

ISAAC

INTERNATIONAL

STUDY OF

ASTHMA AND

ALLERGIES IN

CHILDHOOD

NEWSLETTER – FEBRUARY 2001

On the 13th and 14th of October 2000 the ISAAC Steering Committee held the Eleventh International Workshop on International Study of Asthma and Allergies in Childhood (ISAAC) conference in Auckland, New Zealand.

The following nineteen members attended the conference:

Associate Professor Innes Asher, Chair, *Auckland, New Zealand*; Professor Richard Beasley, *Wellington, New Zealand*; Professor Bengt Björkstén, *Stockholm, Sweden*; Professor Neil Pearce, *Wellington, New Zealand*; Professor David Strachan, *London, United Kingdom*; PD Dr Stephan Weiland, *Münster, Germany*; Professor Nadia Ait-Khaled, *Paris, France*; Professor H Ross Anderson, *London, United Kingdom*; Dr Michael Burr, *Cardiff, Wales*; Associate Professor Julian Crane, *Wellington, New Zealand*; Dr Chris Lai, *Hong Kong, SAR China*; Professor Javier Mallol, *Santiago, Chile*; Associate Professor Ed Mitchell, *Auckland, New Zealand*; Dr Stephen Montefort, *Naxxar, Malta*; Dr Joseph Odhiambo, *Nairobi, Kenya*; Dr Colin Robertson, *Melbourne, Australia*; Dr Jayant Shah, *Mumbai, India*; Mr Alistair Stewart, *Auckland, New Zealand*; PD Dr med Erika von Mutius, *München, Germany*.

With apologies from:

PD Professor med Ulrich Keil, *Münster, Germany*; Professor Fernando Martinez, *Tucson, USA*; Professor Gregory J Redding, *Seattle, USA*; Professor Hywel Williams, *Nottingham, United Kingdom*.

The conference was a resounding success with focused discussions and meaningful contributions from all that attended.

This success can also be attributed to the:

- ◆ generous sponsorship of GlaxoWellcome New Zealand
- ◆ conference venue Te Whau Lodge, Waiheke Island - Auckland

The Eleventh International Workshop on International Study of Asthma and Allergies in Childhood (ISAAC) conference concentrated on ISAAC Phase Two, which is being completed in 30 centres in 20 countries, and ISAAC Phase Three.

The pilot studies of the Environmental Questionnaire for Phase Three were reviewed and the modifications have been finalised. The large interest in ISAAC Phase Three is illustrated later in the newsletter.

Thank you all for your participation, contributions and support. We wish all our ISAAC collaborators and friends a happy and successful New Year.

CORRESPONDENCE TO:

Dr Innes Asher

ISAAC International Data Centre
Division of Paediatrics
Faculty of Medical & Health Sciences
University of Auckland
Private Bag 92 019
Auckland
NEW ZEALAND

Ph: 64 9 373 7599 ext 6451
Fax: 64 9 373 7602
Email: mi.asher@auckland.ac.nz
Website: <http://isaac.auckland.ac.nz>

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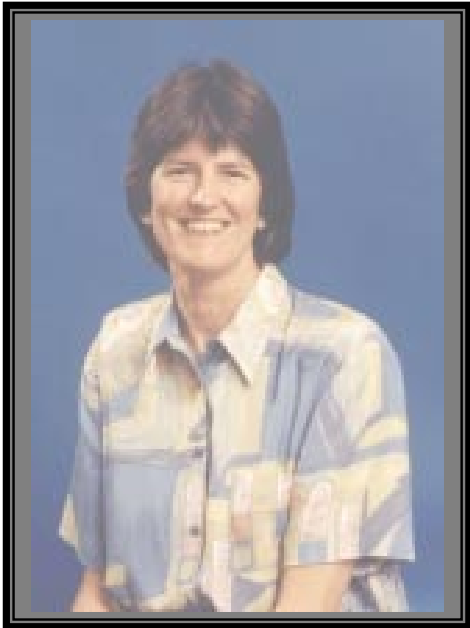
On behalf of the ISAAC International Data Centre and Steering Committee
mi.asher@auckland.ac.nz

Innes Asher

ISAAC PROFILE

The ISAAC mailing list consists of over 300 members worldwide. In order to inform our members, future ISAAC Newsletters will profile key ISAAC members, describing their roles, interest and families.

ISAAC profile: Associate Professor Innes Asher, Chairperson ISAAC



Innes currently resides in Devonport, Auckland, and New Zealand. Devonport is a peninsula near Auckland City centre, with wonderful beaches and friendly small town atmosphere. As Innes works in Auckland, she usually opts to travel to and from work by ferry.

Innes attended Auckland Girls Grammar School and from there completed her tertiary education at the University of Auckland where she attained her BSc in Human Biology, MBChB, and FRACP Paediatrics.

Innes undertook her paediatric training in Auckland, her home city. Towards the end of this she helped set up a Child Health Clinic for Tuhoe Maori at Ruatoki, a valley near Whakatane where she worked as Paediatrician. Whakatane is a coastal township located in a beautiful part of the East Coast of the North Island of New Zealand. Then she spent 3 years at the Montreal Children's Hospital training as a Paediatric Pulmonologist, before returning to the University of

Auckland as a Senior Lecturer in Paediatric Respiratory Medicine.

Innes coordinates the Child Development and Family Study and has a large role in undergraduate and postgraduate teaching. She is the editorial councillor for Southern Hemisphere for the journal Paediatric Pulmonology.

Innes has developed and heads the Starship Paediatric Respiratory Service, a large multidisciplinary team that receives complex cases from throughout New Zealand. She is an active advocate for children, including the effects on them of respiratory illness, hospitalisation and poverty.

Her roles in ISAAC are:

- ◆ Steering Committee, Chair
- ◆ Executive Committee member
- ◆ Steering Committee member
- ◆ National Coordinator
- ◆ Principal Investigator
- ◆ Director of IIDC

Outside of work, Innes enjoys supporting her two sons with their activities. Harry (14 years old) is a rower and both boys play hockey. Robert (12 years old) is a keen drummer. Innes plays celtic Penny Whistle, collects seashells, enjoys music and the outdoors and spending time with family and friends.

mi.asher@auckland.ac.nz

INCEPTION OF ISAAC

At the beginning, Hippocrates recognised the importance of the environment for many diseases, including asthma. Hippocrates identified environmental factors although he was not an epidemiologist, as he did not carry out numerical analyses. There was no epidemiology of asthma until the 20th century. Before the 20th century we only knew about the association with other allergic diseases and environmental effects. In the 19th century known associations with asthma, included the effects of weather, pressure, thunderstorms, environmental tobacco smoke (ETS), 'fenny' country, season, occupation, diet, exercise, the 'passions', feather beds, animals and pollen. The only major risk factor missing from this list is infection due to the lack of germ theory.

The year is 1990, the place Bochum and the focus of discussion, epidemiology. It was at these discussions that ISAAC was born with the recognition that Asthma epidemiology had only got so far looking at disease within populations. Geoffrey Rose's work was a strong influence on the development of ISAAC. The importance of ISAAC stems from the large number of centres, the heterogeneity in prevalence that has been identified, and the simple design.

ISAAC was formally created in 1991. A graph of participating centres shows initial slow growth, followed by large surge in centres. This increase reflected the efforts of the Regional Co-ordinators and self-recruitment, and showed how positively participation in ISAAC was viewed by investigators around the world.

1991 ISAAC Members:

Professor Ross Anderson
Associate Professor Innes Asher
Associate Professor Julian Crane
PD Professor Ulrich Keil
Professor Fernando Martinez
Associate Professor Ed Mitchell
PD Dr Erika von Mutius
Professor Neil Pearce
Dr Colin Roberston
Dr Bonnie Sibbald
Professor David Strachan
PD Professor Ulrich Wahn
PD Dr Stephan Weiland

Over the last ten years the ISAAC Steering Committee has grown and now comprises of twenty-three members from nine regions throughout the world.

ISAAC STEERING COMMITTEE CONFERENCE TIMELINE:

1990	Bochum
1991	Bochum
1992	London
1993	Geneva
1994	Nice
1995	Barcelona
1996	Stockholm
1997	Berlin
1998	Geneva
1999	Madrid
2000	Auckland

SUCCESS OF ISAAC

The success of ISAAC is due to the way we work together, set aims and communication emphasising the following ISAAC key words:

- ◆ Vision
- ◆ Simplicity
- ◆ Standardisation
- ◆ Enthusiasm
- ◆ Participation
- ◆ Communication
- ◆ Consensus
- ◆ Manuals
- ◆ Multidisciplinary
- ◆ Worldwide
- ◆ Regional
- ◆ National
- ◆ Local
- ◆ Networks
- ◆ Self-recruitment
- ◆ Rigorous
- ◆ Efficient
- ◆ Friendly

Based on presentations by Prof Ross Anderson, Assoc Prof Innes Asher and Dr Colin Robertson

Summarised by Mr Tadd Clayton
t.clayton@auckland.ac.nz
ISAAC International Data Centre

ISAAC REGIONAL CO-ORDINATORS REPORTS

ASIA-PACIFIC AND SOUTH EAST ASIA

Auckland Conference Region Report

So far, the following countries in our region have expressed interest in conducting Phase Three:

China, South Korea, Japan, Taiwan, Hong Kong, Thailand, Philippines, Malaysia, Singapore and perhaps Indonesia.

We are going to hold a meeting in Sydney during the ICACI meeting. I am still awaiting replies from the national co-ordinators regarding funding.

We shall be able to complete the pilot EQ questionnaire in Hong Kong by the end of October. I have not asked the national co-ordinators in our region to do the pilot study. As I indicated earlier, I would suggest leaving the EQ optional, as the time and work required for this part of the study may not be acceptable by some of the schools.

Post-Auckland Region Reports

An Asia-Pacific Regional Meeting was held on 17th October 2000 in Sydney. The main focus of the meeting was those centres implementing Phase Three in Asia-Pacific and South East Asia. We confirmed that the following 10 countries will be participating in Phase Three.

- ◆ China, three centres
- ◆ Hong Kong, one centre
- ◆ Indonesia, one centre
- ◆ Taiwan, one centre
- ◆ Singapore, one centre
- ◆ South Korea, two centres
- ◆ Philippines, one centre
- ◆ Japan, one centre
- ◆ Thailand, one centre
- ◆ Malaysia, two centres

All centres except those in China will conduct the study on both age groups (6-7 and 13-14 years old school children) but China will only do the older age group. Korea will begin their Phase Three in November 2000 while the others will commence after January 2001.

It was resolved that the 10 participating countries will include a short questionnaire on risk factors, which are relevant to the Asia-Pacific and South East Asian region.

Dr Chris Lai

keilai@netvigator.com

ISAAC Regional Co-ordinator, Asia Pacific & South East Asia

OCEANIA

Auckland Conference Region Report

As the new Regional Co-ordinator for Oceania I am catching up fast. In Phase One Oceania consisted of Australia and New Zealand only. There was little difference in Phase One between the Oceania centres and prevalence was similar to other English speaking countries. This finding was surprising to New Zealand collaborators, as the expectation was that New Zealand would have the highest prevalence and severity.

The following Centres that participated in Phase One intend to take part in Phase Three:

- ◆ Sydney (Australia)
- ◆ Melbourne (Australia)
- ◆ Perth (Australia)
- ◆ Auckland (New Zealand)
- ◆ Wellington (New Zealand)
- ◆ Christchurch (New Zealand)
- ◆ Nelson (New Zealand)
- ◆ Bay of Plenty (New Zealand)

Two centres that took part in Phase One (Adelaide (Australia) and Hawkes Bay (New Zealand)) are not planning to take part in Phase Three.

The following Centres have already taken part in an ISAAC Phase One/Phase Two study for which the Phase I data can be used for Phase Three:

New Caledonia – 7,000 13-14 year olds
French Polynesia – 4339 13-14 year olds

The following new Centres intend to take part in Phase Three:

- ◆ Rarotonga (Cook Islands)
- ◆ Suva (Fiji)
- ◆ Apia (Samoa)
- ◆ Nuku'alofa (Tonga)

A number of Pacific centres have also verbally expressed an interest in conducting Phase Three in their centres but are yet to formally register.

Neil Pearce together with Dr Sunia Foliaki from Tonga is conducting the recruitment and co-ordination of new Phase Three centres in the Oceania region. A meeting of the national/centre Co-ordinators will be held early in 2001.

Professor Neil Pearce

n.e.pearce@massey.ac.nz

ISAAC Regional Co-ordinator, Oceania

INDIAN SUB-CONTINENT

Auckland Conference Region Report

Communication:

Although communication between India and neighbouring countries of Bangladesh and Sri Lanka are good due to email and fax facilities, communication within India with the principal investigators remains a problem. This is primarily due to lack of email and fax facilities with greater reliance on postal and courier services, which cause delay and increase the cost of carrying out the study.

Meetings:

During Phase One ISAAC study, 3 national meetings were held of principal investigators, one was in Delhi for investigators from North and Eastern India. The other was in Mumbai for central India and the third was in Madras for principal investigators of south India.

For Phase Two we have had 6 useful meetings, 3 of each for private and municipal investigators. The final meeting of both the groups involved a workshop where demonstration of allergen testing and salient features of clinical examination were shown and discussed respectively. For Phase Two we propose to hold the meeting once the questionnaire, clinical examination and allergy test are completed by the field workers and before saline challenge, blood collection and dust collection are carried out. This is in addition to our regular visits to the schools with the field workers to manage day to day problems.

For Phase Three, zonal meetings as were done in Phase One would again have to be carried out to familiarise the principal investigator with the protocol and details of Phase-III studies. We propose to have at least 3 such meetings, one each for Northern, Western and Southern India. Such zonal meetings involve a sizeable cost as airfares and accommodations of principal investigators have to be reimbursed.

Printing & Translations:

For Phase Three study translations of questionnaire into regional languages of Hindi, Gujarati, Marathi, Malayalam and Tamil are required. The translation and printing of the translated questionnaires would be entrusted to a key principal investigator from each of these regions that could then distribute the questionnaires to principal investigators who require such translations.

Drop-outs:

It was observed in Phase One ISAAC study that although we initially funded 20 Indian centres, only 14 completed the study. The Sri Lankan principal investigator of Phase One study also dropped out after having been given initial funding for his project. In Phase-II, we do not expect any field worker to drop out as the entire study is being carried out in Mumbai under our close supervision. For Phase One studies however, we expect a 30 to 40% dropout and therefore the necessity of recruiting additional centres.

Current status of Phase-II and Phase-III in India:

Phase Two fieldwork was started in August where children in Municipal and private schools are being investigated. Support from Bombay Municipal Corporation has been obtained. It is expected that Phase-II studies will be completed by April 2001.

Recruitment of centres for Phase Three is on. Presently expression of interest has been obtained from 9 Indian centres and 2 from Sri Lanka and one from Bangladesh. Dr. Kabir from Bangladesh has already completed over 3000 written questionnaires in each age group and has forwarded the material to IIDC.

Question 4: Parents could understand vigorous physical activity as well as breathing hard.

Rest of the questions could be answered satisfactorily when they were translated in the regional languages where required.

Post-Auckland Conference Report

ISAAC activity in Mumbai got a big boost following Dr. J.R. Shah's visit to Auckland.

Phase Two fieldwork was started in August 2000 being carried out in 2 groups. Private group comprised of consultant pediatricians and municipal group comprised of full time municipal medical officers. 6 useful meetings, 3 of each group and final meeting of both groups involved a work shop where demonstration of allergen testing and salient features of clinical examination were shown and discussed.

Up till now municipal medical officers have completed questionnaire and allergen testing with skin examination on more than 500 students.

As most of the parents of these students are illiterate these medical officers are filling questionnaire themselves after interviewing parents personally. Other groups of consultant pediatricians have completed approximately 200 students. We are planning to do videography of fieldwork being carried out and also planning to take photographs while students are being clinically examined and while doing allergen testing. We have Dr. Mantri Sumant as a research fellow who is helping in co-ordinating and supervising the activities of Phase Two.

Current Status of Phase Two:

We are planning to arrange zonal meeting of principal investigator to familiarise them with protocol and details of Phase Three studies. 6 centres who have participated in Phase One are willing to carry out Phase Three in addition to this centre from Sri Lanka have shown expression of interest.

Dr. K. Gunasekera is the principal investigator in Sri Lanka. He is doing study in all the nine provinces of Sri Lanka with the help of some consultants in respiratory medicine and pediatrician. GlaxoWellcome Ceylon Ltd. has agreed to sponsor the study. In Bangladesh Dr. Kabir has already completed his Phase Three study on 3000 children in each group and has submitted his abstract to IIDC.

Dr. Jayant R. Shah

jaslok@giasbm01.vsnl.net.in

ISAAC Regional Co-ordinator -India Sub-continent

ISAAC REGIONAL CO-ORDINATORS REPORTS CONTINUED

AFRICA-ANGLOPHONE

Although Africa contributes only 12.9% of the world population (6 billion, 2000), it has the potential of contributing significantly to the objectives of ISAAC since nearly half of Africa's population consists of children, the subject of ISAAC and amongst whom there is growing epidemiological evidence for the importance of allergic disorders including asthma.

Out of 156 centres from 56 countries that participated in ISAAC Phase One, Anglophone Africa had 4 countries (Kenya, South Africa, Nigeria and Ethiopia) with 6 centres participating (4%). I wish to acknowledge the contribution of Professor Gabriel Anabwani, my predecessor, and the respective centre Principal Investigators that contributed to the activities and achievements of International Study of Asthma and Allergies in Childhood Phase One.

While these have been covered somewhat in the Publications that have arisen from the International Data Base, plans are underway to have Anglophone Africa data published in the near future. This has, in my view, the advantage of putting Africa in focus with sufficient details that, for understandable editorial considerations, could not feature in the global profile publications.

For the activities of ISAAC Phase Three (Anglophone Africa), I wish to make the following observations:

- ◆ I expect many more centres to participate.
- ◆ I am grateful to the ISAAC Secretariat for 7,000 pounds grant-in-aid to support my work as Regional Co-ordinator.
- ◆ I am equally grateful to the ISAAC Secretariat for the pledge to support 4 centres (2 in Kenya, 1 each in Nigeria and Ethiopia) to implement ISAAC Phase Three.
- ◆ I expect additional centres that can self-support ISAAC Phase Three to participate. Such centres may be from Zimbabwe, South Africa, Namibia and others.

Finally I am grateful to the ISAAC Secretariat for supporting my recent trip to attend the ISAAC Steering Committee Meeting in Auckland 13-15th October 2000. Both the content and spirit of the meeting, my view, fulfilled the intended objectives and I will always have fond memories of your beautiful country and people.

Dr Joseph Odhiambo

Crdr@todays.co.ke
ISAAC Regional Co-ordinator, Anglophone Africa

AFRICA-FRANCOPHONE

Expression of Interest

Six A centres have sent an expression of interest: Casablanca; Marrakech; Rabat (Morocco); Algiers (Algeria); Conakry (Guinea); Sousse (Tunisia)

Eight B centres have also sent an expression of interest:

- ◆ Kinshasa (Republic Democratic Congo)
- ◆ Brazzaville (Congo)
- ◆ Abidjan (Ivory Coast)
- ◆ Bamako (Mali)
- ◆ Dakar (Senegal)
- ◆ Lome (Togo)
- ◆ Tunis (Tunisia)
- ◆ Yaounde (Cameroon)

Advocacy has been stopped, please see map of African (Anglophone and Francophone) centres that have been recruited.

At present there is only one non-coastal centre. I believe that there will be great value in the collaboration with Dr Joseph Odhiambo for gaining new centres and countries.

Environmental Questionnaire

The Environmental Questionnaire has been piloted in Conakry, Guinea with the following findings:

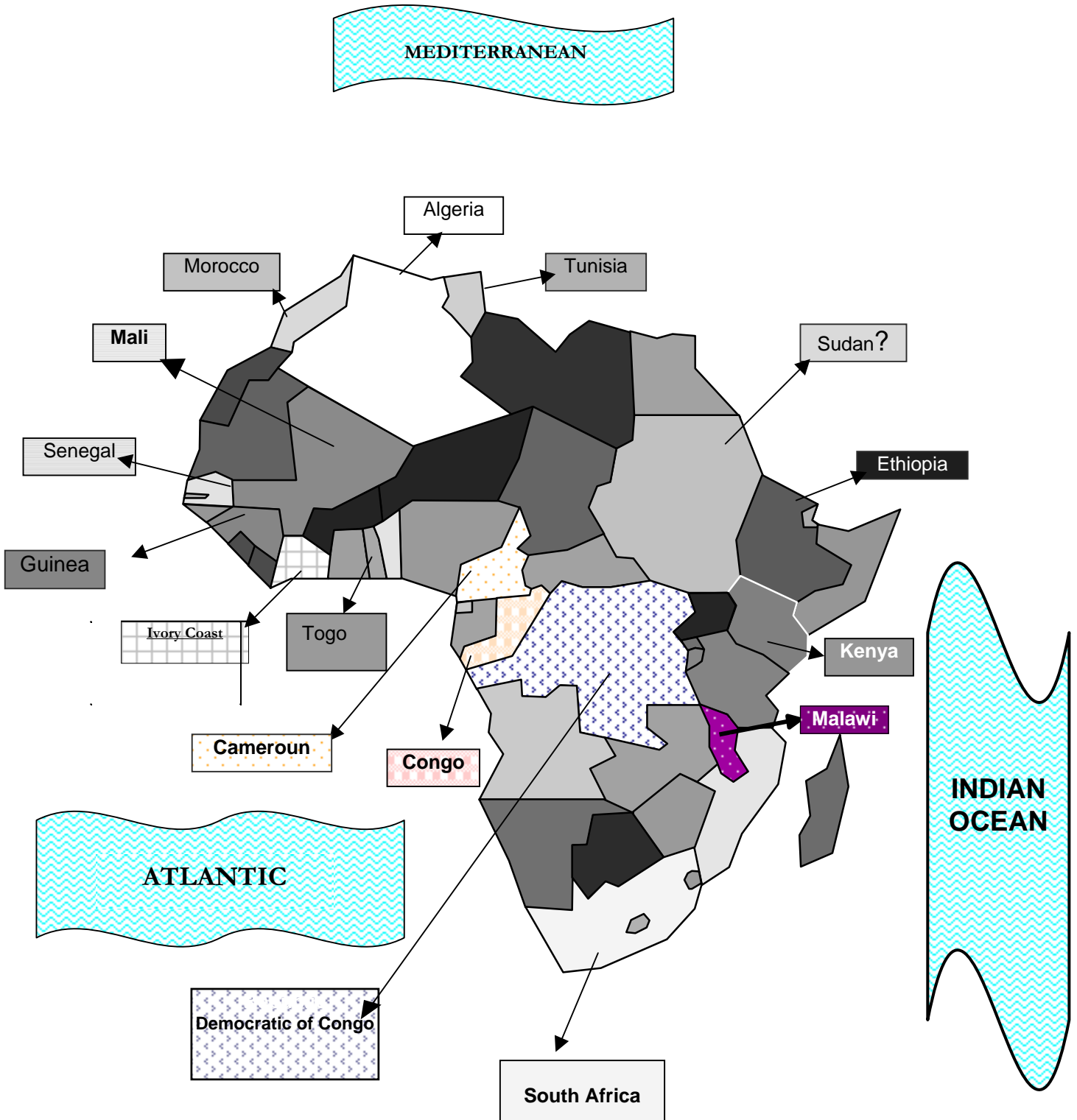
- 1 There was a problem with the ethnic groups, which were not appropriate for Guinea. Many students and parents did not understand 'unit'.
- 2 Some of the food questions components were also not appropriate. For example fast food is not present in Guinea and the word 'nuts' is equivalent to 'peanuts'. Some of the researchers wanted to add 'manioc' (legume used as flour) as some of the respondents did not understand the word 'pasta'.
- 3 We used brand names for paracetamol.
- 4 The education levels in Guinea are different to those proposed in the questionnaire and the terms 'hay fever' and 'eczema' is unknown in Francophone Africa.
- 5 Height proved to be a problem, with weight answered by some respondents and all knew the birth weight.
- 6 Eight of the respondents understood the 'past 12 months'. Only one of the eleven could answer the diet question.

The Environmental Questionnaire took 15 minutes to answer, which was acceptable for 43 of the 50 adolescents. Adolescents had problems with the weight; height, weight at birth, asthma, hay fever, eczema and the researchers suggested using local dialect for some words.

Professor Nadia Aït-Khaled

NaitKhaled@iuatld.org
ISAAC Regional Co-ordinator, Francophone Africa

ISAAC PHASE THREE
EXPECTED CENTRES IN AFRICA



ISAAC REGIONAL CO-ORDINATORS REPORT CONTINUED

EASTERN MEDITERRANEAN

Phase One centres that have expressed an interest in Phase Three are as follows:

Tehran, Rasht, Zanjan and Birjand (Iran) of which Zanjan and Birjand were late Phase One centres, Kuwait, Beirut (Lebanon), Malta, Al-Khod (Oman), Karachi (Pakistan).

New centres that have expressed an interest in Phase Three are:

- ◆ Ramalah and North Gaza (Palestine)
- ◆ Ad Dammam (Saudi Arabia)
- ◆ Khartoum (Sudan)
- ◆ Aleppo, Lattakia and Tartous (Syria)

All Phase One centres are participating in Phase Three. To date Phase Three Registration Documents have been received from Aleppo (Syria).

Dr Stephen Montefort

Stevemonte@waldonet.net.mt

ISAAC Regional Co-ordinator, Eastern Mediterranean

NORTHERN AND EASTERN EUROPE

The Phase Three situation is encouraging with 15 of the 18 phase one centres planning to participate in Phase Three. Therefore, it is foreseen that there will be good data for analysis of time trends. The centres, which participated in Phase One and will perform a Phase Three study in 2001, are situated in Albania, Estonia, Finland, Georgia, Latvia, Poland, Romania, Russia, Sweden and Uzbekistan.

There are nine new centres:

- ◆ Sofia (Bulgaria)
- ◆ Dubrava (Croatia)
- ◆ Pavlodar (Kazakhstan)
- ◆ Kaunas (Lithuania)
- ◆ Reykjavik (Iceland)
- ◆ Oslo (Norway)
- ◆ Belgrade (Yugoslavia)
- ◆ Sombor (Yugoslavia)
- ◆ Nis (Yugoslavia)

Iceland will be of particular interest as it was an outlier for the ECRHS and is also participating in Phase Two.

There is also good news for Phase Two with four centres completed and another three to finish early in 2001.

Professor Bengt Björkstén

Bengt.Bjorksten@admin.ki.se

ISAAC Regional Co-ordinator, Northern & Eastern Europe

WESTERN EUROPE

The recruitment of new centres in Western Europe has been limited, as there was a concentrated effort of the centres in Phase One.

It has been indicated that the majority of the 14 Phase One participating countries (41 centres) will continue onto Phase Three.

Münster has completed Phase Three with a surprising finding of increase of approximately 20% in prevalence of wheeze

Dr Stephan Weiland

weilans@nwz.uni-muenster.de

ISAAC Regional Co-ordinator: Western Europe

LATIN AMERICA

ISAAC in Latin America is going quite well. Recently several abstracts on ISAAC were presented at the Meeting of the Latin American Thoracic Association (ALAT) and they motivated an interesting debate on their results. A paper on ISAAC in Latin America was accepted for publication in *Pediatric Pulmonology* and will be appearing in one of the next issues.

There is great interest from many new centers in the region to collaborate with ISAAC Phase Three, the latter has meant that about 18 (or maybe more) centers from Mexico, Central America, Ecuador, Bolivia and Argentina will participate in the third phase of ISAAC in Latin America.

A direct, fluent and effective communication has been established between collaborating centers in this region and central co-ordinators in New Zealand which has been very useful and has saved a considerable amount of time in redirecting questions and information.

The region (as probably other developing areas of the world, is crossing through an "unstable" economic situation (a bit worse than always...). Thus, most of the centers, which participated in the Phase One will need help to undertake Phase Three (as did in Phase One).

At our Department we have been trying a modern optic system that would let us avoid hiring persons to enter data in the ISAAC database. Using this system will drastically reduce the time employed as well as the costs and possibilities of typing mistakes (see page 13).

In summary, an enthusiastic participation is expected for ISAAC Phase Three in Latin America, with several new centers that have very interesting (and diverse) ethnic, social, ecological and geographic characteristics, which certainly will enrich our knowledge on asthma and allergies in our children.

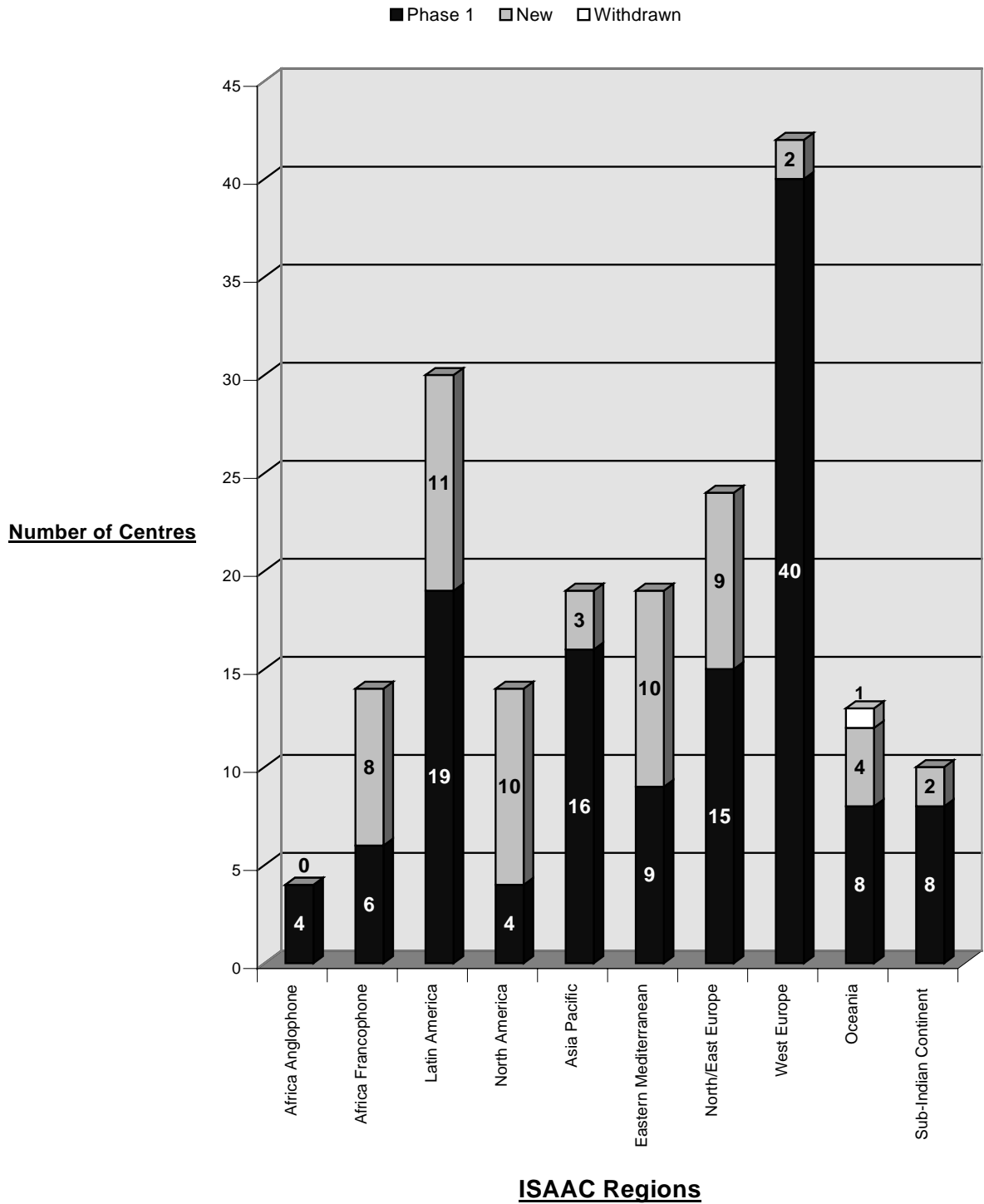
Regarding the pilot EQ (forms Quest 061 and Quest 131): I am finishing the translation and trying to give the meaning to questions to be certain they will be properly understood when the EQ is applied here. There are some questions that could not be reflecting the reality, as occurs for the tobacco smoke passive exposure (form 131): the mother or female guardian perhaps do not smoke but all the other people in the house do (as we have found in our locality where close to 60% of schoolchildren are exposed to tobacco smoke in their houses). Furthermore, we have previously found that 9-12% of the 13-14 year olds are currently smoking tobacco. Thus, and at least in this place, we should add a question for active tobacco smoking. Although important, the vehicle exhaust is not as important here (Santiago) as the particulated material (PM_{2.5} and PM₁₀). I think that here, and also in other air polluted cities of developing countries the word "smog" could be better understood; maybe it could be also added. The questionnaires should be ready to be presented to our Ethic committee in a couple of weeks and to go to schools during the last week of October (hopefully).

Professor Javier Mallol

jmallol@lauca.usach.cl

ISAAC Regional Co-ordinator: America Latin

Phase Three Expression of Interest



ISAAC PHASE THREE

The International Data Centre (IIDC) has had expressions of interest from 190 centres from 86 countries, of which 59 centres are NEW (that is did not participate in Phase One). We welcome the inclusion of new centres provided that they are able to independently fund the study in their area. Please contact the IIDC (p.ellwood@auckland.ac.nz Philippa Ellwood) for further information.

When an 'expression of interest' (EOI) form is sent to the IIDC, the prospective centre is entered into the EOI database and a package sent to them. This package contains three copies of the Phase Three Manual, two copies of the international version of the video and a copy of the Phase Three Manual on disk. A letter is included which instructs each centre, when they receive the package, to copy the Registration Document on page 61 of the Manual, and send copies to the IIDC and the Regional Co-ordinator for their region. If a centre has sent an 'EOI' to the IIDC and not received the Package of Phase Three materials please contact the IIDC to arrange further copies to be sent. When the IIDC receives the completed and signed Registration Document, a Centre Report is generated for each age group to be studied and sent to the centre to complete as the study progresses. The completed Centre Report is sent back to the IIDC at the same time that the data is submitted.

The list below shows the 39 centres that have already sent the Registration Document to the IIDC. Included in this list is the country and centre number, the date the Registration Document was received and the age groups that are being studied in each centre (v equates to the video questionnaire).

ID	Country	Centre	Date	Study Age	ID	Country	Centre	Date	Study Age
251001	Syria	Aleppo	29/08/00	v13/14	083004	Mexico	Monterrey	10/11/00	13/14 & 6/7
151001	Bangladesh	Dhaka	30/08/00	v13/14 & 6/7	0100010	Italy	Ascoli Piceno	11/11/00	v13/14 & 6/7
008001	Spain	Cartagena	07/09/00	v13/14 & 6/7	065002	Morocco	Casablanca	21/11/00	v13/14
001001	New Zealand	Auckland	15/09/00	v13/14 & 6/7	065003	Morocco	Marrakech	21/11/00	v13/14
023001	Yugoslavia	Belgrade	15/09/00	v13/14 & 6/7	251002	Syria	Lattakia	24/11/00	v13/14 & 6/7
252001	Tunisia	Sousse	18/09/00	13/14	034001	Estonia	Tallin	24/11/00	v13/14 & 6/7
091001	Kenya	Eldoret	20/09/00	v13/14	254001	Palestine	Ramalah	28/11/00	13/14 & 6/7
111001	China	Beijing	20/09/00	v13/14 & 6/7	254002	Palestine	North Gaza	28/11/00	13/14 & 6/7
001002	New Zealand	Wellington	26/09/00	v13/14 & 6/7	006014	USA	Sacramento	29/11/00	v13/14 & 6/7
055001	Iran	Tehran	04/10/00	v13/14 & 6/7	023002	Yugoslavia	Sombor	11/12/00	v13/14 & 6/7
055002	Iran	Rasht	04/10/00	v13/14 & 6/7	106001	Congo	Brazzaville	12/12/00	v13/14
055003	Iran	Zanjan	04/10/00	v13/14 & 6/7	063001	Jordon	Irbid	19/12/00	v13/14 & 6/7
055004	Iran	Birjan	04/10/00	v13/14 & 6/7	074009	Argentina	Santa Fe	29/12/00	v13/14 & 6/7
001003	New Zealand	Christchurch	05/10/00	v13/14 & 6/7	074003	Argentina	Cordoba	30/12/00	v13/14 & 6/7
114001	SAR China	Hong Kong	11/10/00	v13/14 & 6/7	067002	Pakistan	Islamabad	08/01/01	v13/14 & 6/7
192001	Lithuania	Kaunas	24/10/00	v13/14 & 6/7	074006	Argentina	Salta	09/01/01	v13/14 & 6/7
072007	Brazil	Uberlandia	30/10/00	v13/14 & 6/7	074001	Argentina	Buenos Aire	09/01/01	v13/14 & 6/7
039001	Bulgaria	Sofia	01/11/00	v13/14 & 6/7	023003	Yugoslavia	Nis	10/01/01	v13/14 & 6/7
008004	Spain	Castellon	08/11/00	v13/14 & 6/7	152020	India	Davangere	15/01/01	v13/14 & 6/7
251003	Syria	Tartous	09/11/00	v13/14 & 6/7					

We look forward to receiving further Registrations, either by fax, email or by post. It is a pleasure communicating with you all and I look forward to working with you on Phase Three.

Best wishes for a happy New Year and success for Phase Three.

Philippa

Mrs Philippa Ellwood
p.ellwood@auckland.ac.nz
ISAAC International Data Centre

ISAAC PHASE THREE

HIGHLIGHT FROM THE PHASE THREE MANUAL

Group A:

Will conduct Phase Three in the same way as Phase One following, as precisely as possible, the details of the centre methodology documented in the Phase One Centre Report.

Each Principal Investigator was sent a final copy of the Phase One Centre Report from the IIDC (example page 64-73). However, further copies are available on request from the IIDC.

Group A will use:

- ◆ The same sampling frame, the exact same set of schools should **not** be aimed for, but some schools may be reselected by the random sampling process. It is acknowledged that some centres will need to use all schools and therefore not select by random sampling.
- ◆ The same age group/s.
- ◆ The same sample size (see page 18 – sample size and power consideration).
- ◆ The same method of choosing the children.
- ◆ The same written questionnaires (plus an environmental module).
- ◆ The same translation (if applicable).
- ◆ The same time of year for data collection.
- ◆ The international version of the video (AVQ 3.0) for the 13/14 year olds.

The ISAAC Steering Committee would like you to discuss any proposed departure from these conditions with your National and Regional Coordinator before starting your study.

IIDC ISAAC CENTRE REQUIREMENTS

The IIDC has summarised below requirements for centres for Phase Three:

Completion of centre report which will include:

- ◆ Adequate description of sampling frame and schools including map.
- ◆ Adequate description of classes and children.
- ◆ Month and year of study.

Data entry;

- ◆ Double entry (minimum check on data entry).
- ◆ Changes after data entry (minimum no changes to core questionnaires).

Participation rates;

- ◆ Schools (minimum >10 – less if complete sample).
- ◆ Number of children (target 3000).
- ◆ Rate (target >90%).

Translation of questionnaires (minimum back translation).

Video (completion of questions).

Data checking process completed:

- ◆ Use of expected codes.
- ◆ Range checks.
- ◆ Ages and calculated ages consistent.
- ◆ Number of schools matches centre report.
- ◆ Number of children matches centre report.
- ◆ Appropriate proportion of apparent inconsistencies.
- ◆ Prevalence values consistent with collaborator expectations.

Submitted by
ISAAC International Data Centre

ISAAC PUBLICATIONS

A number of ISAAC investigators have asked me about possible ecologic analyses of the ISAAC Phase I data. Of course, ISAAC investigators are free to publish their own data at the centre level, the country level (with the National Coordinator) or the regional level (with the Regional Coordinator). However, there are also a number of interesting ecologic analyses that can be done using the entire international Phase One data set. In many instances, such analyses are already being done, but we are also keen for ISAAC investigators to make proposals for further analyses that they wish to undertake.

The following Phase One ecologic publications have been published, are in press, or are in preparation:

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: 2040-41.

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: 449-53.

Ellwood PE, Asher MI, Björkstén B, Burr M, Pearce N, Robertson CF on behalf of the ISAAC 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). *Eur Respir J*, in press.

Stewart AW, Mitchell EA, Pearce N, Strachan DP, Weiland SK, on behalf of the ISAAC Study Group. The relationship of per capita gross national product to the prevalence of symptoms of asthma and other atopic diseases in children. *Int J Epidemiol*, in press.

Anderson R, et al. Immunisation. *Am J Publ Health*, in press.

Anderson R, et al. Air pollution. In preparation.

Björkstén B, Kildegaard Nielsen, et al. Antibiotics. In preparation.

Mitchell EA, Stewart AW. The 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). In preparation.

Burr M, Treu R, Emberlin JC, Pearce N, on behalf of the ISAAC Study Group. Pollens. In preparation.

Shirtcliffe P, Beasley R, on behalf of the ISAAC Study Group. Other infections. In preparation.

Ross Anderson, Richard Beasley, David Strachan, Colin Robertson. Mortality and hospitalisation rates. In preparation.

Weiland S, Hüsing A, Strachan DP, Pearce N, on behalf of the ISAAC Study Group and ISAAC Europe. Climate and the prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema in children. In preparation.

There are also the following papers (other than ecologic analyses) using Phase One data:

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 on asthma prevalence in the ISAAC and the ECRHS. *Eur Resp J* 2000; 16: 420-6.

Crane J, Beasley R, Mallol J, on behalf of the ISAAC Study Group. Agreement between written and video questions for comparing asthma symptoms in ISAAC (the International Study of Asthma and Allergies in Childhood). In preparation.

Anderson R, et al. Synthesis/overview of Phase I data. In preparation.

Stewart AW, Mitchell EA. Month of birth and childhood atopic diseases: the International Study of Asthma and Allergies in Childhood (ISAAC). In preparation.

However, if you have further ideas for Phase One ecologic analyses, I would be pleased if you could contact me with a proposal, which can be placed before the ISAAC Executive.

Professor Neil Pearce
Chair, ISAAC Publications Committee
ISAAC Executive
E-mail: n.e.pearce@massey.ac.nz

OPTICAL MARKING RECORDERS - SCANNERS

In South-Santiago (Chile), at our Department of Pediatric Respiratory Medicine we have been trying entering data from written questionnaires by using a scanning system based on optic marks reading (OMR). It is able to read marks and digitalize them onto an electronic sheet from where it can be exported to Excel.

It is very friendly and easy to use and require minimal training to be operated. It calibrates by itself and is able to discriminate errors in the way questions were responded (double yes/no responses and also when the question has not been responded), has quite good velocity of reading (using manual feeding is about of 1.5 sec per page, and the half when attaching an automatic feeding device). The software allows for several configurations on sensitivity, colors, sizes, etc).

We have been using a form (one page) that contains all the ISAAC written questions on asthma, rhinitis and eczema, and another form (one page) video-questionnaire. The ISAAC questionnaire set in a form for scanner has been very well accepted for children and parents, and has demonstrated to be very easy to complete, just filling up, or doing a mark (x), in the oval corresponding to the alternative response.

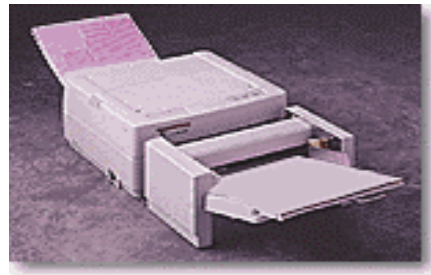
This machine has also been used to correct written (multiple alternatives) evaluations of our pre-grade and post-grade students, as well as in other assessments related to our daily medical routine (outpatient clinics, quality control, stock inventories, etc.).

However, the more important factor for us is the saving we could make in time and money, both of them being dramatically decreased. Another very important advantage of scanning systems is the avoidance of typing mistakes when entering data manually from forms to computer.

At present we are starting a pilot study comparing the double entry system and the scanner system in several aspects; we expect it will provide us with more information on this relatively new system and its implications for ISAAC data entering process.



Chatswood System OMR100



Scanning Systems

More information on OMR contact:	
Chatswood Data Email: frankL@chatsworthdata.com Website: www.chatsworthdata.com	Scanning Systems Email: tharmon@scansys.com Website: www.scansys.com

Submitted by Professor Javier Mallol
 ISAAC Regional Co-ordinator, Latin America

HORSES FOR COURSES

Horses suffer a disease, which is, in many ways, similar to asthma in people. This condition goes by many names, currently the most popular is Recurrent Airway Obstruction (RAO). In veterinary medicine, RAO is regarded as a syndrome with clinical signs ranging from exercise intolerance in the performance horse to expiratory dyspnoea, chronic purulent nasal discharge, cough and weight loss if very severe. Synonyms for RAO include heaves, chronic emphysema, alveolar emphysema, (somewhat erroneously) chronic obstructive pulmonary disease, small airway disease, chronic bronchitis, chronic bronchiolitis and hay sickness. It is suggested that equine RAO was the closest animal disease to asthma, and that RAO fulfilled the 1962 American Thoracic Society definition for asthma. Unfortunately, whilst there is quite a lot of information regarding the pathophysiology of RAO, there is a dearth of epidemiological data.

Typically RAO has been associated with management practices, particularly the type of housing and bedding, and the feeding of hay, and has been referred to as an occupational disease of horses. The factors which result in hypersensitivity to the allergens are unknown, but may have a genetic basis and may follow persistent bouts of airway inflammation, or certain patterns of antigen exposure during early life. Previous viral infections have been suggested as a risk factor of RAO and in one study horses with RAO had increased antibodies against influenza A equine 1. However, whilst respiratory virus infection can cause a transient airway obstruction and non-specific hyperresponsiveness to inhaled agents in experimental animals, and may provoke acute episodes in RAO susceptible horses, there is no compelling evidence that viral infection causes RAO.

The most commonly implicated allergens include fungal spores commonly found in hay and straw. Less commonly, the condition is associated with pasture allergens, probably pollens, and occurs during spring and summer. Multiple allergies are not infrequent. The most important organisms, in terms of RAO, are acinetomycetes and moulds such as *Micropolyspora faeni*, *Thermoactinomyces vulgaris*, *Aspergillus fumigatus* and *Faenia retivirgula*. Natural challenge results in more severe signs than does challenge with single antigens, suggesting that a number of factors, such as the duration of exposure, a combination of antigens and the presence of other factors may be important in clinical RAO.

The incidence of RAO is unknown but is likely to vary widely throughout the world. It is apparently most common in the northern hemisphere, where horses are stabled for a greater proportion of the year. It would appear to be rare in warm, dry climates such as Australia and California. A *post mortem* survey of Swiss horses found a prevalence of chronic small airway disease in 37%, while an abattoir survey from the northern USA found a 12% prevalence of chronic bronchitis.

At present diagnosis of RAO relies on clinical impressions, bronchoscopy, cytological evaluation of tracheal washes or bronchoalveolar lavage samples and occasionally, pulmonary function tests. Whilst horses generally tolerate bronchoscopy well, the technique is invasive and costly. Pulmonary function testing is only available in a very limited number of referral centres and is more often used in research than for clinical diagnosis.

The invasive nature of current diagnostic tests means that there is an almost complete absence of epidemiological information concerning RAO. However, the study of the epidemiology of RAO in horses is, in some ways, analogous to that of asthma in children, particularly where parents or carers have completed questionnaires. The use of such questionnaires for diagnosis of RAO in horses has not been assessed.

However, the results of several studies suggest that further investigation be warranted. Horses with RAO often have characteristic signs. For example, 88% of horses with RAO diagnosed histologically have a history of coughing, whilst 17/20 horses with clinician diagnosed RAO had cough at rest (compared with 0/38 control horses), 13/20 had cough during exercise (1/20 controls) and 15/20 had a forced abdominal expiratory effort (0/38 controls). In addition the following findings are significantly more common in horses with RAO than normal controls; poor work performance, a history of previous febrile illness, chronic cough, dyspnoea, double expiratory effort, increased breath sounds, wheezing and crepitant breathing sounds. Indeed, several findings (such as the presence of coughing and poor work performance) had 100% sensitivity, whilst others had 100% specificity (such as increased breathing sounds, wheezing sounds, and crepitant breathing sounds). A clinical score, based on just three clinical findings, has been demonstrated to be associated with the presence of the pasture associated form of the disease, and to be highly correlated with more invasive measures of disease including changes in intra-pleural pressure ($r=0.96$) and histological changes ($r=0.78$).

The University of Glasgow Veterinary School has recently received funding from an UK based charity, the Home of Rest for Horses, to develop and validate the use of a questionnaire for the diagnosis of RAO. If, as we believe, such a technique proves effective, we will have a tool to enable, for the first time, the investigation of the epidemiology of RAO in horses.

The study will be in three phases. The first phase will develop a number of questionnaires, based on available literature and expert opinion. The second phase will investigate the sensitivity and specificity of the preferred questionnaire whilst the third phase will investigate the prevalence of, and risk factors for, RAO in horses in the UK. It is also hoped that, through international collaboration, variation in the epidemiology of RAO can be investigated.

Anyone interested in further information about this project can contact:

Dr Rob Christley

Weipers Centre for Equine Welfare, University of Glasgow Veterinary School
r.christley@vet.gla.ac.uk