

Asthma Disparities: A Global View

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SLIDE 1

Tēnā koutou katoa.

Kei te mihi ahau ki ngā tāngata
whenua.

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Innes Asher
Department of Paediatrics: Child and Youth Health
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Chair of the International Study of Asthma and Allergies in Childhood (ISAAC)

17 May 2010



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SLIDE 2

I am from New Zealand.

In Maori language I have
acknowledged the indigenous
people of America.

I am enjoying being in ‘Nawlins’ for
the first time. I wish to honour the
courage of all those affected by
Hurricane Katrina.

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Thank you for your invitation to speak today.

I will be speaking on behalf of the ISAAC research programme which has provided the first
global data on asthma in children.

SLIDE 3

Disparities are great differences

In this talk I will use ISAAC data to illustrate global disparities in prevalence of asthma symptoms.

And I will examine associations of asthma symptoms with:

- Country income and income inequality;
- Environmental factors; and
- Atopy.

Disparities = Great Differences
(Oxford dictionary)

In this talk I will use ISAAC data to illustrate global disparities in prevalence of asthma symptoms.

I will examine associations of asthma symptoms with:

- country income and income inequality
- environmental factors
- atopy



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SLIDE 4

ISAAC is a global research programme. It was founded because of increasing concern about asthma and rhinitis and eczema.

Today I will be presenting findings only for asthma.

There has been huge worldwide interest in ISAAC, especially from developing countries where these conditions are becoming significant health issues, even though infectious diseases remain the most important.

The total participation in ISAAC to date – all 3 phases – has involved 423 centres in 105 countries and nearly 2 million children.

ISAAC
The International Study of Asthma and Allergies in Childhood

Increasing concern about asthma, rhinitis and eczema

A fresh look was needed
with a world population view



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SLIDE 5

The ISAAC programme has had three phases so far – Phase One, Phase Two and Phase Three. The dates of data collection are given here.

In this talk I will summarise some key findings from each of these Phases.

I will start with Phase Three.

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Phase Three, like Phase One, was a multicentre cross-sectional study, selecting children from randomly sampled schools.

Two age groups were studied:

- 13-14 year olds, and 6-7 year olds (optional).
- 3000 per age group per centre.
- Simple standardised, validated written questionnaires, and an optional video questionnaire on asthma symptoms in 13-14 year olds.

The ISAAC Programme

ISAAC Phase One 1991 – 1998

- Worldwide prevalence (questionnaires)
- ISAAC Phase One ecological analyses

ISAAC Phase Two 2000 – 2004

- Questionnaires & additional markers

ISAAC Phase Three 2001 – 2005

- Repetition of Phase One
- Addition of more centres
- Environmental questionnaire



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ISAAC Methods: Phase Three

- Multicentre cross-sectional study of children in randomly sampled schools
- 13-14 year olds and optional 6-7 year olds
- 3000 per age group per centre
- Standardised validated simple written questionnaires (optional video asthma questionnaire in 13-14 yr olds)

Asher MI *et al.* Eur Respir J 1995; 8: 483-91.
Ellwood P *et al.* Int J Tub Lung Dis 2005; 9: 10-16.



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SLIDE 7

This shows participation in Phase Three.

There was an amazing number of centres and countries which took part, with a high response rate of the children.

ISAAC Phase Three				
	Countries	Centres	Participants	Response Rate (%)
13-14 year	97	233	798,685	88
6-7 year	61	144	388,811	85



SLIDE 8

Firstly, Disparities in prevalence.

In this talk the asthma symptom I will be talking about is 'current wheeze'. This is defined as a positive answer to this question:

"Have you (Has your child) had wheezing or whistling in the chest in the past 12 months?"

Disparities in the Prevalence of Asthma Symptoms Between Populations

Definition of current wheeze

Yes to:

"Have you (Has your child) had wheezing or whistling in the chest in the past 12 months?"

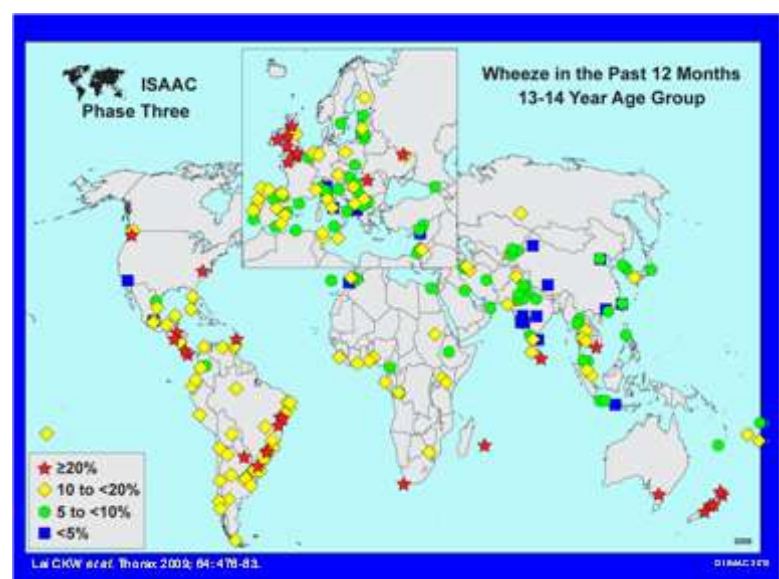


SLIDE 9

Now for some key results.

I will show several maps with this format.

For brevity I will be showing results only for the written questionnaire for 13-14 year olds.



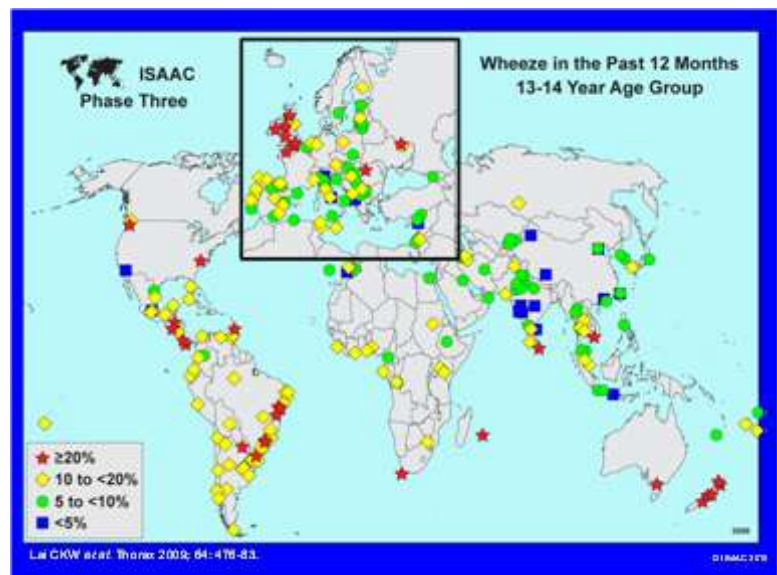
SLIDE 10

Europe is shown in an expanded scale.

Each symbol is a centre.

For most centres there had been no prevalence data before ISAAC began.

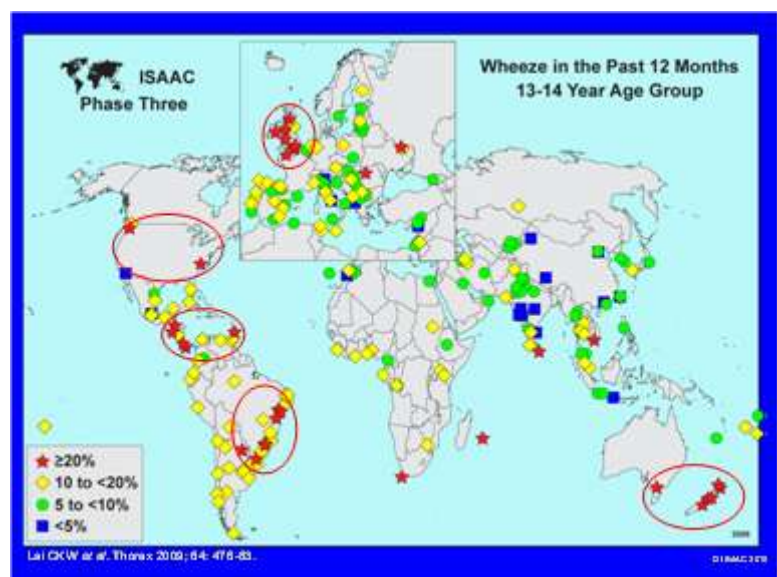
The key at bottom left shows the range of prevalence of current wheeze for each centre.



There were striking variations in the prevalence between different geographic areas and populations – 9 fold differences between countries.

SLIDE 11

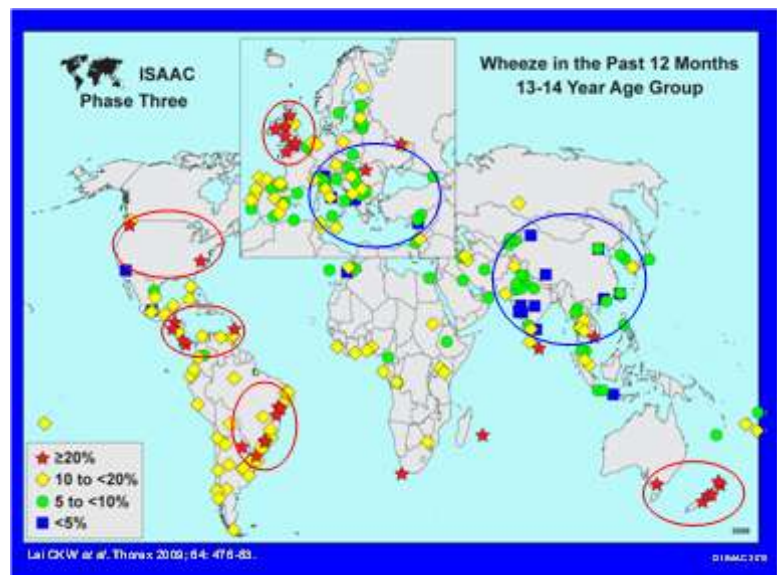
Centres with the highest prevalence values – the red stars – were found as indicated by the large red circles; mainly in New Zealand and Australia, the UK, parts of Central and South America and in the USA, Seattle, and Chapel Hill.



SLIDE 12

Centres with the lowest prevalence values – the blue squares – were found as indicated by the large blue circles – in Asia, India, Eastern Mediterranean and Southern Europe.

Other centres were of intermediate prevalence levels.



Similar patterns of prevalence were also found with the video questionnaire in 13-14 year olds, and also with the written questionnaire in 6-7 year olds.

Such large world wide variations in the prevalence of asthma symptoms, many in populations of similar genetic stock, suggest that environmental factors play a key role.

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I will now turn to symptoms of severe asthma. These were defined as follows.

Definition of Symptoms of Severe Asthma

Wheezing in the past 12 months and at least one of :

- >4 attacks of wheeze
- >1 night per week sleep disturbance from wheeze
- wheeze limiting speech

Lai CKW et al. Thorax 2009; 64: 476-83.

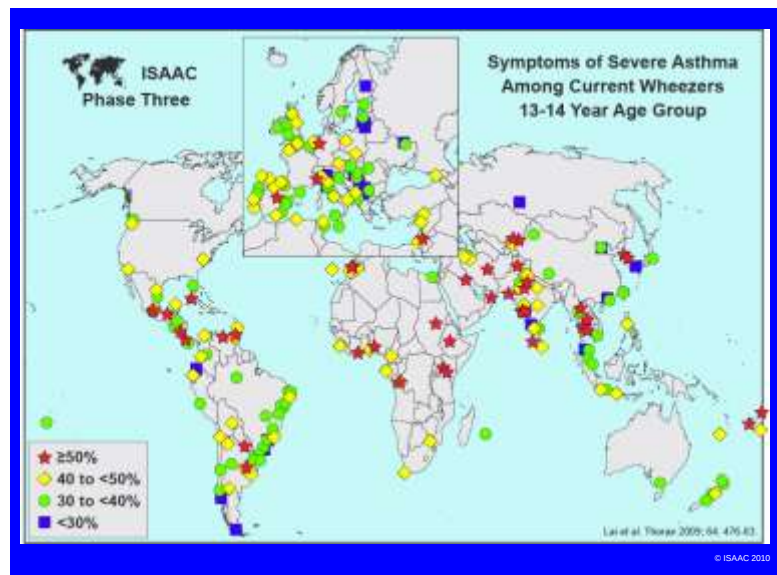


SLIDE 14

The map shows those children with symptoms of severe asthma among current wheezers.

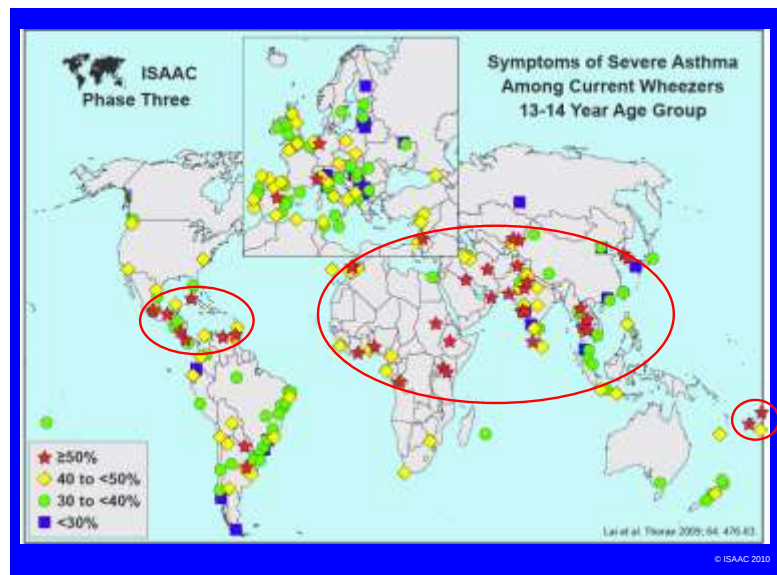
It has a similar format to the previous maps, but the key has a different range.

The red stars are prevalence values $> 50\%$ and the blue squares $< 30\%$.



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You can see that the centres with the highest proportion of severe wheezers among current wheezers were found mainly in lower and middle income countries – as shown in the large red circles – the Pacific, Asia, India, Africa, eastern Mediterranean, parts of Latin America.

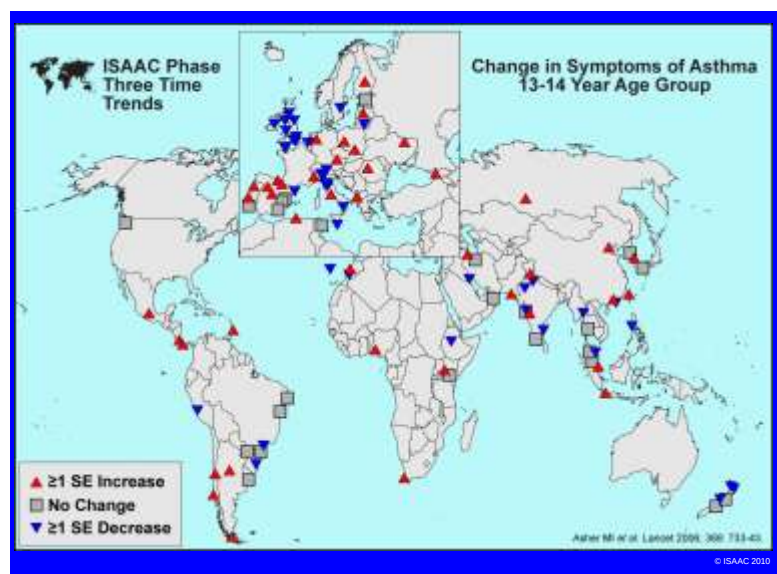


SLIDE 16

In Phase Three we were able to examine changes in prevalence over time – prevalence in Phase One, then in Phase Three on average 7 years later.

We achieved this comparison in 104 centres in 55 countries.

For most centres it was their first opportunity to obtain time trends information.



The key here is different.

The red triangles indicate an increase in prevalence of at least 1 standard error.

The blue triangles indicate a decrease in prevalence of at least 1 standard error.

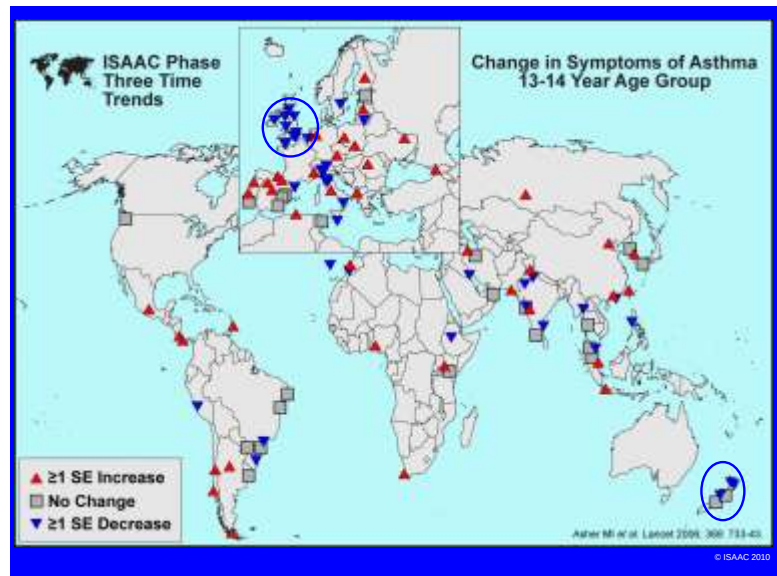
And the grey squares indicate no change.

SLIDE 17

We had expected prevalence would continue to increase in the high prevalence English language countries, but this was not the case.

They changed little or even decreased.

There were increases in asthma symptom prevalence in locations of high population density such as Africa, Latin America and parts of Asia. This new data indicates the surprising finding that the global burden of asthma is continuing to rise, and at the same time the global disparities are lessening.



SLIDE 18

Do country income and inequality influence disparities?

Country income and income inequality

Do they influence disparities?



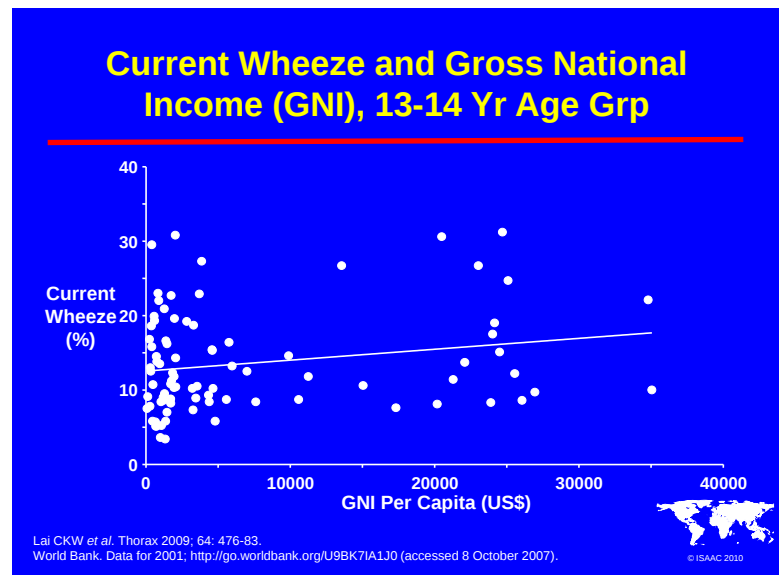
SLIDE 19

We undertook this ecological analysis with ISAAC Phase Three data. Each dot is a country.

Gross National Income per capita is on the x axis, with high income countries having incomes greater than about 10,000 US dollars.

As GNI increases, so does the prevalence of current wheeze.

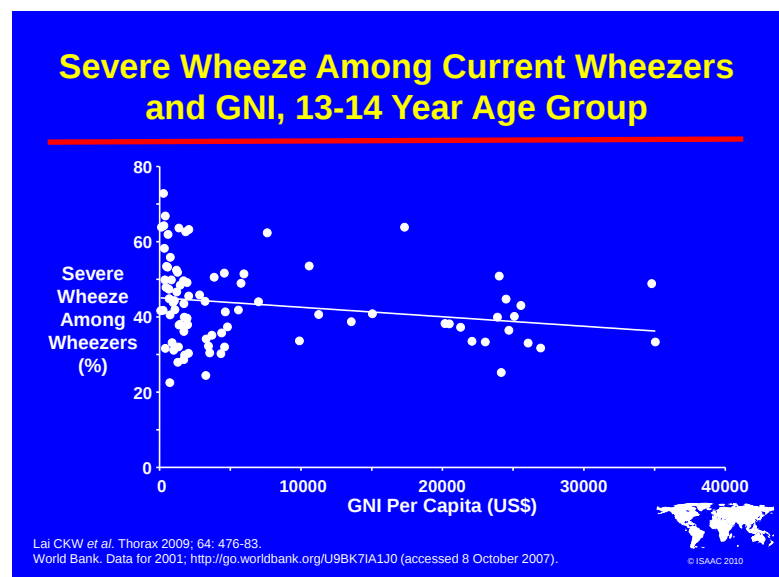
You can see that most ISAAC centres were in low and middle income countries.



SLIDE 20

This shows similar data, but this time the y axis is the proportion of severe wheezers among children with current wheeze.

The trend is reversed.

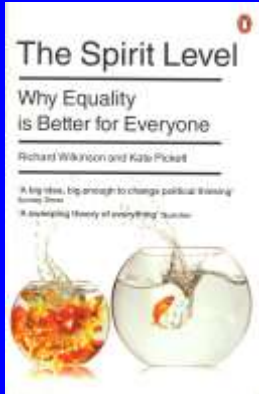


SLIDE 21

This recent publication written by Richard Wilkinson and Kate Pickett describes the far reaching effects of income inequality on indicators of societal health and well being.

The measure of income inequality used was the ratio of the income share of the richest 20% of country population to the poorest 20%.

Income Inequality



The measure (World Bank):
The ratio of the income share of the richest 20% of country population to the poorest 20%.

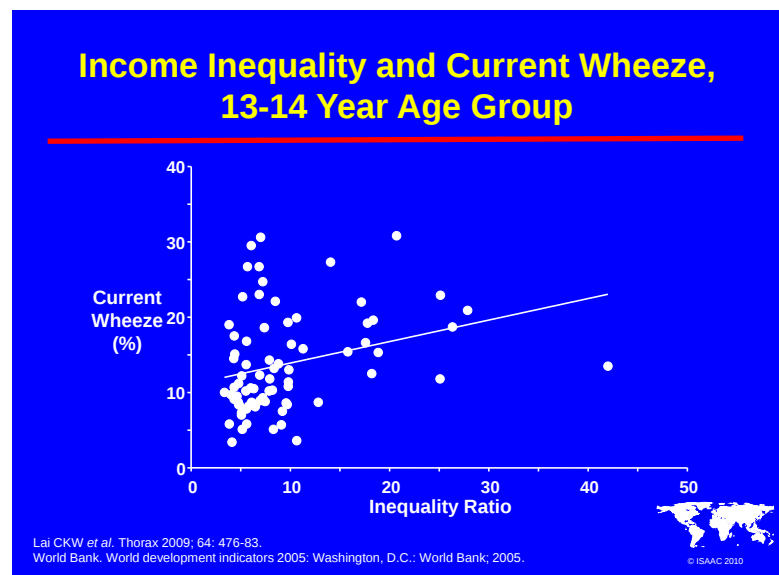


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SLIDE 22

And is shown on the X axis here.

The higher number, the more income inequality there is within the country.



SLIDE 23

Which environmental factors may explain disparities in asthma symptoms?

Which environmental factors may explain disparities in asthma symptoms?



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SLIDE 24

Firstly we undertook ecological analyses with Phase One data.

This table summarises our findings.

Four factors showed a positive association with current wheeze.

Five showed a negative association. These are potentially protective factors.

And three showed no association.

Associations Between Current Wheeze and Environmental Factors	
ISAAC Phase One ecological analyses:	
Exposure	Direction of Association
GNP (GNI)	
Tobacco (females)	↑
Paracetamol sales	
Trans fatty acids	
Plant-based foods	
Immunisations	
TB rates	↓
Tobacco (males)	
Pollens	
Antibiotics	
Climate	-
Air pollution	

Asher MI *et al.* Resp Research 2010; 11: 8.

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SLIDE 25

We explored many of these factors further in ISAAC Phase Three. For the first time we now have individual questionnaire data on environmental exposures.

These data shown here are for 6-7 yr old children.

To date three analyses have been published. We have found a positive association between current wheeze and reported antibiotic use, paracetamol use, truck traffic exposure. These findings all need further investigation.

Current Wheeze and Environmental Factors (6-7yr olds)	
	Multivariate analysis Odds Ratio (95%CI)
Antibiotic use in the 1 st year of life	1.70 (1.60-1.80)
Paracetamol use in the 1 st year of life	1.46 (1.36-1.56)
Truck traffic in street of residence	1.35 (1.22-1.48)

Foliaki S *et al.* J Allergy Clin Immunol 2009; 124: 982-9.
Beasley R *et al.* Lancet 2008; 372: 1039-48.
Brunekreef B *et al.* Environ Health Perspect 2009; 117: 1791-98.

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SLIDE 26

Does atopy influence disparities in asthma symptoms?

Although asthma in children is commonly described as an atopic disease, there is mounting evidence that many children with asthma do not have an atopic constitution.

Does atopy influence disparities in asthma symptoms?



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The role of atopic sensitization in determining asthma prevalence in children was explored in ISAAC Phase Two.

ISAAC Phase Two:

- Multicentre cross-sectional study of school children in randomly sampled schools.
- 30 centres in 22 countries. A smaller number of centres took part because of the intensity of the measurements.
- Participants were 9-11 year olds.
- 1000 per age group per centre.
- Simple core written questionnaires.
- Child contact assessments including atopy.

ISAAC Phase Two Methods

- Multicentre cross-sectional study of school children in randomly sampled schools
- 30 centres in 22 countries
- 9-11 year old participants
- 1000 per age group per centre
- Simple core written questionnaires
- Child contact modules including skin prick tests

Weiland SK et al. Eur Respir J 2004; 24: 406-12.

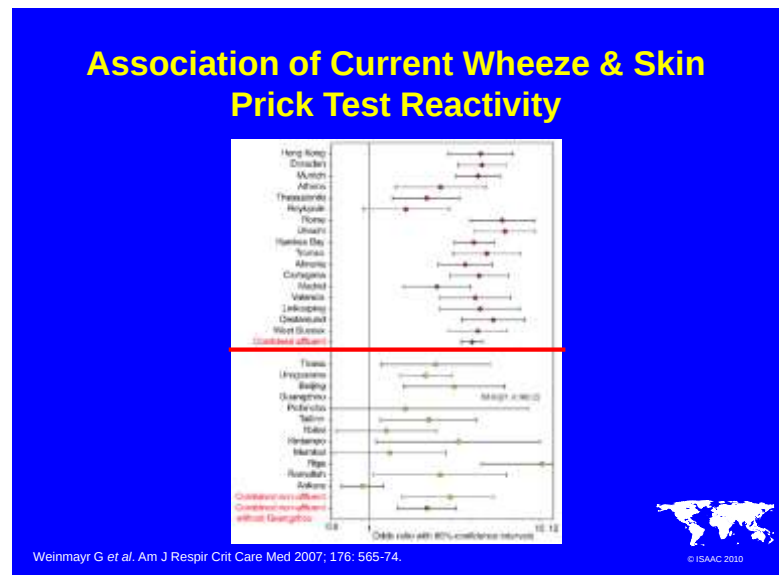


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In this analysis the skin prick test reactivity was used as the measure of atopy.

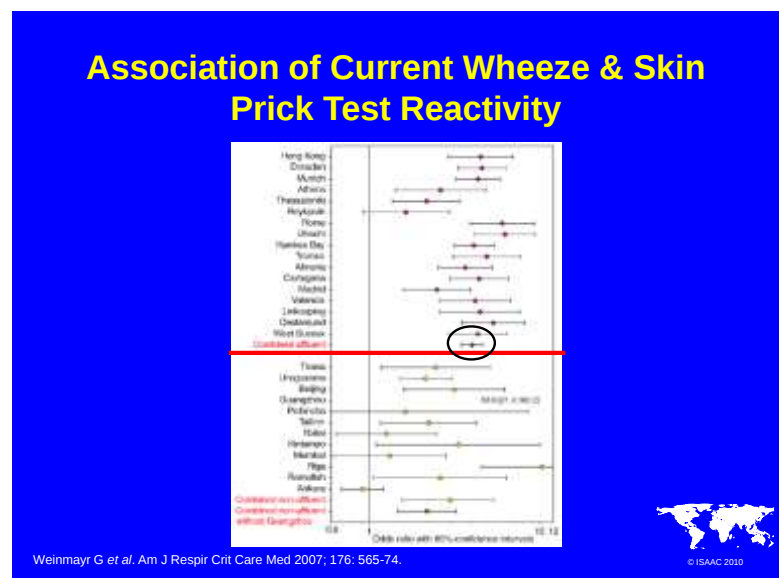
This shows odds ratios for skin prick test reactivity on current wheeze.

The centres in affluent countries are above the line and non-affluent below.



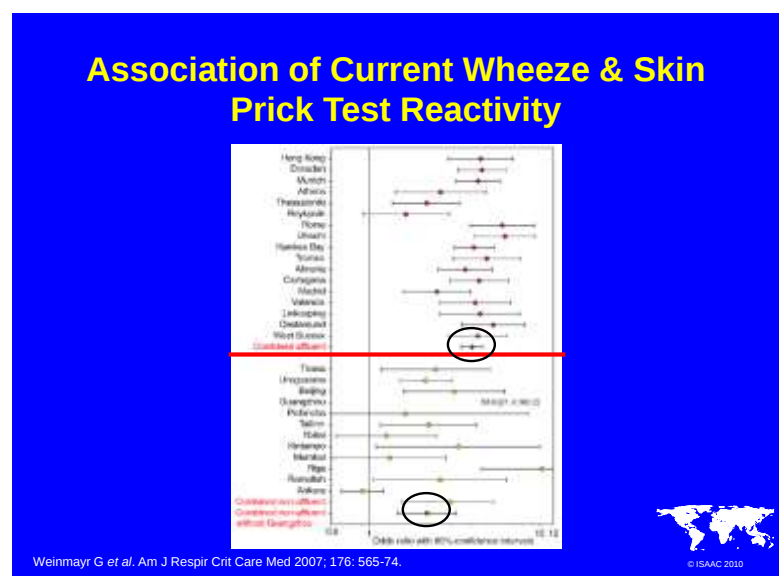
SLIDE 29

The effect size for affluent was...



SLIDE 30

About double that of non-affluent countries, which is where most of the world's children live.



SLIDE 31

In a more recent analysis from ISAAC Phase Two, any breastfeeding was associated with less wheeze in countries of all income levels.

Protective Effect of Breastfeeding		
<u>Centres</u>	<u>Current wheezers</u>	
	Non-atopic	Atopic
Low and middle income countries	0.69 (0.53-0.90)	0.86 (0.55-1.35)
High income countries	0.87 (0.72-1.06)	0.85 (0.67-1.08)

Nagel G et al. Eur Respir J 2009; 33: 993-1002. © ISAAC 2010

SLIDE 32

This shows Odds ratios and 95% CIs for four categories. The only significant finding was for non-atopic wheeze in low and middle income countries where the effect size was the greatest.

Most research to date on atopy and asthma has been done in high income countries where atopy may be a more important determinant, to the detriment of exploration of the non-atopic mechanisms of asthma. This result illustrates where future research should focus.

Protective Effect of Breastfeeding		
<u>Centres</u>	<u>Current wheezers</u>	
	Non-atopic	Atopic
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Nagel G et al. Eur Respir J 2009; 33: 993-1002. © ISAAC 2010

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- There are large global disparities in prevalence of asthma symptoms, and these are lessening.
- There is increasing prevalence in many populous countries – the global burden is increasing.

Summary

- There are large global disparities in prevalence of asthma symptoms, and these are lessening
- There is increasing prevalence in many populous countries – the global burden is increasing



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Country Economic Influences:

- Positive associations with GNI and income inequality.
- In less affluent countries, asthma symptoms are more commonly severe.

Environmental Factors

- Several associations – inverse and positive – warrant further exploration. Loss of protective factors may be as important as addition of risk factors.

Root causes?

Country Economic Influences

- Positive associations with GNI and income inequality
- In less affluent countries, asthma symptoms are more commonly severe

Environmental Factors

- Several associations – inverse (protective) and positive (risk) – warrant further exploration.



SLIDE 35

Influence of Atopy:

- Less effect in low and middle income countries.
- Protective effect of breastfeeding only for non-atopic wheeze in low and middle income countries.

Root causes?

Influence of Atopy

- Less effect in low and middle income countries
- Protective effect of breastfeeding only for non-atopic wheeze in low and middle income countries



SLIDE 36

We need to:

- Understand the influences of income inequality;
- Seek the key environmental factors in low and middle income countries;
- Understand the mechanisms of and influences on non-atopic asthma; and
- Delivering good asthma management to all children with asthma in the world.

SLIDE 36

I would like to thank the children, parents, school staff, funders, ISAAC staff and collaborators.

This is our website.

Thank you.

Global solutions?

We need to:

- understand the influences of income inequality
- seek the key environmental factors in low and middle income countries
- understand the mechanisms of and influences on non-atopic asthma
- deliver good asthma management to all children with asthma in the world



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**Thanks to children, parents, school staff,
ISAAC staff and collaborators, funders**



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