | 900 |

5.4 Study design

5.4.1 Details of Phase One core modules

Three one page questionnaires have been developed by the current collaborators. These were agreed for use at the International Study of Asthma and Allergies in Childhood at a workshop in Bochum, Germany, 8-10 December 1991. The aim of compiling a "core" questionnaire is to ensure that comparable information on the basic epidemiology of wheezing illness and its diagnosis is obtained from as many surveys as possible. The exact wording of questions follows, as far as possible,

questions which have been used on published questionnaires and which have found differences between populations.

It is anticipated that individual investigators may wish to supplement them with questions of their own, but they should endeavour to retain the general form of the questionnaire, including the flow and stemming, as indicated. Any additional questions should come at the end of the four core modules. Consideration must be given to the effect this may have on participation.

In Section 7, the core questionnaires are presented, along with a commentary about their development and validation. The 13-14 year olds will be presented with the written questionnaires on wheezing, rhinitis and eczema, and if feasible, the video questionnaire. Investigators are also encouraged to recruit the sample of 6-7 year olds, whose parents will be asked to complete the appropriate written questionnaires on wheezing, rhinitis and eczema. The following outline summarises this design:

| <u>Phase I Modules</u> | <u>13-14 years</u> | <u>6-7 years</u> |
|------------------------------|----------------------|----------------------|
| 1.1 Core quest. on wheezing | compulsory | strongly recommended |
| 1.2 Core quest. on rhinitis | compulsory | strongly recommended |
| 1.3 Core quest. on eczema | compulsory | strongly recommended |
| 1.4 Video quest. on wheezing | strongly recommended | not used |

5.4.2 Plans for Phase Two Supplementary Modules

The December 1992 London meeting established working groups with a coordinator to develop the instruments for Phase II. This manual covers only Phase I, but collaborators are invited to contribute to the design of Phase II instruments. It is envisaged that there will be at least the following modules:

Module 2.1: Management – medications
 – health service delivery

Module 2.2: Indoor environmental risk factors
 – physical conditions
 – chemical irritants
 – allergens

Module 2.3: Other respiratory symptoms

Module 2.4: Bronchial responsiveness testing

Module 2.5: Skin tests for atopy

Module 2.6: Serum IgE

Module 2.7: Physical examination

Development of these modules will include pilot studies in some centres.

It is anticipated that there will be future phases of the study, probably including the following: repeat prevalence and severity studies; cohort follow-up studies; case control studies.

5.4.3 Season of data collection

It is recognised that the season of the year may influence the reported prevalence of symptoms of rhinitis or eczema. However there is little evidence that the reported one year prevalence of symptoms of asthma varies over seasons from studies which have included Autumn, Winter, and Spring. Analysis of data in adults (Wellington, New Zealand), young adults (London, United Kingdom) and in children (Munich, Federal

Republic of Germany) shows no significant monthly variation in the reported one year prevalence. The date of data collection must be documented and at least half of the study population should be investigated before the main pollen season of the study area.

5.5 Non-participation

A participation rate of at least 90% will be sought. It is a concern that absent children may be away from school because of asthma or allergies. Therefore strenuous efforts need to be made to contact these children and offer the opportunity of participation in the study. In the case of children where consent has been refused, demographic data (age, sex, ethnic group) from the school will be sought.

In the case of the younger age group, if the initial questionnaire is not returned within one week, the information letter and questionnaire will be sent again.

5.6 Quality control

There is particular importance attached to the quality of the data collection and procedures in ISAAC, so that there will be confidence in the results. Prospective research centres must produce a detailed research protocol showing how the ISAAC Phase I protocol will be implemented locally. Key issues to be addressed include: the method for sampling schools; the geographical definition of the centre; the approach to ethnic group comparisons if these are being made; the season of data collection; if appropriate, method of translating ISAAC core questionnaire into other language(s); evidence that ethical and other necessary permissions have been granted. In addition, a statement should be included indicating the intent to achieve a high participation rate and no more than 5% of the data missing from the completed questionnaire forms.

6.0 Data handling and analysis

Each group of subjects will be treated separately: 6-7 year olds, 13-14 year olds, and subjects of each ethnic group where a major comparison is being made (sample size 3000 for each ethnic group). Each parameter of

prevalence and severity will be compared between locations. The cluster effect is not expected to be great, but will be adjusted for in the analysis.

6.1 Data quality and handling

The completed questionnaire must not be changed under any circumstances. Data should be entered on the computer exactly as recorded on the completed questionnaire. Any changes to data entered should be done so for an explicit reason and documented. Those changes should be made to a copy of the original computer data file.

If questions 1 and 2 are not completed in the wheezing questionnaire, that questionnaire will be excluded from analysis, but all available data should still be entered on the computer. A coding manual is necessary so that the core questions will be coded in a standard manner (see Section 9).

A scheme to handle blank or inconsistent stem and branch questions will be developed so that a single denominator for prevalence can be used. This will assume that parents of symptomatic children will be unlikely to leave questions blank and that the category "in the last 12 months" in a branch question overrides a negative or blank stem. A range check will be used to identify any other inconsistency.

Each centre will be responsible for coding its own data and data entry, although in some regions/countries one centre may take responsibility for this. One Data Centre will be chosen for the international comparison of the core data set. Data will be sent to the Data Centre as ASCII files in standard format, detailed in the coding manual; data on disks will be returned to each centre for their own use. A copy of data required for international comparisons will be retained in the Data Centre for analysis along with data received from the other centres. Data will be entered on a PC with the requisite capacity and memory, interfacing with a mainframe for more complex analyses. The results of data analyses will be communicated to the other centres as information is produced, and input on the data analyses will be sought from the other collaborators. Collaborators are encouraged to visit the Data Centre and work with its staff on collaborative analyses.

6.2 Analyses

The objective of the study is “to describe the prevalence and severity of asthma, rhinitis and eczema in children living in different centres and to make comparisons within and between countries (See section 4, Part 1).

Basic descriptive summaries of the data will be compiled and presented in an ISAAC Data Book. This Data Book will be the basic reference for the whole study and will describe prevalence and severity of asthma, rhinitis and eczema in both age groups for males and females in each of the countries participating.

Comparisons between different centres on the rates of events will be made using methods appropriate to the situation. Crude rates can be compared by using contingency tables or logistic regression. Comparison of standardized rates or data that needs controlling for confounding will require analysis by suitable multivariate methods (most probably logistic regression).

The ancillary questions will be treated in the same manner as the major questions on prevalence and severity. Summaries for each centre will be recorded in the Data Book and comparisons made appropriately.

Data will be analysed within each country (and centre if large enough) as well as the international comparisons. This will allow for the introduction of additional variables that the country may have incorporated.

Seasonality, methods of survey sampling, age standardisation and any other issues will be considered in the analysis of the ISAAC data.

6.3 Ownership of data

Each centre owns their own data. However, the collaborating centres will be recognised by the group title “International Study of Asthma and Allergies in Childhood” (ISAAC). All publications and communications involving international comparisons will be authored by the ISAAC Study Group whose collaborators will be identified.

7.0 Study instruments

The content of the questionnaires which appear below is fixed. See section 7.1 for further comments.

7.1 Instructions for completing questionnaire and demographic questions

Examples of instructions for completing questionnaires and demographic questions are given below.

13 and 14 year olds

On this sheet are questions about your name, school, and birth dates. Please write your answers to these questions in the space provided.

All other questions require you to tick your answer in a box. If you make a mistake put a cross in the box and tick the correct answer. Tick only one option unless otherwise instructed.

Examples of how to mark questionnaires: Age years

YES

NO

SCHOOL:

TODAY'S DATE:

Day Month Year

YOUR NAME:

YOUR AGE:

years

YOUR DATE OF BIRTH:

Day Month Year

(Tick all your answers for the rest of the questionnaire)

Are you:

MALE

FEMALE

Optional questions on ethnicity here

6 and 7 year olds

On this sheet are questions about your child's name, school, and birth dates. Please write your answers to these questions in the space provided.

All other questions require you to tick your answer in a box. If you make a mistake put a cross in the box and tick the correct answer. Tick only one option unless otherwise instructed.

Examples of how to mark questionnaires: Age
years

YES NO

SCHOOL:

TODAY'S DATE:

| | | |
|----------------------|----------------------|----------------------|
| <input type="text"/> | <input type="text"/> | <input type="text"/> |
| Day | Month | Year |

CHILD'S NAME:

CHILD'S AGE:

years

CHILD'S
DATE OF BIRTH:

| | | |
|----------------------|----------------------|----------------------|
| <input type="text"/> | <input type="text"/> | <input type="text"/> |
| Day | Month | Year |

(Tick all your answers for the rest of the questionnaire)

Is your child a:

| | |
|--------------------------|--------------------------|
| BOY | GIRL |
| <input type="checkbox"/> | <input type="checkbox"/> |

Optional questions on ethnicity here

7.2 Module 1.1 Core questionnaire for wheezing and asthma

Questionnaire for 13 and 14 year olds

- 1 Have you ever had wheezing or whistling in the chest at any time in the past? Yes
No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

- 2 Have you had wheezing or whistling in the chest in the last 12 months? Yes
No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

- 3 How many attacks of wheezing have you had in the last 12 months? None
1 to 3
4 to 12
More than 12

- 4 In the last 12 months, how often, on average, has your sleep been disturbed due to wheezing?
Never woken with wheezing
Less than one night per week
One or more nights per week

- 5 In the last 12 months, has wheezing ever been severe enough to limit your speech to only one or two words at a time between breaths? Yes
No

- 6 Have you ever had asthma? Yes
No

- 7 In the last 12 months, has your chest sounded wheezy during or after exercise? Yes
No

- 8 In the last 12 months, have you had a dry cough at night, apart from a cough associated with a cold or chest infection? Yes
No

Questionnaire for 6 and 7 year olds

- 1 Has your child ever had wheezing or whistling in the chest at any time in the past? Yes
No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

- 2 Has your child had wheezing or whistling in the chest in the last 12 months? Yes
No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

- 3 How many attacks of wheezing has your child had in the last 12 months? None
1 to 3
4 to 12
More than 12

- 4 In the last 12 months, how often, on average, has your child's sleep been disturbed due to wheezing?
Never woken with wheezing
Less than one night per week
One or more nights per week

- 5 In the last 12 months, has wheezing ever been severe enough to limit your child's speech to only one or two words at a time between breaths? Yes
No

-
- 6 Has your child ever had asthma? Yes
No

- 7 In the last 12 months, has your child's chest sounded wheezy during or after exercise? Yes
No

- 8 In the last 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or chest infection? Yes
No

7.2.1 Development, validation

These questions are designed as a minimum set for inclusion in self-completed or interview-administered questionnaires used in population surveys of respiratory disease in children. Note that enquiry about symptoms proceeds from the relatively mild to the relatively severe, and precedes enquiry about diagnosis.

These questions (self-complete version) were included in a pilot study conducted among 8,000 13-14 year olds in four centres during 1991.

The justification for the individual questions is as follows:

- Qu. 1. This is based on the IUATLD questionnaire. It does not mention "attacks" of wheezing, in order to identify children with persistent symptoms which are not obviously characterised as episodes or attacks. This is seen as a very sensitive question.
- Qu. 2. Limitation to a 12 month period reduces errors of recall and (at least in theory) should be independent of month of completion. This is considered to be the most useful question for assessing the prevalence of wheezing illness.
- Qus. 3,4. These questions offer two alternative quantitative measures of the frequency of wheezing. Problems with the concept of attacks (see above) and difficulty in quantifying the frequency of recurrent asthma lead to the inclusion of question 4 to identify and quantify persistent wheeze.
- Qu. 5. There is a dearth of epidemiological information relating to acute severe asthma, which is of direct relevance for international comparisons of hospital admissions and mortality statistics. This question aims to fill this gap.
- Qu. 6. All respondents are asked about diagnosed asthma, as occasionally asthma may be diagnosed in the absence of wheeze (on the basis of recurrent nocturnal cough etc.).
- Qu. 7. Although logically this question belongs as a stem question under number 2 (where it was used in the pilot study), it has been found in certain Australasian surveys to identify some

children who deny (or whose parents deny) wheezing or whistling at question 1 or 2.

- Qu. 8. Nocturnal cough is widely accepted as an alternative presentation of asthma, and this question has been included to increase the overall sensitivity of the questionnaire, although its specificity in population surveys remains unclear.

7.3 Module 1.2: Core questionnaire for rhinitis

7.3.1 Questionnaires

Questionnaire for 13 and 14 year olds

All questions are about problems which occur when you DO NOT have a cold or the flu.

- 1 Have you ever had a problem with sneezing, or a runny, or blocked nose when you DID NOT have a cold or the flu? Yes
No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

-
- 2 In the past 12 months, have you had a problem with sneezing, or a runny, or blocked nose when you DID NOT have a cold or the flu? Yes
No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

-
- 3 In the past 12 months, has this nose problem been accompanied by itchy-watery eyes? Yes
No

- 4 In which of the past 12 months did this nose problem occur? (Please tick any which apply)

| | | | | | |
|----------|--------------------------|--------|--------------------------|-----------|--------------------------|
| January | <input type="checkbox"/> | May | <input type="checkbox"/> | September | <input type="checkbox"/> |
| February | <input type="checkbox"/> | June | <input type="checkbox"/> | October | <input type="checkbox"/> |
| March | <input type="checkbox"/> | July | <input type="checkbox"/> | November | <input type="checkbox"/> |
| April | <input type="checkbox"/> | August | <input type="checkbox"/> | December | <input type="checkbox"/> |

- 5 In the past 12 months, how much did this nose problem interfere with your daily activities?:

| | |
|-------------------|--------------------------|
| Not at all | <input type="checkbox"/> |
| A little | <input type="checkbox"/> |
| A moderate amount | <input type="checkbox"/> |
| A lot | <input type="checkbox"/> |

-
- 6 Have you ever had hayfever? Yes
No

Questionnaire for 6 and 7 year olds

- 1 Have your child ever had a problem with sneezing, or a runny, or blocked nose when he/she DID NOT have a cold or the flu? Yes
No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

- 2 In the past 12 months, has your child had a problem with sneezing, or a runny, or blocked nose when he/she DID NOT have a cold or the flu? Yes
No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

- 3 In the past 12 months, has this nose problem been accompanied by itchy-watery eyes? Yes
No

- 4 In which of the past 12 months did this nose problem occur? (Please tick any which apply)

| | | | | | |
|----------|--------------------------|--------|--------------------------|-----------|--------------------------|
| January | <input type="checkbox"/> | May | <input type="checkbox"/> | September | <input type="checkbox"/> |
| February | <input type="checkbox"/> | June | <input type="checkbox"/> | October | <input type="checkbox"/> |
| March | <input type="checkbox"/> | July | <input type="checkbox"/> | November | <input type="checkbox"/> |
| April | <input type="checkbox"/> | August | <input type="checkbox"/> | December | <input type="checkbox"/> |

- 5 In the past 12 months, how much did this nose problem interfere with your child's daily activities?:

| | |
|-------------------|--------------------------|
| Not at all | <input type="checkbox"/> |
| A little | <input type="checkbox"/> |
| A moderate amount | <input type="checkbox"/> |
| A lot | <input type="checkbox"/> |

- 6 Has your child ever had hayfever? Yes
No

7.3.2 Development, validation

The principal aims are to: (1) distinguish between rhinitic and non-rhinitic individuals in the general population; (2) predict which subjects with rhinitis are likely to be atopic; and (3) give some indication of the severity of rhinitis among affected individuals.

The justification for individual questions is as follows:

- Qu. 1. This question was found to have a positive predictive value of 80% in detecting rhinitis in a community sample of adults (aged 16-65 years) in south west London.
- Qu. 2. As for "1" above.
- Qu. 3. This symptom had the highest positive predictive value (78%) in detecting atopy among subjects with rhinitis.
- Qu. 4. This question permits subjects with rhinitis to be separated into those with seasonal symptoms alone and those with a perennial problem. The method maximises precision in classification, is devoid of subjective definitions of "season", and could be used by any country regardless of climate. The number of months a subject is affected could be used as a quantitative indicator of "severity". Seasonal exacerbations had a positive predictive value of 71% in detecting atopy among subjects with rhinitis.
- Qu. 5. While this is a crude qualitative measure of severity, it correlated well with other indicators of morbidity including reported symptom severity, interference with specific activities of daily living and medical service use.
- Qu. 6. This question permits investigation of the labelling of rhinitis in relation to the prevalence of rhinitic symptoms. The label "hayfever" had a positive predictive value of 71% in detecting atopy among subjects with rhinitis.

7.4 Module 1.3: Core questionnaire for eczema

7.4.1 Questionnaires

Questionnaire for 13 and 14 year olds

- 1 Have you ever had an itchy rash which was coming and going for at least six months?
- Yes
- No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

-
- 2 Have you had this itchy rash at any time in the last 12 months?
- Yes
- No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

-
- 3 Has this itchy rash at any time affected any of the following places?
- Yes
- No

the folds of the elbows, behind the knees,
in front of the ankles, under the buttocks,
or around the neck, ears or eyes?

- 4 Has this rash cleared completely at any time during the last 12 months?
- Yes
- No

- 5 In the last 12 months, how often, on average, have you been kept awake at night by this itchy rash?

Never in the last 12 months

Less than one night per week

One or more nights per week

-
- 6 Have you ever had eczema?
- Yes
- No

Questionnaire for 6 and 7 year olds

- 1 Has your child ever had an itchy rash which was coming and going for at least six months? Yes
No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

- 2 Has your child had this itchy rash at any time in the last 12 months? Yes
No

IF YOU HAVE ANSWERED "NO" PLEASE SKIP TO QUESTION 6

- 3 Has this itchy rash at any time affected any of the following places: Yes
No

the folds of the elbows, behind the knees,
in front of the ankles, under the buttocks,
or around the neck, ears or eyes?

- 4 At what age did this itchy rash first occur? Under 2 years
Age 2-4 years
Age 5 or more

- 5 Has this rash cleared completely at any time during the last 12 months? Yes
No

- 6 In the last 12 months, how often, on average, has your child been kept awake at night by this itchy rash?

Never in the last 12 months
Less than one night per week
One or more nights per week

- 7 Has your child ever had eczema? Yes
No

7.4.2 Development, validation

These questions are 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.

It is anticipated that individual investigators may wish to supplement them with questions of their own, but they should endeavour to retain the general form of the questionnaire, including the flow and stemming, as indicated. Note that enquiry about symptoms proceeds from the relatively mild to the relatively severe, and precedes enquiry about diagnosis.

The justification for the individual questions is as follows:

The numbering refers to the version for completion by parents. The question on age at onset has been excluded from the self-reported version because recall of rashes in infancy by children in their teens is likely to be incomplete.

- Qu. 1. This screening question was evaluated in a UK pilot study of factors which discriminated “typical” mild-moderate atopic dermatitis from non-atopic eczema and other inflammatory dermatoses presenting for the first time in British hospital outpatient clinics. A positive response to this question was obtained for all 36 cases of atopic dermatitis presenting at ages 5-19 years, and 91% of 120 cases of all ages. Taken alone, however, it had specificity of only 44% at ages 5-19 and 48% at all ages.
- Qu. 2. Following the form of the core questionnaires for wheezing and rhinitis, further enquiry focuses only on those children with recent rashes, to minimise problems of incomplete and selective recall.
- Qus. 3,4. In the UK study, the specificity (i.e. the power to exclude non-atopic forms of eczema and other inflammatory dermatoses) was improved substantially by considering flexural involvement and age at onset. In the 5-19 age group (based on 36 cases of atopic dermatitis and 27 control subjects) the sensitivity was 94% and specificity 81% if flexural involvement

alone were included, and sensitivity 92% with specificity 96% if case-definition was based on both flexural involvement and onset before 5 years of age.

- Qus. 5,6. These two questions have been included as measures of the severity of the dermatitis, one assessing chronicity, the other morbidity. A question on the extent of skin involvement was considered and rejected as infeasible for questionnaire-based studies.
- Qu. 7. This question may need to be modified slightly in countries where a number of diagnostic labels are in common use (e.g. Has your child ever had any of the following: ...?). A supplementary stem question (If yes, was this diagnosed by a doctor?) was considered optional.

7.5 Module 1.4: Video questionnaire

7.5.1 Questionnaire

- | | | | | | |
|----|--|-----|--------------------------|----|--------------------------|
| 1. | Has your breathing ever been like this?: | | | | |
| | at any time in your life? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| | if YES,; in the last year? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| | if YES,; one or more times a month? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| 2. | Has your breathing been like the girl's in the video following exercise? | | | | |
| | at any time in your life? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| | if YES,; in the last year? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| | if YES,; one or more times a month? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| 3. | Have you been woken like this at night?: | | | | |
| | at any time in your life? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| | if YES,; in the last year? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| | if YES,; one or more times a month? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| 4. | Have you been woken like this at night?: | | | | |
| | at any time in your life? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| | if YES,; in the last year? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| | if YES,; one or more times a month? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| 5. | Has your breathing been like this?: | | | | |
| | at any time in your life? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| | if YES,; in the last year? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |
| | if YES,; one or more times a month? | YES | <input type="checkbox"/> | NO | <input type="checkbox"/> |

7.5.2 Development, validation

In response to translation problems with written questionnaires a video questionnaire has been developed and validated in Wellington, New Zealand. This attempts to minimise difficulties of comparability of information in large surveys among diverse populations. In particular the video questionnaire was developed to avoid problems of translation and comprehension of terms such as “wheeze” or “whistling from the chest” and their use in culturally heterogeneous populations.

The video involves sequences of asthma symptoms in young persons (generally late teens); three sequences involve various scenes of wheezing whereas the final two sequences involve other asthma symptoms. The five sequences are:

1. A young person wheezing (while at rest)
2. Wheezing after exercise
3. Waking at night with wheezing
4. Waking at night with coughing
5. A severe attack of asthma, involving difficulty breathing at rest.

After each sequence, students are asked to write down their answers to questions presented on the video. These are presented in Module 1.4. They are asked to specify whether their breathing has ever been like that of the person in the video; if so they are asked whether this has occurred in the last year; if so they are asked whether this occurs more often than once a week. The video takes less than 10 minutes to play.

Centres are strongly encouraged to present the video questionnaire. However it is acknowledged that in some centres, logistic or technical factors may make this impossible. The video has the advantage of obtaining data from a large number of children quickly and efficiently.

7.6 Further comments on validation of instruments

We have set out to use questionnaires with both sensitive and specific questions. The validity of questionnaire measurements of asthma or wheeze to be used in the core study have been considered as follows:

1. Repeatability

Several studies indicate that questionnaires of this type about asthma, have a good level of repeatability even when translated into languages other than English (Salome et al 1987, Burney et al 1989, Clifford et al 1989). Earlier versions of the written and video questionnaires on wheezing and asthma have been shown to be repeatable (Shaw et al).

2. Content validity

The questions have face validity; for some questions on severity it is very difficult to obtain data to validate the questions (e.g. for questions on night waking a true validation would require prospective home data collection for one year; for questions about the worst attack it would require prospective observations on all asthma attacks).

3. Construct validity

There has already been a major pilot study of written and video questionnaires on wheezing and asthma, which are very similar to the Phase I core questionnaires (Pearce et al). It was the first occasion in which the video questionnaire had been used in an international comparison. The similarities and differences found between countries were generally consistent with previously published work, and the video and written questionnaires showed a similar pattern of results.

The questionnaires were generally answered in a consistent fashion.

4. Concurrent validity

In the pilot study the reported prevalences of wheezing were relatively high in this self-reporting sample of 12-15 year olds compared with estimates in previous surveys involving parental completion of questionnaires. Therefore further investigation of this observation will be made in at least two centres: parent-completed and self-completed

questionnaires will be simultaneously compared in this age group. Anderson et al will be studying the validity of the three core questionnaires among 13 year olds using a detailed interview.

The pilot study has demonstrated that presentation of the written questionnaire before the video does not affect responses to the video; however presentation of the video first does affect responses to the written questionnaire.

5. Predictive validity

Frequent and persistent wheezing episodes are associated with chest deformity, residual airways obstruction, radiological evidence of hyperinflation, and presence of rhonchi in the interval phase (Gillam et al 1970, McNicol et al 1970). Wheezing at age 7 years predicts later wheezing and this is increased if one uses frequency of episodes at age 7 (Anderson et al 1986).

Although bronchial hyperresponsiveness (BHR) has in the past been equated with asthma, population studies have shown that its relationship to asthma symptoms and asthma diagnosis is not close (Josephs, Pattemore et al). This is probably because it is only one of several mechanisms underlying clinical asthma. BHR cannot be regarded as the gold standard (the one objective indicator of asthma). Nevertheless, BHR is an important factor in asthma, and its relationship to the tools being used is of particular interest. The prevalence of wheeze found by questionnaire relates to the response to an exercise provocation test (Barry & Burr 1991) and other measures of BHR (Burney et al 1989). Previous work with the video questionnaire has shown it to have reasonable sensitivity and specificity for BHR in an English-speaking population (Shaw et al).

7.7 Presentation and translation

It is important that the questionnaires are prepared in a consistent manner. The order of yes/no responses has been defined. The layout and printing of the questionnaires will be standard with each module being printed on a single page. The 4 questionnaires for 13-14 year olds are usually presented on one piece of folded paper with the video questionnaire to be showing on the back when folded. Alternatively they may be presented separately with adequate identification on each page.

Translation of questionnaires from English to other languages will be standardised. The English version will be translated, and then that version translated back to English. These procedures will involve several translators, in an attempt to define the best non-English version for each region. In some countries (e.g. New Zealand) the information sheet may be translated into the main non-English languages, but not the questionnaires, providing the vast majority of the population are conversant with written English.

8.0 Ethics and conduct

8.1 Ethical committee approval

Each centre will need to obtain the necessary Ethics Committee approval prior to the start of the study. Sample information sheets appear below.

8.2 Model for approaching schools

What follows is one example of the approach to schools. Centres must proceed according to their local rules. A final goal should be a high participation rate.

Once Ethics Committee approval has been obtained, the school principal will be approached for his/her cooperation with the study. Then the data collection will be able to commence with the cooperation of the class teachers. It is very important that the asthma, allergies, rhinitis and eczema are not explicitly mentioned to school staff pupils and parents in relationship to the study.

8.2.1 Sample information letter for 13-14 year olds

Dear Chairman of Board of Trustees/Principal/Teachers

re: New Zealand Survey of Breathing, Nose and Skin Problems in Children

We are inviting some children at your school to take part in an important study about child health with the approval of their parents. Many schools in Auckland are taking part in the study, and by random sampling

techniques, your school has been selected. We wish to study children aged 13 and 14 years.

This survey is being carried out in randomly selected schools in Auckland, Wellington, Christchurch, Nelson and Hawke's Bay, and also in many overseas countries including Australia, Canada, USA, Britain and Germany. The Auckland survey is funded by the Health Research Council of New Zealand. The purpose of the study is to understand more about the increasing problem of respiratory symptoms in children of this age group.

For your school, it would mean:

1. Identifying classes in which 13-14 year olds are found and making available a copy of the class lists with date of birth if possible.
2. During this term one of our research team would bring information sheets for parents (copy enclosed) to the school, to be distributed to all the selected children one week before the study team come to your school.
3. We would return the next week to ask these children to complete written questionnaires (copy enclosed) and to watch a video about exercise and breathing which lasts about ten minutes. We would require about 40 minutes in total.
4. We would come back about a week later, with the questionnaires and show the video to any children who were absent on the first occasion and ask them to complete the survey.

One of our research team will be in contact with you soon to discuss this survey further. In the meantime if there is any further information you require about the survey, please do not hesitate to contact one of us. If you are unable to reach us directly by telephone, please leave a message with our secretary Mrs Chris Thomas.

This survey has the approval of the University of Auckland Human Subjects Ethics Committee, whose Chairman you may contact directly about ethical matters (care of the Secretary, University of Auckland Human Subjects Ethics Committee, University of Auckland, Private Bag 92019, Auckland; phone 373-7599, ext 6204).

Yours sincerely

.....

8.2.2 Sample information letter for 6-7 year olds

Dear Chairman of Board of Trustees/Principal/Teachers

re: New Zealand Survey of Breathing, Nose and Skin Problems in Children

We are inviting some children at your school to take part in an important study about child health with the approval of their parents. Many schools in Auckland are taking part in the study, and by random sampling techniques, your school has been selected. We wish to study children aged 6-7 years.

This survey is being carried out in randomly selected schools in Auckland, Wellington, Christchurch, Nelson and Hawke's Bay, and also in many overseas countries including Australia, Canada, USA, Britain and Germany. The Auckland survey is funded by the Health Research Council of New Zealand. The purpose of the study is to understand more about the increasing problem of respiratory symptoms in children of this age group.

For your school, it would mean:

1. Identifying classes in which 6-7 year olds are found and having ready a copy of the class lists for the researcher.
2. One of our research team will then come and name each survey form and distribute them by class to be taken home.
3. We will send information sheets, and questionnaires (copies enclosed) to the parents of the children who will be asked to complete the questionnaire and return it to your school, to be collected by the researcher.
4. We would follow-up any non-returned forms.
5. We would wish to have information on the date of birth and sex of any potentially eligible children who do not participate in the survey.

One of our research team will be in contact with you soon to discuss this survey further. In the meantime if there is any further information you require about the survey, please do not hesitate to contact one of us. If you are unable to reach us directly by telephone, please leave a message with our secretary Mrs Chris Thomas.

This survey has the approval of the University of Auckland Human Subjects Ethics Committee, whose Chairman you may contact directly about ethical matters (care of the Secretary, University of Auckland Human Subjects Ethics Committee, University of Auckland, Private Bag 92019, Auckland; phone 373-7599, ext 6204).

Yours sincerely

.....

8.3 Model for approaching parents

An information sheet will be sent home with each participating child, giving details about the study. The information sheet will be translated up to four of the most common languages used by families of eligible children.

13-14 year olds: The information sheet has an additional paragraph giving the parent the right to refuse their child's participation in the study.

6-7 year olds: Parents completion of the questionnaire implies consent.

8.3.1 Sample information sheet for parents/guardians of 13-14 year olds

Dear Parent/Guardian

We are inviting your child to take part in an important survey about child health with the approval of your school. Many schools in Auckland are taking part in the study and all classmates of your child are being asked to take part. First, your child will be asked to complete three brief questionnaires. Then a 10 minute video about exercise and breathing will be shown to your child in his/her class and your child will be asked to complete a further brief questionnaire. This will take up to 40 minutes of class time.

This survey is being carried out in randomly selected schools in Auckland, Wellington, Christchurch, Nelson, Hawke's Bay and also in many overseas countries including Australia, Canada, USA, Britain and Germany. The Auckland survey is partly funded by the Health Research Council of New Zealand.

We ask you to consider this information sheet, and if you agree to your child taking part in the survey, then you need to take no action. If you do not wish your child to answer the questionnaire, please telephone the number listed at the bottom of this page tomorrow. Your child's questionnaire will be treated confidentially; only a code number will be entered in the computer.

This survey has the approval of your child's school's Board of Trustees, Principal and teachers. It also has the approval of the University of Auckland Human Subjects Ethics Committee.

If there is any further information you require about the study, please contact one of us.

Yours sincerely

.....

8.3.2 Sample information sheet for parents/guardians of 6-7 year olds

Dear Parent/Guardian

We are inviting your child to take part in an important survey about child health with the approval of your school. Many schools in Auckland are taking part in the study and all classmates of your child are being asked to take part. For each child, a parent/guardian is being asked to complete a questionnaire.

This survey is being carried out in randomly selected schools in Auckland, Wellington, Christchurch, Nelson, Hawke's Bay and also in many overseas countries including Australia, Canada, USA, Britain and Germany. The Auckland survey is partly funded by the Health Research Council of New Zealand.

We ask you to consider this information sheet, and if you agree to your child taking part in the survey, then we would like you to complete the attached questionnaire. Your child's questionnaire will be treated confidentially; only a code number will be entered in the computer.

This survey has the approval of your child's school's Board of Trustees, Principal and teachers. It also has the approval of the University of Auckland Human Subjects Ethics Committee.

If there is any further information you require about the study, please contact one of us.

Yours sincerely

.....

8.4 Guidelines for field workers

ISAAC research staff and field workers should not use the terms “asthma”, “allergy”, “rhinitis” or “eczema” when

- (i) advertising the study
- (ii) presenting written material about the study
- (iii) speaking about the study to school staff, parents, children
- (iv) speaking to 13-14 year old children in the classroom.

The phrases “breathing survey” or “a survey about breathing problems” are acceptable terms to use.

The title of the questionnaires must not include the words asthma, allergy, rhinitis, eczema or ISAAC. An alternative title could be “A survey of Breathing, Nose and Skin Problems”. Coding should not appear on the questionnaires delivered to the children or their parents. Improved layout of the questionnaires is being developed and tested by the New Zealand steering committee members, and will be recommended for use in the field. Please contact Innes Asher for copies of these questionnaires.

6-7 year olds

Once eligible children are identified, ISAAC staff will send the questionnaire to the parent/guardian either through the school or by post. The parent/guardian will be asked to return the questionnaire by a mechanism which incurs no financial cost to them.

13-14 year olds

The questionnaires will be administered to a group of children in a school in one session at a time. Each session will comprise verbal instructions on the three sections before handing the questionnaires out and instructions to leave the video questions until the video is shown. Alternatively, the questionnaires may be presented on separate sheets of paper. Administration will then include:

- (i) handing out and completion of the written questionnaire on wheezing
- (ii) handing out and completion of the written questionnaire on rhinitis
- (iii) Handing out and completion of the written questionnaire on eczema

The order of presentation of the core questionnaires is of importance: they should always be presented wheezing-rhinitis-eczema.

- (iv) Handing out the written questions for the video questionnaire followed immediately by the showing of the video questionnaire; the written questions are completed while this is being shown. The video questionnaire must always be shown after the written questionnaires

In presenting the video, there must be adequate technical adequacy and visual and audio quality to ensure subjects see it well and hear it correctly.

If questionnaires have clearly not been completed in a comprehensible fashion, then they could be represented to the person who originally completed them for one further attempt. The research worker should not give advice about the responses that might be given. Once the questionnaire is completed, it must not be changed by research workers under any circumstances.

9.0 Data Transfer

The coding manual is available upon request from the regional coordinators.

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