

Newsletter - January 1995

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I S A A C I N T E R N A T I O N A L S T U D Y O F A S T H M A A N D A L L E R G I E S I N C H I L D H O O D

The Newsletter

Thank you for your positive responses to the June Newsletter. I would welcome items from anyone for inclusion in the next newsletter.

- Innes Asher
Auckland

PS Please let me know if you do NOT want to receive the ISAAC Newsletter.

Excerpt III from "Organisation of the ISAAC Study"

Regional Coordinators

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

Responsibilities:

- recruit national coordinators
- help national coordinators with translation and production of

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UPDATE ON PARTICIPATION IN PHASE I ISAAC PROGRAMME

Participation in Phase I of the ISAAC Programme continues to progress well in all WHO regions. To date over 100 centres have registered from 51 countries. Over 60 centres have now started data collection, with about one half of these having completed this part of the study.

In view of this situation, the priority has shifted from the recruitment and registration of further centres to participate in Phase I, to the support of those centres that have already registered, to ensure their successful completion of the data collection in Phase I.

As a result, although registration for the ISAAC Programme remains "open" to allow further interested centres the opportunity to take part, further registrations will be actively encouraged only in high priority areas, not currently well represented in ISAAC.

As previously noted, the deadline for completing Phase I of the ISAAC Programme has already been extended on two occasions, to allow for participation of centres from as many countries as possible. At its recent meeting, the Steering Committee considered that it was important that the current timetable was confirmed. As a result, all participating centres are encouraged to complete data collection by 1 July 1995, so that data can be forwarded to the International Data Centre by 1 December 1995 for inclusion in the initial Phase I analysis and publication. It was recognised that this timetable will create difficulties for some centres which have only just registered and for this reason, a second deadline of 1 December 1996 was established for the second Phase I analysis and publication, which will hopefully include all centres participating in the ISAAC Programme.

Richard Beasley

Note from the International Data Centre

The Steering Committee has resolved that double entry of data is required for Phase One data to limit data entry errors and ensure the quality of data used in international comparisons. Use of single entry may prevent data from being used in all ISAAC international comparisons.

When sending data to the International Data Centre please note carefully the coding for the question "In which of the past 12 months did this nose problem occur?" (question 4 of the rhinitis questionnaire). The coding for the variables concerning this question should be '1' or '9' if the child or parent did not tick the box for the month and '2' if they did tick the box. This is a bit different to most of the other questions where a '1' is coded if the child or parent answered yes.

Tadd Clayton, Data Manager, International Data Centre.

Excerpt III from "Organisation of the ISAAC Study" cont.

- 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
 - 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

Progress from Brazil

National Coordinator, Dr Renato Stein from Porto Alegre has overseen translation of the protocol into Portuguese. In Brazil 6 centres are enrolled: Porto Alegre and Curitiba (2 large southern cities) have finished data collection; São Paulo will start data collection soon under the leadership of Professor Julio Croce; Salvador and Recife (2 large northeastern cities) have started data collection; and Manaus (Amazon region) will start data collection early in 1995.

Dr Stein is moving to Tucson, Arizona to do his PhD in Epidemiology at the University of Arizona with Dr Fernando Martinez. Professor Charles Naspitz from São Paulo will become the National Coordinator for Brazil during this period.

Video Questionnaire

There was an omission from the earliest versions of the ISAAC Manuals (October 1992 and June 1993 editions). Section 8.4, Module 1.4, Video Questionnaire, Question 3:

Have you been woken like this at night:
 At any time in your life? YES NO
 if YES, in the last year? YES NO

Omitted was the third response:
 if YES, one or more times YES NO
 a month

This third response appears in the original ISAAC Video, the ISAAC Coding and Data Transfer Manual and in the revised ISAAC Manual (2nd Edition, December 1993).

Thanks to Professor Malcolm Sears, St Joseph's Hospital, McMaster University, Hamilton, Ontario for finding this error. The original ISAAC Steering Committee apologises for this error and any difficulties encountered as a result.

ISAAC Steering Committee Meeting

The annual ISAAC Steering Committee Meeting was held in Nice on the 5th and 6th of October 1994. There was a great deal of discussion about the progress of Phase One and plans for Phase Two. The degree of interest in ISAAC has exceeded all plans, expectations and projections. To date over 100 centres in 51 countries have registered in ISAAC Phase One.

Summaries reports from the ISAAC regions presented at the meeting are included here:

1.1 Reports of Regional Coordinators

North America -Fernando Martinez / USA - Victoria Persky

In the USA Phase One has commenced in the Chicago area with funding obtained for two areas. Chicago was chosen due to a high mortality rate of African Americans. A local feature of interest is the effect of the extensive flooding of the Mississippi river on respiratory disease. Data collection has been completed in the older age group (90% participation). Preliminary analysis indicated that the prevalence of current asthma is lower than in Australia/New Zealand but higher than England. The male:female ratio of the survey population was approximately 1:2. Translations of the questionnaires have not been necessary for rural areas but a spanish language version will be required for urban areas. The spanish translation will probably differ significantly from a European spanish translation.

Phase One is also under way in Seattle.

In Canada Phase One studies have been completed in Hamilton and Saskatoon.

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Western Europe - Stephan Weiland/Ulrich Keil

Spain is the most advanced country in Western Europe with seven centres, most having completed data collection. One data set from Spain has been forwarded to the International Data Centre in Auckland.

France also has seven centres. Two have started data collection and the other five are planning to start by the end of 1994.

In the United Kingdom data has been collected in London/Sussex and a copy of the data has been sent to the International Data Centre. Funding has been obtained for a national survey with data collection due to commence in the spring of 1995. The national survey will use an alternative design which is intended to better illustrate geographic variations, sampling one school per administration area. An extended questionnaire will be used, including questions on indoor pollutants and other respiratory symptoms.

One centre in Portugal has completed data collection and a copy has been forwarded to the International Data Centre. Two other centres are also participating and another two may also participate.

Italy has eight participating centres with data collection due to start in autumn. An extended questionnaire will be used.

Germany has funding for six centres. Münster has completed data collection.

A regional meeting is planned for 9-10 December in Münster.

The European Pediatric Asthma Survey is now effectively merged with ISAAC.

Asia/Western Pacific - Chris Lai

Eight countries are participating to date.

China has five centres although funding problems may affect participation. Some of the funding provided by Glaxo International has been used as seeding money in China. The Chinese centres are aiming to start data collection in 1-2 months and finish by April 1995. The emphasis has firmly been placed on ensuring the quality of the data rather than speed.

Japan has two collaborating centres and there is one each in Korea and Singapore.

Hong Kong has one combined centre.

Malaysia and the Philippines also have one centre each.

Taiwan currently has five participating centres and the national coordinator is intending to recruit at least another five. The target for participants at each centre in Taiwan is 50 000 individuals.

One regional meeting has taken place and another is planned. A national meeting was held for China three weeks ago. All National Coordinators are very enthusiastic and funding only appears to be a problem in China. Communications have been a problem due to language problems. Improvement in communication in the future is essential. A Chinese translation of the questionnaire has been developed and will be piloted. Other translations will be necessary.

Central/South America - Richard Beasley for Javier Mallo

There has been good progress in the last year with centres from eight countries registered in the programme (including Argentina and Bolivia) and with Phase One already completed in Santiago, Chile. Funding is the major restriction on participation. The World Health Organisation (WHO) letter of support from Tord Kjellström is specifically intended to assist with funding applications.

Anglophone Africa - Gabriel Anabwani

Communication difficulties caused by language differences required division of the coordinating responsibilities for Africa. French speaking Africa will be coordinated by Nadia Ait-Khaled.

Three centres are certainly participating (Capetown, Eldoret and Nairobi) with one further centre (Addis Ababa) possible.

Funding is a major limitation as only Capetown was able to secure local funding. The other participating centres are dependent on the regional funding from Glaxo International.

Other problems include the absence of transportation and communications infrastructure, linguistic differences and a shortage of trained research personnel.

A regional meeting was held in Nairobi on June 17-18 1994 and a further meeting is planned for June 1995.

All centres are planning to collect data between January and May 1995.

Southeast Asia - Richard Beasley for JR Shah

Twenty one centres have been recruited in India with a further one each in Indonesia and Thailand. The regional funds provided by Glaxo International have been equally divided between the Indian centres.

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Two national meetings for India have been held. Dr Shah has used monthly updates from all centres to maintain good communication links. Medical staff and students have been used as field workers to limit costs. The importance of using the ISAAC methodology has been stressed by Dr Shah at the meetings. The fieldwork guidelines included in the appendices to the 1993 ISAAC Steering Committee meeting have been most useful.

Eastern Mediterranean - Stephen Montefort

Centres from seven countries have been recruited to date.

Funding has been obtained in Iran for surveys in six areas, covering 4-6 provinces.

Morocco has one participating centre (Rabat) with the possibility of another one (Meknès). Regional funds may be allocated to Meknès as it is high altitude. Rabat will use a french translation but a further translation will be needed for Meknès as the population is predominantly Berber.

Funding may also be available for Casablanca.

Lebanon has one centre participating (Beirut) with funding obtained and data collection scheduled to start in October or November 1994. Communication is extremely difficult as all messages must go via the United States diplomatic bag to New York.

Saudi Arabia has two participating centres, one of which is funded.

Kuwait has one centre covering the whole country. Some translations will be needed.

Malta has completed data collection in the younger age group (78% participation) and will collect the data for the older age group from November 1994. State schools only have been sampled.

A small regional meeting was held during the European Respiratory Society meeting in Nice. The great distance between countries in the region and variable funding make further meetings difficult.

Eastern Europe/Baltics - Bengt Björkstén

Five countries will have finished data collection by the end of October 1994. A good sampling of Eastern Europe has been obtained including Sweden, Poland, Russia, Estonia and Finland.

Problems have included communication and the lack of experienced scientific workers.

The region has required a unique approach which has included a strict approach to funding and a strict communication policy. Regional funds have only been

available for extra expenses. Each centre has had to find local funding for the bulk of the study. Communication directly with the active worker has been important, rather than through the hierarchy of the institution.

Oceania - Innes Asher

New Zealand (six centres) and Australia (four centres) are the only participating countries at present. All centres apart from Perth have completed data collection and data entry.

An interest was expressed by doctors in Tonga but, with scarce local resources, ISAAC is not being pursued there.

Preliminary analysis of seasonal, centre and ethnic variations has been carried out for New Zealand. The Nelson centre appears to be much lower than all other centres for most variables in the younger age group. Ethnic differences have also been identified in the younger age group with Maori showing much higher prevalence for allergic conditions. An abstract of the seasonal analysis has been prepared and is included in the briefing material.

Important features of the New Zealand study have been regular meetings (sponsored by Glaxo New Zealand) and good communications.

Increased communication between workers in the centres has been a major benefit of the Australian study.

Resolved: Successful communication between researchers and regional coordinators is crucial to the success of Phase One. Early national and regional meetings therefore should have the highest priority. Consideration should also be given to a formal requirement for regular communication between centres and the regional/national coordinator.

Note: The documents that each collaborating centre should have available include:

- (i) The Registration Document (to be completed and returned to the regional coordinator)
Document 031
- (ii) The ISAAC Manual **Document 006**
- (iii) The ISAAC Coding and Transfer Manual
Document 007
- (iv) ISAAC in the Field (providing some practical guidelines for implementing Phase One)
Document 053
- (v) Guidelines for the Translation of Questionnaires
Document 054
- (vi) The Video Questionnaire (international version)
Document 055

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- (vii) Guidelines for the administration of the Video Questionnaire **Document 056**

1.2 Particular Regional Issues

A tally of the centres noted during the reports from the regional coordinators indicates that approximately 50 countries and 130 centres are registered or participating. This raises issues of priority for further recruitment, a limit on further enrolment and a time frame for Phase One.

A discussion of these issues concluded that a closed study was more desirable than a completely open ended approach and that it is important to publish results from Phase One as quickly as possible. However, it is also important not to limit additional centres from using the tools and contributing to Phase One in the future.

Resolved: Further enrolment of centres will be accepted but not actively encouraged.

Regional coordinators will have discretion regarding new centres and may encourage participation if appropriate to improve geographic coverage.

A clean dataset must be lodged with the International Data Centre by 1 December 1995 if the data is to be included in initial Phase One publications. In order to meet this deadline it is recommended that data collection be completed by 1 July 1995.

Presentations of Papers and Posters at International Scientific Meetings 1994

International Union Against Tuberculosis and Lung Disease, Annual Scientific Meeting, Mainz, Germany, June 1994.

Erika von Mutius presented this poster:

Progress report of European ISAAC surveys (the International Study of Asthma and Allergies in Childhood)

Erika von Mutius on behalf of the ISAAC Study Group. University Children's Hospital, Lindwurmstr. 4, D-80337 Munich, Germany

Background: The etiology of asthma and allergic diseases in childhood remains poorly understood. Epidemiological 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. The aims of ISAAC are to describe the prevalence and the severity of asthma, rhinitis and eczema in children living in different centers and to make comparisons within and between countries. A framework for further etiological research into genetic, lifestyle, environmental and medical care factors affecting these diseases in different parts of the world will be provided. Furthermore, the purpose of ISAAC is to obtain baseline measures for assessment of future trends in the prevalence and severity of these diseases. Methods: The ISAAC study design comprises three phases: phase 1 is a compulsory core study designed to assess the prevalence and severity of these diseases in 6-7 and 13-14 year old children; phase 2 will investigate possible etiological factors and phase 3 will be repetition of phase 1 after 3 years. Three standardized one page questionnaires on wheezing, rhinitis and eczema have been developed for phase 1. In addition, a video questionnaire on wheezing will be used for self-completion by the 13-14 year old children. Standardized protocols for skin prick testing and assessment of bronchial reactivity, and questionnaires on other respiratory symptoms, environmental factors and medical care have been developed for phase 2. Results: 45 European centers in Germany, Great Britain, France, Italy, Spain, Switzerland, the Netherlands, Austria, Greece, Ireland and Malta have expressed their interest to participate in ISAAC. In several centers data collection for phase 1 has started. Conclusion: The ISAAC initiative provides a standardized methodology to study and compare the prevalence of asthma, rhinitis and eczema in children living in different parts of the world. Moreover, a common protocol has been established to study the trends and determinants of these disorders worldwide.

The Third Congress of the Asia Pacific Association for Respiratory Care, Christchurch, New Zealand, August 1994.

Innes Asher presented a similar overview paper entitled "ISAAC - where asthma epidemiology is heading".

European Respiratory Society, Annual Congress, Nice, France, October 1994.

Joseph Reidler presented this paper about the hyperosmolar challenge chosen for ISAAC Phase Two. *Eur. Resp. J.* 1994; 7: supp. 18, p129.

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**PREVALENCE OF BRONCHIAL
RESPONSIVENESS TO HYPERTONIC SALINE
AND ITS RELATIONSHIP TO ASTHMA IN
CHILDREN**

J. Reidler, M. Dalton, D. Holst, T. Reade, CF. Robertson.

Department of Thoracic Medicine, Royal Children's Hospital, Melbourne, Parkville, Australia

To determine the prevalence and assess sensitivity and specificity of a 4.5% hypertonic saline (HS) challenge as a screening test for a diagnosis of asthma, we studied 393 schoolchildren aged 13-14 years with 'current wheeze', and without a history of wheeze. The children were selected from 2836 schoolchildren who took part in an International Study of Asthma and Allergies in Childhood (ISAAC) and who completed a self administered questionnaire on respiratory symptoms. 174/393 children were interviewed by a paediatric respiratory physician to assess the diagnosis of asthma. Good agreement between the response to the questionnaire and a respiratory physician diagnosis of asthma was found ($\kappa=0.72$). The prevalence of reported 'wheeze in the last 12 months' was 27.3%. 382/393 successfully completed the HS challenge test with 4.5% saline and increasing inhalation periods, and 365/393 also performed a standardised 6 min free running challenge test (EX). The prevalence of bronchial responsiveness to HS was 20.4% and for EX was 23.4%. Sensitivity and specificity for the HS challenge to identify children with 'current wheeze' were 47% and 93% and for the EX challenge 46% and 88% respectively. These values did not differ significantly when compared to a doctor diagnosis of asthma. These results suggest that the 4.5% HS challenge test is a simple, safe and convenient test to assess bronchial reactivity in children in a community based survey and shows similar sensitivity and specificity to identify asthma as a standardised exercise challenge. Although there was a strong relationship between 'current wheeze' and response to HS, sensitivity was not high enough for the test to be able to 'detect' asthma in a community based survey in children. Nevertheless, we think that bronchial challenge tests are of value when comparing prevalence of bronchial responsiveness or asthma over time and between different countries.

Charlotte Braun-Fahländer presented this poster examining self reported prevalences of respiratory symptoms in teenagers. *Eur. Resp. J.* 1994; 7: supp. 18, p480s.

P2152

Prevalence of wheezing reported by parents and self-reported by 14 year olds (written and video questionnaire)

Braun-Fahländer Ch., Gasser I., Minder Ch, Sennhauser F.M., Vuille J.C. and the SCARPOL-Team. Departement of Health of the city of Berne, Switzerland.

In the framework of the Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution (SCARPOL), 1388 parents and 8th grade students (mean age 14 y) completed the ISAAC (International Study of Asthma and Allergies in Childhood) core questions for wheezing and asthma. In addition to the written questionnaire (SWQ), the students answered the video-questionnaire (VIDEO) shown in class. 874 (63 %) of the students also had serological allergy tests (SX1 screening test for 8 common aeroallergens, Pharmacia, Sweden).

Parents (parents written questionnaire =PWQ) reported a higher prevalence of "wheezing ever": 20.7% (PWQ) vs 17.9% (SWQ) and 14.2% (VIDEO), but students reports were higher for "wheezing past year": 9.7% SWQ, 7.9% VIDEO vs 7.1% PWQ. For "wheezing after exercise past year" (PWQ: 9.7%, SWQ: 18.3%, VIDEO: 19.5%) and "dry cough apart from colds" (PWQ: 12.4%, SWQ: 18.4%, VIDEO: 14.5%), students reported significantly higher prevalences.

The kappa-coefficient of agreement was higher between parents and students written answers and students written and video answers than parents reports and video answers.

To assess the validity of the answers yielded by these three sources of information, the proportion of students with a positive reaction to the allergy screening test (SX1) was calculated for each question assuming that in this age group atopy is an important etiologic factor for asthma symptoms. There were no significant differences in the proportion of atopy-positive students between the three sources of information.

We conclude that for this age group self reported prevalences by students are reliable and that the prevalence rates reported by parents might be underestimating.

At the Nice ERS congress representatives of the ISAAC Steering Committee were invited to address the business meetings of two ERS Scientific Committees to give an update on ISAAC:

Paediatric Respiratory Epidemiology (Erika Von Mutius)

Paediatric Asthma and Allergy (Innes Asher)

*Seasons Greetings and
Happy New Year*