

# INTERNATIONAL STUDY OF ASTHMA AND ALLERGIES IN CHILDHOOD

## NEWSLETTER – NOVEMBER 2011

Dear ISAAC colleagues and friends,

The end of the year is rapidly approaching and this will be the last newsletter for 2011. The ISAAC Steering Committee joins me in hoping that you have had a productive and fruitful year and that the year 2012 will be kind to you.

We are still trying to trace 9 original articles for the compilation of ISAAC publications held by the IIDC (see pages 7&8) *Please check and contact Eamon if you can help* ([e.ellwood@auckland.ac.nz](mailto:e.ellwood@auckland.ac.nz)).

The ISAAC website development has been completed (<http://isaac.auckland.ac.nz/index.html>) and the number of hits accessing the website has increased a lot (see page 7). The finalised ISAAC Story (<http://isaac.auckland.ac.nz/story/>) is now available via the website and can also be downloaded in pdf format as a lasting record (but think carefully before you print as it is 420 pages). Thank you very much indeed to all of the contributors.

Over the past 3 years the ISAAC Steering Committee has been developing its ideas about future use of the ISAAC data. There is a general trend to make large data sets more accessible so as to maximise the potential of data. We have evolved an approach to the ISAAC data which we describe on pages 3-4. *This asks for your assent by 31 December 2011* to making the individual data available within the ISAAC consortium. We look forward to your responses on this.

The [Global Asthma Report](#) has now been completed and was launched in New York in September of this year at the NonCommunicable Diseases (NCD) Alliance event 2 days before the UN Summit on NCDs. This completes ISAAC Phase Four with a flourish. Copies have already been posted to our collaborators.

As you know, funding for ISAAC is drawing to a close, and as we discussed at the Steering Committee meeting on Waiheke Island in January of this year, ISAAC will finish next year. This will ring to an end our extraordinary research programme 22 years after it started. Unfortunately our superb staff are having to find new employment. Tadd Clayton has found a new 5-year full time position as Data Manager with the Section of Epidemiology and Biostatistics with The University of Auckland. He will continue to work for ISAAC 2 days a week until funding runs out sometime in April 2012. Eamon Ellwood is actively seeking employment as a web designer. Philippa will continue to be supported by ISAAC funding until middle of 2012, and is looking for further opportunities in the asthma research field. These are major changes, which will affect all of us. We have been blessed by having such wonderful people working for ISAAC for such a long time, with such commitment and with such excellence, contributing to ISAAC's success.

### CORRESPONDENCE TO:

#### Professor Innes Asher

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### NEWSLETTER CONTENT:

- ◆ [Editorial: Innes Asher](#)
- ◆ [Congratulations to: our ISAAC Colleagues from China](#)
- ◆ [Data sharing within ISAAC](#)
- ◆ [The Global Asthma Report](#)
- ◆ [ISAAC website Report](#)
- ◆ [Publication check](#)
  - ◆ [ISAAC Phase One Publications](#)
  - ◆ [ISAAC Phase Two Publications](#)
  - ◆ [ISAAC Phase Three Publications](#)

Sub editor - P Ellwood

I wish you and your families a happy festive season

*Innes*

Professor Innes Asher ONZM  
Chair of ISAAC

# Congratulations to:

Professor Yu-Zhi Chen (ISAAC National Coordinator for China and Principal Investigator for Phases One, Two Three in Beijing and Phase Three in Tong Zhou) and her colleagues, Professor Kun-Hua Chen (Principal Investigator for Phase One in Chonqqing), Dr Mao Bao-Shan (Principal Investigator for Shanghai in Phase One), Professor Man-Lin Xiao (Principal Investigator for Wulumuqi in Phase One), Professor Nan-Shan Zhong, (Principal Investigator for Phases One, Two and Three in Guangzhou), Assistant Professor Osamu Kunii (Principal Investigator for Phase Three in Tibet) and Dr Qiao Li Pan (Principal Investigator for Phase Three in Wulumuqi) for being awarded the:

**“Science and Technology Advancement Prize” awarded by the Beijing Municipal Government in 2006**

For their ISAAC Phases One, Two and Three studies.



Overall, in 12 years of ISAAC Study from Phase One to Phase Three, about 90,000 chinese children joined the study.

*Congratulations Yu-Zhi and her team*

During its meetings in 2008, 2009 and January 2011, the Steering Committee has considered possible arrangements for wider sharing of the ISAAC datasets to facilitate the maximum potential of the ISAAC data to be realised. By the “ISAAC datasets”, we mean the **individual-level** data (such as the responses of an individual child), not the summary information at centre level (such as the prevalence of asthma symptoms in Auckland). The individual-level data include the responses to symptom questionnaires (Phases One, Two and Three), clinical and biological measurements (Phase Two), and risk factor questionnaires (Phases Two and Three).

Individual-level data from ISAAC Phase One have recently been made available to members of the ISAAC consortium (under username / password control) via the ISAAC website. Only one centre disagreed with this arrangement, and the majority of ISAAC centre principal investigators positively agreed. No response was obtained from about one-third of the PIs, and so far we have not made available the Phase One datasets from centres who did not reply.

As ISAAC draws to a close at the end of 2012, the ISAAC Executive now feels that it is appropriate to extend data access, within the ISAAC consortium, to ISAAC Phase Two and Phase Three datasets. This will allow ISAAC collaborators to analyse these global data with their own resources, independent of the ISAAC data centres in Auckland and Ulm, each of which has limited capacity. After careful consideration we make the following proposal:

1. The arrangements will take effect from 1 January 2012.
2. Data sharing will occur within ISAAC Study Groups. Thus, Phase Two datasets will be shared within the Phase Two Study Group (which includes the Steering Committee) and Phase Three datasets will be shared within the Phase Three Study Group (which also includes the Steering Committee).
3. Access to individual-level datasets will use the ISAAC website and the username / password control mechanisms already developed for access to the Phase One datasets.
4. Potentially disclosive or sensitive data items, including exact dates of birth, names and/or addresses (if supplied), and genotype data will be removed from the datasets before they are made available on the ISAAC website.
5. Centre investigators who agree to share individual-level data under these arrangements should contact Philippa Ellwood ([p.ellwood@auckland.ac.nz](mailto:p.ellwood@auckland.ac.nz)) to indicate their approval, **before the end of 2011**. These investigators **will** be allowed to access data from other centres within their ISAAC Study Group.
6. Centre investigators who do not wish the individual-level data from their centre to be shared within their ISAAC Study Group should make their views known to Philippa Ellwood ([p.ellwood@auckland.ac.nz](mailto:p.ellwood@auckland.ac.nz)) **before the end of 2011**. These investigators **will not** be allowed to access data from other ISAAC centres.
7. All centres are strongly encouraged to make their views known. However, if no response has been received from a centre by 31 December 2011, the datasets for that centre **will** be included in the shared data. But, investigators from these centres **will not** be allowed to access data from other centres until they have indicated their approval as in point 5 above.

8. Phase One datasets from all the centres who have not yet responded regarding Phase One data sharing (despite repeated reminders) **will** be made available to all members of the Phase One, Phase Two and Phase Three Study Groups.
9. Centres who have access to the shared datasets will be required to notify the ISAAC Executive ([i.asher@auckland.ac.nz](mailto:i.asher@auckland.ac.nz)) of the statistical analyses that they propose. The intention of this is not to prevent analyses being done, but to identify any potential overlap or duplications which could be resolved by discussion among collaborators. The intention is also to encourage collaborations with other members of the ISAAC network. In some instances, the Executive may recommend or require that the investigators consult with the relevant Regional or National Coordinators. These proposals for data analysis can be submitted at any time during 2012.
10. For the calendar year 2012, at least, ISAAC datasets will not be shared outside the ISAAC consortium. External investigators who wish to access the ISAAC data during this period will need to collaborate closely with an ISAAC centre, or a member of the ISAAC Steering Committee who would be responsible for the data analysis. All such external collaborations should be notified to the ISAAC Executive ([i.asher@auckland.ac.nz](mailto:i.asher@auckland.ac.nz)).
11. All journal publications and conference abstracts, arising from analyses of ISAAC data under the arrangements described above, should include the relevant ISAAC Study Group in the authorship listing. This should follow the convention of recent global ISAAC publications (“... and the ISAAC Phase One/Two/Three Study Group” with the full listing of study group members at the end of the manuscript). The ISAAC Executive ([i.asher@auckland.ac.nz](mailto:i.asher@auckland.ac.nz)) can provide detailed advice, and recommendations on how ISAAC should be acknowledged in other forms of output (for example, book chapters or review articles).
12. A copy of any manuscript prepared for journal publication should be sent to the ISAAC Executive ([i.asher@auckland.ac.nz](mailto:i.asher@auckland.ac.nz)) at least two weeks before the intended date of submission, so that it can be circulated to the relevant ISAAC Study Group for information. This follows the conventions already established for publications led by the ISAAC Steering Committee.

The ISAAC Steering Committee is developing detailed proposals for the longer-term secure storage of ISAAC datasets and possible arrangements for access by non-ISAAC investigators, from 2013 onwards. We will consult all members of the ISAAC collaboration about these proposals in a future newsletter.

Meanwhile, please take a little time to consider your views on our proposals for data sharing within the ISAAC consortium, and let Philippa Ellwood know, **before the end of 2011** if you are willing to share your individual-level data as described above.

The more centres that respond, the more confident we can be, at the ISAAC International Data Centre, that we are accurately reflecting the views of the whole consortium. Thank you.



*Embargoed until Saturday, 17 September, at 00:01*

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## **Global Asthma Report 2011 shows the tools to manage asthma exist but are not reaching many of the 235 million people affected**

New York, 17 September 2011 — Asthma is the most common chronic disease among children and also affects adults. Worldwide, 235 million people have asthma. For these people, asthma can mean struggling for breath when they have an asthma attack, a diminished quality of life, disability and even death. Although effective treatment is available, many people with asthma, especially in low- and middle-income countries, are unable to access or afford it.

To highlight the issues surrounding this major non-communicable disease, the **International Union Against Tuberculosis and Lung Disease (The Union)** and the **International Study of Asthma and Allergies in Childhood (ISAAC)** have collaborated to produce the **Global Asthma Report 2011**, which will be launched at an event sponsored by the Non-Communicable Disease Alliance on Saturday, 17 September at 10:45 am at the New York Academy of Medicine, 1216 Fifth Avenue (at 103rd Street). Release of the report coincides with the UN High-Level Meeting on NCDs taking place on 19–20 September.

Designed for stakeholders from government ministers and policy-makers to health workers and people with asthma, the **Global Asthma Report 2011** is a richly illustrated “atlas” that provides an overview of what is known about the causes and triggers of the disease, the global prevalence, the progress being made and the significant challenges today and for the future.

### **Key findings in the report:**

- ISAAC data show that asthma in children is increasing in low- and middle-income countries, where it is more severe than in high-income countries.
- The World Health Survey found an 8.2% prevalence of diagnosed asthma among adults in low-income countries and 9.4% in the richest countries. Middle-income countries had the lowest prevalence at 5.2%.
- Smoking and secondhand smoke are two of the strongest risk factors — and triggers — for asthma.
- Although asthma is frequently thought of as an allergic disease, this does not apply to all cases, and the non-allergic mechanisms need to be the focus of more research.
- Surveys around the world found asthma treatment falling short, with few patients consistently using the inhaled corticosteroids that effectively manage the disease. For example, the Asthma in America survey found only 26.2% of patients with persistent asthma used these medicines.
- While many countries now have asthma management guidelines, many health workers do not know how to diagnose or treat asthma and health systems are not organised to handle this type of long-term, chronic disease.
- A 2011 Union survey of the pricing, affordability and availability of essential asthma medicines in 50 countries found dramatic variations. For example, one generic Beclometasone 100µg inhaler in a private pharmacy cost the equivalent of nearly 14 days’ wages — and a patient with severe asthma requires about 16 of these inhalers per year.
- The Asthma Drug Facility established by The Union has been able to bring down the cost of treating a patient with severe asthma to approximately US\$ 40 per year.

**PRESS RELEASE**

- When people do not have access to ongoing care, they often end up in emergency rooms and hospitals — a costly and unnecessarily disruptive process for all involved.
- Although economic data are unavailable for almost all low-income countries, a 2009 systematic review found annual national costs (in 2008 US dollars) ranging from \$8,256 million in the United States to \$4,430 million in Germany.
- Success stories from five high- and low-income countries that have implemented asthma management activities show that well-managed asthma saves money – and enables people to get on with their active lives. For example, in Finland, the mortality, number of hospital days and disability due to asthma fell 70–90% between 1994 and 2010 and a conservative estimate of the savings was \$300 million in 2007 alone.

“The tools to treat asthma are already available – there is no reason to delay”, says **Dr Nils E Billo, Executive Director of The Union**. “Moreover, when asthma is not diagnosed, not treated or poorly managed, and when people can not access or afford treatment, they regularly end up having to miss school or work, they are unable to contribute fully to their families, communities and societies, they may require expensive emergency care, and everyone loses. The obstacles to well-managed asthma can be overcome. Asthma is a public health problem that can – and should be addressed now.”

Learn more at our interactive website: [www.globalasthmareport.org](http://www.globalasthmareport.org). You may also download the complete report from this site.

### **About The Union**

The mission of the International Union Against Tuberculosis and Lung Disease (The Union) is to bring innovation, expertise, solutions and support to address health challenges in low- and middle-income populations. With nearly 10,000 members and subscribers from 150 countries, The Union has its headquarters in Paris and offices serving the Africa, Asia Pacific, Europe, Latin America, Middle East, North America and South-East Asia regions. Its scientific departments focus on tuberculosis and HIV, lung health and non-communicable diseases, tobacco control and research. Learn more at [www.theunion.org](http://www.theunion.org)

### **About ISAAC**

The International Study of Asthma and Allergies in Childhood (ISAAC) is the only global study of paediatric asthma and allergy currently in existence. In the 21 years it has been running, the ISAAC programme has completed three phases involving 306 research centres in 105 countries with nearly two million children. ISAAC findings are cited by world organisations involved in monitoring and preventing chronic respiratory diseases (CRDs) and are used to inform global health initiatives. Learn more at <http://isaac.auckland.ac.nz/>

## ISAAC Editorials

Asher MI. *Urbanisation, asthma and allergies*. Thorax December 2011 Vol 66 No 12 1025-1026 originally published online September 22, doi: 10.1136/thoraxjnl-2011-201019

Langan SM, Fewtrell M. *Does breastfeeding protect against the development of eczema?* British Journal of Dermatology, December 2011; 165(6): 1157–1158.

In response to

Flohr C, Nagel G, Weinmayr G, Kleiner A, Strachan DP, Williams HC and the ISAAC Phase Two Study Group. *Lack of evidence for a protective effect of prolonged breastfeeding on childhood eczema: lessons from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two*. Br J Dermatol 2011; 165(6): 1280-1289 Epub 2 Nov.

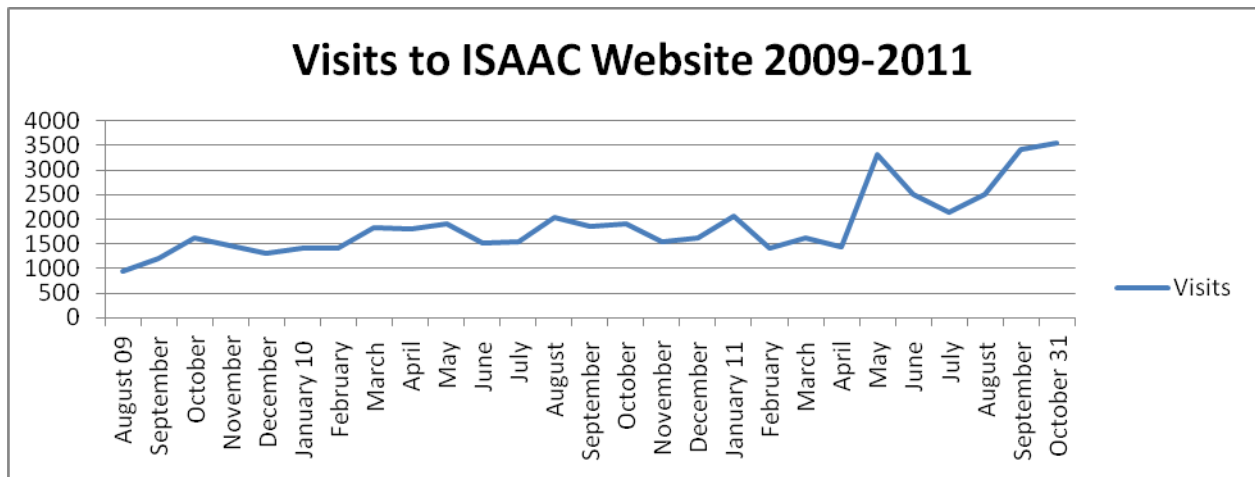
### Commentary

Ellwood P. *The ISAAC Story*. Journal of Medical academy – US Medical School Medicine and Health Sciences. Vol 1 (2011) No 1. Page 68.

## Website Report

Eamon Ellwood November 2011

The ISAAC website has seen consistent usage and growth since its re launch in 2009. It is designed to be a repository of all ISAAC information.



The ISAAC website is intended to be a resource for you, the collaborators. As such the focus of the development is towards the publications section, Phase Four, which is the resources section of the ISAAC website, and the Phase One and Three data pages. It now also hosts the ISAAC Story, a 20 year history of ISAAC.

## ISAAC Publications

We are continually updating the publications database with new ISAAC papers as they are published or located, and continuing to search for full text articles (see below). Currently we have 483 journal articles in the database (as well as various manuals and other publications) and full text access for 346 of these. All other articles are linked to the abstract on the journals website (where the journal has a website). The ISAAC publications can be found at <http://isaac.auckland.ac.nz/publications/publicationsintro.html>.

We also maintain a pdf library of ISAAC articles, including those we do not have permission to make available on the website. We continue to search for missing pdf files of ISAAC articles. Currently we have 9 articles that we are unable to locate pdf files for. If you are able to assist in locating these, please contact me ([e.ellwood@auckland.ac.nz](mailto:e.ellwood@auckland.ac.nz)).

Chereches-Panta P, Popa M, Iacob D, Muresan M, Dumitrascu D, Ichim G, Mirestean I, Nanulescu MV. [Prevalence of bronchial asthma in 7 years -old children in Cluj-Napoca, an ISAAC study], *Pneumologia*. 2003 Apr-Jun;52(2):134-40. Románian.

Cherecheş-Panţa P, Popa MD, Iacob D, Mureşan M, Man SC, Farcău M, Indolean C, Ichim GE, Mireştean I, David L, Nanulescu MV. [Increase of the prevalence of bronchial asthma and related symptoms in students in Cluj-Napoca. Epidemiologic study with a five-years interval] *Pneumologia*. 2004 Jan-Mar;53(1):47-52.

Charpin D, Penard-Morand C, Raheison C, Kopferschmitt C, Lavaud F, Caillaud D, Annesi-Maesano I. Long-term exposure to urban air pollution measured through a dispersion model and the risk of asthma and allergy in children. *Bull Acad Natl Med* 2009; 193(6): 1317-1328

Masjedi MR, Fadaizadeh L, Najafzadeh K, Dokouhaki P. A Study of the Prevalence and Severity of Rhinitis in Children in Tehran: ISAAC Study. *Journal of Isfahan Medical School (I.U.M.S)* Spring 2005; 23(76):36-41.

Fadaizadeh L, Keyvan S, Najafzadeh K, Masjedi MR. Evaluation of Agreement between Video and Written Questionnaires for Asthma Symptoms Among Children of Tehran: ISAAC Study. *Journal of Shahid Sadoughi University of Medical Sciences and Health Services*, summer 2008; 16(2):36-43.

Moghadam M, Jou S. Prevalence of Asthma Symptoms among 13-14 years old Children in Birjand. *TABIB-E-SHARGH* Fall 2004; 6(3):183-192.

Riedler J, Reade T, Dalton M, Holst D, Robertson CF. Hypertonic saline challenge in an epidemiological survey of asthma in children. *Am J Respir Crit Care Med* 1994; 150:1632-1639.

Eder W, A Gamper, G Oberfeld, J Riedler. Clinical follow-up of an epidemiological study of asthma and allergies in children [Klinische Nachuntersuchung einer epidemiologischen Studie über Asthma und Allergien im Kindesalter.] (article in German). *Wien Klin Wochenschr* 1998; 110(19):678-685.

Luss LV, Aripova TU, Ilyina NI, Lysikova IV. Prevalence of bronchial asthma symptoms (ISAAC programme result). *Asthma* 2000; 1(1): 52–59.

Our aim is for the ISAAC publications database to be the definitive record of articles produced by ISAAC collaborators including articles from centres published in local journals.

However, being based in New Zealand means that we can only find journals that are indexed by large journal services such as Medline. If you have published articles in local journals that are not indexed by these services, could you please check to see if your article is on the ISAAC website (the easiest way to do this is an author search publications search page), and if not, please send it to me. ([e.ellwood@auckland.ac.nz](mailto:e.ellwood@auckland.ac.nz))

Also, when you publish a new article could you please send me the details, and preferably a pdf.

As always, we encourage you to make use of the publications facility (<http://isaac.auckland.ac.nz/publications/publicationsintro.html>) Please check to see that your articles have been included. If not please contact me at [e.ellwood@auckland.ac.nz](mailto:e.ellwood@auckland.ac.nz).



## **ISAAC Resources**

The ISAAC Resources' section (<http://isaac.auckland.ac.nz/resources/resources.php>) including the comprehensive list of management guidelines and 'ISAAC Tools' section- a collection of manuals and questionnaires for ease of use – has seen consistent use in the 6 months since its introduction. We still wish to increase the management guidelines in this section. We currently have 15 from various countries. It is important that these guidelines are NOT sponsored by the pharmaceutical industry. If you know of any such guideline, we would like to hear from you and receive the link or a pdf of the guideline, with permission to use it.

We aim for the Phase Four/Resources page to have a wide range of useful resources, so if you have any information that could be added to the website such as useful links to good research /resource sites, asthma information sites open journal sites etc, management recommendations or entry level 'information pages' about asthma, eczema and rhinitis, please forward them to me. ([e.ellwood@auckland.ac.nz](mailto:e.ellwood@auckland.ac.nz))

Also in the resources section, there are links to talks given by Steering committee members at various symposiums. This includes the presentation slides, and audio or video.

## **Phase One Individual Data**

Last year we started to request permission from Principal Investigators to display the individual level Phase One Data. We have now received a response from 131 centres. The original embargo expired at the end of June 2011 and the Phase One Individual data has been moved to the public section of the ISAAC website. Further data sharing has been discussed earlier in this newsletter.

## **Phase One and Three Results**

Last year we added the Phase Three Results page (<http://isaac.auckland.ac.nz/phases/phasethree/results/results.php>) to accompany the Phase One Results page (<http://isaac.auckland.ac.nz/phases/phaseone/results/results.php>). This includes the summary centre level results as well as selected information about the study centre. As this is a collation of summary level data that has already been published in the worldwide publications, we have displayed the data on the website unless the centre specifically requests that we do not. This data was made available on the 1<sup>st</sup> of June.

## **ISAAC News**

The News page contains the latest ISAAC papers published and other noteworthy events. There is also now a News Articles Page <http://isaac.auckland.ac.nz/news/media.html>. This contains links to ISAAC related news items in mainstream media.

We are always looking for noteworthy information to go on our news and announcements page. This is intended to keep the ISAAC community up to date with what is happening in the ISAAC study more frequently than the bi-annual newsletter. If you have any noteworthy events or announcements, please let me know and I will add them to the webpage.

## **The ISAAC Story**

The ISAAC Story website is now complete. This includes a modified print layout that can be viewed using the print preview function in your web browser, and an accompanying pdf version of the website. This can be downloaded in sections or complete, and is available in low resolution and high resolution versions from <http://isaac.auckland.ac.nz/story/print.php>.

We are awaiting content from centres, including images to make it a really collaborative experience. The intent of the ISAAC Story is to recognize the entire ISAAC collaboration, as it

is this collaboration that has made ISAAC the huge success that it is. This is the ideal opportunity for the ISAAC collaborators who are not Principal Investigators to be properly acknowledged. We wish to include photographs, and anecdotes from fieldwork and other matters of interest from behind-the-scenes. It is time to dust off those old boxes of ISAAC records!

To view your centre, select it from the menu at <http://isaac.auckland.ac.nz/story/centres/centres.html>. To add your contribution, please send a word document with your information and any photographs you may have to Eamon Ellwood ([e.ellwood@auckland.ac.nz](mailto:e.ellwood@auckland.ac.nz)). While these contributions can still be added to the website, it is unfortunately too late to add them to the pdf version.

### **Current responses**

Centres: 124/306  
Countries: 47/81 (National Coordinators)  
Regions: 9/9

The ISAAC Story can be viewed at:  
<http://isaac.auckland.ac.nz/story/index.html>

To ensure a comprehensive document we need to have up to date contact details for all the ISAAC collaborators. If you know of any collaborators whose emails have changed, particularly those listed below, please send these to Eamon Ellwood ([e.ellwood@auckland.ac.nz](mailto:e.ellwood@auckland.ac.nz)).

Dr Mao Bao-Shan – Shanghai, CHINA	Prof Abedelkrim Bennis - Rabat, MOROCCO
Dr Marco Biocca – Bologna, ITALY	Dra Eliana Cortez – Santiago, CHILE
Dr G Jayaraj – Chennai, INDIA	Dr Mohan Keshav Joshi – Mumbai, INDIA
Dr Antti Koivikko – Turku, FINLAND	Dr Ramesh M. Maheshwari – Akola, INDIA
Dr Gustavo A Ordoñez – Cali, COLUMBIA	Prof Berhane Seyoum - Addis Ababa, ETHIOPIA
Dr Lim Wee Yeong – Ipoh, MALAYSIA	Prof Tamara Aripova – Tashkent, UZBEKISTAN

Kind regards  
Eamon Ellwood  
ISAAC Webmaster  
[e.ellwood@auckland.ac.nz](mailto:e.ellwood@auckland.ac.nz)

# ISAAC Publications of worldwide analyses (updated November 2011)

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## ISAAC Phase One Publications (worldwide)

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### 1.0 Preliminary Papers

- 1.1 ISAAC Phase One Manual. 2nd ed. Auckland and Münster: ISAAC Steering Committee, 1993.
- 1.2 Pearce N, Weiland S, Keil U, Langridge P, Anderson HR, Strachan D, Bauman A, Young L, Gluyas P, Ruffin D, Crane J, Beasley R. Self-reported prevalence of asthma symptoms in children in Australia, England, Germany and New Zealand: an international comparison using the ISAAC protocol. *Eur Respir J* 1993; 6: 1455-61. [263 citations]
- 1.3 Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, Mitchell EA, Pearce N, Sibbald B, Stewart AW, Strachan D, Weiland SK, Williams HC. International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur Respir J* 1995; 8: 483-91. [1104 citations]

### 2.0 Main Findings

- 2.1 Strachan D, Sibbald B, Weiland S, Aït-Khaled N, Anabwani G, Anderson HR, Asher MI, Beasley R, Björkstén B, Burr M, Clayton T, Crane J, Ellwood P, Keil U, Lai C, Mallol J, Martinez F, Mitchell E, Montefort S, Pearce N, Robertson C, Shah J, Stewart A, von Mutius E, Williams H. Worldwide Variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC). *Pediatr Allergy Immunol* 1997; 8(4): 161-76. [264 citations]
- 2.2 The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *The Lancet* 1998; 351(9111): 1225-32. [1717 citations]
- 2.3 Williams H, Robertson C, Stewart A, Aït-Khaled N, Anabwani G, Anderson HR, Asher MI, Beasley R, Björkstén B, Burr M, Clayton T, Crane J, Ellwood P, Keil U, Lai C, Mallol J, Martinez F, Mitchell E, Montefort S, Pearce N, Shah J, Sibbald B, Strachan D, von Mutius E and Weiland S. Worldwide variations in the prevalence of symptoms of atopic eczema in the international study of asthma and allergies in childhood. *J Allergy Clin Immunol* 1999; 103(1 Pt 1): 125-38. [359 citations]
- 2.4 The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998; 12(2): 315-335. [580 citations]

### 3.0 Other Overview Papers

- 3.1 Asher MI, Weiland SK on behalf of the ISAAC Steering Committee. The International Study of Asthma and Allergies in Childhood (ISAAC). *Clin Exp Allergy* 1998; 28 Suppl 5: 52-66. [112 citations]
- 3.2 Beasley R, Ellwood P, Asher I. International patterns of the prevalence of pediatric asthma the ISAAC program. *Pediatr Clin North Am* 2003; 50(3): 539-53. Copyright© Elsevier 2003 [42 citations]
- 3.3 Lai C, Pearce N. The contribution of ISAAC to the understanding of asthma. *Leukotriene Res & Clin Rev* 2001; 2: 1-4.
- 3.4 Mallol J, Asher MI, Williams H, Clayton T, Beasley R. ISAAC findings in children aged 14 years: an overview. *Allergy Clin Immunol Int* 1999; 11: 176-82.
- 3.5 von Mutius E. Epidemiology of asthma: ISAAC--International Study of Asthma and Allergies in Childhood. *Pediatr Allergy Immunol* 1996; 7(9 Suppl): 54-6. [6 citations]

### 4.0 Ecological Analyses

- 4.1 Anderson HR, Gupta R, Kapetanakis V, Asher MI, Clayton T, Robertson CF, Strachan DP and the ISAAC Steering Committee. International correlations between indicators of prevalence, hospital admissions and mortality for asthma in children. *Int J Epidemiol* 2008; 37(3):573-82. [9 citations]
- 4.2 Anderson HR, Poloniecki JD, Strachan DP, Beasley R, Björkstén B, Asher MI and the ISAAC Phase One Study Group. Immunization and symptoms of atopic disease in children: Results from the International Study of Asthma and Allergies in Childhood. *Am J Publ Health* 2001; 91(7): 1126-9. [68 citations]
- 4.3 Burr ML, Emberlin JC, Treu R, Cheng S, Pearce NE and the ISAAC Phase One Study Group. Pollen counts in relation to the prevalence of allergic rhinoconjunctivitis, asthma and atopic eczema in the International Study of Asthma and Allergies in Childhood (ISAAC). *Clin Exp Allergy* 2003; 33(12): 1675-80. [33 citations]
- 4.4 Ellwood P, Asher MI, Björkstén B, Burr M, Pearce N, Robertson CF, and the ISAAC Phase One Study Group. Diet and asthma, allergic rhinoconjunctivitis and atopic eczema symptom prevalence: An ecological analysis of the International Study of Asthma and Allergies in Childhood (ISAAC) data. *Eur Respir J* 2001; 17(3): 436-443. [88 citations]
- 4.5 Foliaki S, Kildegard Nielsen S, Björkstén B, von Mutius E, Cheng S, Pearce N, and the ISAAC Phase I Study Group. Antibiotic sales and the prevalence of symptoms of asthma, rhinitis, and eczema: The International Study of Asthma and Allergies in Childhood (ISAAC). *Int J Epidemiol* 2004; 33(3): 558-63. [24 citations]
- 4.6 Mitchell EA, Stewart AW, on behalf of the ISAAC Phase One Study Group. The ecological relationship of tobacco smoking to the prevalence of symptoms of asthma and other atopic diseases in children: The International Study of Asthma and Allergies in Childhood (ISAAC). *Eur J Epidemiol* 2001; 17(7): 667-73. [19 citations]
- 4.7 Shirtcliffe P, Weatherall M, Beasley R on behalf of the ISAAC Phase One Study Group. An inverse correlation between estimated tuberculosis notification rates and asthma symptoms. *Respirology* 2002; 7(2): 153-5. [18 citations]
- 4.8 Stewart AW, Mitchell EA, Pearce N, Strachan DP, Weiland SK on behalf of the ISAAC Steering Committee. The relationship of per capita gross national product to the prevalence of symptoms of asthma and other atopic diseases in children (ISAAC). *Int J Epidemiol* 2001; 30: 173-9. [66 citations]
- 4.9 von Mutius E, Pearce N, Beasley R, Cheng S, von Ehrenstein O, Björkstén B, Weiland S, on behalf of the ISAAC Steering Committee. International patterns of tuberculosis and the prevalence of symptoms of asthma, rhinitis and eczema. *Thorax* 2000; 55(6): 449-453. [112 citations]
- 4.10 Weiland SK, von Mutius E, Hüsing A, Asher MI, on behalf of the ISAAC Steering Committee. Intake of trans fatty acids and prevalence of childhood asthma and allergies in Europe. *Lancet* 1999; 353(9169): 2040-1. [92 citations]
- 4.11 Weiland SK, Hüsing A, Strachan, Rzehak P, Pearce N, and the ISAAC Phase One Study Group. Climate and the prevalence of symptoms of asthma, allergic rhinitis and atopic eczema in children. *Occup Environ Med* 2004; 61(7): 609-15. [70 citations]
- 4.12 Anderson HR, Ruggles R, Pandey KD, Kapetanakis V, Brunekreef B, Lai CKW, Strachan DP, Weiland SK. Ambient particulate pollution and the world-wide prevalence of asthma, rhinoconjunctivitis and eczema in children: Phase One of the International Study of Asthma and Allergies in Childhood (ISAAC). *Occup Environ Med* 2010; 67(5): 293-300. doi:10.1136/oem.2009.048785. epub: 9 October 2009. [1 citations]
- 4.13 Asher MI, Stewart AW, Mallol J, Montefort M, Lai CKW, Aït-Khaled N, Odhiambo J, and the ISAAC Phase One Study Group. Which population level environmental factors are associated with asthma, rhinoconjunctivitis and eczema? A review of the ecological analyses of ISAAC Phase One. *Respiratory Research*. 2010; 11(8) [5 citations]

## **5.0 Other Papers**

- 5.1 Crane J, Mallol J, Beasley R, Stewart A, Asher MI, on behalf of the International Study of Asthma and Allergies in Childhood (ISAAC) Phase I study group. Agreement between written and video

questions for comparing asthma symptoms in ISAAC. *Eur Respir J* 2003; 21(3): 455-61. [45 citations]

- 5.2 Pearce N, Sunyer J, Cheng S, Chinn S, Björkstén B, Burr M, Keil U, Anderson HR, Burney P, on behalf of the ISAAC Steering Committee and the European Community Respiratory Health Survey. Comparison of asthma prevalence in the ISAAC and the ECRHS. *Eur Respir J* 2000; 16(3): 420-6. [93 citations]

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## ISAAC Phase Two Publications (worldwide)

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### 1.0 Preliminary Papers

- 1.1 ISAAC, ISAAC Phase II Modules. Münster, Germany. May 1998.
- 1.2 von Mutius E, Weiland SK, Keil U and the ISAAC Steering Committee. The International Study of Asthma and Allergies in Childhood (ISAAC): study design and methods of phase II. *Allergologie* 1999; 22(5):283-288 [1 citations]
- 1.3 Weiland SK, von Mutius E, Keil U and the ISAAC Steering Committee. The International Study of Asthma and Allergies in Childhood (ISAAC): rationale methods and outlook. *Allergologie* 1999; 22(5):275-282 [3 citations]
- 1.4 Weiland SK, Björkstén B, Brunekreef B, Cookson WO, von Mutius E, Strachan DP and the International Study of Asthma and Allergies in Childhood Phase II Study Group. Phase II of the International Study of Asthma and Allergies in Childhood (ISAAC II): rationale and methods. *Eur Resp J* 2004; 24(3): 406-12. [123 citations]

### 2.0 Main Findings

- 2.1 Weinmayr G, Weiland SK, Björkstén B, Brunekreef B, Büchele G, Cookson WO, García-Marcos L, Gotua M, Gratziau C, van Hage M, von Mutius E, Riiikjäv MA, Rzehak P, Stein RT, Strachan DP, Tsanakas J, Wickens K, Wong GW and the ISAAC Phase Two Study Group. Atopic sensitization and the international variation of asthma symptom prevalence in children. *Am J Respir Crit Care Med* 2007; 176(6): 565-74. [85 citations]
- 2.2 Flohr C, Weiland SK, Weinmayr G, Björkstén B, Bråbäck L, Brunekreef B, Büchele G, Clausen M, Cookson WOC, von Mutius E, Strachan DP, Williams HC, and the ISAAC Phase Two Study Group. The role of atopic sensitization in flexural eczema: Findings from the International Study of Asthma and Allergies in Childhood Phase Two. *J Allergy Clin Immunol* 2008; 121(1): 141-7. [26 citations]
- 2.3 Weinmayr G, Forastiere F, Weiland SK, Rzehak P, Abramidze T, Annesi-Maesano I, Björkstén B, Brunekreef B, Büchele G, Cookson WO, von Mutius E, Pistelli R, Strachan DP; the ISAAC Phase Two Study Group\*. International variation in prevalence of rhinitis and its relation with sensitization to perennial and seasonal allergens. *Eur Respir J* 2008; 32: 1250–1261 [16 citations]
- 2.4 Gehring U, Strikwold M, Schram-Bijkerk D, Weinmayr G, Genuneit J, Nagel G, Wickens K, Siebers R, Crane J, Doekes G, Di Domenicantonio R, Nilsson L, Priftanji A, Sandin A, El-Sharif N, Strachan D, van Hage M, von Mutius E, Brunekreef B, and the ISAAC Phase Two Study Group. Asthma and allergic symptoms in relation to house dust endotoxin: Phase Two of the International Study on Asthma and Allergies in Childhood (ISAAC II). *Clin Exp Allergy* 2008; 38: 1911–1920 [17 citations]
- 2.5 Flohr C, Weinmayr G, Weiland SK (deceased), Addo-Yobo E, Annesi-Maesano I, Björkstén B, Bråbäck L, Büchele G, Chico M, Cooper P, Clausen M, El-Sharif N, Martínez Gimeno M, Mathur RS, von Mutius E, Morales Suárez-Varela MM, Pearce N, Svabe V, Wong GWK, Yu M, Zhong NS, Williams HC. How well do questionnaires perform compared with physical examination in detecting flexural eczema? Findings from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two. *Br J Dermatol* 2009; 161(4): 846-853. Epub 27 May. [8 citations]
- 2.6 Nagel G, Büchele G, Weinmayr G, Björkstén B, Chen Y-Z, Wang H, Nystad W, Saraçlar Y, Bråbäck L, Batllés-Garrido J, García-Hernández G, Weiland SK, the ISAAC Phase Two Study Group. Effect of Breastfeeding on Asthma, Lung function, and Bronchial Hyperreactivity in

- ISAAC-Phase-Two. *Eur Resp J*. 2009; 33: 993–1002; Epub 2009 Jan22. [11 citations]
- 2.7 Genuneit J, Cantelmo JL, Weinmayr G, Wong GWK, Cooper PJ, Riiikjäär MA, Gotua M, Kabesch M, von Mutius E, Forastiere F, Crane J, Nystad W, El Sharif N, Batllés-Garrido J, García-Marcos L, García-Hernández G, Morales Suárez-Varela MM, Nilsson L, Bråbäck L, Saraçlar Y, Weiland SK, Cookson WOC, Strachan DP, Moffatt MF, ISAAC Phase Two Study Group. A multi-centre study of candidate genes for wheeze and allergy. The International Study of Asthma and Allergies in Childhood Phase Two. *Clin Exp Allergy* 2009 Dec; 39(12): 1875-1888 [9 citations]
  - 2.8 Weinmayr G, Genuneit J, Nagel G, Björkstén B, van Hage M, Priftanji A, Cooper P, Rijkjäär M-A, von Mutius E, Tsanakas J, Forastiere F, Doekes G, Garrido JB, Morales Suárez-Varela MM, Bråbäck L, Strachan DP, the ISAAC Phase Two Study Group. International variations in associations of allergic markers and diseases in children: ISAAC Phase Two. *Allergy* 2010; 65(6): 766–775. epub 21 Dec 2009. DOI:10.1111/j.1398-9995.2009.02283.x [7 citations]
  - 2.9 Nagel G, Weinmayr G, Kleiner A, Garcia-Marcos L, Strachan DP, the ISAAC Phase Two Study Group. Effect of diet on asthma and allergic sensitisation in the International Study on Allergies and Asthma in Childhood (ISAAC) Phase Two. *Thorax* 2010; 65(6): 516-522 doi:10.1136/thx.2009.128256 [13 citations]
  - 2.10 Büchele G, Genuneit J, Weinmayr G, Björkstén B, Gehring U, von Mutius E, Priftanji A, Stein RT, Addo-Yobo EO, Priftis KN, Shah JR, Forastiere F, Svabe V, Crane J, Nystad W, García-Marcos L, Saraçlar Y, El-Sharif N, Strachan DP and the ISAAC Phase Two Study Group. International Variations in Bronchial Responsiveness in Children: Findings From ISAAC Phase Two. *Pediatr Pulmonol* 2010; 45(8): 796–806 [3 citations]
  - 2.11 Flohr C, Nagel G, Weinmayr G, Kleiner A, Strachan DP, Williams HC and the ISAAC Phase Two Study Group. Lack of evidence for a protective effect of prolonged breastfeeding on childhood eczema: lessons from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two. *Br J Dermatol* 2011; 165: 1280-1289. DOI: 10.1111/j.1365-2133.2011.10588.x

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### ISAAC Phase Three Publications (worldwide)

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#### 1.0 Preliminary Papers

- 1.1 Ellwood P, Asher MI, Beasley R, Clayton TO, Stewart AW on behalf of the ISAAC Steering Committee and the ISAAC Phase Three Study Group. ISAAC Phase Three Manual. Auckland. July 2000. ISBN 0-473-06910-5.
- 1.2 Ellwood P, Asher MI, Beasley R, Clayton TO, Stewart AW and the ISAAC Steering Committee. The International Study of Asthma and Allergies in Childhood (ISAAC): Phase Three rationale and methods. *Int J Tuberc Lung Dis* 2005; 9(1): 10-6. [80 citations]

#### 2.0 Main Findings

- 2.1 Asher MI, Montefort S, Björkstén B, Lai CKW, Strachan DP, Weiland SK, Williams H, and the ISAAC Phase Three Study Group. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *The Lancet* 2006; 368(9537): 733-743. [606 citations]
- 2.2 Pearce N, Ait-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E, Robertson C, and the ISAAC Phase Three Study Group. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2007; 62(9): 758-66. [158 citations]
- 2.3 Björkstén B, Clayton T, Ellwood P, Stewart A, Strachan D, and the ISAAC Phase Three Study Group. Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma and Allergies in Childhood. *Pediatr Allergy Immunol* 2008; 19(2): 110-24. [50 citations]
- 2.4 Williams H, Stewart A, von Mutius E, Cookson B, Anderson HR and the International Study of Asthma and Allergies in Childhood (ISAAC) Phase One and Three Study groups. Is eczema really

on the increase worldwide? *J Allergy Clin Immunol* 2008; 121(4): 947-54. [42 citations]

- 2.5 Aït-Khaled N, Pearce N, Anderson HR, Ellwood P, Montefort S, Shah J, and the ISAAC Phase Three Study Group. Global map of the prevalence of symptoms of rhinoconjunctivitis in children: The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three. *Allergy* 2009; 64: 123–148 [29 citations]
- 2.6 Lai CKW, Beasley R, Crane J, Foliaki S, Shah J, Weiland S, and the ISAAC Phase Three Study Group. Global variation in the prevalence and severity of asthma symptoms: Phase Three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2009; 64: 476–483. Epub 2009 Feb22. [46 citations]
- 2.7 Odhiambo J, Williams H, Clayton T, Robertson C, Asher MI, and the ISAAC Phase Three Study group. Global variations in prevalence of eczema symptoms in children from ISAAC Phase Three. *J Allergy Clin Immunol.* 2009;124(6):1251-8. [20 citations]

### **3.0 Environmental Questionnaire Analyses**

- 3.1 Beasley R, Clayton T, Crane J, von Mutius E, Lai CKW, Montefort S, Stewart A, for the ISAAC Phase Three Study Group. Association between paracetamol use in infancy and childhood, and risk of asthma, rhinoconjunctivitis, and eczema in children aged 6-7 years: analysis from Phase Three of the ISAAC programme. *Lancet* 2008; 372(9643): 1039-48. [76 citations]
- 3.2 Brunekreef B, Stewart AW, Anderson HR, Lai CKW, Pearce NE, and the Phase Three Study Group. Self Reported Truck Traffic on the Street of Residence and Symptoms of Asthma and Allergic Disease: A Global Relationship in ISAAC Phase Three. *Environ Health Perspect* 2009; 117(11): 1791-98. Epub July 2009. doi:10.1289/ehp.0800467. [10 citations]
- 3.3 Foliaki S, Pearce N, Björkstén B, Mallol J, Montefort S, von Mutius E and the ISAAC Phase Three Study Group. Antibiotic use in infancy and risk of symptoms of asthma, rhinoconjunctivitis and eczema in 6 to 7 year old children: ISAAC Phase Three. *J Allergy Clin Immunol* 2009;124(5):982-9. [15 citations]
- 3.4 Beasley RW, Clayton TO, Crane J, Lai CKW, Montefort SR, von Mutius E, Stewart AW, and the ISAAC Phase Three Study Group. Acetaminophen Use and Risk of Asthma, Rhinoconjunctivitis and Eczema in Adolescents: ISAAC Phase Three. *Am J Resp Crit Care Med.* 2011; 183(2): 171-178. epub 13 August 2010 [4 citations]
- 3.5 Björkstén B, Aït-Khaled N, Asher MI, Clayton TO, Robertson C, the ISAAC Phase Three Study Group. Global analysis of breast feeding and risk of symptoms of asthma, rhinoconjunctivitis and eczema in 6—7 year old children: ISAAC Phase Three. *Allergol Immunopathol (Madr)*; 2011. doi:10.1016/j.aller.2011.02.005

### **4.0 Other papers**

- 4.1 Ellwood P, Williams H, Aït-Khaled N, Björkstén B, Robertson C, ISAAC Phase III Study Group. Translation of questions: The International Study of Asthma and Allergies in Childhood (ISAAC) experience. *Int J Tuberc Lung Dis.* September 2009; 13(9): 1174-1182 [7 citations]
- 4.2 Asher MI. Recent perspectives on global epidemiology of asthma in childhood. *Allergol Immunopathol(Madr).*2010;38(2):83-7. epub Jan [4 citations]
- 4.3 Flohr C. What can we learn about eczema from the International Study of Asthma and Allergies in Childhood (ISAAC)? *Allergologie* 2010; 33(6): 242–250 [1 citations]
- 4.4 Ellwood P, Asher MI, Stewart AW and the ISAAC Phase III Study Group. The impact of the method of consent on response rates in the ISAAC time trends study. *Int J Tuberc Lung Dis.* 2010 Aug;14(8):1059-65. [2 citations]
- 4.5 Flohr C. Recent perspectives on the global epidemiology of childhood eczema. *Allergol Immunopathol (Madr).* 2011;39(3):174-182

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