

INTERNATIONAL STUDY OF ASTHMA AND ALLERGIES IN CHILDHOOD

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(Attention Innes Asher)

ISAAC WEB SITE ONLINE JANUARY 1999

<http://isaac.auckland.ac.nz>

At the Berlin meeting of the Steering Committee (Sept 1997) it was resolved to develop a World Wide Web site for the promotion of ISAAC and to facilitate communication.

Tadd Clayton has developed this site on behalf of the Steering Committee and the International Data Centre (IDC) in Auckland.

The ISAAC web site will provide information on Phase One, Phase Two, Phase Three, Publications and the Steering Committee. for both collaborators and casual visitors. The web site will also provide an opportunity for comment from visitors and a forum for communication between collaborators and interested visitors. Ctd/

NEWSLETTER - 1998

Welcome back to the ISAAC Newsletter, the first since May 1996. We have been in touch with you in many ways since then, but feel it is time to revive the newsletter in an ongoing way.

We welcome contributions to the newsletter from any ISAAC collaborators. Scientific achievements, "bits and pieces" on your own area of interest or from your local centre, and items of fun would be welcomed.

You will see in this newsletter brief summaries and commentaries from members of the ISAAC Steering Committee and the ISAAC International Data Centre.

ISAAC has really come of age this year with the first four worldwide publications being produced. For members of the ISAAC Steering Committee and collaborators, you will find enclosed a reprint of the paper on **Worldwide variations in the prevalence of asthma symptoms** published in the European Respiratory Journal in August 1998.

The ISAAC programme is thriving and we have an annual meeting of the Steering Committee on the Friday and Saturday preceding the European Respiratory Society Annual Meeting. This year's meeting in Geneva confirmed the ongoing ISAAC research programme, progressing now to ISAAC Phase Two and ISAAC Phase Three (see pages 4-5).

Major funding is being sought for these phases, including the running of International Data Centres for Phase Two in Münster, and Phase Three in Auckland, and co-ordination of these phases.

The 1999 Madrid meeting of the Steering Committee (October 8 & 9) is planned to be held in conjunction with the "Collaborators' Get-together" on the evening of Saturday, 9 October, which has been much enjoyed in the past.

The ISAAC Steering Committee wishes to continue active communication with ISAAC collaborators as needed, and to encourage the appropriate development and execution of the further phases of ISAAC. We believe that the development of the ISAAC web site should help us a step further.

The ISAAC Steering Committee would like to express admiration for the efforts of the ISAAC collaborators in contributing in such an excellent way to this very important programme.

On behalf of the ISAAC Steering Committee and the Auckland International Data Centre, I wish you, your families and colleagues the very best for the festive season and the New Year.



Innes Asher

Chairperson, ISAAC Steering Committee

December 1998

ISAAC Web site Development (Continued from previous page)

The construction of this site has been quite an experience for Tadd who has established it whilst carrying out his many tasks as Data Manager for the IIDC. He welcomes suggestions for modifications or additional content and can be contacted through our "address for correspondence" or the web site!!

We look forward to viewing, and utilising, the fruits of your labour, Tadd!

ISAAC STEERING COMMITTEE MEETING, SEPTEMBER 1998

Overview provided by David Strachan, Professor of Epidemiology, Department of Public Health Sciences, St George's Hospital Medical School, London, United Kingdom

Seventeen members of the ISAAC Steering Committee met in Geneva for two days prior to the ERS congress in September. Hospitality was kindly provided at Geneva University by Prof Ragnar Rylander.

In 1993 many of us met with representatives of WHO in Geneva to discuss the implementation of ISAAC in developing countries. The intervening five years have seen ISAAC Phase One completed on a truly global scale. Innes Asher and colleagues from Auckland presented a report of this success story to WHO representatives before the start of the Steering Committee meeting.

Phase One

Although Hywel Williams was unable to attend due to illness, we were delighted to receive his news that the global comparisons of eczema prevalence, based on the Phase One ISAAC surveys, have been accepted for publication in the Journal of Allergy & Clinical Immunology. This completes the suite of four descriptive papers publicising the Phase One prevalence data.

The Steering Committee is actively involved in preparing a series of papers relating to "ecological analyses" of disease prevalence in relation to measures of economic prosperity, climate, air pollution, aeroallergen exposures, diet, infections and immunisation rates, and routinely available data on mortality and hospital admissions for asthma. Centres have already been contacted to request additional data for some of these, for example the immunisation rates, and the response has been encouraging. Discussion of these papers addressed both administrative and intellectual issues (in equal measure).

A few centres have contributed Phase One data after the deadline for inclusion in the first four publications. Alternative means of publishing these prevalence figures, perhaps through the ISAAC website or in printed format as a WHO publication, are being explored. Meanwhile a paper synthesising the findings of Phase One and addressing the interrelationships of the three diseases has been proposed and will aim to include these additional centres. From the repeated requests for review articles relating to ISAAC, it is clear that the Phase One results have already attracted widespread interest.

Phase Two (see also pages 4-5)

Studies, using the ISAAC Phase Two modules, are completed or in progress in Germany, Netherlands, Sweden, Estonia, and China (including Hong Kong). Funding has been obtained for studies in UK and France and there has been interest expressed from centres in Albania, Australia, Brazil, Chile, Costa Rica, Kenya, India, Iran, Japan and New Zealand. Some funding has been raised through the European Union Biomed programme to support co-ordination and training for Phase Two studies in Europe, but funding is still being sought for a Phase Two data centre, to be located in Münster.

It is clear that Phase Two has passed the stage of isolated studies and the challenge is now to collate existing data and co-ordinate the collection of further data from interesting and informative centres around the world.

Phase Two modules are available from Stephan Weiland in Münster and will be provided on the ISAAC website in future. The possibility of a journal publication describing the Phase Two methodology was discussed.

Phase Three (see also page 5)

Centres received an outline of the aims and methods of Phase Three in May 1998 and replies have been received from 72 centres, of whom 65 expressed a firm interest in participating. A minimum of 5 years should elapse between Phases One and Three in the same centre, implying that most centres will need to wait until the year 2000 or later. The ISAAC International Data Centre in Auckland will be ready to receive Phase Three data by November 2000, and it was decided that centres wishing to contribute to Phase Three must provide a clean dataset by November 2002. Centres who have not previously participated in ISAAC are encouraged to do a Phase One survey during the years 2000-2001, for comparison with the Phase Three surveys in other places. The global co-ordination of Phase Three will be undertaken by Richard Beasley and colleagues in Wellington (see page 5), using the established network of regional co-ordinators or direct contact with centres as appropriate. So far, applications for central funding of Phase Three have not met with success, although a number of avenues are being pursued.

D.Strachan@sghms.ac.uk

Steering Committee Snippets.....



JAVIER MALLOL, LATIN AMERICA

After a quite busy and productive Phase One, ISAAC in Latin America has entered into a "resting" phase waiting for Phase Three. However, some centres are undertaking Phase Two studies in an attempt to provide data from this region to add to those being collected from other parts of the world. Considerable interest has been expressed to me, from individuals and institutions that will do studies using ISAAC Phase One core questionnaires, looking at the possible relationship between parasites or pollution and symptoms of asthma, rhinitis and eczema; or simply determining the prevalence of these symptoms in their localities. Researchers from the NIH in Ecuador will conduct one of these studies; another will be undertaken in Mexico by the Mexican Society of Allergy and Immunology. The participating centres in the Region have started to publish their results in journals of national and regional circulation, which will certainly disseminate the ISAAC findings in Latin America. jmallol@lauca.usach.cl



MICHAEL BURR, CARDIFF, UK

"...Data are available on pollen counts from a wide variety of countries. With Dr Jean Emberlin of the National Pollen Research Laboratory, I hope to examine the relationships between pollen counts

and the prevalence of rhinoconjunctivitis and asthma. We should have some data by the end of January. It is relatively easy to obtain information from European countries, but it may take a little longer to cover all available sources.

WANTED – Ideas on how to gather data on exercise from ISAAC centres – everything considered! Please contact ↓

MICHAEL.BURR@bro-taf-ha.wales.nhs.uk



ROSS ANDERSON, ST GEORGES HOSPITAL MEDICAL SCHOOL, LONDON, UK

(Opinions expressed are those of the author and not the institution)

AIR POLLUTION AND ASTHMA

We all want to know the degree to which variations in asthma prevalence are explained by variations in air pollution. If we could get air pollution data from ISAAC centres the question would be answered!

All centre collaborators have had a letter asking if there are air pollution data for their area, and if so to give some simple summaries. The response has been good and we now have data from all over the world. We shall be following up some of the responses to clarify the information. If you have not replied, please do so even if there are no data.

IMMUNISATION ANALYSIS

The collection of immunisation data from centres is now completed and the Steering Committee are now preparing a paper for publication. Thanks to all who provided centre data. We also obtained national data from WHO and these did not always agree with the centre data – confirming the importance of centre data. randerso@sghms.ac.uk



**HYWEL WILLIAMS, UNIVERSITY HOSPITAL
NOTTINGHAM, UNITED KINGDOM**

"Flexural Eczema In Different Coloured Skins"

Researchers often ask me whether our visible flexural dermatitis protocol is equally useful in darker coloured skins as in white skin. The answer is "probably yes".

In the past, dermatologist colleagues have been keen to point out to me that the distribution of atopic eczema is often different in black skins, for example in Afro-Caribbean children living in the UK when compared with their white counterparts. Having worked in Brixton, London, where 40% of the population is Afro-Caribbean, I would certainly agree that eczema affecting the extensors (fronts as opposed to backs of the knees) is common.

Despite these observations, the available evidence suggests that flexural eczema is still a hallmark of atopic eczema in children with more darkly pigmented skins. Gabriel Anabwani's team showed that the pattern of atopic eczema in black children living in Kenya had more similarities, rather than differences, to the traditional pattern described in white skins. Another study, with which I am involved, compares atopic eczema prevalences in Jamaica and London and suggests that the pattern of eczema is in fact very similar, regardless of ethnic groups. The visible flexural dermatitis protocol developed for the ISAAC study was derived from children of mixed ethnic groups, and photographs of different coloured skins have been deliberately included to train observers.

We still do not really know why atopic eczema has this predilection for the flexures, but irritation from sweat and trapping of allergens and irritants has been a favourite story. Atopic eczema can of course affect any area of the body, including the scalp, but at some time it does appear to favour the

flexural sites. If you hardly ever see atopic eczema settling in the flexures, then I would like to hear from you by email. I would also welcome review of our training manual on recording atopic eczema and how it can be improved.

Please do not forget to think about atopic eczema in your rush to record allergic disease in future allergic disease surveys - it is very easy to record in an objective way, and it will help you to say more about the totality of expressed atopic disease in your population.

muzhw@mmn1.medical.nottingham.ac.uk

Hywel is "I tching to hear from you" !!

ISAAC PHASE TWO

- The ISAAC Steering Committee is proposing a co-ordinated international study to follow Phase One.
- This next study, known as "ISAAC Phase Two - International", will investigate hypotheses generated by Phase One.
- Comparisons between populations (centres) will be undertaken using objective measures of disease, and assessment of environment, lifestyle, and clinical management.
- Populations that are potentially informative will be chosen, such as those with contrasting prevalence of disease, environmental exposures, management or genetic factors.
- Measurements on representative samples of these populations will be undertaken using standardised ISAAC instruments

The ISAAC Steering Committee has developed additional standardised tools (published in the Phase Two Manual):

- Questionnaires about cough, and the medical care of asthma, rhinitis and eczema.
- Standardised protocols for physical examination:
 - of the skin for flexural dermatitis
 - airway responsiveness testing using hypertonic saline aerosol challenge
 - skin prick tests for atopy
 - total and specific serum IgE
 - storage of blood samples for potential future genetic analyses.

Phase Two Co-ordinator:

Dr Stephan Weiland

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Westfälische Wilhelms Universität
Domagkstrasse 3
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ISAAC PHASE THREE

- Phase Three of the ISAAC Programme will be a repeat of Phase One after a minimum of 5 years.
- ISAAC Phase Three will provide vital information concerning time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema.
- Evidence of increases (or decreases) in the prevalence of symptoms will be a strong indication that these diseases are more dependent on environment than genetics.

REGISTRATION OF INTEREST

Centres interested in participating in Phase Three should complete the enclosed "Expression of Interest" form – (only enclosed for centres whose interest has not yet been registered).

Phase Three Co-ordinator:

Professor Richard Beasley

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Wellington School of Medicine
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Phase Three Data Centre:

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Recent Quotes Received at the IIDC ...

"... I hope that the asthma and allergy story will be unravelled in the next century 'und wir können sagen, wir sind dabeigewesen' (Goethe) and we can say we have been part of it" –

Ulrich Keil

"Hywel rhymes with towel" - Hywel Williams

From the Back-Translations...

Beirut, Lebanon:

Arabic "sadr" has a double meaning
CHEST and BREAST

"During the last 12 months did your breast wheeze during or after exercise?"

Our minds boggle at the prospect - IIDC

Update of ISAAC Database & Review of ISAAC Directory

It would be appreciated if you could supply details as per the proforma below (especially if you have new team members) or recent changes and preferably email or fax/post to:

Chris Thomas
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ISAAC International Data Centre
Department of Paediatrics
Faculty of Medicine & Health Science
University of Auckland
Private Bag 92 019
Auckland, NEW ZEALAND

Email: cr.thomas@auckland.ac.nz
Fax: 64 9 373 7602

Personnel: Names of all members in your team including their current positions
Address: }
Telephone Number: } Common address where possible, otherwise specify individually
Fax Number: }
Email Address: }

ISAAC STEERING COMMITTEE 1998-9

Professor Gabriel Anabwani
Gaborone, Botswana
Professor Ross Anderson
London, United Kingdom
Dr Innes Asher (Chair)
Auckland, New Zealand
Professor Richard Beasley
Wellington, New Zealand
Prof Dr med Ulrich Keil
Münster, Germany
Dr Chris Lai
Hong Kong, China
Professor Bengt Björkstén
Linköping, Sweden
Dr Michael Burr
Cardiff, United Kingdom
Dr Julian Crane
Wellington, New Zealand
Associate Professor Ed Mitchell
Auckland, New Zealand

Dr Stephen Montefort
G'Mangia, Malta
Professor Javier Mallo
Santiago, Chile
Dr Fernando Martinez
Tucson, Arizona, USA
Professor Neil Pearce
Wellington, New Zealand
Dr Colin Robertson
Melbourne, Australia
Mr Alistair Stewart
Auckland, New Zealand
Professor David Strachan
London, United Kingdom
Dr med Erika von Mutius
München, Germany
Dr Stephan Weiland
Münster, Germany
Dr Hywel Williams
Nottingham, United Kingdom

Professor Neil Pearce, Chair, ISAAC Publications Committee, Wellington

Many of you have been wondering (and asking me!) about progress on further analyses of the ISAAC Phase One study findings. Until earlier this year, our priority was to complete and publish the four initial papers, and this task has now been completed. We are now focusing on ecologic analyses of the Phase One data. In each instance, the analysis and manuscript preparation is being organised by a Steering Committee member, together with a Writing Group that primarily comprises Steering Committee members, but may also include other colleagues where appropriate.

I should stress that the preparation of these “global” analyses does not preclude ISAAC investigators conducting and publishing further analyses of ISAAC data:

- from a particular region (with the approval of the Regional Coordinator)
- a particular country (with the approval of the National Coordinator)
- or the data from their own centre.

In addition, the ISAAC Phase One findings are already beginning to be widely quoted in various reviews and commentaries, both by ISAAC Steering Committee members, and by other investigators.

To date, only one ecologic analysis has been submitted for publication (a paper by von Mutius et al on tuberculosis notification rates and asthma prevalence). However, several other manuscripts have been drafted, and a number of ecologic analyses have been presented as Conference abstracts. The analyses/manuscripts currently in preparation are:

Topic	Probable first author	Writing Committee
Economic development	Alistair Stewart	Ed Mitchell, Neil Pearce, David Strachan, Stephan Weiland, Bengt Björkstén, Alistair Stewart, Javier Malloj
Diet	Philippa Elwood	Innes Asher, Philippa Elwood, Neil Pearce, Colin Robertson, Bengt Björkstén, Michael Burr
Infections	Erika von Mutius	Erika von Mutius, (Ondine von Ehrenstein), Bengt Björkstén, Richard Beasley, Neil Pearce
Immunisation	Ross Anderson	Ross Anderson, Richard Beasley
Climate	Stephan Weiland	Stephan Weiland, David Strachan
Tobacco	TBA	Ulrich Keil, (C Currie)
Outdoor air pollution	Ross Anderson	Ross Anderson, Chris Lai
Pollens	Michael Burr	Michael Burr, Bengt Björkstén, David Strachan
House dust mites	Julian Crane	Julian Crane
Cat	Michael Burr	Michael Burr
Month of birth	Ed Mitchell	Ed Mitchell, Alistair Stewart
Mortality and hospitalisation rates	Ross Anderson	Ross Anderson, David Strachan, Richard Beasley

Other related papers in preparation include:

- a comprehensive analysis of the ISAAC findings for Europe (David Strachan)
- a comparison of the ISAAC written and video questionnaire findings (Julian Crane)
- a comparison of the ISAAC and ECRHS findings (Neil Pearce, Jordi Sunyer)
- a more detailed synthesis and analysis of the ISAAC Phase One findings for asthma, rhinitis and eczema (Ross Anderson).

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