The Global **Asthma** Report 2011

International Union Against Tuberculosis and Lung Disease

Health solutions for the poor

ISAAC

The International Study of Asthma and Allergies in Childhood

Asthma affects 235 million people today and the prevalence is rising.

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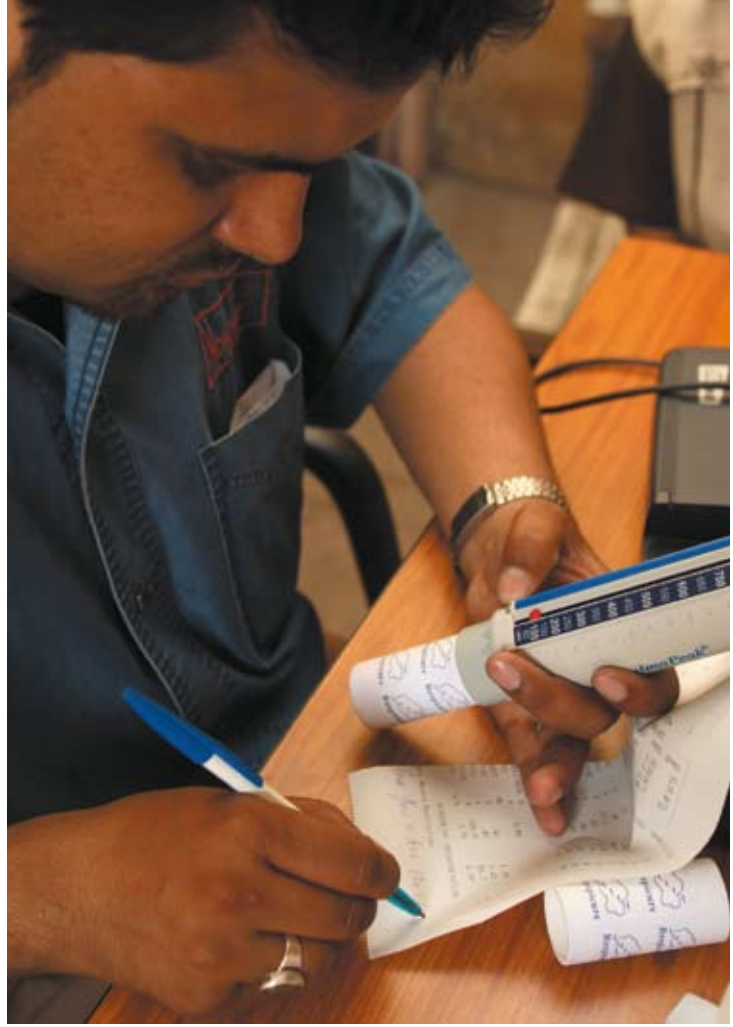
GLOBAL ASTHMA REPORT 2011

Why Asthma?

Asthma is the most common chronic disease among children and also affects millions of adults. Some 235 million people worldwide suffer from this non-communicable disease.

The causes of asthma are not well understood, but effective medicines are available that can treat it, thus largely avoiding the diminished lives, disabilities and death it can bring.

Unfortunately, for many people with asthma – particularly the poor – this effective treatment is too costly or not available at all.



Why Now?

The burden of asthma has been growing over the past 30 years, particularly in the low- and middle-income countries least able to absorb its impact. In September 2011, a UN High-Level Meeting on Non-Communicable Diseases (NCDs) was held to focus world attention on the increasing threat of asthma and other NCDs to global health, social welfare and economic development.

The Global Asthma Report 2011

The Global Asthma Report has been prepared through the collaboration of the International Study of Asthma and Allergies in Childhood (ISAAC) and the International Union Against Tuberculosis and Lung Disease (The Union), two organisations that have been dedicated to helping countries identify and address the problem of asthma for more than two decades.

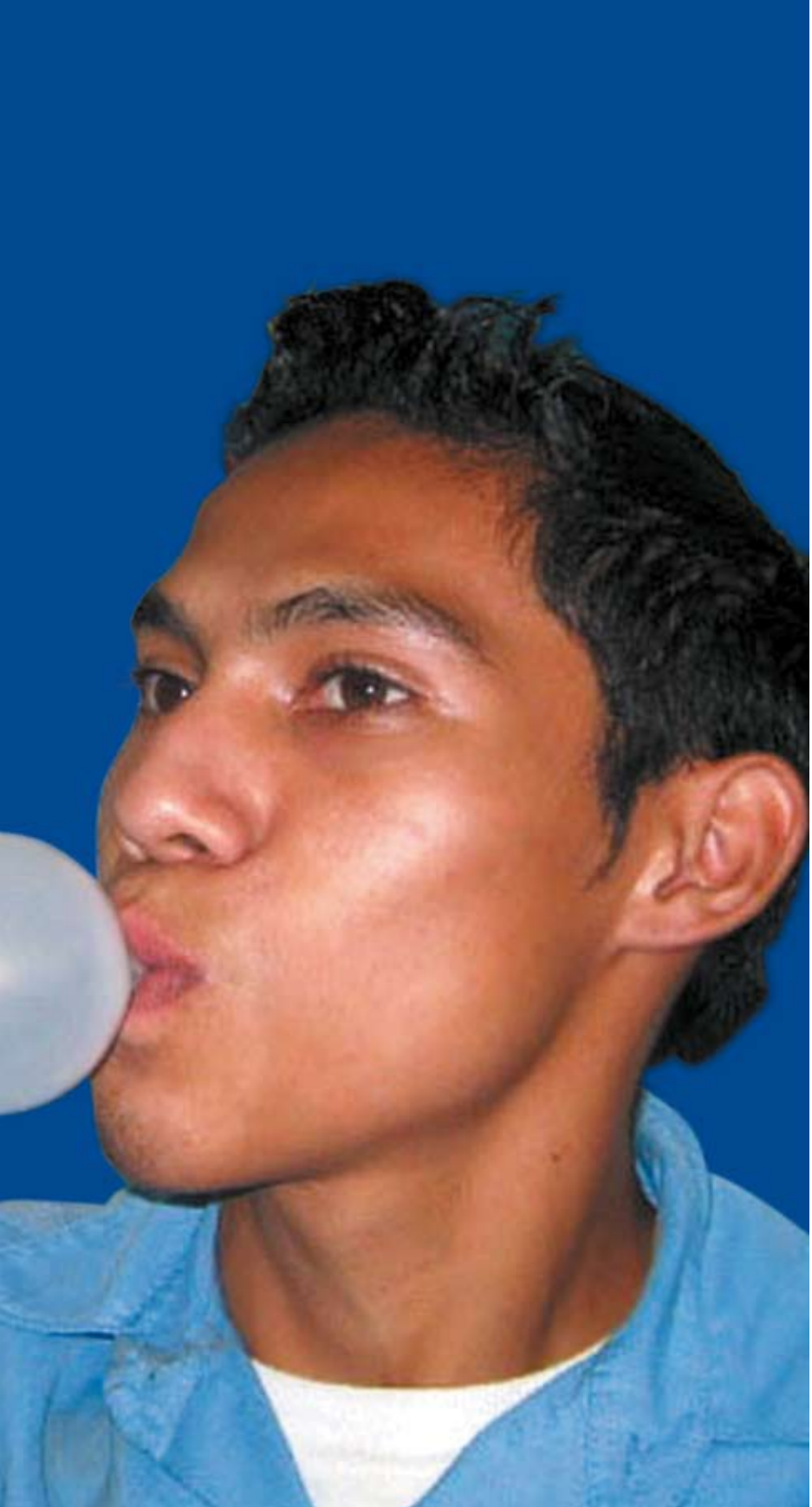
Designed for stakeholders from government ministers and policy-makers to health workers and people with asthma, the report provides an overview of what is known about the causes and triggers of the disease, the global incidence, the progress being made and the significant challenges today and for the future.

It demonstrates that the suffering and waste of resources caused by not managing asthma effectively are much greater than the cost of effective action.

Asthma is a public health problem that can – and should – be solved now.

Nils E Billo, MD MPH
Executive Director
International Union Against
Tuberculosis and Lung Disease
(The Union)

With asthma, breathing is not something you take for granted.



PART ONE:

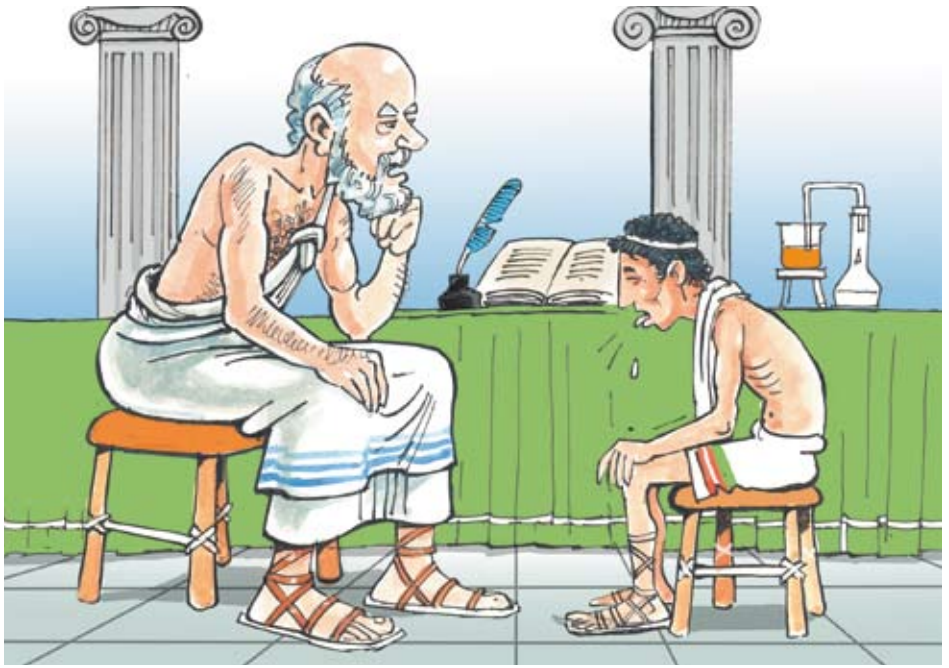
ABOUT ASTHMA

1. What Is Asthma?

Neil Pearce, David Strachan

Asthma is a disease of the bronchial tubes (the "airways") that typically presents with "wheezing", a high-pitched whistling sound heard during breathing, especially when breathing out. However, wheezing does not always occur, and asthma can also involve shortness of breath or coughing, particularly in children.

Asthma most commonly develops in early childhood, and more than three-quarters of children who develop asthma symptoms before age 7 no longer have symptoms by age 16. However, asthma can develop at any stage in life, including adulthood.



A centuries-old puzzle

Asthma has puzzled and confused physicians from the time of Hippocrates to the present day. The word "asthma" comes from a Greek word meaning "panting", but reference to asthma can also be found in ancient Egyptian, Hebrew and Indian medical writings. There were clear observations of patients experiencing attacks of asthma in the 2nd century, and evidence of disordered anatomy in the lung as far back as the 17th century.

A subject of controversy

With the advent of anatomic pathology, the differing factors leading to airway obstruction were observed. It was noted that external factors such as allergen exposure could induce attacks. The similarities with anaphylaxis (severe allergic reaction) prompted consideration of asthma as an allergic disease. This evolution in understanding has been reflected in many attempts to define asthma, and such definitions have steadily evolved

from clinical descriptions to encompass physiological and pathological features. Nevertheless, the definition and classification of asthma has continued to be a subject of controversy.

1959: The cardinal feature of asthma defined

In modern times, the cardinal clinical feature of asthma, reversible airflow obstruction, has formed the basis of the definition of asthma. For example, the definition initially proposed at the CIBA Foundation conference in 1959, and endorsed by the American Thoracic Society in 1962, is that "asthma is a disease characterised by wide variation over short periods of time in resistance to flow in the airways of the lung". In elaborating this definition, the American Thoracic Society introduced the characteristic of hyperreactivity of the airways as a feature that would usually (but not always) be present in asthma.

Subsequently it has been proposed that this phenomenon of bronchial hyperreactivity might be the unifying mechanism underlying the range of disorders encompassed by the term asthma. However, it has been demonstrated that people with clinical asthma may have normal bronchial reactivity, that people without clinical asthma may have enhanced bronchial reactivity, and that there is a poor correlation between current asthma severity and the degree of bronchial hyperreactivity. As a result, while bronchial hyperreactivity may be present in many asthmatics, it is no longer considered to be synonymous with asthma.

1992: Asthma defined as a chronic Inflammatory disorder

Recently the major clinical and physiological characteristics of asthma have been incorporated in an operational definition, which also recognises the underlying disease mechanisms. In this way the International Consensus Report on the Diagnosis and Treatment of Asthma defines asthma as "a chronic inflammatory disorder of the airways in which many cells play a role, including mast cells and eosinophils. In susceptible individuals this inflammation causes symptoms which are usually associated with widespread, but variable, airflow obstruction that is often reversible either spontaneously or with treatment, and causes an associated increase in airway responsiveness to a variety of stimuli."

These three components: chronic airways inflammation, reversible airflow obstruction and enhanced bronchial reactivity form the basis of this current definition of asthma. They also represent the major pathophysiological events leading to the symptoms of wheezing, breathlessness, chest tightness, cough and sputum production by which physicians clinically diagnose this disorder.

WHAT IS ASTHMA?

THE SYMPTOMS OF ASTHMA	THREE COMPONENTS USED TO DEFINE ASTHMA:
• wheezing • breathlessness • chest tightness • cough • sputum production	• chronic airways inflammation • reversible airflow obstruction • enhanced bronchial reactivity

Asthma is an allergic disease: Yes, no, maybe

In recent decades it has become routine to describe asthma as an allergic disease. A theoretical paradigm has evolved in which allergen exposure produces sensitisation to allergens, and continued exposure leads to clinical asthma through the development of airways inflammation, reversible airflow obstruction, and enhanced bronchial reactivity.

However, it has been acknowledged that not all cases of asthma fit this paradigm, for example, some occupational causes of asthma do not appear to involve allergy. In fact, it is now widely recognised that at most one-half of asthma cases, in both children and adults, involve allergic mechanisms. The majority of the cases probably involve non-allergic mechanisms, including non-allergic inflammation of the airways. These non-allergic mechanisms are currently not well understood.

One disease or multiple conditions resulting in the same effect?

Although asthma's main characteristic –variable airways obstruction– is well-established and relatively easy to diagnose, the underlying mechanisms (both allergic and non-allergic) are not well understood. It is therefore currently unclear whether asthma is a single disease, with a single underlying causal mechanism, or if it is in fact a grouping of different conditions which all result in the same clinical effect, i.e., variable airways obstruction.

2. Asthma in Children

Innes Asher, Tadd Clayton

It used to be thought that asthma primarily affected people in high-income countries. However, by the 1980s, several research groups had become concerned about signs that asthma was increasing in high-income countries, and that it was possibly much more common in low-income countries than initially presumed.

The resulting 20-year international study has shown that childhood asthma is a common disease in both high-income and lower-income countries. It is relatively more severe and increasing in prevalence in many lower-income countries.

ISAAC: A RECORD-BREAKING EPIDEMIOLOGICAL STUDY

ISAAC made the Guinness Book of World Records in 2004 when it was recognised as the largest epidemiological study among children ever conducted. Since then it has grown even more:

- 1.96 million children
- 306 research centres
- 105 countries
- 53 languages
- more than 500 publications
- more than 20 years of research

ISAAC is established

Concern that asthma, rhinitis and eczema were on the increase led to a unique worldwide epidemiological research programme – the International Study of Asthma and Allergies in Childhood (ISAAC). Established in 1991 and coordinated from New Zealand and Germany, ISAAC has conducted research over a 20-year period. For many of the countries involved, the ISAAC research was their first-ever population-based assessment of the prevalence and severity of asthma among children. ISAAC data offers the most comprehensive and up-to-date information available.

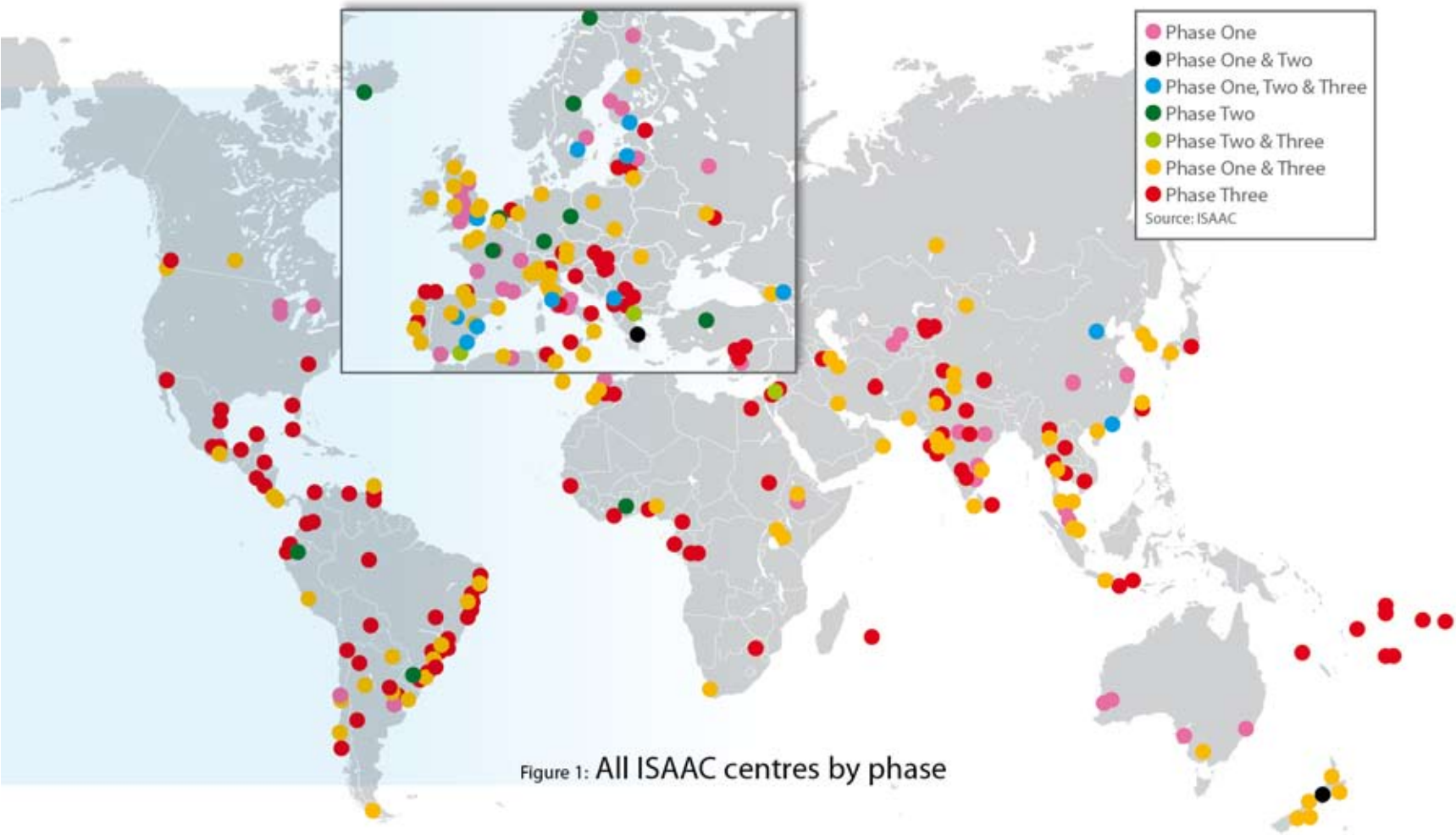


Figure 1: All ISAAC centres by phase

How ISAAC collected its data

ISAAC Phase One (1993–1997) and ISAAC Phase Three (2000–2003) were multi-centre, multi-country cross-sectional studies involving two age groups of school children: 13–14 year olds (adolescents) and 6–7 year olds (children).

Schools were randomly selected for participation from a defined geographical area. Written questionnaires on symptoms of asthma, rhinitis and eczema (translated from English, where necessary) were completed at school by the adolescents, and at home by the parents of the children. An asthma symptoms video questionnaire was also available for the adolescents. A sample size of 3,000 per age group was used to give sufficient confidence in the results from each area, and a high participation rate was required.

ISAAC Phase Two (1998–2004) conducted more intensive studies including clinical tests involving children aged 10–12 years old and was designed to investigate the relative importance of hypotheses of interest that arose from the Phase One results.

Which parts of the world participated in ISAAC?

ISAAC was the first truly global study of asthma and allergies in children. In Phase One adolescents and children from 165 centres in 62 countries took part. ISAAC Phase Two involved children in 30 centres in 22 countries. In Phase Three adolescents and children from 237 centres in 98 countries took part. In all, 306 centres in 105 countries participated in one or more phases of ISAAC (Figure 1). The countries were from all the regions of the world, representing 86.9% of the world's population. While most countries had more than one centre, findings should not be assumed to represent the situation countrywide. In particular, most ISAAC centres were urban, so the findings are less likely to be representative of rural locations.

The 113 countries that did not participate in ISAAC represent only 13.1 % of the world's population.

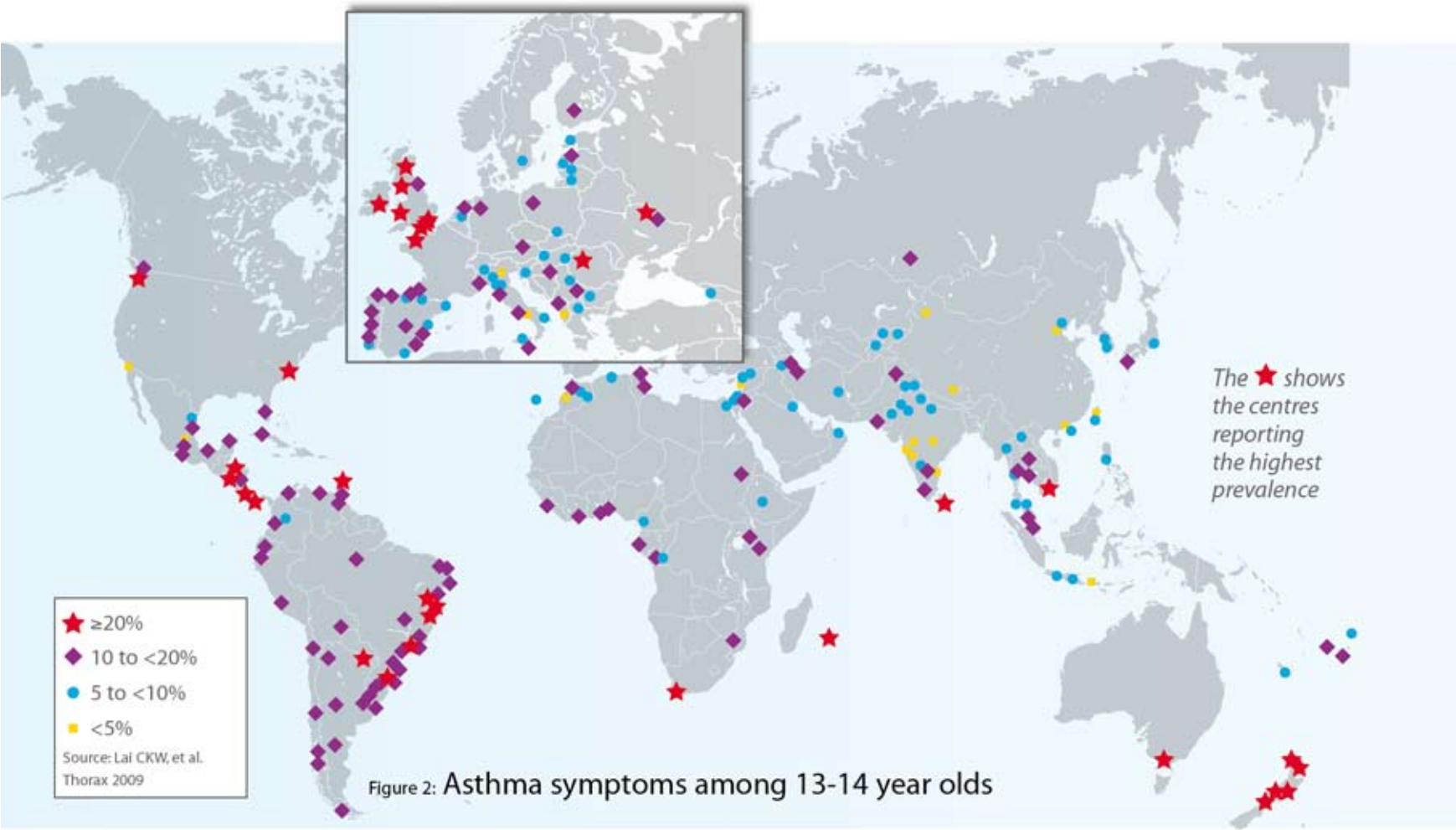


Figure 2: Asthma symptoms among 13-14 year olds

What ISAAC found

Asthma is a disease of low- and middle-income, as well as high-income, countries

ISAAC Phase One found that asthma symptoms (wheeze in the past 12 months) occurred in all countries studied. Although asthma symptoms were more common in some high-income countries, some low- and middle-income countries also had high levels of asthma symptom prevalence. In addition, there were striking variations in the prevalence of asthma symptoms throughout the world – up to 15-fold between countries. In Phase Three, it became clearer that a high prevalence of asthma symptoms is not restricted to high-income countries (Figures 2 and 3).

Asthma is more severe in low- and middle-income countries

In ISAAC Phase Three, the highest prevalence of symptoms of severe asthma* among participants with current wheeze was found in low- and middle-income countries, not high-income countries.

Asthma is on the increase in many countries

Research from English-language countries published in the 1990s reported increases in asthma prevalence from the 1980s, and continuing increases in prevalence had therefore been expected. However, ISAAC found that in most high-prevalence countries, particularly the English-language countries, the prevalence of asthma symptoms changed little between Phase One and Phase Three (1993–2003), and even declined in some cases as shown in Figures 4 and 5.

** See Appendix A: Table 1 for definition*

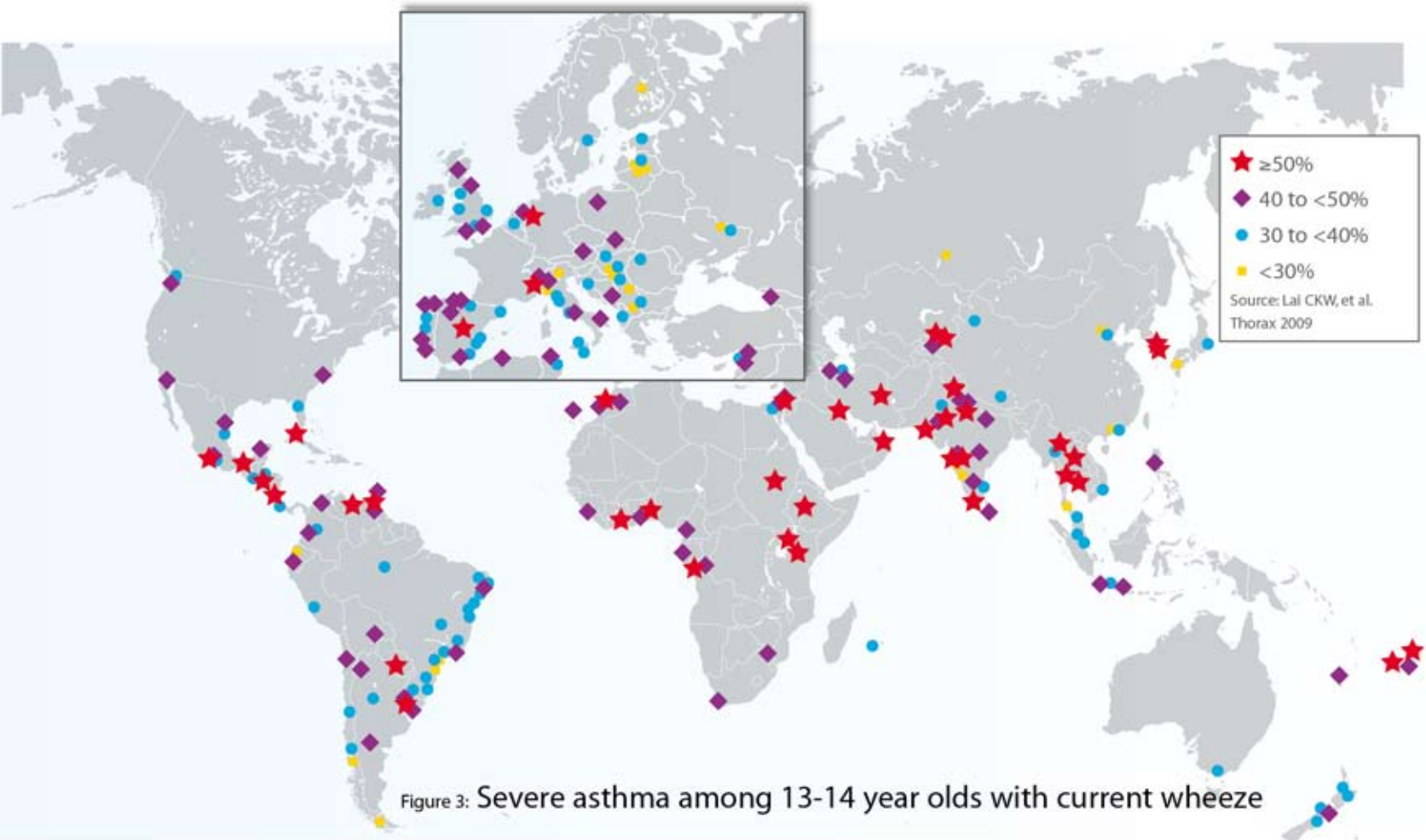


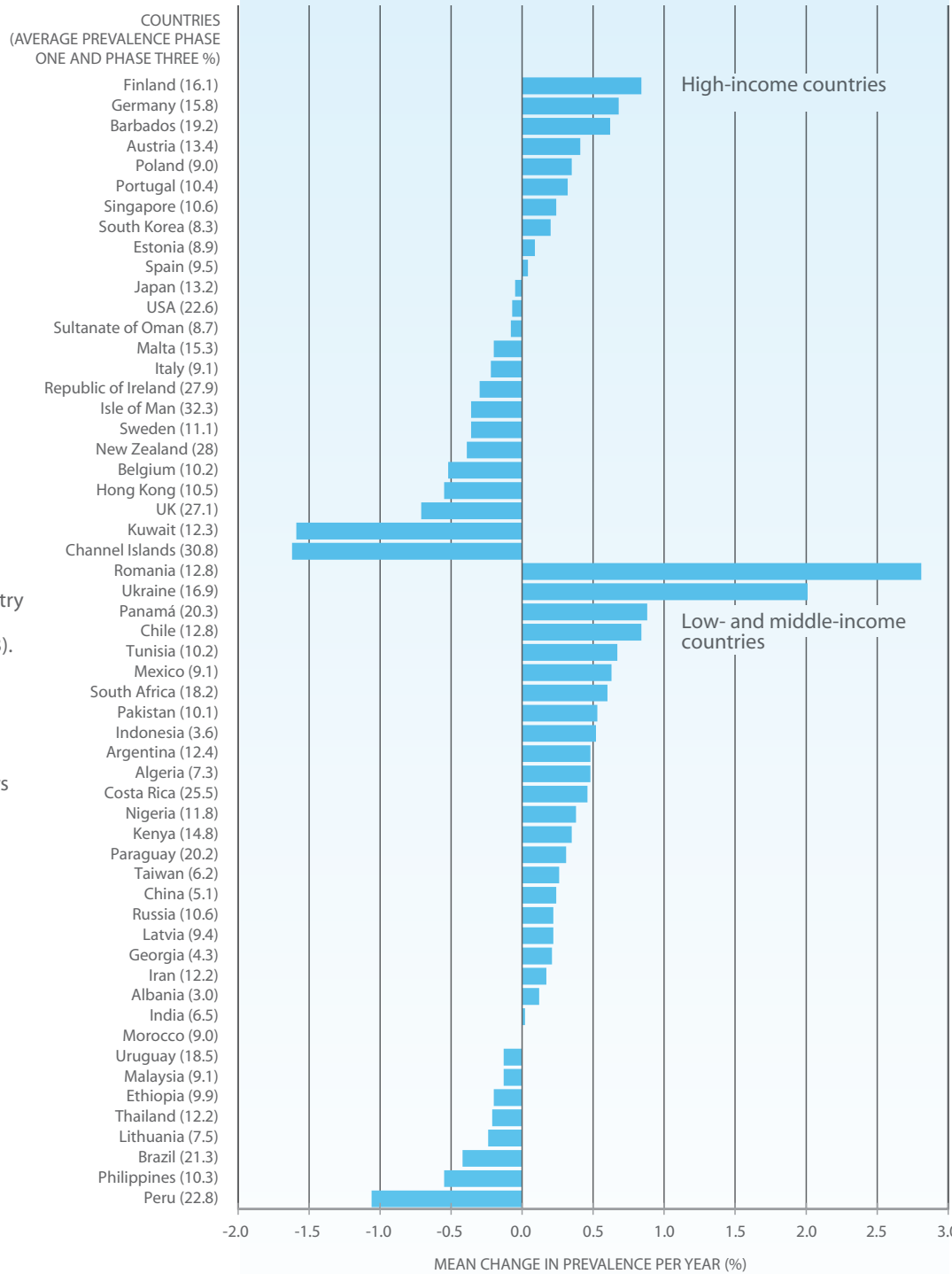
Figure 3: Severe asthma among 13-14 year olds with current wheeze

In contrast, a number of countries that had high or intermediate levels of symptom prevalence in Phase One showed significant increases in prevalence in Phase Three. Examples include Latin American countries, such as Costa Rica, Panama, Mexico, Argentina and Chile, and Eastern European countries, such as the Ukraine and Romania. Most of the countries with very low symptom prevalence rates in Phase One reported increases in prevalence in Phase Three.

The overall percentage of children and adolescents reported to have ever had asthma increased significantly, possibly reflecting greater awareness of this condition and/or changes in diagnostic practice.

Figure 4:

Changes in asthma prevalence among 13-14 year olds ranked by affluence and mean change per year



KEY TO TIME TRENDS CHART

Brackets contain the average prevalence of asthma in the country based on ISAAC Phase One and Phase Three data (1993–2003).

The blue bars indicate the change in prevalence per year between Phase One and Three.

Bars going to the right show an increase in prevalence and bars to the left show a decrease.

The length of the bar indicates the magnitude of the change.

Source: ISAAC Phase Three

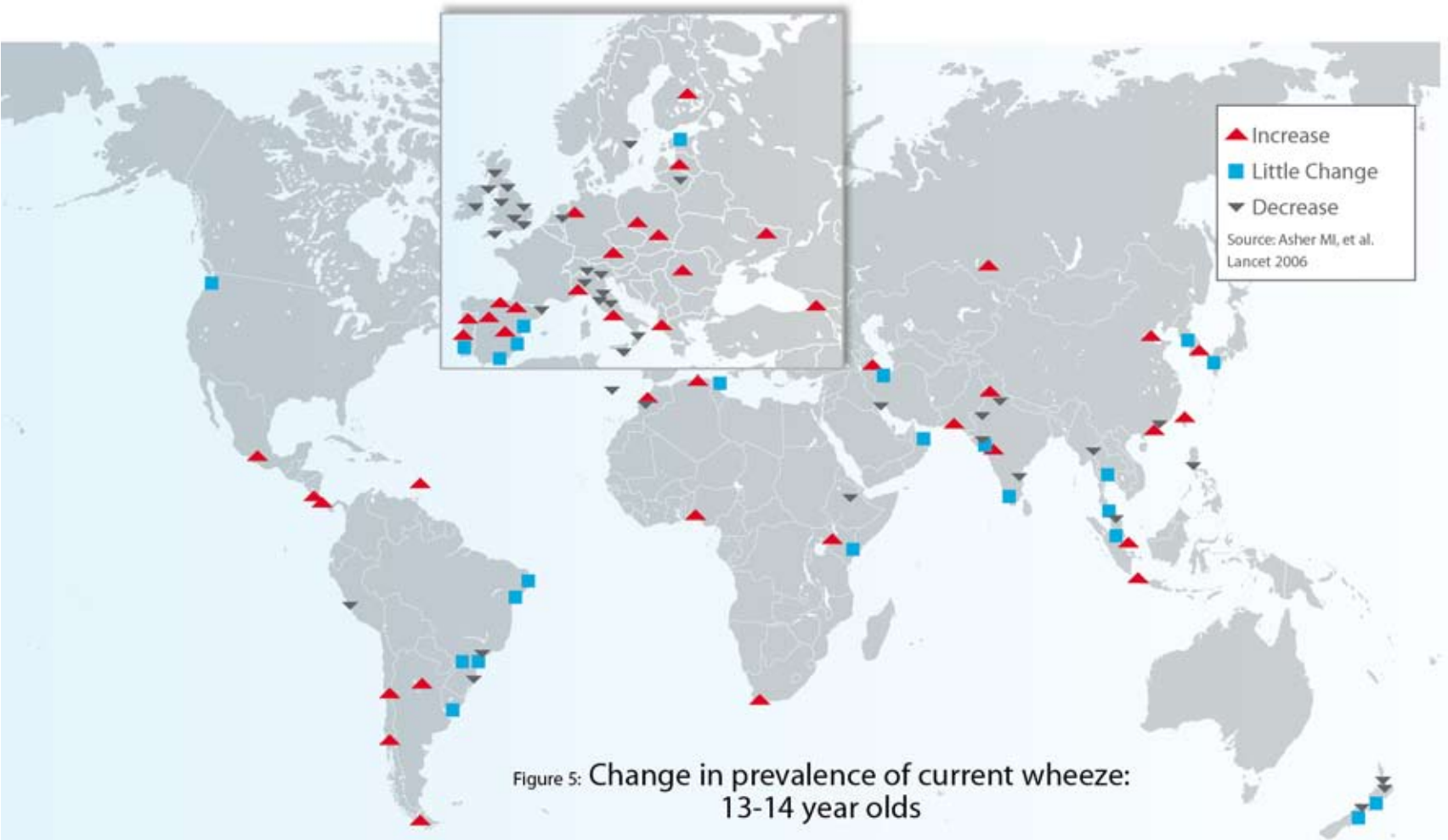


Figure 5: Change in prevalence of current wheeze: 13-14 year olds

Asthma is increasing in many low- and middle-income countries

The ISAAC Phase Three time trends analysis showed that while asthma has become more common in some high-prevalence centres in high-income countries, in many cases the prevalence stayed the same or even decreased. At the same time, many low- and middle-income countries with large populations showed an increase in prevalence, suggesting that the overall world burden is increasing, and global disparities are decreasing.

What has happened to the prevalence and severity of asthma since 2003?

Funding has not yet been found for a further phase of ISAAC and there have been no other comparable standardised studies with wide international participation. It is therefore not possible to estimate whether the prevalences and severity of asthma have changed since 2003.

3. Asthma in Adults

Peter Burney, Deborah Jarvis, Elizabeth Limb

Identifying people with asthma

Comparing the prevalence and severity of asthma across countries is difficult because asthma is poorly defined and is hard to identify with certainty. The study of asthma in young adults, however, has fewer problems than in older adults or in children. This is because conditions that can be easily confused with asthma – wheezy bronchitis in childhood and the chronic obstructive lung disease of older age groups – are much less common between the ages of 20 and 45 years.

Early population surveys

In the 1980s The Union developed methods to survey populations for asthma using both questionnaires[1-4] and measures of airway responsiveness.[5, 6] From these questionnaires further definitions have been derived, though these are not yet commonly reported.[7, 8]

The European Community Respiratory Health Survey (ECRHS)

Following on from the earlier work, the European Community Respiratory Health Survey (ECRHS) assessed the prevalence of atopy, symptoms of airway disease, diagnoses and airway responsiveness in the general population aged 20 to 44 years at a number of sites, mostly in Western Europe.[9] The initial survey showed wide variations in the prevalence of common conditions related to asthma (see Table at right).

[1] *All references can be found in Appendix C.*

Table:

Range of prevalence for common outcomes related to asthma from the first European Community Respiratory Health Survey

	Minimum (%)	Median (%)	Maximum (%)	Fold range*
Sensitivity to common allergens	16.2	33.1	44.5	**3**
Nasal allergies/hayfever	9.5	20.9	40.9	**4**
Wheeze	4.1	20.7	32.0	**8**
PD20<1mg methacholine	3.4	13.0	27.8	**8**
Waking with breathlessness	1.5	7.3	11.4	**8**
On current asthma medication	0.6	3.5	9.8	**16**

The range is expressed as a "fold range", that is, how many times the maximum value is compared with the minimum.

There has been a continuous increase in sensitivity to common allergens among people born in each decade from the 1940s to the 1970s.

The most common condition was sensitivity to allergens with a median of 33% and a 3-fold range from 16% to 45%. Hay fever symptoms were slightly less prevalent (21%) with a similar variation. Signs and symptoms associated with asthma all had an 8-fold range in prevalence with median values of 21% (wheeze) 13%, (airway response to < 1 mg methacholine) and 7% (waking with breathlessness).

Current treatment for asthma was less commonly reported than any of these conditions and was far more variable. Only 3.5% of participants said that they were currently taking asthma medication, and there was a 16-fold difference between the lowest and highest report.[10-12] This is twice the variation in the prevalence of symptoms and signs of asthma.

The principal limitation of the ECRHS data has been that it is almost entirely confined to the richer countries with the exception of Tartu (Estonia), Mumbai (India) and, for the initial survey, Algiers (Algeria). Although others have collected data using the same or similar methods,[13-21] this has not been systematic.

Where surveys have been done in the same place, there is a good association between the prevalences reported by the International Study on Asthma and Allergies in Childhood (ISAAC) in children and by ECRHS in adults,[22] but it is unwise to rely on an extrapolation of this association beyond those centres in which it was measured.

World Health Survey reports on the prevalence of asthma and wheeze

The best source of information on asthma in adults in low-income countries comes from the World Health Survey.[23] This shows that there are very wide variations in the prevalence of wheeze and asthma regardless of overall national income. The mean prevalence of wheeze was highest in the poorest countries (13.3%) followed closely by that in the richest countries (13%) (Figure 1); the mean prevalence of diagnosed asthma was highest in the richest countries (9.4%) followed closely by the poorest countries (8.2%). The middle-income countries had the lowest prevalence in each case (wheeze: 7.6%; asthma: 5.2%). In each case, these averages disguise a wide variation between countries.

Severity of disease

Because of the rather poorly defined threshold at which asthma is diagnosed, it is difficult to assess relative severity and its distribution. The Asthma Insights and Reality (AIRE) studies categorised people identified from a telephone survey as having asthma. They categorised them according to the Global Initiative on Asthma (GINA) definitions of severity [24] as either intermittent or persistent and, if persistent, as either severe, moderate or mild. Severe persistent disease was relatively more common in Eastern and Central Europe (32%) and less common in the Asia-Pacific region (11%) (Figure 2). This was also true if the intermittent disease was excluded (Figure 3). The proportion of patients who had persistent disease ranged from 41% in Central and Eastern Europe to 23% in the Asia-Pacific Region. [25] The proportion in Latin America was close to that for Central and Eastern Europe (22% of all "asthma" identified, and 41% of all persistent asthma identified).[26]

Trends in disease over time

The clearest evidence on time trends comes from data in the ECRHS on sensitisation (presence of specific IgE) to common allergens. This has demonstrated a continuous increase in sensitisation among people born in successive decades from the 1940s to the 1970s.[27] Another study has shown that this trend goes back at least to people born in the 1930s.[28]

Evidence on symptoms and reported diagnoses are more difficult to interpret. Within the ECRHS cohort, the prevalence of reported asthma increased markedly between the early 1990s and the turn of the millennium, but there was little increase in symptoms.[29] This could easily be explained as an artifact due to the greater willingness to diagnose asthma, a trend that has been well documented.[30] However, in the light of the rising prevalence in sensitisation and the strong association between sensitisation and airway disease, it might be premature to conclude that this is the whole explanation. Other changes may have altered the prevalence of symptoms, including a reduction in cigarette smoking[31] and an increase in the use of inhaled steroids, and this may have been enough to offset the increase in symptoms due to increasing allergy.

Figure 1:
Prevalence of wheeze and asthma according to Gross National Income (GNI)
Source: Redrawn from data in Sembajwe G, et al., Eur Respir J. 2010

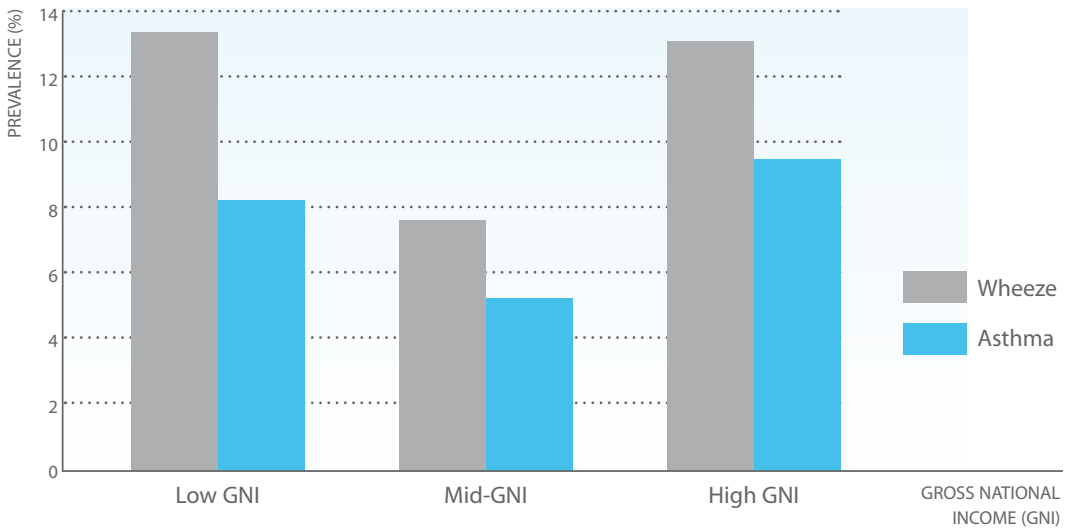


Figure 2:

Proportions of participants with any asthma whose asthma was graded Severe, Moderate or Mild in the AIRE studies

Source: Redrawn from data in Rabe K, et al., J Allergy Clin Immunol. 2004.

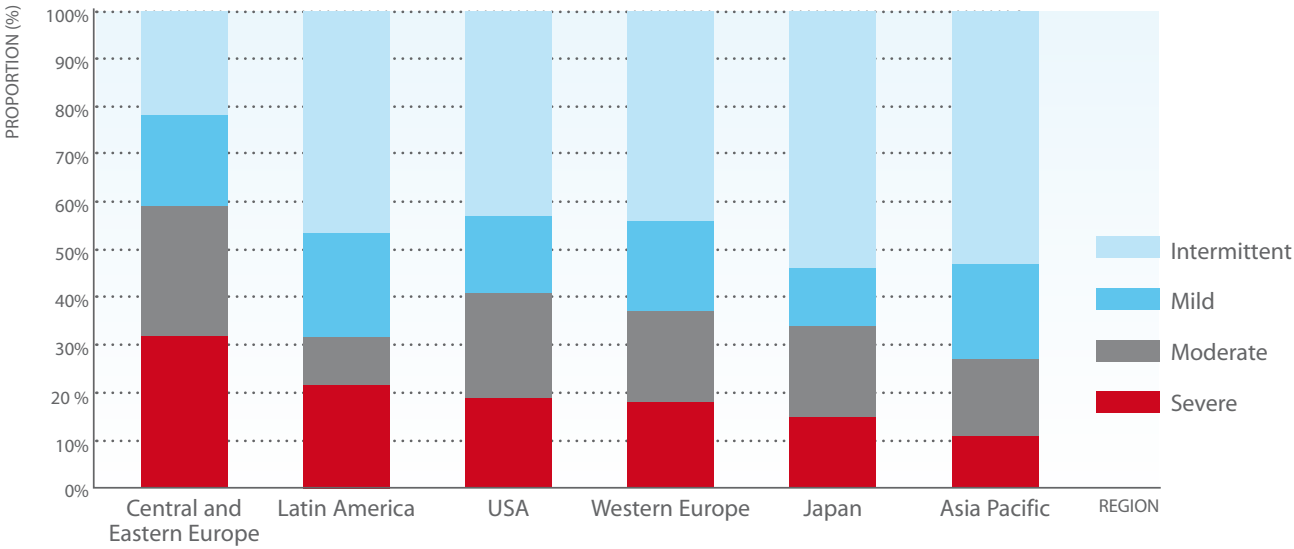
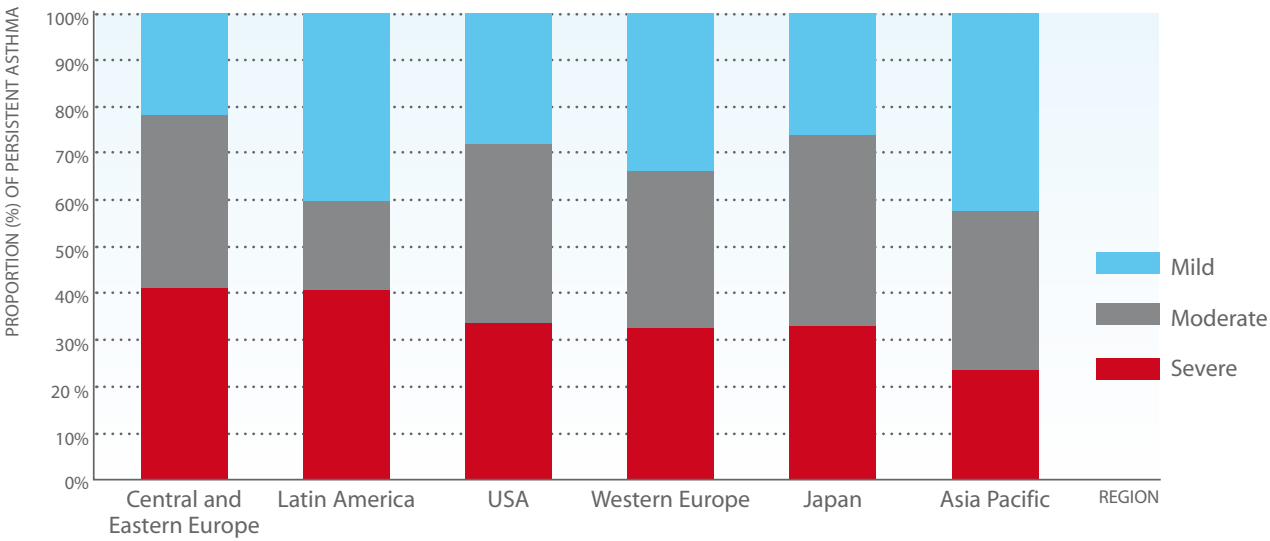


Figure 3:

Proportions of participants with persistent asthma whose asthma was graded Severe, Moderate or Mild in the AIRE studies

Source: Redrawn from data in Rabe K, et al., J Allergy Clin Immunol. 2004.



4. Factors Affecting Asthma

David Strachan, Neil Pearce

A wide variety of factors are known to affect asthma, but no one specific cause, either biological or environmental, has been identified.

Studies indicate the contribution of both genetic and non-genetic factors. When considering non-genetic factors affecting asthma, it is important to distinguish between the triggers of asthma attacks (which are widely recognised) and the causes of the underlying asthmatic trait (about which much less is known). Both groups of factors may contribute to the severity and persistence of asthma.

It is important to distinguish between the triggers of asthma attacks (which are widely known) and the causes of the underlying asthmatic trait (about which much less is known).

Genetics: One part of the picture

Asthma often runs in families, and identical twins are more likely to both be asthmatic than are non-identical twins. Nevertheless, only about half of the identical twins with an asthmatic co-twin are themselves asthmatic, indicating a contribution from both genetic and non-genetic factors.

Large studies of asthma in the general population have recently identified a small number of genetic variants that influence asthma risk, mainly in children. These variants are frequently found in populations of European origin, but their association with asthma is too weak to predict reliably which individuals will develop the disease.

Common triggers: The common cold and exercise

Asthma attacks are commonly triggered by upper respiratory tract infections, including common colds, and by exercise. Less frequently, they are related to acute emotional stress or to the consumption of certain foods, beverages or medicines.

Environmental factors that may provoke asthma attacks include inhaled allergens (commonly dust mites and animal fur; less commonly pollens, moulds and allergens encountered in the workplace) and inhaled irritants (cigarette smoke, fumes from cooking, heating or vehicle exhausts, cosmetics and aerosol sprays).

Environmental factors: Facts and theories

Secondhand smoke is a confirmed risk

Secondhand tobacco smoke is associated with asthma risk both in childhood and adulthood. Pre-natal exposure may also be important. This is considered to be a causal association, implying that the prevalence (and severity) of asthma would be reduced if exposure to secondhand smoke could be reduced. The role of other indoor air pollutants as causes of the asthmatic tendency is less clear and less consistent than for tobacco smoke.

Link to mould and damp is uncertain

Dampness and mould growth are more common in the homes of asthmatic children and adults. However, the causal nature of this link remains uncertain, because few asthmatic individuals are demonstrably allergic to fungal moulds, and dampness is associated with both allergic and non-allergic forms of asthma.

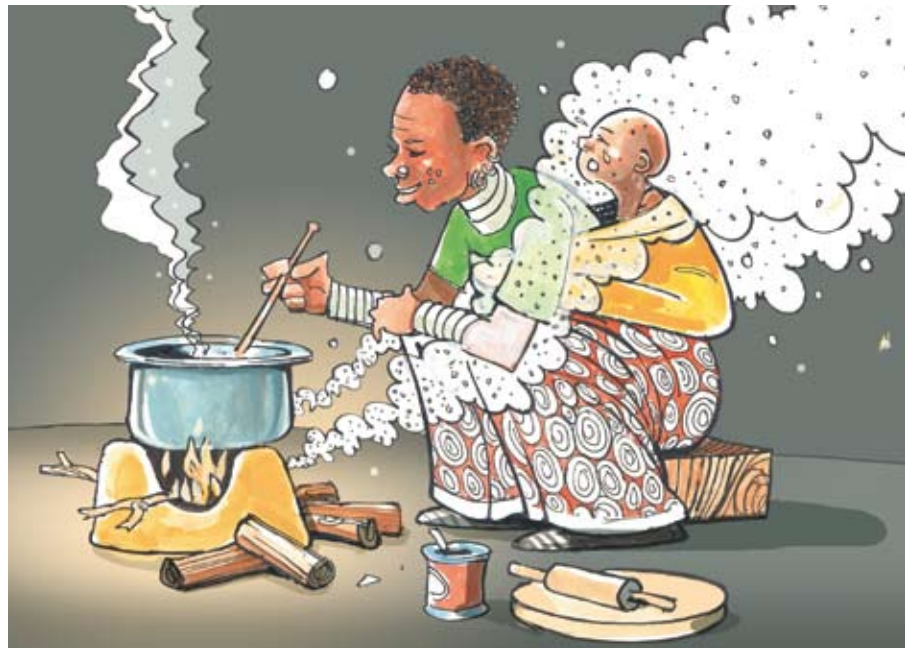
Animals in the home and on the farm

Exposure to furry pets is often less common among asthmatic children and adults, due to avoidance or removal of pets by allergic families. When this is taken into account, there is no consistent evidence that pets are either a risk factor or a protective factor.

In contrast, several large studies, mainly in temperate countries, have shown a lower prevalence of asthma among children living on farms. These children also have fewer allergies, but this does not totally explain the apparent protection against asthma. No specific cause has been identified for this protective effect of farm upbringing, but diversity of microbial exposure may be an underlying factor.

Antibiotics and paracetamol: cause or effect?

Asthmatic symptoms are more common among children who were treated with antibiotics in early childhood. However, the direction of cause and effect here is uncertain. Symptoms of wheezing commonly develop for the first time in infancy and may be treated with antibiotics before they are recognised as the early manifestations of asthma.



Similar considerations of "reverse causality" apply to the possible link between paracetamol (acetaminophen) exposure in infancy and asthma at school age – paracetamol may have been given for early symptoms of asthma, or for infections that may themselves increase the risk of asthma. Recent paracetamol use by adolescents and adults is also more common among those with asthmatic symptoms, but this may also be "reverse causality" in that people with asthma symptoms may avoid using aspirin, since it is a known trigger of wheezing attacks in a small proportion of asthmatics.

Preventive and remedial measures

Eat a balanced diet

Prolonged exclusive breastfeeding was once thought to protect against allergic diseases, including asthma, but this is no longer thought to be the case. Many components of diet during later childhood and adult life have been studied in relation to asthma. The balance of evidence suggests that "prudent diets", those that are widely recommended to prevent cardiovascular diseases and cancer, are unlikely to increase the risk of asthma and may reduce it slightly.

Avoid exposure to causal agents

Occupational exposures provide some of the clearest examples of remediable causes of asthma. Occupational asthma may develop in persons with no previous history of chest disease and can sometimes persist after exposure to the causal agent is removed. High-risk occupations include baking, woodworking, farming, exposure to laboratory animals, and use of certain chemicals, notably paints containing isocyanates. Perhaps the most widespread "occupational" exposure is to chemical cleaning agents, both in workplace and domestic settings.

Don't smoke

Little is known about the factors affecting asthma after middle age, when there is substantial overlap between the reversible airflow obstruction, which is typical of asthma, and the irreversible airflow obstruction of chronic obstructive pulmonary disease (COPD). Active smoking is a major and remediable cause of COPD and probably contributes to some cases of adult-onset asthma. It should therefore be discouraged among both asthmatics and non-asthmatics alike.

5. Asthma and Air Pollution

H Ross Anderson, Bert Brunekreef, David Strachan

One characteristic of asthma is that the airways are more reactive to a range of environmental stimuli, and it is reasonable to assume that asthmatics would be adversely affected by inhaling airborne pollutants.

This has been the subject of a large amount of experimental, clinical and epidemiological research that suggests that, in the real world, air pollution plays a role in exacerbating symptoms in asthmatics. It is not clear however that air pollution causes the asthmatic disease itself.

Exacerbation, not cause

The question is complicated not only by the need to distinguish between exacerbations of existing asthma and the incidence of the disease asthma, but also by the complex nature of air pollution. In the outdoor environment, air pollution may arise from a variety of sources, the most important being from the combustion of fossil or biomass fuels. In the indoor environment, the most common sources are also from combustion with the main processes being cooking or tobacco smoking. The pollution mixture comprises particulate matter with a wide range of physical and chemical characteristics and a range of gases, including nitrogen dioxide, sulphur dioxide and ozone. The study of asthma and air pollution is constrained by the lack of good measures of asthma and by the lack of personal exposure data.

Outdoor air pollution: The impact of traffic

There have been substantial trends in asthma and in outdoor air pollution throughout the world, but overall these do not correlate with one another. For example, asthma has tended to increase in developed countries while, over the same time period, there have been very large overall reductions in outdoor air pollution concentrations.

While this negative correlation over time suggests that air pollution is unlikely to be responsible for asthma trends, it should be noted the increase is correlated with increases in traffic-related pollution. In cross-sectional studies, variations in asthma prevalence are not associated with variations in community-wide average concentrations of air pollutants. However, there is evidence from within-community studies that the prevalence of asthma symptoms is higher in children living near sources of traffic pollution. With rapid urbanisation across the world, and poor pollution control and vehicle maintenance in poorer countries, asthma related to traffic pollution may become more important in the near future.

In contrast to the rather weak and conflicting evidence concerning prevalence and incidence, there is more convincing evidence that air pollution can exacerbate existing asthma. This evidence is based on analyses of hospital admissions data and panels of asthmatic patients. However, the effect of air pollution on asthma exacerbations is relatively small in comparison with that of other exacerbating factors, especially respiratory virus infections.

Asthmatics are often sensitive to inhaled allergens, such as from house dust mites, and laboratory studies suggest that allergens interact with air pollutants to exacerbate symptoms. It is not clear whether this happens in real-world situations. Apart from asthma, it should be emphasised that there is quite strong evidence that air pollution causes respiratory symptoms and exacerbates upper and lower respiratory infections in children.

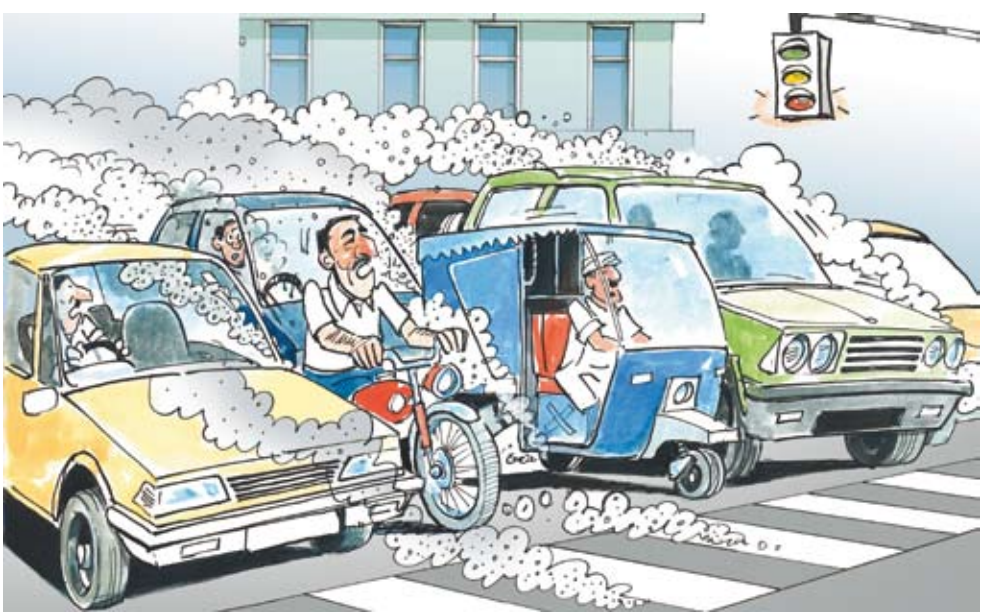
Indoor air pollution: The impact of tobacco and solid fuels

For children, one of the most important exposures to pollution indoors is secondhand smoke from parental tobacco smoking. This is somewhat easier to study than outdoor air pollution because better information on personal exposure can be obtained by asking about smoking in the home or measuring cotinine in biological samples, such as saliva.

The evidence from a large number of studies worldwide is that secondhand smoke is a cause of wheezing illness in early childhood, probably interacting with acute respiratory virus infections. This wheezing illness tends to be mild and transient, and the association with secondhand smoke becomes progressively less apparent in the school years. There is also evidence associating secondhand smoke with the onset of asthma in later childhood.

The other major source of indoor air pollution is from combustion of cooking fuels. About half of the world's population is exposed to smoke from cooking with solid fuels, often in poorly ventilated conditions. This exposure is associated with increased respiratory symptoms in children but there is little evidence to suggest that there is an effect on asthma incidence. In the developed world, gas cooking is the main source of cooking pollution, and this differs from exposure to solid fuel pollution in that particulate concentrations are much lower. The evidence of a large number of studies is not entirely consistent but suggests that gas cooking is associated with respiratory symptoms in children with asthma, and an increased severity of asthma associated with respiratory viral infections.

Broadly, the evidence from studies of outdoor and indoor pollution points in the same direction; that air pollution plays a role in causing symptoms in children with asthma, but has an uncertain role in causing healthy children to become asthmatic.



The prevalence of asthma is higher in children living near sources of traffic pollution.

6. Asthma and COPD

Chiang Chen-Yuan, Nadia Aït-Khaled, Donald A Enarson

COPD is the major killer with the unfamiliar name. Chronic Obstructive Pulmonary Disease (COPD) is the term now used to describe chronic bronchitis and emphysema. COPD is defined as a preventable and treatable disease characterised by airflow limitation that is not fully reversible and usually progressive.

According to the World Health Organization, more than three million people died of COPD in 2005, 90% of them in low- and middle-income countries. By 2030, the WHO predicts that COPD will be the 3rd leading cause of death worldwide. However, data available for these estimates were limited, since COPD is frequently undiagnosed in low- and middle-income countries.

Diagnosing COPD

The diagnostic marker for COPD is the deterioration of lung function as shown by a decline in the forced expiratory volume of air in one second (FEV1). The Global Initiative for Chronic Obstructive Lung Disease (GOLD) classifies COPD into four stages based on the percentages of predicted FEV1 from 80% to 30% of normal. The level of FEV1 has been shown to be associated with mortality in COPD patients.

Smoking is the leading risk factor

To date, smoking is the most important risk factor for developing COPD in most countries. The growing burden of COPD is closely related to the epidemic of smoking. To reverse the epidemic of COPD, it is essential to reduce the proportion of the population who smoke. Other factors associated with COPD include specific genetic syndromes, occupational exposures, traffic and other outdoor pollution, secondhand smoke, biomass smoke and dietary factors. Chronic asthma and tuberculosis have also been shown to be associated with irreversible airflow limitation.

Asthma and COPD: Two distinct diseases or different manifestations of the same disease?

Both asthma and COPD are syndromes of airflow limitation, but with significant differences. Typical COPD patients include a high proportion of smokers or ex-smokers;

their symptoms rarely develop before age 40; difficult breathing is persistent, progressive and worsens with exertion; night-time attacks of difficult breathing are uncommon; and day-to-day variability of symptoms is rare.

Among asthma patients, a high proportion are non-smokers; symptom onset prior to age 40 is common; variability of symptoms is usual; and patients may be asymptomatic between attacks.

Differences have also been noted in the pulmonary inflammation caused by asthma and COPD in terms of cells, mediators and the anatomic sites of the disease. These differences support the hypothesis that asthma and COPD are distinct diseases with different underlying mechanisms.

However, distinguishing asthma from COPD can be difficult. In reality, there is substantial overlap between them. Patients with asthma who smoke or have been exposed to air pollution may have non-reversible airflow limitation. Likewise, a substantial proportion of patients who meet the definition of COPD have reversible airflow limitation with a positive bronchodilator test, both criteria of asthma. It has been suggested that asthma and COPD are different manifestations of the same underlying disease.

Tracking the prevalence of COPD

Diagnosis of COPD requires spirometry, a test of lung function that measures both the speed and volume of air being inhaled or exhaled. However, quality-assured spirometry is usually unavailable at both primary health care and first-level referral facilities in most countries. Consequently, the majority of patients with COPD are unrecognised or under-diagnosed, especially in low- and middle-income countries.

The Burden of Obstructive Lung Disease (BOLD) Initiative developed a standardised protocol for estimating the prevalence of COPD and its risk factors in various countries around the world. Results from the initial 12 sites (Australia, Austria, Canada, China, Germany, Iceland, Norway, Philippines, Poland, South Africa, Turkey, USA) were published in 2007 and demonstrated that the prevalence of stage II or higher COPD was 10.1% overall, with 11.8% for men, and 8.5% for women.

The PLATINO study, launched in 2002, evaluated the prevalence of COPD in five large Latin American cities: Sao Paulo (Brazil), Santiago (Chile), Mexico City (Mexico), Montevideo (Uruguay) and Caracas (Venezuela). The study showed crude rates of COPD ranged from 7.8% in Mexico City to 19.7% in Montevideo, suggesting that COPD is a greater health problem in Latin America than previously realised.

Treating COPD

Like asthma, COPD is mainly treated with inhaled bronchodilators and inhaled corticosteroids. To date, smoking cessation is the only convincing intervention that has reduced the rate of decline of the FEV1 in patients with COPD.

While it is crucial to ensure the accessibility of essential diagnostics and medicines for COPD, tobacco control and reducing exposure to other risk factors for COPD must be given high priority by all countries in their national strategy for the prevention and management of COPD.

ASTHMA AND COPD COMPARED

ASTHMA	COPD
High proportion of non-smokers	High proportion of smokers/ex-smokers
Symptom onset before age 40 is common	Symptoms develop after age 40
Breathing difficulty is intermittent ("attacks")	Breathing difficulty is persistent and progressive
Night-time symptoms and/or attacks are common	Night-time attacks are uncommon
Patients may be asymptomatic or with minimal symptoms between attacks	Variability of symptoms is rare
Symptoms may be affected by exercise	Symptoms worsen with exercise


Lack of access to quality-assured affordable medicines is a major obstacle to effective asthma management.

PART TWO:

THE CHALLENGES OF MANAGING ASTHMA

7. Essentials of Asthma Management

Chiang Chen-Yuan, Nadia Aït-Khaled

The criteria for successfully managed asthma have been described by the Global Initiative for Asthma (GINA). The Union follows these same criteria closely in its own guidelines:

- no symptoms or very mild symptoms
- no attacks
- no emergency department visits
- no limitation of activities
- no airflow limitation (PEF ≥ 80% of predicted value)
- minimal bronchodilator use (< 2 times/week)
- the least side effects possible.

The under-use of inhaled corticosteroids results in poor asthma control, frequent unplanned visits to the emergency room, more hospitalisations, and an unnecessary reduction in quality of life for those who live with asthma.

Inhaled corticosteroids are essential to success

Inhaled corticosteroids are essential for achieving these goals and managing patients with persistent asthma over the long-term. However, studies have found that health care workers often don't prescribe inhaled corticosteroids for asthma. When they do prescribe them, patients often abandon them and rely on bronchodilators instead. They believe that bronchodilators are effective because these medicines provide quick relief from symptoms and that inhaled corticosteroids are not effective because they observe no immediate, obvious effect from them. Consequently patients are likely to under-use inhaled corticosteroids.

Projects undertaken by The Union evaluated asthma treatment outcomes after one year of follow-up. They found that asthma severity and symptom frequency reduced significantly when patients took treatment regularly. However, practitioners demonstrated only moderate adherence to guidelines for grading the severity of their patients' asthma, and poor adherence to guidelines as regards prescribing inhaled corticosteroids. A substantial proportion of patients also stopped taking their inhaled corticosteroids.

Falling short of success

Survey after survey shows these effective medicines are not being used.

The USA

The Asthma in America national population survey revealed that only 26.2% of persons who had had persistent asthma symptoms in the previous month reported using inhaled corticosteroids. The percentage was even lower among smokers and persons reporting lower income, less education and present unemployment, all of whom were significantly less likely to report current use of inhaled corticosteroids.

Europe

The Asthma Insights and Reality in Europe study revealed that 46% of patients had daytime symptoms, and 30% had asthma-related sleep disturbances at least once a week. In the past 12 months, 25% of patients reported an unscheduled urgent care visit; 10% had one or more emergency room visits; and 7% were hospitalised overnight due to their asthma. Yet, the proportion of patients who used inhaled corticosteroids was low. The study found that in the previous four weeks, 63% of patients had used bronchodilators, but only 23% used inhaled corticosteroids.

Asia Pacific

The Asthma Insights and Reality in the Asia-Pacific study revealed that in China, Hong Kong, Korea, Malaysia, The Philippines, Singapore, Taiwan and Vietnam, 51.4% of respondents had daytime asthma symptoms, and 44.3% reported sleep disturbances caused by asthma in the preceding four weeks. Survey respondents also reported that 43.6% had been hospitalised, attended an emergency room or made unscheduled emergency visits to other health care facilities for treatment of asthma during the previous 12 months. While 56.3% reported using bronchodilators, only 13.6% reported current use of inhaled corticosteroids.

Globally

The global Asthma Insights and Reality surveys observed that asthma had a substantial impact on patients' lives with considerable loss of school days and work days and that the current level of asthma control worldwide was unsatisfactory.

What is needed to manage asthma effectively in low- and middle-income countries?

The under-use of inhaled corticosteroids results in poor asthma control, frequent unplanned visits to the emergency room, more hospitalisations, and an unnecessary reduction in quality of life for those who live with asthma. To turn this situation around requires action on several fronts:

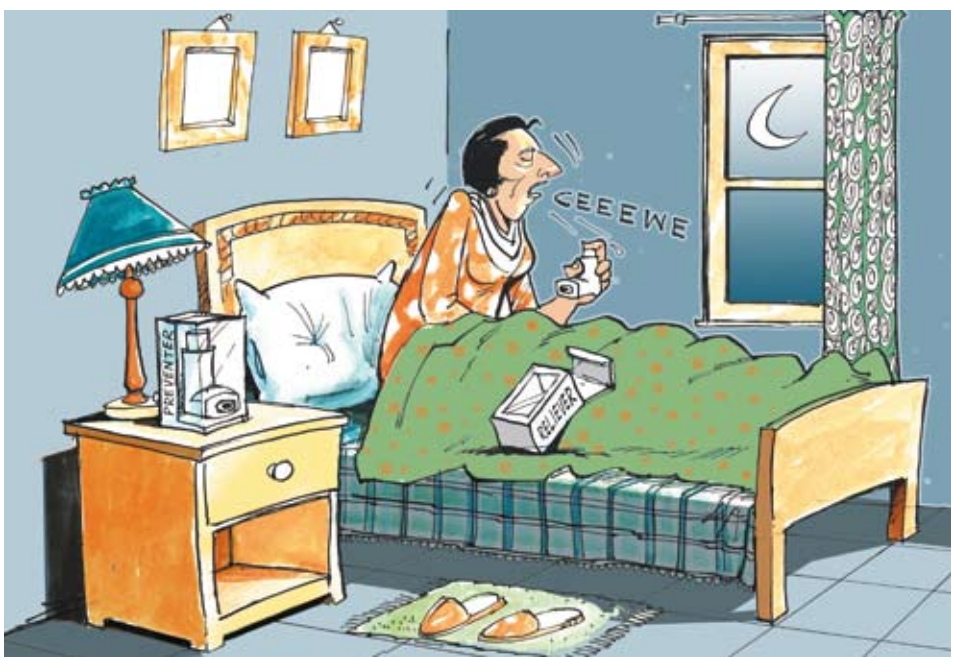
Apply guidelines for standard case management of asthma

The Union's asthma guidelines were pilot tested in health centres in Algeria, Guinea, Ivory Coast, Kenya, Mali, Morocco, Syria, Turkey and Vietnam. Investigators concluded that the measures were feasible, effective and cost-effective, with reductions in the severity of asthma for the majority of patients, and the almost complete disappearance of visits to emergency services and hospitalisations.

Train clinicians and health care workers to identify asthma patients

In Huaiyuan County, Anhui Province, China, a project with The Union revealed that asthma was not being diagnosed in the participating facilities before the project was introduced. Patients presenting with cough and difficult breathing were usually diagnosed with chronic bronchitis and treated with a combination of antibiotics, systemic steroids, xanthine derivatives and/or oral beta-2 agonists.

Inhaled corticosteroids had never been available prior to the project. After training, health workers identified a substantial number of asthma patients who were treated with inhaled corticosteroids and inhaled salbutamol. This project suggested not only that asthma can be a "hidden disease", but also that health workers can be trained to provide standardised case management of asthma.



Ensure quality-assured essential asthma medicines are accessible and affordable

The high cost of inhaled corticosteroids is a major barrier to asthma management in low- and middle-income countries. The Union's Asthma Drug Facility, along with several countries running pilot projects, has demonstrated that quality-assured essential asthma medicines can be procured at low prices.

Serve chronic patients effectively

The huge majority of asthma patients are only being treated on an emergency basis – when they arrive in the emergency department with an acute attack of asthma. Health services need to be organised for the long-term management of asthma, with trained health care workers and regular follow-up of patients. This will reduce emergency visits and hospitalisations, and empower patients and their families to manage their asthma.

Collect and monitor data to assure quality of care

To evaluate the effectiveness and quality of asthma care, an information system allowing outcome assessment of registered asthma patients and overall evaluation of asthma management should be established for facilities providing care.

Educate patients to overcome fears and encourage self-management

Patient education is essential to prevent unnecessary concerns about asthma and asthma medicines. Patients need to learn that inhaled corticosteroids are not addictive or dangerous. They need to understand that their condition is ongoing, possibly lifelong, and that it is variable (i.e., the timing and extent of symptoms varies). They also need to learn how to manage their asthma: how and when to take their medicines and when to seek help from health care facilities.

Governments need to help set up long-term management of asthma

An uninterrupted supply of essential asthma medicines, organised services and trained human resources are the minimum requirements for health services to manage asthma.

8. The Role of Guidelines in Managing Asthma

Philippa Ellwood, Innes Asher, Eamon Ellwood

Despite the success of asthma management guidelines so far, increased efforts are required to improve adherence to guidelines and promote the delivery of quality asthma care.

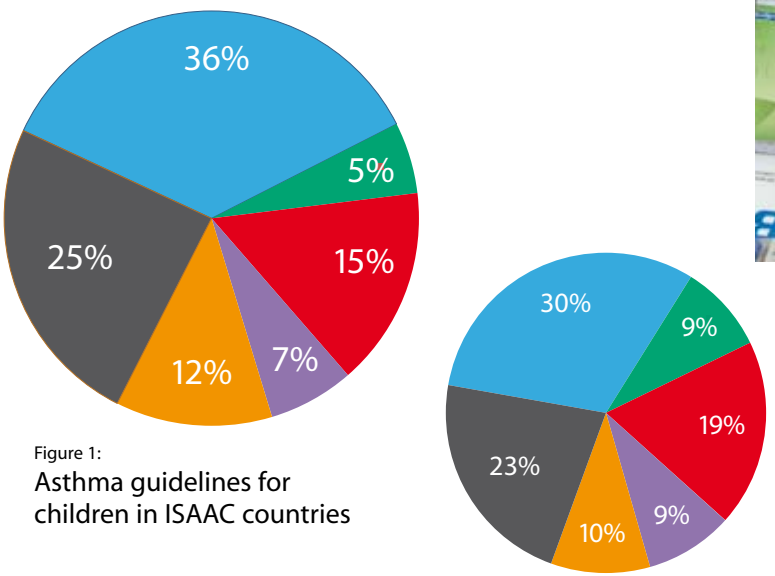


Figure 1:
Asthma guidelines for children in ISAAC countries

Asthma guidelines for adults in ISAAC countries

The role of guidelines

The WHO reports that lack of awareness probably represents the most important barrier to progress in the diagnosis, treatment and care of individuals with non-communicable diseases, including asthma. Asthma management guidelines encourage awareness and play an important role in patient care, focusing on the assessment of asthma symptoms and their severity, and recommendations for effective medicines in children and adults, as well as non-pharmacological measures.

Who determines the guidelines?

When the first guidelines were created in the late 1980s, it was almost uniform that pharmaceutical companies sponsored the consensus meetings. In more recent times, where there are alternative sources of funding available, in many cases doctors are choosing to create evidence–based guidelines, without the involvement of pharmaceutical companies in any aspect of the process.

Some groups developing asthma management guidelines have been instrumental in constraining the pharmaceutical industry, where attempts have been

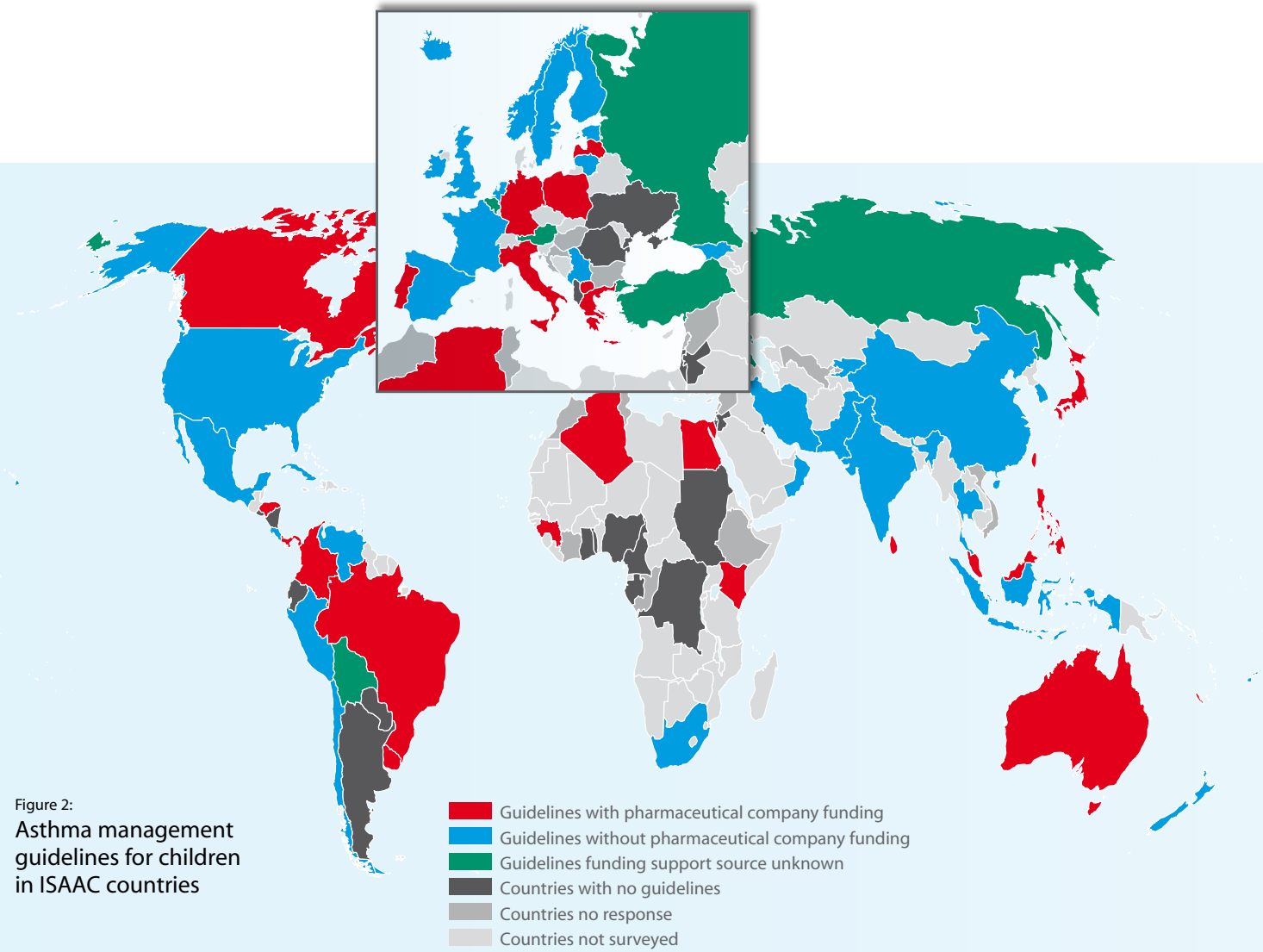


Figure 2:
Asthma management guidelines for children in ISAAC countries

made to broaden the therapeutic indications for a particular type of medication. Others have been able to discuss recommendations within guidelines where these have not been based on evidence.

However, asthma prevalence is increasing, and the global economic burden is substantial. Despite the success of asthma management guidelines so far, increased efforts are required to improve adherence and promote recognition of quality asthma care. The use of asthma guidelines should be encouraged to reduce hospital admissions and improve asthma control for the benefit of both patients and the health systems that serve them.

The ISAAC survey of national guidelines 2011

To identify countries with existing asthma management guidelines for children and adults, ISAAC canvassed its collaborators from the 105 countries that participated in Phases One, Two and Three. They were asked if they had guidelines for children, for adults and also if the development of the guidelines had been supported with pharmaceutical company funding. *

There was an 88% (92/105) response rate to the survey. Of the 92 countries that responded, 69 (75%) said they used asthma management guidelines for children, and 71 (77%) said they used them for adults.

For the children, 58/69 countries (84%) had their own national asthma management guidelines. Of these, 34 (59%) did not receive pharmaceutical company financial support, 14 (24%) said they did and 4 countries did not know if they had received pharmaceutical company financial support or not.

For the adults, 61/71 countries (87%) reported they had their own national asthma management guidelines. Of these 28 (46%) did not receive pharmaceutical company financial support, 18 (29%) said they did, and 8 countries did not know if they had received pharmaceutical company

** Detailed results are shown in Appendix A.*

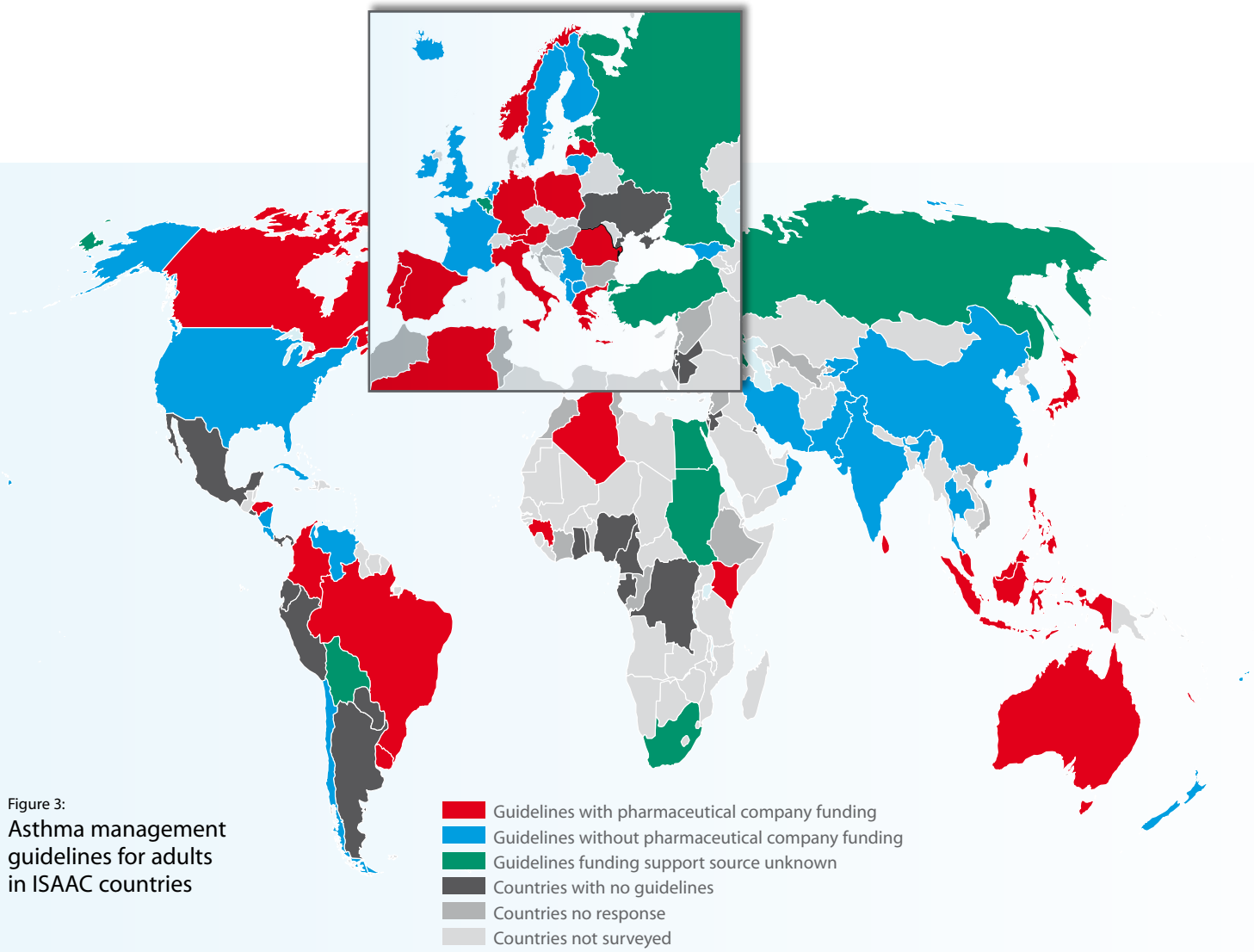


Figure 3:
Asthma management guidelines for adults in ISAAC countries

financial support or not. The results are shown in Figure 1 with a more detailed description in Appendix A.

Clearly, asthma management guidelines appear to be an important part of medical practice in the majority of countries. It is encouraging that, in the 58 countries with guidelines for children, more than half (59%) were developed without pharmaceutical company funding. While the percentage is lower (46%) in the 61 countries with guidelines for adults, this is still an improvement over the situation when guidelines were first introduced in the 1980s. Independently developed guidelines avoid any perception of influence by the pharmaceutical industry regarding branding and allow the most appropriate therapeutic drugs to be recommended. They can also be regularly updated based on new evidence.

Asthma management guidelines are an essential part of efforts to provide access to effective, appropriate drug therapy and management.

9. Essential Medicines: Pricing, Availability and Affordability

Zaheer-Ud-Din Babar, Charon Lessing, Karen Bissell, Cécile Macé

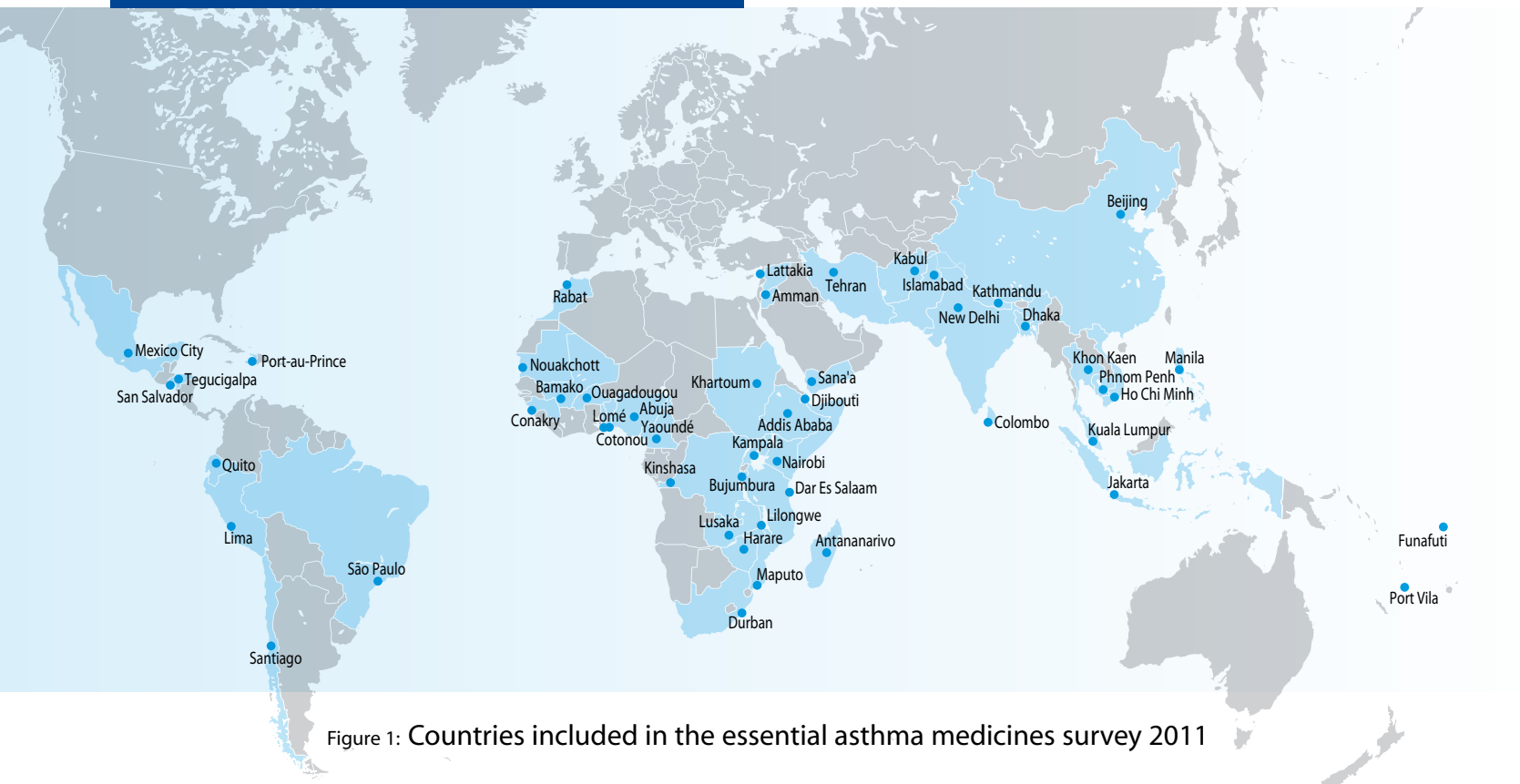


Figure 1: Countries included in the essential asthma medicines survey 2011

Although effective treatment for asthma exists, many people, especially in low- and middle-income countries, are unable to access the medicines needed to manage this chronic condition. Poor availability of medicines is one barrier, another is price - many medicines are unaffordable for patients who have to purchase them out-of-pocket.

Providing affordable essential medicines for developing countries is a target within goal 8 of the Millennium Development Goals and a particular focus of the World Health Organization (WHO).

Measuring and understanding the price of medicines is the first stage in developing pricing policies that can improve both the availability and affordability of medicines. However, data on medicine prices and availability are still limited in low- and middle-income countries.

Essential asthma medicines: A survey in 2011

A cross-sectional 'snapshot' survey was conducted by The Union and the University of Auckland's School of Pharmacy to measure the availability and prices in low- and middle-income countries of three essential asthma medicines: beclometasone 100 µg/puff inhaler, salbutamol 100 µg/puff inhaler, and budesonide 200 µg/puff inhaler (all with 200 doses and HFA i.e., CFC-free). For each of these inhalers, the price and availability of both an innovator or reference product and the lowest-priced generic product was sought. Qvar® from 3M was used as the reference medicine for beclometasone; Pulmicort® from Astra Zeneca as the innovator for budesonide. For salbutamol, innovator brands from GlaxoSmithKline (such as Ventolin®, Aerolin®, or Salbutan®) were sought. Union contacts in 50 countries collected data by making one visit to a public hospital, a public sector national procurement centre and two private retail pharmacies in the capital or main provincial city of each country during the months of May-July 2011.

The price ratios of each medicine were calculated by comparison with the Management Sciences for Health 2010 International Reference Prices (IRPs). IRPs are the medians of recent procurement or tender prices offered by predominantly not-for-profit suppliers to developing countries for multi-source products. Affordability for patients was calculated using the surveyed price of each inhaler and the daily wage of the lowest-paid unskilled government worker of the particular country.

Survey results

Pricing of medicines

International Reference Prices (IRPs) were used to assess pricing and procurement efficiency and some pricing information is provided in Appendix B. However, this approach should be taken with some caution, as IRPs are only indicators. In addition, these IRPs appear to be on the higher side, for example, the IRP for beclometasone (US$ 8.06) is much higher than the current price obtained by the Asthma Drug Facility (ADF) (US$ 1.28 FCA price). Likewise the IRP for budesonide (US$ 10.55) is much higher than ADF's price (US$ 2.60). Therefore, public sector procurement agencies and other sectors should definitely aim to obtain prices significantly lower than the IRPs for these products.

Median prices of the surveyed inhalers are shown below in US$ (Table 1).

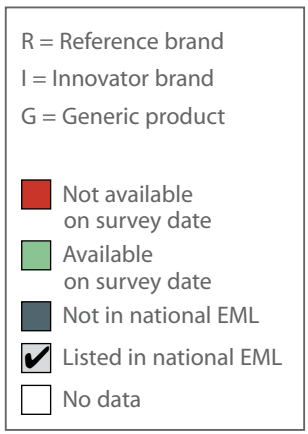
Median Price (US $)	Private Pharmacy		National Procurement Centre		Public Hospital Pharmacy	
	Reference	Generic	Innovator	Generic	Innovator	Generic
Beclometasone 100µg	26.00	6.29	n/a	3.09	n/a	4.43
Salbutamol 100µg	6.57	3.59	3.69	1.67	5.48	2.63
Budesonide 200µg	29.94	15.15	16.70	4.28	23.77	6.76

Table 1: Median price of surveyed inhalers in 50 low- and middle-income countries

Note: Not all countries or facilities had all products. In the table, n/a means no country had that product.
For details on availability, see Table 2, p. 34.

Table 2:

Availability of surveyed inhalers by country, type of health facility and national Essential Medicines List (EML)



	Beclometasone 100µg							Salbutamol 100µg							Budesonide 200µg						
	Private Pharmacy		National Procurement Centre		Public Hospital Pharmacy		EML	Private Pharmacy		National Procurement Centre		Public Hospital Pharmacy		EML	Private Pharmacy		National Procurement Centre		Public Hospital Pharmacy		EML
	R	G	R	G	R	G		I	G	I	G	I	G		I	G	I	G	I	G	
Afghanistan														✔							
Bangladesh																					
Benin																					
Brazil														✔							
Burkina Faso														✔							
Burundi														✔							
Cambodia																					
Cameroon														✔							
Chile							✔							✔							✔
China (Beijing)														✔							
Congo														✔							
Djibouti																					
Ecuador														✔							
El Salvador														✔							
Ethiopia							✔							✔							
Rep Guinea																					
Haiti														✔							
Honduras							✔							✔							
India (New Delhi)														✔							
Indonesia														✔							✔
Iran														✔							✔
Jordan														✔							✔
Kenya														✔							
Madagascar														✔							
Malawi														✔							
Malaysia							✔							✔							✔
Mali														✔							
Mauritania														✔							
Mexico														✔							
Morocco														✔							
Mozambique																					
Nepal																					
Nigeria														✔							
Pakistan														✔							
Peru														✔							
Philippines														✔							
South Africa							✔							✔							✔
Sri Lanka							✔							✔							
Sudan														✔							
Syria							✔							✔							✔
Tanzania														✔							
Thailand							✔							✔							✔
Togo																					
Tuvalu							✔							✔							
Uganda														✔							
Vanuatu														✔							
Vietnam														✔							✔
Yemen																					
Zambia																					
Zimbabwe							✔							✔							

Availability of medicines (Table 2)

Beclometasone 100µg/dose was on the national Essential Medicines List (EML) of only 10 countries (20%). Others listed only 50µg and 250µg strengths, despite the fact that 250µg is no longer in the WHO EML. Generic beclometasone was available in 41% of private pharmacies, 15% of national procurement centres and 17% of public hospitals.

Salbutamol 100µg/dose was on the EML of almost all countries. Generic salbutamol was available in 82% of private pharmacies, 54% of national procurement centres and 57% of public hospitals.

Budesonide 200µg/dose was on the EML of 9 countries (18%). In at least 20 countries, neither the innovator nor generic brand was available. Generic budesonide was available in 31% of private pharmacies, 12% of national procurement centres and 17% of public hospitals.

Affordability of medicines purchased from private pharmacies

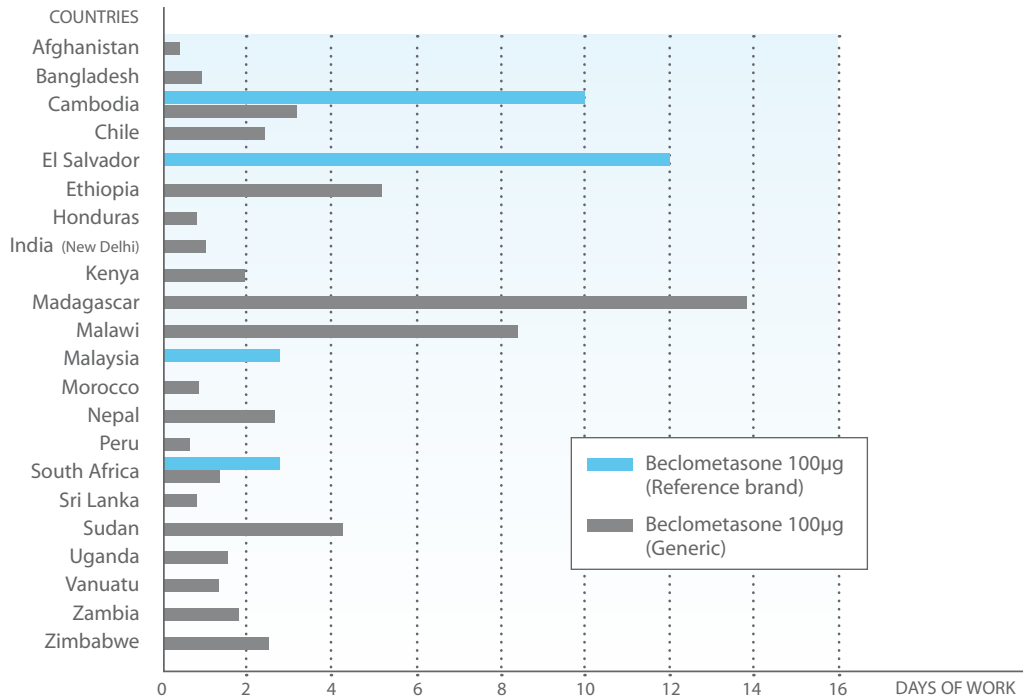
Affordability was based on inhaler prices and a generalised daily minimum wage. Affordability in private pharmacies is presented here (see Figure 2 at right) and in Appendix A (Figures 3 and 4). It should be noted that in some of these countries, medicines may be provided free in the public sector, and social insurance may exist in the private sector. The tables do, however, show what patients would have to pay out-of-pocket, if they have no alternative.

Given that a patient with severe asthma needs about 16 beclometasone inhalers per year and 8 salbutamol inhalers per year, all prices per inhaler need to be multiplied to estimate the cost of a year's supply. For example, to purchase one reference brand inhaler of beclometasone in Cambodia and in El Salvador, more than 10 days' wages are needed (160 days' wages per year for severe asthma). For one generic beclometasone inhaler, less than 5 days' wages are needed (less than 80 days' wage/year) in all countries except Ethiopia, Madagascar and Malawi.

One generic salbutamol inhaler requires 4 or less days' wages (32 days' wages/year) in all countries. Innovator brands of salbutamol are less than 8 days' wages per inhaler in all countries, except the Republic of Guinea.

Affordability of budesonide demonstrates wider extremes: for generic budesonide, it ranges from less than one day's wage (16 days' wages/year for severe asthma) in Iran, Jordan and Malaysia to more than 50 days' wages (800 days' wages/year) in Mozambique. In the Republic of Guinea, the innovator brand costs 107 days of wages (1712 days' wages/year).

Figure 2:
Affordability of Beclometasone 100µg inhaler in private pharmacies
(Number of days of wages required to purchase one inhaler)



Using results to improve access

This preliminary analysis reveals issues around the pricing, availability and affordability of essential medicines recommended by the WHO. It is of concern that beclometasone 100µg and budesonide 200µg are absent from so many Essential Medicines Lists (EMLs). The integration of these essential medicines into national EMLs is an important first step for improving the availability of these products in the public sector.

The fact that corticosteroid prices continue to remain so high in many countries is reflected in the International Reference Prices (IRPs): IRP for beclometasone is 6 times higher than the ADF's current price; IRP budesonide is 4 times higher. Hopefully this preliminary report and the upcoming detailed analysis will alert policy-makers and health services to the disparities that exist within and between countries. Most health systems are spending much more than they need, and there are many examples of acute lack of affordability for patients.

10. A Practical Solution: Asthma Drug Facility

Cécile Macé, Karen Bissell

With proper management and medicines, the severity of asthma can be dramatically reduced, and a person's quality of life significantly improved. Yet for millions of people with asthma, especially those in low- and middle-income countries, these benefits are unattainable.

Although several effective asthma medicines are on the WHO Essential Medicines List, the most commonly reported obstacle to successful asthma management is the lack of access to essential medicines. For many patients and health systems, asthma medicines are prohibitively expensive and frequently not available.

A practical solution to the problem of access

The Asthma Drug Facility (ADF), a project of The Union, is helping to overcome this obstacle by making it possible for low- and middle-income countries to obtain quality-assured essential medicines at affordable prices. Through the ADF, the cost of one year of treatment for a patient with severe asthma has already come down to about US $40. In some countries, this is half of what they were paying before the ADF.

Assuring both quality and affordability

The Union places the highest importance on providing not only affordable but also quality-assured medicines. The ADF has a quality-assurance system based on WHO norms and standards. Since asthma inhalers are not part of the WHO Prequalification Programme, the ADF has to organise the selection of manufacturers and products. It keeps prices down by having a limited competitive process among selected manufacturers, based on annual estimated volumes. Countries can then purchase these affordable products through the ADF.

ADF PRODUCTS	
Inhaled HFA corticosteroids	
BECLOMETASONE	100µg / puff, 200 doses, HFA inhaler
BUDESONIDE	200µg / puff, 200 doses, HFA inhaler
FLUTICASONE	125µg / puff, 120 doses, HFA inhaler
Inhaled HFA short-acting beta2-agonist	
SALBUTAMOL	100µg / puff, 200 doses, HFA inhaler

Improving quality of care takes more than medicines

To address the other aspects of asthma care, the ADF provides The Union's asthma management guidelines and training materials. These help clients build their capacity for asthma management and establish an information system for monitoring patient outcomes. By tracking the reduction in patients' emergency visits and hospitalisations, health care providers and administrators see the health benefits and financial advantage of providing appropriate care and medicines. They can also evaluate and improve patient management.

Financing asthma medicines

Countries that have chosen to purchase quality-assured medicines through the ADF have done so using a variety of mechanisms. Some examples are:

The Global Fund

Countries may purchase asthma medicines through the ADF with funds from the Practical Approach to Lung Health (PAL) component of their TB grants from the Global Fund to Fight AIDS, TB and Malaria. Burundi and Guinea Conakry, for example, are using their PAL funds to purchase through the ADF.

Revolving drug funds

Another approach is for the government or a donor to make an initial capital investment to purchase medicines through the ADF. The medicines are then sold to patients with a small margin to cover local charges and increase the fund progressively. New orders are placed and the fund becomes self-financing. Sudan and Benin are using this approach. By applying a 12–18% margin, these countries have managed to make prices affordable for patients and replenish the funds for future orders.

Health budgets

Ministries of Health can ensure that asthma care is provided at primary health care level as well as reference levels by including this cost in their budgets. In El Salvador, for example, medicines are provided free-of-charge to patients in areas that are implementing the PAL strategy.

Scaling up

Some countries have developed sustainable financing solutions to guarantee continuous availability of medicines for this chronic condition. However, only a very small number of countries and patients have so far benefited from the ADF.

COUNTRIES USING THE ADF TO IMPROVE ASTHMA CARE

El Salvador *> The National Tuberculosis Programme (NTP) is working with El Salvador's PAL programme. The price of medicines decreased by more than 50% when purchased through the ADF.*

Benin *> began receiving medicines through ADF in 2009. The NTP is running the asthma project, using the systems and experience from the DOTS model for managing tuberculosis.*

Sudan *> EpiLab is working with the government to achieve a national asthma control strategy. Sudan has been piloting standardised asthma management based on the DOTS model since 2006.*

Kenya *> is focusing on patients in and around Nairobi. The Kenya Association for the Prevention of Tuberculosis and Lung Disease purchased inhalers with funds from the World Lung Foundation.*

Burundi *> The NTP is using Global Fund money to pilot PAL. Asthma medicines are making the asthma component of PAL an affordable reality.*

Vietnam *> is decentralising care to health posts attended by the poor in Vietnam. Inhalers are being purchased with funds raised by The Union's staff, consultants and Board.*

Guinea Conakry *> The NTP has placed its first order, using funds from the Global Fund. The inhalers will be used for the country-wide implementation of PAL.*

11. Asthma Management Country Profiles

Countries around the world are beginning to address the challenges of asthma management using a variety of approaches, strategies and structures. In the following pages, countries share experiences of pilots and programmes, challenges and improvements in quality of life for patients and in efficiency for the health services.

Benin

Martin Gninafon, Leon Tawo

Revolving fund provides sustainable supply of asthma medicines

Asthma comes under Benin's National Programme Against Non-Communicable Diseases, but currently there are no national guidelines on asthma management. Instead, Benin's National Tuberculosis Programme (NTP) has been working on how to provide asthma care. The NTP adapted The Union's asthma guide and has piloted it in two phases so far: the first was the Comprehensive Approach to Lung Health project in 2008, financed by the World Bank, with technical support from The Union. The second project is still underway and is also supported by The Union, with medicines supplied through the Asthma Drug Facility (ADF).

Benin's current asthma project has been implemented in six health facilities. Health workers from these sites have been trained in all aspects of asthma management, including diagnosis, treatment, monitoring and long-term management. Sites received peak flow meters, mouthpieces and the monitoring and evaluation forms and tools. Medicines were procured through the ADF and stored at the pharmacy in Cotonou's National Respiratory Hospital.

Revolving fund proves its worth

Recognising the need for a sustainable supply of asthma medicines for its project sites, the NTP established a revolving fund in 2008, using a one-off capital sum provided by the World Bank. The fund continues to operate today.

The NTP adds a 12% margin to the price it paid for the medicines. Health centres participating in the project then sell asthma inhalers to their patients – at what is still a low price for patients – and the money recovered replenishes the fund. Money collected in the centres is transferred to an account managed by the NTP.

The fund's capital was further strengthened when The Union donated an order of medicines through the ADF in 2009. Benin's NTP has recently managed to place two further orders through the ADF and pay for them exclusively from the revolving fund.

Tackling the challenges

One challenge is that patients who are extremely poor are still unable to buy the asthma inhalers despite the low price. These patients may require different solutions. Some have already been given medicines free of charge.

Another is that some health care workers still prescribe too many bronchodilators and too few inhaled corticosteroids for patients with persistent asthma. This indicates that not all health care workers

fully understand the importance of long-term treatment. Their patients are therefore unlikely to be hearing the right messages about how to manage their asthma. The NTP is dealing with this through training, supervision and an increased focus on patient education.

Sometimes, some of the sites receive fewer asthma patients per month than they had planned for. Therefore these sites do not use their stock of inhalers as expected. Over time, this could mean that some inhalers expire, causing a loss for the revolving fund. The NTP is working on how to cope with these fluctuations between estimated and actual demand.

A "decrease" in the number of registered patients returning to the health centre may in fact be a good sign. It may indicate that some patients finally have their asthma under control with their prescribed medicines and that the severity of their asthma has reduced. This would mean they need less medicines and fewer visits to the health centres. A small phone survey among patients lost to follow-up suggested this, but properly funded operational research would allow the NTP to analyse more thoroughly the reasons for patients not returning.

The revolving fund is playing a vital role in the management of asthma in Benin. It has provided a self-financing and a sustainable supply of asthma medicines, so that the health centres can provide ongoing care, and patients can purchase quality-assured medicines at low prices.

Chile

Ricardo Sepúlveda

Chile's de-medicalised programme for ACRD at the primary care level: Impact on asthma control

The mortality rate for chronic respiratory diseases in Chile was 21/100,000 inhabitants in 2008 with a DALY of 567 attributed to the same cause. Therefore, a programme using Primary Health Care Centers (PHCCs) for the outpatient management of Adult Chronic Respiratory Disease (ACRD) was launched in 2001.

ACRD patients have access, free of charge, to spirometry and treatment.

Developing the ACRD Programme

To implement the ACRD Programme, practical clinical guides based on evidence and international consensus were developed for bronchial asthma, chronic obstructive pulmonary disease (COPD) and community-acquired pneumonia (CAP). Local teams consisting of a nurse, a physiotherapist and a part-time general physician were trained to take care of patients following predefined criteria and specific algorithms.

Drugs are ordered centrally at a national level, providing a significant economy of scale. A patient's level of asthma control is assessed using a five-point scale combining clinical and functional scores based on pre- and post-bronchodilator peak flow (PEF) evaluation. Patients with inadequate asthma control, important complications or co-morbidities are referred to the secondary health care level.

From 15 to 534 participating PHCCs in a decade

The ACRD Programme has grown from 15 participating PHCCs in 2001 to 534 by 2010. Their coverage exceeds 85% of the population who use the public health system. In December 2010, the Programme was serving 136,000 asthmatics, 24.5% of them under 10 years old. A random sample of 1,200 patients showed 87% had good treatment adherence. Acceptable asthma control scores and PEF measurements were achieved by 84%, and only 1.9% were referred to the secondary level.

Asthma mortality dropped 26.9%

Although the use of hospital beds for asthma patients remained stable at an average of 3/1000 inhabitants per year, mortality decreased by 26.9% (from 1.7 to 1.2/1000.000) when comparing 1990–2000 with 2001–2007, the first years of the ACRD Programme.

The National ACRD Programme has taken a de-medicalised, primary health care level approach to asthma, and it has had a significant impact in Chile: reducing mortality, obtaining good treatment adherence, and achieving control for most patients' asthma, with limited referral to secondary-level facilities.

El Salvador

Francisco Castillo, Julio Garay

Improving asthma management at the primary health care level

In 2005, the El Salvador Ministry of Health's National Tuberculosis and Lung Disease Programme adopted the PAL strategy (Practical Approach to Lung Health), as part of its efforts to improve health care for patients with respiratory diseases, including asthma. Since then, the programme has improved the care of the asthma patients at health care facilities throughout the country.

Between 2005, when PAL was started, and 2010, the number of patients being referred from primary level to secondary or tertiary level facilities has dropped by 60%.

Developing country guidelines

When PAL was adopted, country guidelines were developed for the standardised care of asthma patients. They were then included in the new 'Guide for the care of patients with asthma, pneumonia and COPD at primary health care level'. Clinical protocols and flowcharts showing how to manage asthma patients were also developed.

Managing asthma

These guides, protocols and flowcharts are now present in all primary health care facilities run by the Ministry of Health (MoH), as well as its national hospitals, which also provide asthma care. Training in asthma management is provided to the whole spectrum of health care workers who should be involved in asthma care: general doctors, specialist doctors, nurses and health promoters, who work in the community visiting patients in their homes.

Care of asthma patients often begins with the health services identifying them in emergency rooms. Acute asthma attacks are managed according to guidelines based on GINA recommendations. Long-term asthma care includes peak flow measurements, spirometry and standardised treatment with quality-assured medicines (salbutamol, beclometasone, etc.) and spacers. The medicines are purchased by the MoH, with some coming through the Asthma Drug Facility. They are then provided free-of-charge to patients when they visit their health centre.

Expanding implementation

The national asthma guidelines were developed with broad input from existing clinical guidelines and experts such as paediatricians, lung specialists and internal medicine specialists, as well as experts from other parts of the health sector, such as the

Social Security Institute and medical associations. The guidelines are therefore relevant for all health care providers, not only the MoH. The MoH is currently applying these guidelines in 100% of its own health care facilities, and it is starting to expand implementation to other health care providers.

Ongoing improvements for asthma care

Uptake of the guidelines by doctors has progressively improved. The programme is currently updating the guides, incorporating lessons learnt from implementation over the years and from a recent project supported by The Union. Since the introduction of the peak flow meter and some innovations in the information system, the programme has noted that the diagnosis, treatment and follow-up of patients have improved. Between 2005, when PAL was started, and 2010, the number of patients being referred from primary level to secondary or tertiary level facilities has dropped by 60%, meaning substantial savings for the health services and care that is more convenient for patients.

Finland

Tari Haahtela and Anne Pietinalho

Finnish asthma and allergy programmes: Community problems need community actions

In Finland, a comprehensive and nationwide Asthma Programme was undertaken from 1994 to 2004 to improve asthma care and prevent the predicted increase in costs. The main goal was to lessen the burden of asthma on individuals and society.

In Finland, mortality, number of hospital days and disability due to asthma fell 70–90% during the period from 1994 to 2010.

Goals of the Asthma Programme

Five specific goals were set, for example, decreasing the number of days patients were hospitalised by 50% and reducing annual costs per patient by 50%. The programme comprised both evidence-based management guidelines, which have been available to general practitioners and nurses via the Internet since 2000, and an action plan with defined tools to achieve the goals.

The action plan focused on implementation of new knowledge, especially for primary care. At that time the new medical knowledge was: "Asthma is an inflammatory disease and should be treated as such from the very beginning". The key to implementation was an effective network of asthma-responsible professionals and development of an evaluation strategy. In 1997 Finnish pharmacies were included in the *Pharmacy Programme*, and in 2002 a *Childhood Asthma Mini-Programme* was launched.

Results: The burden of asthma has decreased

As a result of this programme, the burden of asthma in Finland has decreased considerably. Key indicators have fallen significantly: Number of hospital days by 86% from around 110,000 (1993) to 15,000 (2010) and disability by 76% from 1993 to 2003. In recent years, only a few asthma deaths/year under the age of 65 have been recorded in Finland (total population 5.3 million). In young age groups there is virtually no asthma mortality. In 1993 the number of patients needing regular medication for persistent asthma (entitled to 75% reimbursement of medicine costs) was around 135,000. By 2004 this number was around 212,000, indicating a 57% increase and reflecting earlier and more effective intervention. The most remarkable increase was in the use of inhaled corticosteroids during the early years of the programme (1994–1999).

Prevalence is up; costs are down

In spite of increasing prevalence, the overall costs related to asthma (compensation for disability, medicines, hospital care and outpatient doctor visits) levelled off and then continued to decrease. This has been in stark contrast to what was predicted. The overall costs of asthma in 1993 were circa €285 million, including loss of productivity. By 2007, this figure had dropped to €230 million.

Based on the 1993 trends, the 2007 costs would have been around €800 million. A conservative estimate of the potential savings for the year 2007 alone was around €300 million. Annual costs per patient attributable to asthma have been reduced by more than 50%. The extra costs of planning and implementing the programme have been small, primarily because most of the activities were carried out as part of the routine work of the clinicians and administrators.

Patient benefits: Early detection, timely treatment

For the patients with asthma, the main improvement has been early detection of the disease and its timely treatment: "Hit early and hit hard!" Patients with chronic asthma have been educated to employ guided self-management, an approach that encourages them to be proactive in preventing asthma attacks. Effective networking of specialists with general practitioners (n=200), asthma nurses (n=700) and pharmacists (n=700) has also considerably improved the overall asthma care in Finland.

Expanding the programme's scope

The Finnish experience shows that it is possible to considerably reduce the morbidity of asthma and its impact on individuals, as well as on society. Worrying trends continue to be the still slightly increasing prevalence of asthma and growing drug costs.

A new *Allergy Programme 2008–2018*, which includes asthma, has been launched in Finland to expand the good asthma results to all allergic conditions and to take a step from treatment to prevention. The long-term aim is to have an impact on the incidence of both asthma and allergies.

Sudan

Mai El-Tigany, Asma El Sony

Asthma management in Sudan

In Sudan, a study of asthma management conducted in 2003 found that 95% of the participating patients paid full cost for their asthma medicines; less than 2% of them received regular treatment from a single facility, and there was no overall asthma management plan. In a country where the daily wage of the lowest paid unskilled government worker is US$ 2.20 per day, the cost of one day of hospitalisation for asthma was $79.60 and patients were responsible for medicines and other costs on top of that.

By 2008, in the Asthma Project pilot sites, the number of emergency room visits for participating patients had been reduced by 97%.

Developing asthma management guidelines

Since Sudan had no asthma guidelines, initially The Union guidelines were adopted. They then formed the basis for the first Sudan Asthma Guidelines, which were developed in 2002. Due to limited resources, these guidelines made it mandatory to use only essential medicines. A pilot project testing the guidelines was launched in 2003 and evaluated by The Union in 2005.

In 2006 the Epi-Lab in Khartoum received funds from the World Bank to launch the 'Comprehensive Lung Health' project that included asthma, as well as pneumonia and other respiratory diseases. The Union provided technical assistance, and the Asthma Project evolved from this first project.

Implementing the guidelines in test sites

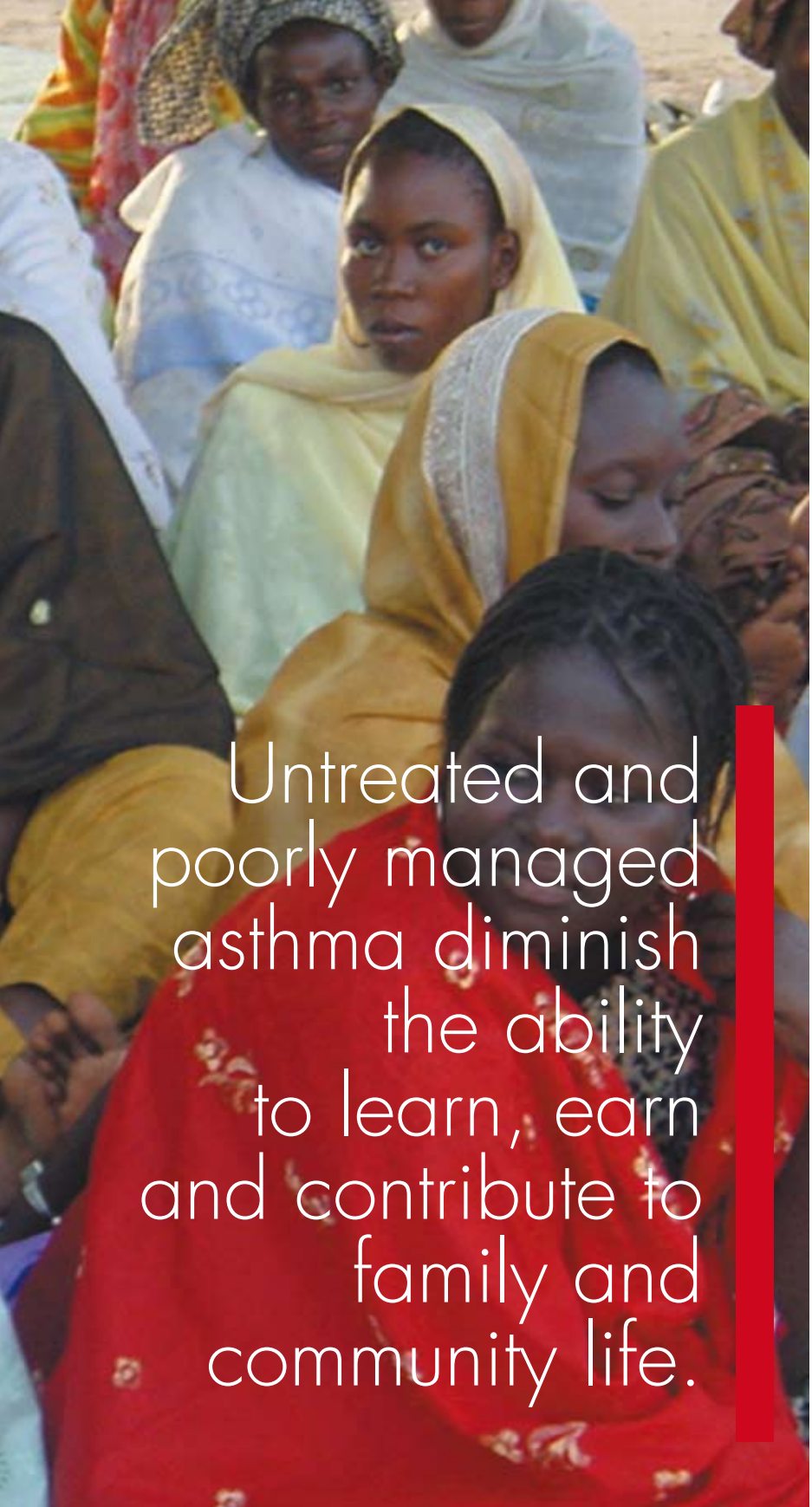
Asthma Project activities included a training programme for doctors, nurses, statisticians and medical assistants that covered both standard case management and patient education. The project also mobilised community doctors, chest physicians, paramedics and patients' communities as advocates for improved asthma care. Patients came forward for treatment, and, by 2008, the number of emergency room visits for participating patients had been reduced by 97% in the pilot sites. There was also an improvement in the severity of patients' asthma. By 2009, the Asthma Project was functioning in 19 first-referral level hospitals in central Sudan.

Access to essential medicines and care

In 2010, Sudan purchased medicines through the Asthma Drug Facility (ADF) to address the low availability and prohibitive cost of asthma inhalers. Sudan set up pilot sites in Gezira State to test this ADF approach, which combines access to affordable essential medicines with the monitoring and evaluation of asthma case management. The Ministry of Health judged the pilots successful and has requested that these activities be expanded to cover the whole Gezira State.

Making asthma a countrywide priority

Practical Approach to Lung Health (PAL) activities are also now being initiated in Sudan and are expected to help provide care for asthma patients at the primary health care level. Epi-Lab and its partners in the Department of Non-Communicable Diseases at the Ministry of Health are continuing to negotiate for a nationwide asthma programme that will make asthma a high priority and ensure quality care and a regular supply of medicines for all patients who need them.



PART THREE:

THE GLOBAL IMPACT

12. Access to Health Care

Donald A Enarson

For many people living with asthma, it is a chronic disease that they have to cope with throughout their lives. For those with severe asthma, the effort simply to breathe can be an all-consuming challenge.

Fortunately, the regular use of medications – and particularly the use of inhaled corticosteroids – can provide relief from asthma symptoms, substantially for most and entirely for some.

Asthma can be a matter of breath or death

For people with severe persistent asthma, their condition dominates their lives. The disability is costly – both in terms of the health care required and the loss of income it can entail. Frequent crises in their clinical condition force them to seek urgent care, which is costly both for them and the health care systems that serve them. Without appropriate long-term treatment, they are at substantial risk of dying of the disease.

For patients with moderate or mild persistent asthma, effective treatment can mean the difference between living a life curtailed by disability and taking a full active part in their work, families and communities. Ensuring regular, unobstructed access to appropriate care is therefore crucial to relieving the suffering and restoring the health of all patients with asthma.

Challenges to receiving care for asthma

In spite of the critical need for effective asthma care, numerous studies have shown substantial challenges to accessing appropriate treatment for patients across the spectrum from high-income to low-income countries.

Asthma often goes undiagnosed

The first challenge is the knowledge and practice of the health services personnel providing care for such patients. A recent study in Canada surveyed medical practices to identify the extent to which practitioners routinely diagnosed people living with chronic lung disease. The results showed that a high proportion of such patients were never diagnosed by their health practitioner, even when they attended the health service regularly.

The most effective medicines are not prescribed

Clearly when patients are not diagnosed, they cannot benefit from the medications that would be able to help them. But patients who are diagnosed face obstacles too. Surveys undertaken by The Union among chest specialists have shown that, even though the practitioners surveyed were specialists, and they had access to literature on what constitutes good-quality care for asthma patients, many of them did not prescribe the inhaled corticosteroids so vital to the care of a patient with persistent asthma.

The gap between rich and poor is wide – and gets wider

A number of studies in the United States of America showed, more than 10 years ago, that obstacles to appropriate care for asthma included family income, social status, access to health insurance and race. Even in a wealthy country such as the United States, many who desperately need such care are unable to access it. This leads to poor people becoming steadily poorer due to the cost of care and to the disabling effect of their chronic disease.

In some regions, essential medicines are completely unavailable

Surveys of many countries around the world undertaken by The Union assessed the affordability of aerosol medicines used routinely in the treatment of asthma. The results indicated that the essential medicines were completely unavailable in some locations.

In others, medicines are available – at prices out of reach for most people

In some of the poorest countries of the world, the cost of essential asthma medicines was found to be so high that paying for them would consume a substantial proportion of the income of a professional person. As a result, these life-saving medicines were completely out of reach for many patients, especially the poorest.

Emergency rooms are full of people with asthma

In an effort to improve access to high-quality care in poor communities, The Union and partners in China, Sudan and Benin worked together with funding from the World Bank. The pilot projects they carried out revealed that, while asthma was essentially unrecognised by the practitioners in some communities, the emergency rooms were full of asthma patients in crisis. In some locations, this was due to the fact that emergency care was free-of-charge, while ambulatory care was not. Consequently, patients sought care in the emergency rooms to get temporary relief, but continued to suffer from the ongoing disability caused by their asthma, since they could not access the long-term care they needed.

When health services don't help

In some locations, The Union and its partners learned that patients resorted to finding solutions for their asthma through the 'grapevine'. One such notion was that taking corticosteroid tablets by mouth could help them.

The tragic results of this inappropriate treatment are illustrated by the case of a woman, an elderly farmer. She took corticosteroid tablets for several years to try to control her asthma, but her asthma had not improved. She became virtually house-bound, unable to farm her land, and consequently, desperately poor. When inhaled corticosteroids were finally made available to her, she regained her strength, her breathing improved, and she was able to resume farming. However, her bones had become extremely thin and brittle as an adverse effect of taking corticosteroid tablets, and when she fell one day, she had a severe fracture and died of the complications. For her, the health-restoring inhaled corticosteroids had come too late.

Stopping the cycle of poverty and disease

Asthma is a frequent and, in some cases, debilitating disease whose effects can be avoided or improved in most cases. However, this depends on access to good-quality care, including the proper recognition of the disease, an understanding of the correct way to treat it and regular access to the medications needed to improve health. Unfortunately, although there is excellent evidence to show that, given the systematic application of good practice in the care of people living with asthma, the worst effects of the disease can be avoided, it is clear that many people do not have access to this care. This is worst amongst those who most need it, causing poor people to become even poorer and forever condemning them to a vicious cycle of poverty and disease.

13. Asthma and Poverty

Karen Bissell, Innes Asher, Gillian Mann, Donald A Enarson

In terms of human development, poverty means far more than being economically poor. It includes and overlaps with all types of social vulnerability. In addition to those living in absolute economic poverty, there are disadvantaged populations who have relatively little access to health services because of factors including ethnic group, geographical location, gender, education, living conditions, social exclusion and migration.

Poverty and health

Across the countries of the world, poor people and those from disadvantaged social groups face greater exposure to many health threats, and when they fall sick they are much less likely to receive adequate care than those who are not poor and disadvantaged. When they suffer from a long-term chronic disease such as asthma, lack of access to health care is likely to be an ongoing problem.

The goal of health equity is to accelerate health progress among poor and socially excluded groups. Pro-poor approaches can help to achieve this, by ensuring health services give special attention to the needs of the most disadvantaged groups. Asthma guidelines and services can include such approaches.

Finding and addressing disparity

Special efforts need to be made to address barriers to care and increase early and effective treatment for the poorest and most vulnerable communities. It may be useful to consider the following steps, inspired by efforts to address poverty in tuberculosis control.

Step 1: Promote standardised management of asthma

The first step towards ensuring poor and vulnerable groups receive care is having national asthma guidelines with a standardised approach for diagnosis and treatment of all patients.

Step 2: Identify the poor and vulnerable groups in the country

Countries should be monitoring the prevalence of and deaths from asthma over time (for example, in demographic health surveys). If this surveillance includes geographical and socio-economic data, researchers can assess who is suffering from asthma. If access to services and outcomes of asthma care could also be monitored, countries could work out which groups are not getting adequate access and care.

Step 3: Determine which barriers prevent access of the poor and vulnerable groups to services that provide asthma diagnosis and treatment

These are likely to include:

- Economic barriers
- Geographical barriers
- Social and cultural barriers
- Health system barriers

Many poor and vulnerable groups encounter more than one of these overlapping sets of barriers and have greater difficulty in overcoming them than the non-poor. To identify the barriers, it is helpful to consider all of the steps a person has to take from the onset of symptoms to receiving a diagnosis and treatment. Since asthma is a chronic disease, it is necessary to then consider the person's ongoing access to medicines and care.

Step 4: Assess potential actions to overcome the barriers to access

As asthma is a global challenge, asthma services need to be an integral part of all primary care services. Implementing the Practical Approach to Lung Health (PAL) strategy is one key activity, since it includes asthma diagnosis and care at the primary health care level. By decentralising care according to an integrated and properly resourced strategy, countries should find that patients are less likely to go directly to secondary or tertiary hospitals, or seek out expensive private practitioners.

Step 5: Identity situations and groups that require special consideration

There are some workplaces that can cause or greatly exacerbate asthma, for example, mines, factories and workplaces that involve organic dusts, cleaning products and pollutants. The poor and socially excluded may be more likely to work in these settings where environmental controls are inadequate and where external support is required to highlight and improve conditions. Another issue is indoor air pollution caused by smoke from domestic use of solid fuels, particularly biomass fuels, for cooking and heating. Those most at risk are the most vulnerable, such as the poor, women and young children.

Step 6: Include asthma and other respiratory NCDs in discussions about health financing

Health financing in low-income settings is often focused on communicable diseases. Chronic, non-communicable diseases such as asthma should be included in discussions about financing. When budgeting for asthma, countries should consider evidence-based solutions for overcoming barriers faced by the poor regarding asthma diagnosis, medicines and care.

Step 7: Evaluate the impact of pro-poor measures

Socio-economic questions can be included in asthma prevalence surveys, and periodic studies of care-seeking, use of medicines and services can be conducted.

14. The Economic Burden of Asthma

Innes Asher, Karen Bissell, Eamon Ellwood

Counting up the economic burden of asthma is difficult: It is a disease that is frequently undiagnosed and untreated, yet it is chronic and can affect sufferers throughout their whole lives. Management is often not optimal even in some of the best-resourced health systems. Asthma is also increasing most rapidly in low- and middle-income countries, many of which do not systematically collect data about asthma rates, outcomes or costs.

The high cost of essential asthma medicines has been mentioned frequently in this report. However, treating asthma entails vastly more than the cost of medicines. It amounts to billions of dollars in both direct and indirect costs.

Costs to patients, families, employers, communities

When people with asthma experience the symptoms of airway obstruction, such as shortness of breath, wheezing and coughing, they feel unwell and unable to carry out their usual activities, whether at home, at work or in their communities.

If the asthma becomes abruptly severe, such as in an asthma attack, the person will need acute medical treatment, possibly admission to the hospital and sometimes even intensive care. Occasionally people die.

For all of the people described above – from the person who is not well enough to go to work to the one who ends up in hospital, asthma is incurring both direct and indirect costs. The indirect costs of their symptoms may stem from lost time at work or school, resulting in less income and diminished skills and opportunities. Absent workers, students and citizens also affect the success of the workplaces, businesses, schools and communities counting on their participation. For the families of children with asthma, the children's illness may require them to miss work and other activities, widening the circle of cost. In addition, the regular direct costs of asthma can be considerable, including not only doctor's fees, medicines, inhalers and hospital charges, but also the cost of transportation to and from health care facilities, ambulances, parking and other related expenses.

Costs to health systems

The costs incurred by health systems also cover a broad spectrum: from the human resources, materials and facilities required to train health professionals about asthma to the time and resources required to treat people with asthma both acutely and long term. Direct costs include preventer and reliever medicines, spacers and other devices; acute ambulatory, emergency and inpatient hospital care; as well as asthma management planning and patient education.

Costs go up when the person with asthma has other respiratory tract symptoms that can cause more asthma-related emergency visits. Although diagnostic tests are not usually needed, in cases of high severity, complications or diagnostic uncertainty, chest radiographs and blood tests may be indicated. Total hospital costs may also be higher in women, older patients, those with greater severity of asthma or significant co-morbidities, and those that require use of the intensive care unit and prolonged hospital stay.

Who pays the bill?

The level to which all of these costs are borne directly by the patients with asthma and/or their families, taxpayers or health insurance companies depends on the national or local approach to funding health care.

What are the actual costs of asthma?

The economic costs of asthma are among the highest for non-communicable diseases (NCDs) because of the substantial health service use, in many cases over a lifetime. The largest direct costs are for inpatient care and pharmaceuticals. The principal indirect costs stem from loss of productivity due to missed work and school.

While the exact cost of asthma worldwide cannot be determined, a 2009 systematic review found 8 national studies which reported total cost, illustrating its substantial impact. Of those with a study duration of one year, the costs reported in 2008 US dollars were all very high, but also varied widely: Canada $654 million; Germany $2,740 million and $4,430 million; Singapore $49.36 million; Switzerland $1,413 million; and USA $7,189 million, $8,256 million and $2,300 million. In 2004, new cases of occupational asthma alone in the United Kingdom cost GB£70–100 million.

As the proportion of people with asthma in the population rises, all of these costs will become greater. Clearly more population-based research on the economic burden of asthma is needed, especially in low- and middle-income countries where the prevalence of asthma is increasing.

What can be done to reduce costs?

Most asthma can be controlled, such that symptoms and use of reliever medicines become minimal. Asthma symptoms and acute attacks can be reduced by preventive measures: treatment with preventer medicines, such as inhaled corticosteroids, and other non-drug measures, including asthma education and management plans.

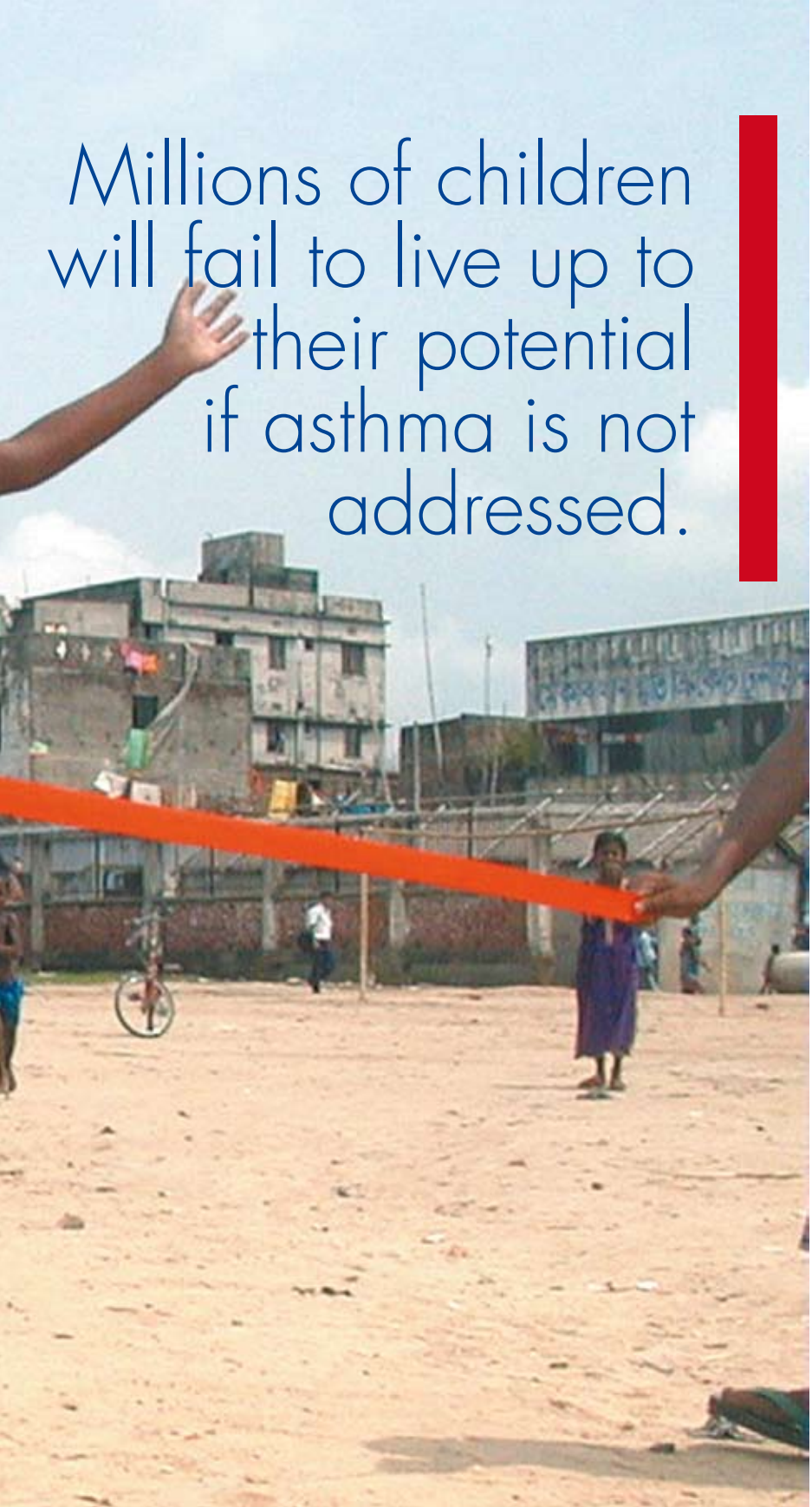
However studies have repeatedly shown that many asthmatics have poor asthma control, and that this is more costly (directly and indirectly) than good asthma control. In other words, inadequate treatment leads to poor control which leads to higher costs for the patients, communities, health services and countries. Thus, one key way to reduce costs is to achieve good asthma control in more people in the population.

How can adequate preventer treatment be achieved? A person with symptoms of asthma needs to be able to reach a health professional who has the skills to assess the pattern and severity of symptoms and the adequacy of asthma control. The appropriate medicine needs to be prescribed, and, along with that, the patient needs to be educated about how to use the medicine and manage asthma symptoms. The prescribed asthma medicines need to be available and affordable for the patient. Regular follow-up is necessary to assess control, check that the patient is using the medicines correctly, and adjust treatment where necessary.

As straightforward as these simple steps may seem, they are currently unachievable for a large proportion of the people with asthma in the world – and at every stage, money, time and resources are leaking away, and millions of people are suffering unnecessarily.

In sum: Poor treatment costs more than good treatment

The costs of asthma are enormous at country and global levels and will increase as the global prevalence of asthma rises. Cost containment will result from achieving better asthma control in symptomatic people, and this requires affordable medicines and access to education and treatment. Future prevalence surveys should be accompanied by estimates of the costs of asthma, especially in low- and middle-income countries.



PART FOUR:

A HEALTH PRIORITY

15. Asthma Research

Luis García-Marcos, Neil Pearce, David Strachan

The focus of asthma research in the past few decades has been prevention and treatment. Research in prevention has aimed to identify risk and protective factors that may determine either the beginning of the disease (primary causes) or may provoke attacks in those who already have the condition (secondary causes). Research in treatment has sought to identify the most effective drug therapy and therapeutic targets.

An interdisciplinary approach is the most likely to open up new avenues of cutting-edge research.

Population-based studies of asthma

The two main research approaches used are cross-sectional prevalence studies involving subjects from many countries, such as ISAAC, and the European Community Respiratory Health Survey (ECRHS) in adults; and longitudinal cohort studies, in which individuals are followed for long periods of time, such as Phases II and III of the ECRHS and birth cohort studies ongoing in many countries, primarily in the developed world.

Studying the mechanics of asthma

Much clinical and basic science research has been dedicated to improve our understanding both of changes in the lung and how they influence its mechanics in asthma; and of the alterations in the immunological pathways that cause inflammation, bronchial constriction and altered mucus secretion, which may end up in irreversible lung damage.

Understanding the role of the immune system and other issues

Research has identified numerous newly discovered molecules secreted by cells either to produce inflammation or to communicate with other cells involved in this process. However, the mechanisms by which the immunological system may shift from a well-regulated situation to a dysfunctional one (as occurs in allergy) have yet to be established. Furthermore, the role of viruses or bacteria, which can mutate with time, is still not definitely known. It is suspected that the immune system may be "programmed" during foetal and/or very early postnatal development. The potential importance of the environment of the developing foetus is being explored.

Combining drugs: a milestone in asthma treatment

Safe and effective drugs capable of preventing asthma attacks and controlling symptoms during exacerbations are essential to effective clinical management of asthma. Inhaled corticosteroids are very effective to reduce bronchial inflammation, and their adverse effects have been diminished in the past years both by using safer molecules and by improving their formulation. Inhaled bronchodilators, such as salbutamol, have been used as efficient bronchodilators for asthma since the 1960s. The discovery of the synergistic effects of adding these drugs to inhaled corticosteroids was a milestone in the treatment of asthma 15 years ago.

Only two new drugs in past 15 years

Since then, only two new and more specific drugs have become commercially available: antagonists to leukotriene (an immunologic mediator) and monoclonal antibodies against immunoglobulin E (a key molecule in the allergic pathway). The former can be used as preventer medication on a regular basis, but the latter are reserved for very severe allergic asthma. Pharmaceutical companies have dedicated considerable resources to finding new therapeutic targets among the newly discovered molecular mediators of asthma and allergy, with very limited success. Research in asthma treatment will probably continue in this direction in the years to come, but significant breakthroughs are considered to be unlikely.

Interdisciplinary approach holds most promise

Perhaps the most promising new direction for asthma research in the 21st century is the development of a truly interdisciplinary approach that integrates the usually separate worlds of epidemiology, social science and biomedical and clinical research. Traditionally these disciplines have conducted their research in relative isolation, a situation that has distinct disadvantages. In particular: (i) many animal models of asthma are only partially applicable to human populations; (ii) clinical studies are generally not well equipped to determine the causal exposures of primary causation; and (iii) epidemiological studies often don't fully acknowledge the complexity of the biological responses involved.

Findings in high-income countries do not apply to all

Another shortcoming has been the common assumption that findings in high-income countries can be extrapolated to the rest of the world. It has taken international collaborations, such as ISAAC, to show that, for example, the strong associations between allergy and asthma symptoms, which have been repeatedly observed in high-income countries, are not so evident in low- and middle-income countries.

Non-allergic asthma more common in low- and middle-income countries

Overemphasis on allergen exposure as the "causal" factor of asthma, as well as the lack of appreciation of the variation in types of asthma in many epidemiological studies, has guided biomedical and clinical research into studying (almost exclusively) allergic mechanisms and allergy-specific treatment options, with very little consideration of other potentially relevant biological pathways. For example, corticosteroid treatment seems to be less effective in asthma phenotypes that do not involve allergic mechanisms and subsequent non-eosinophilic airway inflammation, despite these types of asthma being common in the general population, and probably the most common types in low- and middle-income countries.

Addressing the complex interplay of factors

Considering the complex interplay between environmental exposures, genetic susceptibility, immunological mechanisms, as well as social and cultural factors involved in asthma development – and indeed most non-communicable diseases – an interdisciplinary approach that brings together expertise from each of these disciplines is most desirable. This type of approach is the most likely to open up new avenues of cutting-edge research, yielding greater explanatory power, more efficient use of research funding and more efficient translation into disease prevention.

16. Making Asthma a Global Priority

Innes Asher, Neil Pearce, David Strachan, Nadia Aït-Khaled

The asthma epidemic experienced by high-income nations over the past 30 years is now an increasing problem in low- and middle-income countries as they become more urbanised. Whilst it is true that communicable diseases, such as malaria, still present a major challenge for many of these countries, non-communicable diseases, including asthma, are emerging as serious additional problems. Authorities believe that they will be responsible for tomorrow's pandemics.

Why asthma needs to be a priority

Asthma affects millions of people worldwide

The seriousness with which asthma is viewed within the healthcare community is illustrated by the readiness with which health researchers, including paediatricians, respiratory physicians and epidemiologists, in 306 centres in 105 countries joined the ISAAC research programme to estimate the extent of the problem for children in their locality. The results of the surveys conducted by ISAAC (children) and ECRHS (adults) demonstrate that asthma is now an important non-communicable disease (NCD).

Asthma has a global impact

With millions of people in every region of the world suffering from asthma, it has become an issue of international development. WHO estimates that around 15 million disability adjusted life years (DALYs) are lost annually through this disease. Children with untreated asthma can miss much of their primary school education, which affects their future opportunities. It also impacts the productivity of the parents and relatives who must stay home to care for them, contributing to a cycle of poverty in families and communities. Asthma can also be fatal and causes an estimated 250,000 deaths annually (1 in 250 deaths worldwide).

Asthma is one of the significant NCDs

As a chronic respiratory disease (CRD), asthma is considered one of the major NCDs that have outstripped communicable diseases as the leading causes of death in the world. In 2008 NCDs were responsible for 60% of all deaths worldwide and 80% of these deaths occurred in low- and middle-income countries. Chronic respiratory diseases (CRDs) alone cause 15% of the world's deaths.

WHO has identified CRDs, including asthma, as a priority

The burden and suffering caused by CRDs has been identified by the World Health Organization (WHO) as a priority. The WHO has also resolved that there needs to be "better surveillance to map the magnitude of CRDs and analyse their determinants with particular reference to poor and disadvantaged populations and to monitor future trends". Thus surveillance of asthma needs to continue with simple instruments that can be widely used around the world and repeated at regular intervals, such as those used in ISAAC.

Improved asthma care makes economic sense . . .

People with poor asthma control are less able to work or look after their families, causing them considerable financial and emotional stress, and loss of productivity for the country.

Poorly managed asthma places a disproportionate burden on health care systems that may already be struggling, due to increased emergency room visits, hospitalisations and inadequate or unaffordable treatments.

. . . especially in low- and middle-income countries

For people and health systems in low-income countries, the cost of treating asthma has been a major obstacle that has perpetuated this cycle of suffering and wasted resources.

What needs to be done

Invest in asthma research

Asthma research is decades behind other fields, such as cardiovascular and cancer research, and needs further investment. A key challenge is to identify environmental risk factors modifiable by public health interventions that can reduce the morbidity and severity of this increasing global problem.

Ensure that good-quality asthma drugs are affordable and accessible

Lack of access to affordable, quality-assured medicines is a major obstacle for both asthma and other NCDs. People with asthma need affordable drugs, appropriate to the severity of their asthma, including a beta-2 agonist reliever for all and an inhaled corticosteroid preventer for those with more frequent symptoms. These essential medicines, particularly inhaled steroids, are not available or affordable to patients or health services in many low- and middle-income countries, and as a consequence, people become disabled or die from asthma. The Union's Asthma Drug Facility is an innovative initiative that has demonstrated a way to address this issue successfully, but it needs to be scaled up.

Reorganise health services for long-term treatment

The other major obstacle to effective management of asthma and other NCDs is the fact that health services are not organised for long-term management of patients with regular follow-up. Usually these diseases are treated only on an emergency basis. Health personnel need training and these health services need to be re-organised to handle chronic and long-term care.

Support priority interventions for NCDs

Asthma prevention and management will be aided by two of the five priority interventions for the NCD crisis – improved tobacco control and access to essential drugs. The reduction in obesity that will be achieved through a third priority of improved diets and physical activity is likely to be beneficial, as an association between obesity and asthma has been observed.

WHEN ASTHMA IS TRULY A GLOBAL PRIORITY:

1. Asthma will be recognised as a major global health problem.
2. Affordable, quality-assured asthma medicines will be universally accessible.
3. Correct asthma treatment will reduce suffering and poverty and increase prosperity, especially in low- and middle-income countries.
4. NCD priority actions, such as tobacco control, will be scaled-up massively and will help prevent asthma and other CRDs.
5. Surveillance of asthma will be ongoing and cover all countries in the world.
6. More asthma research will be funded, especially in low- and middle-income countries.

Appendices

Table 1: ISAAC world map data, symptoms of asthma

Country (number of centres)	6-7 Year Age Group				13-14 Year Age Group				
	Current wheeze (%)	Asthma ever (%)	Symptoms of severe wheeze (%)	Symptoms of severe wheeze among current wheezers (%)	Current wheeze (%)	Current wheeze (video) (%)	Asthma ever (%)	Symptoms of severe wheeze (%)	Symptoms of severe wheeze among current wheezers (%)
Albania (1)	5.0	2.6	2.0	38.0	3.4	1.6	3.6	1.1	32.0
Algeria (1)					8.7		7.1	4.3	49.6
Argentina (4)	17.0	6.2	7.2	41.0	12.5	7.7	9.3	5.9	44.0
Australia (1)	20.0	26.0	8.4	40.0	30.6	15.0	37.3	12.1	38.1
Austria (1)	7.4	4.2	2.5	33.0	15.1	8.6	7.0	6.7	44.7
Barbados (1)	20.0	21.0	7.2	37.0	20.8	14.0	24.7	9.8	47.0
Belgium (1)	7.5	6.0	2.9	39.0	8.3		8.5	3.4	39.9
Bolivia (1)					13.5	16.0	12.3	8.0	43.8
Brazil (20)	24.0	10.0	12.0	43.0	18.7	12.0	13.3	8.1	34.1
Bulgaria (1)	5.6	4.3	2.2	35.0	8.2		5.5	4.5	36.1
Cameroon (1)					5.7		6.0	4.3	47.3
Canada (1)	18.0	19.0	6.8	37.0	13.7		16.3	5.0	33.5
Channel Islands (2)					26.5	12.0	26.3	12.2	43.1
Chile (5)	18.0	11.0	6.1	32.0	15.3	15.0	15.1	6.1	32.0
China (4)					3.6	2.0	3.5	1.3	31.1
Colombia (3)	14.0	8.7	4.8	32.0	11.8	10.0	14.2	6.0	39.6
Congo (1)					19.9		9.4	13.4	53.2
Cook Islands (1)					10.6		14.8	5.4	38.3
Costa Rica (1)	38.0	28.0	20.0	49.0	27.3		23.2	16.0	50.5
Côte d'Ivoire (1)					19.3		11.6	12.0	61.9
Croatia (1)	9.7	3.9	2.9	30.0	8.4	4.6	5.2	3.1	35.7
Cuba (1)	32.0	39.0	19.0	61.0	17.8	13.0	30.9	10.3	58.2
Ecuador (2)	17.0	5.0	4.7	28.0	16.6	11.0	10.9	6.3	37.8
Egypt (1)					7.0		5.2	3.9	38.0
El Salvador (1)	19.0	30.0	6.2	28.0	30.8		24.0	10.0	30.3
Estonia (1)	9.6	4.1	2.9	27.0	9.3	2.2	4.8	3.2	30.2
Ethiopia (1)					9.1		2.3	8.2	63.8
Fiji (1)					10.4	16.0	13.6	6.6	63.2
Finland (1)					19.0	3.3	7.7	5.1	25.2
France[1] (5)	8.1	9.3	3.0	37.1	13.5	8.3	12.6	5.7	41.1
Gabon (1)					10.2		11.0	5.9	44.1
Georgia (1)	6.9	3.3	3.3	48.0	5.1		3.3	2.3	44.8
Germany (1)	13.0	4.6	5.2	39.0	17.5	6.8	8.0	9.6	50.8
Greece (1)	7.9	9.8	2.4	28.0					
Honduras (1)	19.0	15.0	9.2	47.0	22.0		18.3	7.6	33.1
Hong Kong (1)	9.4	7.9	3.1	26.0	8.6	6.2	10.1	3.1	33.0
Hungary (2)	6.6	4.9	2.2	32.0	5.8	3.3	7.8	2.6	37.3
India (18)	5.3	4.1	2.8	40.0	5.8	4.7	5.1	3.4	47.8
Indonesia (3)	2.8	4.8	1.1	38.0	5.1	4.5	10.8	2.1	40.5
Iran (4)	9.7	4.0	4.7	38.0	10.8	3.7	3.4	5.9	43.5
Isle of Man (1)	14.0	21.0	6.9	47.0	31.2		28.6	12.4	36.4
Italy (13)	7.4	8.8	2.2	27.0	8.1		11.4	3.3	38.2
Japan (2)	18.0	23.0	3.3	17.0	10.0		14.9	3.4	33.3
Jordan (1)	17.0	10.0	10.0	61.0	12.3	6.8	7.6	7.8	62.6
Kenya (2)					15.8	11.0	14.5	11.3	66.8
Kingdom of Tonga (1)					16.2	11.0	12.5	7.9	48.4
Kuwait (1)					7.6	8.4	14.0	6.8	63.8
Kyrgyzstan (3)	5.8	1.2	4.1	69.0	7.8	2.8	2.5	6.1	72.8
Latvia (1)					10.5	3.1	7.2	3.9	30.4
Lebanon[1] (1)					14.4	4.9	11.6	10.8	58.5
Lithuania (3)	5.4	2.0	1.4	26.0	7.3	6.1	2.5	1.8	24.4

Symptoms of severe wheeze: Respondents with current wheeze who had 4 or more attacks of wheeze in the past year or had 1 or more nights per week sleep disturbance from wheeze in the past year or had wheeze affecting speech in the past year.

Country (number of centres)	6-7 Year Age Group				13-14 Year Age Group				
	Current wheeze (%)	Asthma ever (%)	Symptoms of severe wheeze (%)	Symptoms of severe wheeze among current wheezers (%)	Current wheeze (%)	Current wheeze (video) (%)	Asthma ever (%)	Symptoms of severe wheeze (%)	Symptoms of severe wheeze among current wheezers (%)
Malaysia (3)	5.8	11.0	1.7	25.0	8.9	4.9	12.0	3.3	32.2
Malta (1)	15.0	15.0	4.2	25.0	14.6		14.1	5.4	33.6
Mexico (10)	8.0	5.9	3.3	38.0	8.7	7.2	6.9	4.3	41.8
Morocco (4)					9.0	10.0	13.3	4.9	52.4
Netherlands (1)					12.2		13.0	5.3	43.0
New Zealand (5)	22.0	30.0	9.8	44.0	26.7	11.0	32.4	10.9	38.7
Nicaragua (1)	17.0	17.0	10.0	55.0	13.8		15.2	8.9	55.8
Nigeria (1)	5.6	3.3	6.7	57.0	13.0	10.0	11.7	11.9	64.2
Niue (1)	17.0	28.0	4.3	25.0	12.7		30.4	1.3	10.0
Nouvelle Calédonie (1)					8.2	6.9	12.5	3.6	43.9
Pakistan (2)	6.4	4.8	3.5	44.0	10.7	6.0	6.6	6.6	53.4
Palestine (2)	9.5	8.2	5.2	51.0	8.6		6.0	4.1	46.6
Panamá (1)	23.0	20.0	9.7	36.0	22.9		20.5	9.4	35.1
Paraguay (1)					20.9	11.0	12.8	10.8	51.8
Peru (1)					19.6	16.0	33.1	8.8	37.9
Philippines (1)					8.4	13.0	20.9	3.7	44.3
Poland (2)	14.0	5.8	6.0	43.0	10.2		6.1	5.3	41.3
Polynésie Française (1)					11.3		15.9	4.6	39.7
Portugal (5)	12.0	9.6	5.7	46.0	11.8	7.3	14.7	4.9	40.6
Rép de Guinée (1)					18.6		10.3	9.6	49.8
Rép Dém Congo (1)					7.5		10.2	3.3	41.6
Rep Ireland (1)					26.7		21.5	9.5	33.3
Rep Macedonia (1)					8.8		1.7	2.5	28.6
Reunion Island (1)					21.5		19.1	7.5	35.1
Romania (1)					22.7		8.9	9.0	39.9
Russia (1)	11.0	2.5	3.2	28.0	11.2		3.9	3.3	29.8
Samoa (1)					5.8	5.1	14.1	4.6	63.6
Serbia and Montenegro (5)	11.0	6.3	2.7	23.0	9.5	3.3	5.6	2.7	27.9
Singapore (1)	10.0	16.0	2.6	25.0	11.4	11.0	26.5	4.7	37.2
South Africa (2)	13.0	3.5	11.0	51.0	19.2	11.0	10.7	13.2	45.8
South Korea (2)	5.8	9.3	2.3	34.0	8.7	5.6	5.4	4.9	53.5
Spain (11)	10.0	11.0	3.6	33.0	10.6	7.3	13.9	4.7	40.8
Sri Lanka (1)	28.0	11.0	13.0	47.0	23.0	8.8	11.7	11.9	49.8
Sudan (1)					12.5		15.5	9.5	58.2
Sultanate of Oman (1)	8.4	11.0	5.1	60.0	8.4	8.1	19.9	5.3	62.3
Sweden (1)	10.0	9.3	4.2	39.0	9.7	3.7	12.0	3.4	31.7
Syrian Arab Republic (3)	5.2	4.2	2.9	45.0	5.2	5.1	5.1	3.6	41.9
Taiwan (2)	8.9	14.0	2.3	23.0	6.2	6.1	15.4	2.3	31.8
Thailand (6)	11.0	9.8	4.8	36.0	10.3	6.0	12.0	5.9	49.1
Togo (1)					16.8		10.1	9.9	41.7
Tokelau (1)					19.7	7.6	34.8	13.6	69.2
Trinidad and Tobago (2)					13.2	8.9	13.0	9.2	51.4
Tunisia (2)					14.3		9.3	9.2	45.5
Ukraine (2)	10.0	4.4	3.2	22.0	14.5		4.5	4.1	22.5
United Kingdom (6)	21.0	27.0	11.0	50.0	24.7	10.0	25.1	10.5	40.1
Uruguay (2)	23.0	9.8	9.0	40.0	16.4	10.0	17.0	8.1	48.9
USA (3)					22.1	13.0	17.4	11.5	48.8
Uzbekistan[1] (2)					9.2	1.3	1.7	2.5	25.5
Venezuela (1)	20.0	29.0	12.0	55.0	15.4		29.7	9.7	51.6
Vietnam (1)	18.0	4.5	4.8	27.0	29.5	3.6	5.0	9.3	31.6
Global Totals	**11.5**	**9.4**	**4.9**	**38.5**	**14.1**	**8.6**	**12.6**	**6.8**	**43.2**

[1] Phase One data

Table 2: National asthma guidelines in countries participating in ISAAC

Countries participating in ISAAC	National guidelines for children	Pharmaceutical financial support	National guidelines for adults	Pharmaceutical financial support
Albania	No	N/A	Yes	No
Algeria	Yes	Yes	Yes	Yes
Argentina	Don't know	N/A	No	N/A
Australia	Yes	Yes	Yes	Yes
Austria	Yes	Don't know	Yes	Yes
Belgium	Yes	Don't know	Yes	Don't know
Bolivia	Yes	Don't know	Yes	Don't know
Brazil	Yes[1]	Yes	Yes	Yes
Cameroon	No	N/A	No	N/A
Canada	Yes	Yes	Yes	Yes
Channel Islands	Yes	No	Yes	No
Chile	Yes	No	Yes	No
China	Yes	No	Yes	No
Colombia	Yes[2]	Yes	Yes[2]	Yes
Cook Islands	No	N/A	No	N/A
Costa Rica	Yes	No	Yes	No
Cuba	Yes	No	Yes	No
Ecuador	No[3]	N/A	No[3]	N/A
Egypt	Yes	Yes	Yes	Don't know
El Salvador	No	N/A	No	N/A
Estonia	Yes	No	Yes	Don't know
Fiji	Yes[4]	No	Yes[4]	No
Finland	Yes[4]	No	Yes[4]	No
France	Yes	No	Yes	No
Gabon	No	N/A	No	N/A
Georgia	Yes	No	Yes	No
Germany	Yes	Yes	Yes	Yes
Ghana	No	N/A	No	N/A
Greece	Yes[6]	Yes	Yes[6]	Yes
Honduras	Yes[5]	Yes	Yes[5]	Yes
Hong Kong	Yes	No	Yes[7]	No
Iceland	Yes	No	Yes	No
India	Yes	No	Yes	No
Indonesia	Yes	No	Yes	Yes
Iran	Yes	No	Yes	No
Isle of Man	Yes[8]	No	Yes[8]	No
Italy	Yes[9]	Yes and No[9]	Yes[9]	Yes and No[9]
Japan	Yes	Yes	Yes	Yes
Jordan	No	N/A	No	N/A
Kenya	Yes	Yes	Yes	Yes
Kingdom of Tonga	No	N/A	Yes[4]	No
Kuwait	No	N/A	No	N/A
Kyrgyzstan	Yes	No	Yes	No
Latvia	Yes[5]	Yes	Yes[5]	Yes
Lithuania	Yes	No	Yes	No
Malaysia	Yes	Yes	Yes	Yes

[1] For over 5 year olds
[2] Currently working on new guidelines with no pharmaceutical company financial support
[3] Currently working on their guidelines with pharmaceutical company financial support
[4] Part of a general guideline for management of common conditions
[5] No national guidelines but use GINA guidelines which received pharmaceutical company financial support
[6] National guidelines developed based on GINA
[7] Pharmaceutical company financial support only for printing
[8] No formal guidelines but follow NICE & British Thoracic Society guidelines
[9] Two sets of guidelines. One with pharmaceutical company financial support and one without
[10] Nigerian Thoracic Society planning to develop guidelines but funding is difficult to get
[11] Use guidelines developed in France which received pharmaceutical company financial support
[12] Pharmaceutical company financial support only for distribution
[13] Use GINA guidelines. They have draft independent guidelines but no money to develop them further
[14] Currently working on guidelines with Ministry of Health

Countries participating in ISAAC	National guidelines for children	Pharmaceutical financial support	National guidelines for adults	Pharmaceutical financial support
Malta	Yes	No	Yes	No
Mexico	Yes	No	No	N/A
New Zealand	Yes	No	Yes	No
Nicaragua	No	N/A	Yes	No
Nigeria	No[10]	N/A	No[10]	N/A
Niue	No	N/A	No	N/A
Norway	Yes	No	Yes	Yes
Nouvelle Calédonie	Yes[11]	Yes	Yes[11]	Yes
Pakistan	Yes[12]	No	Yes[12]	No
Palestine	No	N/A	No	N/A
Panamá	Yes[5]	Yes	No	N/A
Paraguay	No	N/A	No	N/A
Peru	Yes	No	No	N/A
Philippines	Yes	Yes	Yes	Yes
Poland	Yes	Yes	Yes	Yes
Polynésie Française	Yes[11]	Yes	Yes[11]	Yes
Portugal	Yes[5]	Yes	Yes[5]	Yes
Rép de Guinée	Yes[13]	Yes	Yes[13]	Yes
Rép Dém Congo	No	N/A	No	N/A
Rep Ireland	Yes	No	Yes	No
Rep Macedonia	Yes[5]	Yes	Yes	No
Reunion Island	Yes[11]	Yes	Yes[11]	Yes
Romania	No	N/A	Yes	Yes
Russia	Yes	Don't know	Yes	Don't know
Samoa	No	N/A	No	N/A
Serbia and Montenegro	Yes[7]	No	Yes[7]	No
Singapore	Yes	No	Yes	No
South Africa	Yes	No	Yes	Don't know
South Korea	Yes	No	Yes	No
Spain	Yes	No	Yes	Yes
Sri Lanka	Yes	Yes	Yes	Yes
Sudan	No[14]	N/A	Yes	Don't know
Sultanate of Oman	Yes	No	Yes	No
Sweden	Yes	No	Yes	No
Taiwan	Yes	Yes	Yes	Yes
Thailand	Yes	No	Yes	No
The Netherlands	Yes	No	Yes	No
Togo	No	N/A	No	N/A
Tokelau	No	N/A	No	N/A
Trinidad and Tobago	Yes	No	Yes	No
Turkey	Yes	Don't know	Yes	Don't know
Ukraine	No	N/A	No	N/A
United Kingdom	Yes	No	Yes	No
Uruguay	Yes	Yes	Yes	Yes
USA	Yes	No	Yes	No
Venezuela	Yes	No	Yes	No

Figure 1: Asthma guidelines for children in ISAAC countries

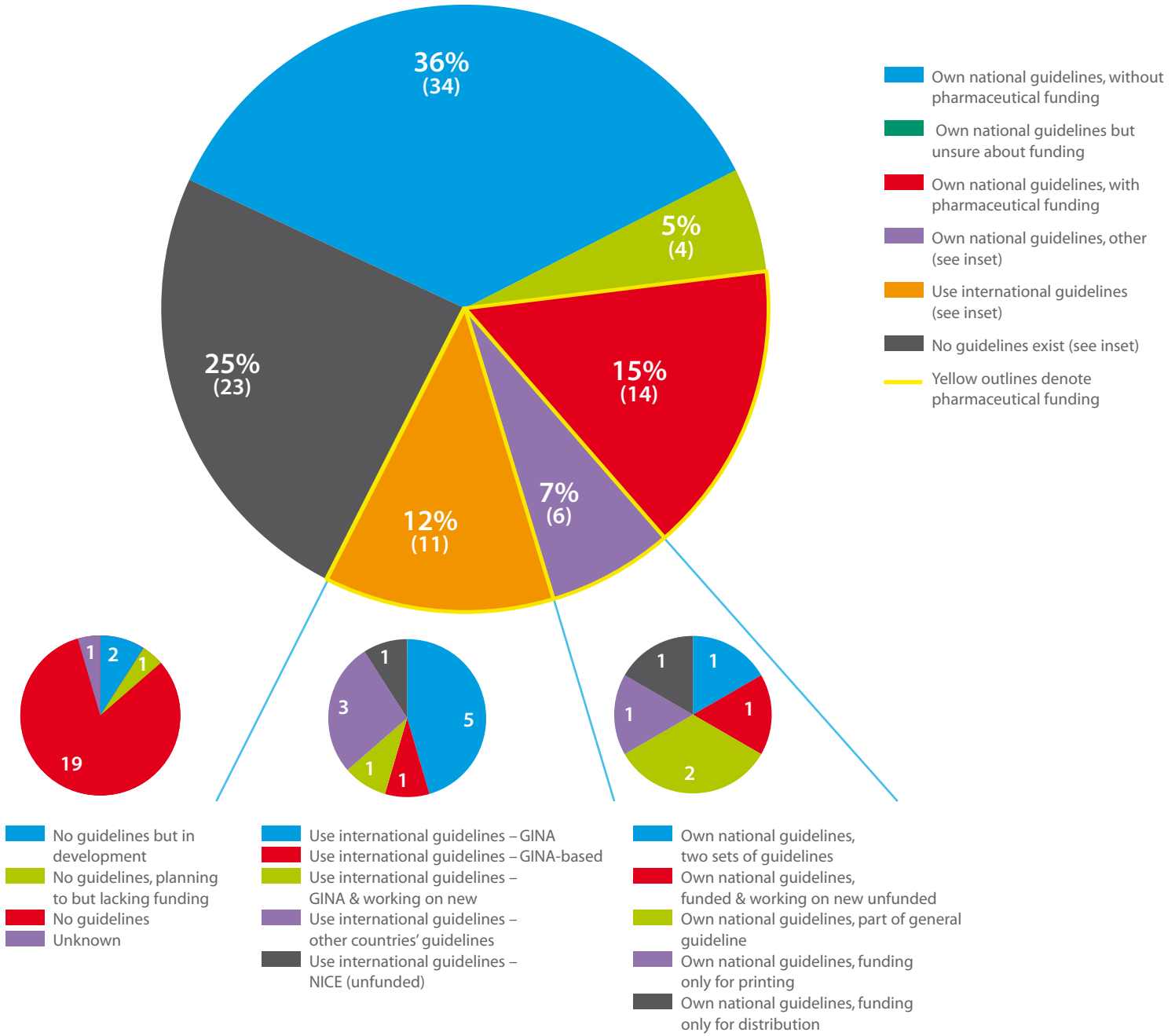


Figure 2: Asthma guidelines for adults in ISAAC countries

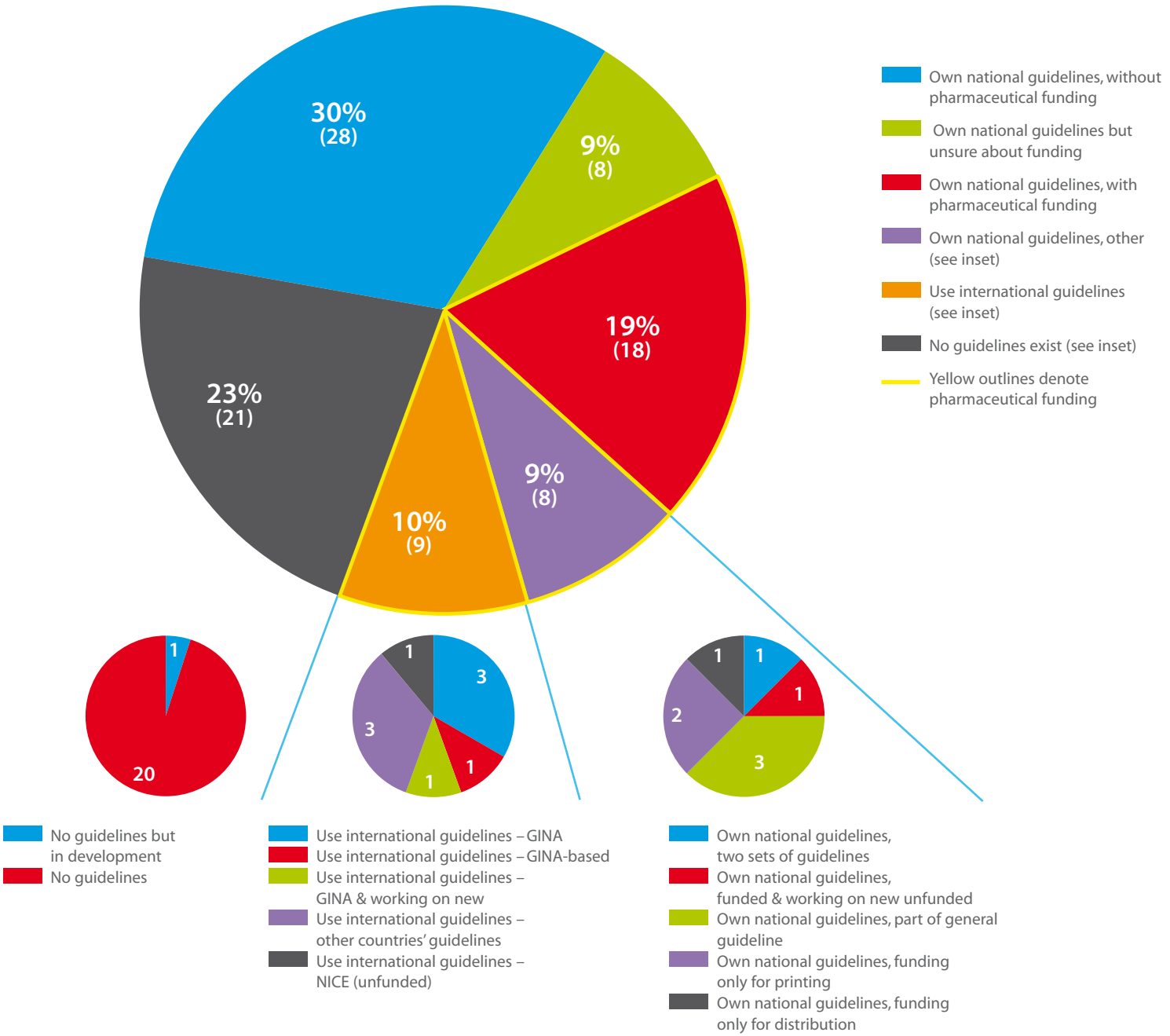


Figure 3: **Affordability of Salbutamol 100µg inhaler in private pharmacies**

(Number of days of wages required to purchase one inhaler)

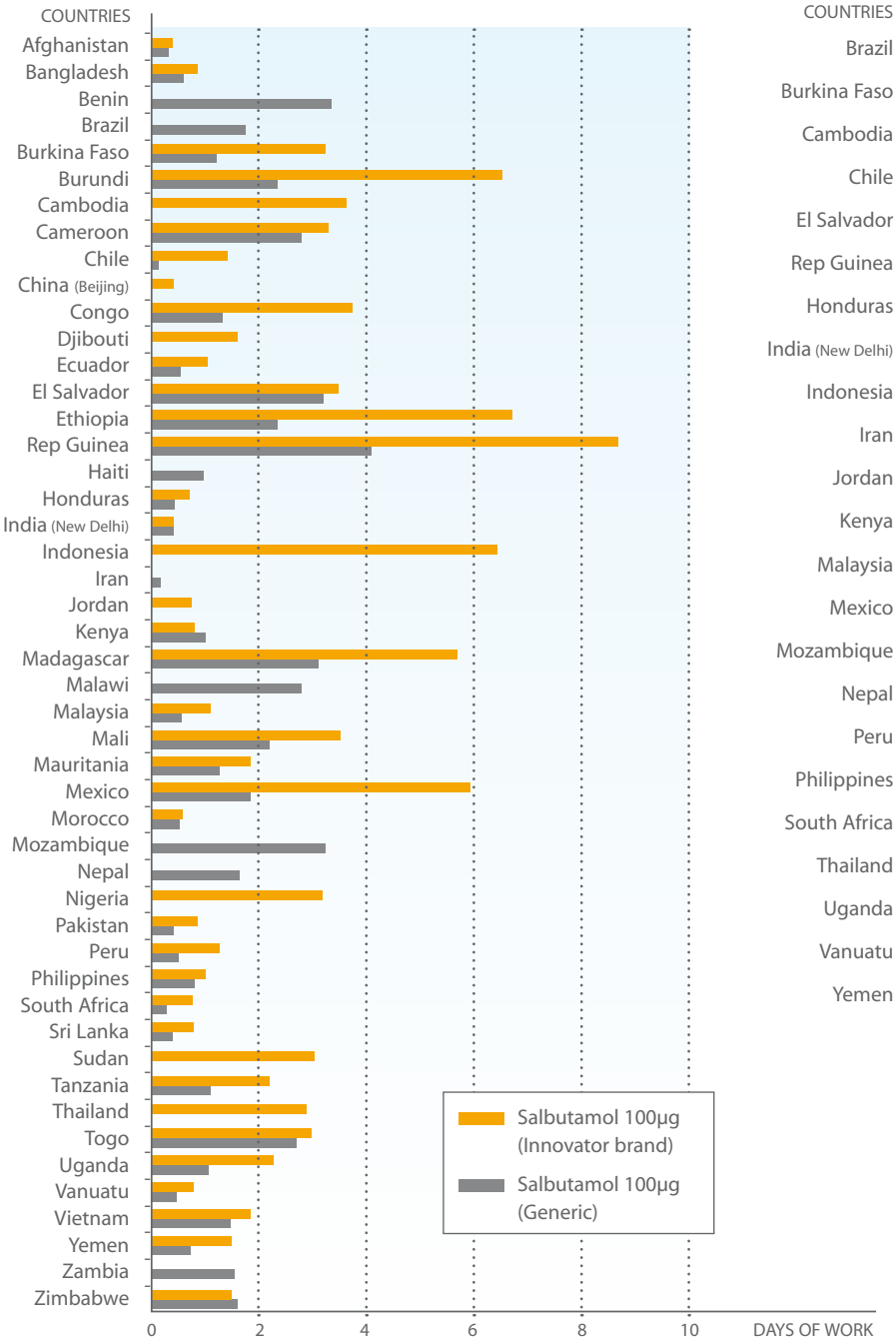
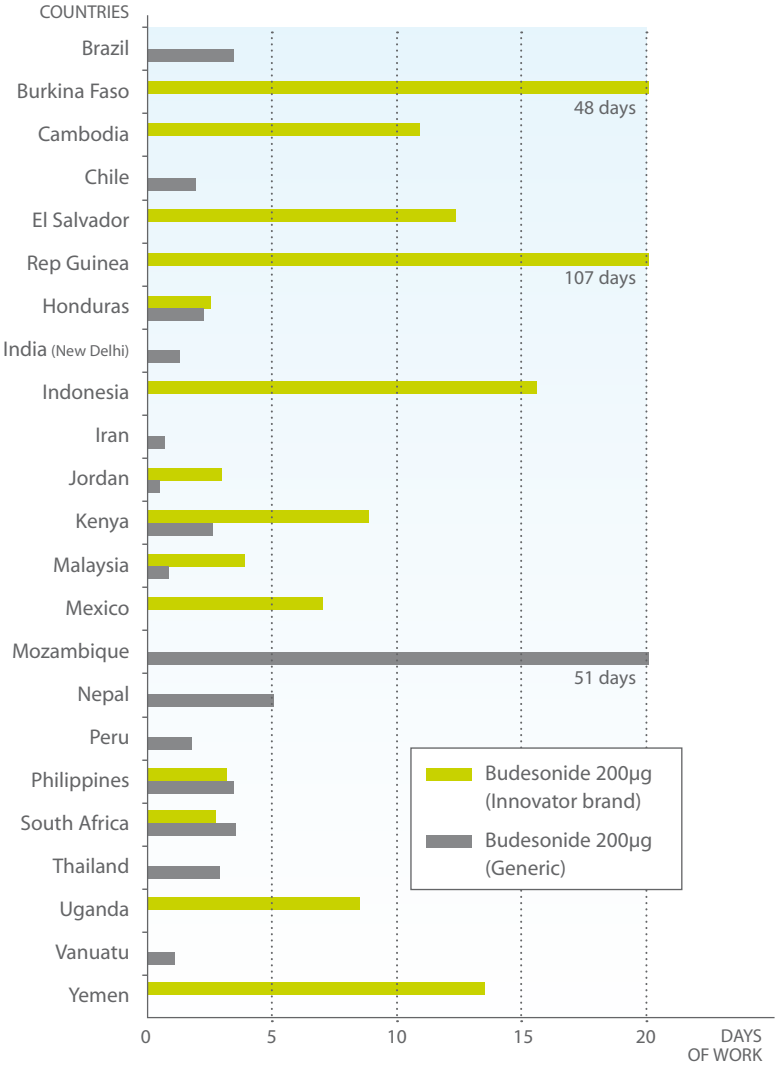


Figure 4: **Affordability of Budesonide 200µg inhaler in private pharmacies**

(Number of days of wages required to purchase one inhaler)



Pricing of Essential Asthma Medicines

In the survey of 50 countries conducted by The Union and the University of Auckland School of Pharmacy in 2011, International Reference Prices (IRPs) were used to assess pricing and procurement efficiency. The price ratios of each medicine were calculated by comparison with the Management Sciences for Health 2010 International Reference Prices (IRPs). IRPs are the medians of recent procurement or tender prices offered by predominantly not-for-profit suppliers to developing countries for multi-source products. Previous studies have considered a median price ratio of 1 or less to demonstrate efficient procurement in the public sector, while below 3 has been considered reasonable for the private sector.

However this approach should be taken with some caution, as IRPs are only indicators. In addition, these IRPs appear to be on the higher side, for example, the IRP for beclometasone (US$ 8.06) is much higher than the current price obtained by the Asthma Drug Facility (ADF) (US$ 1.28 FCA price). Likewise the IRP for budesonide (US$ 10.55) is much higher than ADF's price (US$ 2.60).

BECLOMETASONE 100µg INHALER

All seven countries that provided data from their national procurement centres (Afghanistan, Burkina Faso, Ethiopia, India, Kenya, Mozambique and Vanuatu) had a price ratio for beclometasone inhalers (both generic and reference brands) of less than 1 (i.e., less than the International Reference Price). In the private pharmacies, the price ratio for generic beclometasone inhalers was less than 3 in all 20 countries in which it was available except Chile, (however, asthma medicines are in fact provided free for all asthma patients that are treated within the Ministry of Health's national asthma programme). In 11 out of 20 countries, the price ratio of generic beclometasone in private pharmacies was less than 1. The price ratio for the reference product in private pharmacies was more than 3 in El Salvador and more than 4 in South Africa.

SALBUTAMOL 100µg INHALER

For generic salbutamol in procurement centres, the price ratio was less than 1 in 11 out of 21 countries (Bangladesh, Cameroon, Honduras, India, Jordan, Madagascar, Morocco, Mozambique, Peru, Tanzania and Vanuatu). For generic salbutamol in the public hospital sector, the price ratio was more than 1 in 10 out of 14 countries, suggesting inefficient procurement. For generic salbutamol in the private pharmacies, the price ratio was less than 1 in only 2 countries (Afghanistan and Pakistan) and more than 2 in 21 countries, whilst price ratios for the innovator brands varied widely from less than 1 in Afghanistan to almost 17 in Brazil and Mexico.

BUDESONIDE 200µg INHALER

Generic budesonide was only found in India, Peru, South Africa and Tuvalu's procurement centres and all had price ratios of less than 1. The innovator brand of budesonide was only found in national procurement centres of Indonesia, Iran, and Jordan. Jordan had a price ratio of less than 1, Iran more than 1 and Indonesia was fairly high at 2. For generic budesonide in the public hospitals, price ratios were generally less than 1. In private pharmacies in Burkina Faso and the Republic of Guinea, the price ratio of innovator brand budesonide was 9. In Yemen, the price ratio was 4; in El Salvador and Indonesia, 3. In Mozambique's private pharmacy, the price ratio of generic budesonide was 7; in Brazil and South Africa, it was 5; in Chile and Honduras, it was 2.4; in Vanuatu, it was 1.4.

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TABLES AND FIGURES

2. Asthma in Children

Figures 2 and 3: Asthma symptoms among 13-14 year olds; Severe asthma among 13-14 year olds with current wheeze. From: Lai CKW et al. *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(6): 476-483.

Figure 4: Changes in asthma prevalence among 13-14 year olds ranked by affluence and mean change per year. Adapted from: Asher MI et al. *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.* Lancet 2006: 368(9537): 733-743.

Figure 5: Change in prevalence of current wheeze: 13-14 year olds. From: Asher MI et al. *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.* Lancet 2006: 368(9537): 733-743.

3. Asthma in Adults

Figure 1. Prevalence of wheeze and asthma according to Gross National Income (GNI). From: Sembajwe G, Cifuentes M, Tak SW, Kriebel D, Gore R, Punnett L. *National income, self-reported wheezing and asthma diagnosis from the World Health Survey.* Eur Respir J. 2010;35(2):279.

Figures 2 and 3: Proportions of participants with any asthma whose asthma was graded Severe, Moderate or Mild in the AIRE studies; Proportions of participants with persistent asthma whose asthma was graded Severe, Moderate or Mild in the AIRE studies. From: Rabe K, Adachi M, Lai CKW, Soriano J, Vermeire P, Weiss K, et al. *Worldwide severity and control of asthma in children and adults: The global asthma insights and reality surveys.* J Allergy Clin Immunol. 2004;114(1):40.

Appendix A

Table 1. ISAAC World Map Data, Symptoms of Asthma. Adapted from: Lai CKW et al. *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. And: 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): 315-35

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GLOBAL ASTHMA REPORT: AUTHORS

Prof Nadia Aït-Khaled
Senior Consultant, International Union Against Tuberculosis and Lung Disease (The Union) France

Prof H Ross Anderson
Division of Community Health Sciences
St Georges, University of London, United Kingdom

Prof M Innes Asher
Dept of Paediatrics: Child and Youth Health
Medical and Health Sciences,
The University of Auckland
New Zealand (NZ)

Dr Zaheer-Ud-Din Babar
School of Pharmacy
Medical and Health Sciences,
The University of Auckland, NZ

Dr Karen Bissell
Dept of Research, The Union
France

Prof Bert Brunekreef
Institute of Risk Assessment Sciences
Universiteit Utrecht, The Netherlands

Prof Peter Burney
Dept of Respiratory Epidemiology and Public Health
National Heart and Lung Institute
Imperial College, London, UK

Dr Francisco Castillo
Programa Nacional de Tuberculosis y Enfermedades Respiratorias
Ministry of Health – El Salvador

Dr Chiang Chen-Yuan
Dept of Lung Health and NCDs, The Union
France

Tadd Clayton
Dept of Paediatrics: Child and Youth Health
Medical and Health Sciences,
The University of Auckland, NZ

Eamon Ellwood
Dept of Paediatrics: Child and Youth Health
Medical and Health Sciences,
The University of Auckland, NZ

Philippa Ellwood
Dept of Paediatrics: Child and Youth Health
Medical and Health Sciences,
The University of Auckland, NZ

Prof Asma El Sony
The Epidemiological Laboratory (Epi-Lab)
Sudan

Dr Mai El-Tigany
The Epidemiological Laboratory (Epi-Lab)
Sudan

Prof Donald A Enarson
Senior Advisor, The Union
France

Dr Julio Garay
Programa Nacional de Tuberculosis y Enfermedades Respiratorias
Ministry of Health – El Salvador

Prof Luis García-Marcos
Instituto de Salud Respiratoria
Universidad de Murcia, Spain

Dr Martin Gninafon
Programme National contre la Tuberculose
Ministry of Health – Benin

Prof Tari Haahtela
Skin and Allergy Hospital,
Helsinki University Hospital
Finland

Dr Deborah Jarvis
National Heart and Lung Institute
Imperial College, London, UK

Charon Lessing
School of Pharmacy
Medical and Health Sciences,
The University of Auckland, NZ

Elizabeth Limb
National Heart and Lung Institute
Imperial College, London, UK

Cécile Macé
Asthma Drug Facility, The Union
France

Dr Gillian Mann
CRESTHA
Liverpool School of Tropical Medicine, UK

Prof Neil Pearce
Dept of Medical Statistics, Epidemiology and Public Health
London School of Hygiene and Tropical Medicine, UK

Dr Anne Pietinalho
Peijas Hospital, Helsinki University Hospital
Finland

Prof Dr Ricardo Sepúlveda M.
Respiratory Health Unit Coordinator
Ministry of Health – Chile

Prof David Strachan
Division of Community Health Sciences
St Georges, University of London, UK

Dr Léon Tawo
Programme National contre la Tuberculose,
Ministry of Health – Benin

PHOTOGRAPHY:
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ISAAC PHASE ONE, TWO AND THREE STUDY GROUPS

Steering Committee
(* Regional Coordinator)

N Aït-Khaled*, International Union Against Tuberculosis and Lung Disease [The Union], Cheraga, Algeria

HR Anderson, Division of Community Health Sciences, St Georges, University of London, London, UK

MI Asher, Department of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand

R Beasley*, Medical Research Institute of New Zealand, Wellington, New Zealand

B Björkstén*, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

B Brunekreef, Institute of Risk Assessment Sciences, Universiteit Utrecht, The Netherlands

J Crane, Wellington Asthma Research Group, Wellington School of Medicine, New Zealand

P Ellwood, Department of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand

C Flohr, St John's Institute of Dermatology, St Thomas' Hospital, London, UK

S Foliaki*, Centre for Public Health Research, Massey University, Wellington, New Zealand

F Forastiere, Department of Epidemiology, Rome E Health Authority, Rome, Italy

L García-Marcos, Instituto de Salud Respiratoria, Universidad de Murcia, Spain

U Keil*, Institut für Epidemiologie und Sozialmedizin, Universität Münster, Germany

CKW Lai*, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, SAR China

J Mallol*, Department of Pediatric Respiratory Medicine, Hospital CRS El Pino, University of Santiago de Chile, Chile

EA Mitchell, Department of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand

S Montefort*, Department of Medicine, University of Malta, Malta), J Odhiambo*, Centre Respiratory Diseases Research Unit, Kenya Medical Research Institute, Nairobi, Kenya

N Pearce, Department of Medical Statistics, Faculty of Epidemiology and Public Health, London School of Hygiene and Tropical Medicine, London, UK

CF Robertson, Murdoch Children's Research Institute, Melbourne, Australia

AW Stewart, Epidemiology and Biostatistics, School of Population Health, The University of Auckland, New Zealand

D Strachan, Division of Community Health Sciences, St Georges, University of London, London, UK

E von Mutius, Dr von Haunerschen Kinderklinik de Universität München, Germany

SK Weiland†, Institute of Epidemiology, University of Ulm, Germany (Deceased)

G Weinmayr, Institute of Epidemiology, University of Ulm, Germany

H Williams, Centre for Evidence Based Dermatology, Queen's Medical Centre, University Hospital, Nottingham, UK

G Wong, Department of Paediatrics, Prince of Wales Hospital, Hong Kong, SAR China.

ISAAC International Data Centres

Professor M Innes Asher ONZM, Tadd Clayton, Eamon Ellwood, Philippa Ellwood, Professor Ed Mitchell, Alistair Stewart, The University of Auckland, Auckland, New Zealand

Gisela Büchele, Claudia Dentler, Andrea Kleiner, Dr Gudrun Weinmayr, Ulm University, Ulm, Germany

Principal Investigators
(* National Coordinator)

Africa

Algeria
Algiers, Dr A Bezzaoucha
Wilaya of Algiers, Professor Badia Benhabylès

Cameroon
Yaounde, Professor Christopher Kuaban*

Congo
Brazzaville, Professor Joseph M'Boussa

Côte d'Ivoire
Urban Côte d Ivoire, Dr Bernard Ngoran Koffi*

Ethiopia
Addis Ababa, Associate Professor Kibrebeal Melaku
Jima, Professor Berhane Seyoum

Gabon
Port-Gentil, Dr Isabelle Ekoume Hypolite*

Ghana
Kintampo, Dr Emmanuel OD Addo-Yobo

Kenya
Eldoret, Dr Fabian O Esamai
Nairobi, Dr Joseph A Odhiambo, Dr Lucy Ng'ang'a*

Morocco
Benslimane, Boulmene, Casablanca, Marrakech, Professor Zoubida Bouayad*
Rabat, Professor Abedelkrim Bennis

Nigeria
Ibadan, Professor Babatunde O Onadeko

République de Guinée
Conakry, Professeur Oumou Younoussa Sow

République Démocratique du Congo
Kinshasa, Professor Dr Jean-Marie Kayembe

Reunion Island
Reunion Island, Dr Isabella Annesi-Maesano

South Africa
Cape Town, Dr Hugo Nelson, Professor Rodney Ehrlich, Professor Heather J Zar*
Polokwane, Professor Kuku Voyi

Sudan
Khartoum, Professor Omer Abdel Aziz Musa

Togo
Lome, Professor Osseni Tidjani

Tunisia
Grand Tunis, Professeur Faouzia Khaldi
Sousse, Professeur Mohamed Jerray

Asia-Pacific

China
Beijing, Tong Zhou, Professor Yu-Zhi Chen*
Chongqing, Professor Kun-Hua Chen
Guangzhou, Professor Nan-Shan Zhong
Shanghai, Dr Mao Bao-Shan
Tibet, Assistant Professor Osamu Kunii
Wulumuqi, Professor Man-Lin Xiao, Dr Qiao Li Pan

Indonesia
Bali, Professor Putu Konthen
Bandung, Professor Dr Cissy B Kartasasmita, Professor Dr Karnen Baratawidjaja*
Semarang, Dr Winarto Suprihati

Japan
Fukuoka, Dr Hiroshi Odajima, Professor Sankei Nishima*
Tochigi, Professor Makino Sohei

Malaysia
Alor Setar, Dr Keng Hwang Teh
Ipoh, Dr Lim Wee Yeong
Klang Valley, Associate Professor Jessie de Bruyne*

Kota Bharu, Associate Professor Ban Seng Quah
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Philippines
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Singapore
Singapore, Associate Professor Daniel Yam Thiam Goh, Professor Bee-Wah Lee*

South Korea
Provincial Korea, Seoul, Dr Sang-Il Lee, Professor Ha-Baik Lee*

Taiwan
Taipei, Professor Kue-Hsiung Hsieh (Deceased), Dr Jing-Long Huang*
Taoyuan, Dr Chun-Chieh Kao

Thailand
Bangkok, Dr Pakit Vichyanond*
Chantaburi, Dr Thanong Prasarnphanich
Chiang Mai, Associate Professor Muthita Trakultivakorn
Chiangrai, Dr Rawee Nettagul
Khon Kaen, Associate Professor Jamaree Teeratakulpisarn
Nakorn Pathom, Dr Aree Kongpanichkul

Vietnam
Ho Chi Minh City, Dr Baïch Vaên Cam

Eastern Mediterranean

Egypt
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Iran
Birjand, Rasht, Tehran, Zanjan, Dr Mohammed-Reza Masjedi*

Jordan
Amman, Dr Faisal Abu-Ekteish

Kuwait
Kuwait, Dr Jawad A al-Momen

Lebanon
Beirut, Dr Fuad M Ramadan

Malta
Malta, Professor Stephen Montefort*

Pakistan
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Palestine
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Syria
Aleppo, Dr Khaldoun Tabbah
Lattakia, Professor Yousser Mohammad
Tartous, Dr Samira Mohammad*

Indian Sub-Continent

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Chandigarh, Professor Lata Kumar
Chennai (3), Dr Gururaj Setty
Davangere, Dr P S Suresh Babu
Jaipur, Professor Virendra Singh
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Sri Lanka
Sri Lanka, Dr Kirthi D Gunasekera*

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Ciudad de México (4), Dra Nelly Ramírez-Chanona
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Toluca, Dr Francisco J Linares-Zapién
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Nicaragua
Managua, Dr José Félix Sánchez*

Panamá
David-Panamá, Dr Gherson Cukier*

Paraguay
Asunción, Dr Jaime A Guggiari-Chase*

Peru
Lima, Dr Pascual Chiarella*

Uruguay
Montevideo, Dra Dolores Holgado*
Paysandú, Dra María Cristina Lapides

Venezuela
Caracas, Dr Oscar Aldrey*

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Barbados, Dr Malcolm E Howitt*

Canada
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Vancouver, Professor Alex Ferguson

Trinidad and Tobago
St Augustine, Tobago, Dr Michelle A Monteil

USA
Chapel Hill, Dr Karin Yeatts
Chicago (3), Chicago (4), Professor Victoria Persky
Sarasota, Dr Hugh H Windom
Seattle, Professor Gregory J Redding

Northern and Eastern Europe

Albania
Tiranë, Professor Alfred Priftanji*

Bulgaria
Sofia, Dr Todor Popov*

Croatia
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Estonia
Narva, Tallinn, Dr Mall-Anne Riikjärv*

Finland
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Lappland Area, Dr Leena Soininen
Turku and Pori County, Dr Turku Antti Koivikko

Georgia
Kutaisi, Dr Nino Khetsuriani, Dr Maia Gotua*
Tbilisi, Professor Amiran Gamkrelidze, Dr Maia Gotua*

Hungary
Svábhegy, Dr Györgyi Zsigmond*
Szeged, Dr Zoltán Novák

Iceland
Reykjavik, Dr Michael Clausen

Kyrgyzstan
Balykchi, Bishkek, Dr Cholpon Imanalieva*
Jalalabat, Professor Shairbek Sulaimanov

Latvia
Rural Latvia, Dr Marcis Leja
Riga, Dr Vija Svabe, Dr Marcis Leja

Lithuania
Kaunas, Professor Jurgis Bojarskas, Associate Professor Jolanta Kudzyte*
Panevezys, Siauliai, Professor Jurgis Bojarskas

Poland
Krakow (1993), Kraków (1995), Associate Professor Grzegorz Lis*
Poznan, Associate Professor Anna Brêborowicz

Republic of Macedonia
Skopje, Dr Emilija Vlaski*

Romania
Cluj, Professor Diana Deleanu*

Russia
Moscow, Professor Rakhim M Khaitov*
Novosibirsk, Professor Dr Elena G Kondiourina

Serbia and Montenegro
Belgrade, Dr Zorica Zivkovic*
Nis, Dr Snezana Zivanovic
Novi Sad, Dr Mila Hadnadjev
Podgorica, Dr Omer Adzovic
Sombor, Dr Eva Panic

Sweden
Linköping, Dr Hartmut Vogt, Professor N-I Max Kjellman, Dr Lennart Bråbäck
Östersund, Dr Lennart Bråbäck, Dr Anna Sandin
Stockholm/Uppsala, Dr Tony Foucard

Ukraine
Kharkiv, Rural Kharkiv, Associate Professor Viktor Ognev*

Uzbekistan
Samarkand, Tashkent, Professor Tamara Aripova

Oceania

Australia
Adelaide, Dr Declan Kennedy
Melbourne, Professor Colin F Robertson*
Perth, Professor Louis Landau
Sydney, Professor Adrian Bauman, Dr Jennifer Peat

Cook Islands
Rarotonga, Dr Roro Daniel*

Fiji
Suva, Dr Rosalina Sa'aga-Banuve

New Zealand
Auckland, Professor M Innes Asher ONZM*
Bay of Plenty, Dr Chris Moyes
Christchurch, Associate Professor Philip Pattemore
Hawkes Bay, Dr David Barry, Professor Julian Crane
Nelson, Dr Richard MacKay
Wellington, Professor Neil Pearce, Professor Julian Crane

Niue
Niue Island, Ms Moka Magatogia

Nouvelle Calédonie
Nouvelle Calédonie, Dr Isabella Annesi-Maesano

Polynésie Française
Polynésie Française, Dr Isabella Annesi-Maesano

Samoa
Apia, Ms Peone Fuimaono V Pisi

Tokelau
Tokelau, Dr Tekie Iosefa

Tonga
Nuku alofa, Dr Sunia Foliaki

Western Europe

Austria
Kärnten, Urfahr-Umgebung, Associate Professor Gerald Haidinger*
Salzburg, Dr Josef Riedler

Belgium
Antwerp, Professor Joost Weyler, Professor Paul Vermeire

Channel Islands
Guernsey, Dr David Jeffs, Dr Peter Standring
Jersey, Dr Richard Grainger, Ms Rosie Goulding

France
Créteil, West Marne, Dr Isabella Annesi-Maesano
Marseille, Professor Denis Charpin*
Montpellier, Professor Philippe Godard
Pessac, Professor André Taytard
Strasbourg, Dr Christine Kopferschmitt-Kubler

Germany
Dresden, Professor W Leopold
Greifswald, Professor Axel Kramer
Munich, Professor Erika von Mutius
Münster, Professor Dr Ulrich Keil

Greece
Athens, Associate Professor Christina Gratziou*
Thessaloniki, Associate Professor John Tsanakas

Isle Of Man
Isle of Man, Dr Andreea Steriu, Dr Peter Powell

Italy
Ascoli Piceno, Professor Sergio Bonini
Bari, Dr Lucio Armenio
Colleferro-Tivoli, Dr Valerio Dell'Orco
Cosenza, Dr Enea Bonci
Cremona, Mr Franca Rusconi
Emilia-Romagna, Dr Claudia Galassi, Dr Marco Biocca
Empoli, Dr M G Petronio, Ms Lucia Chetoni
Firenze, Dr Elisabetta Chellini
Frosinone, Mr Roberto Ronchetti
Mantova, Dr Gabriele Giannella
Milano, Dr Luigi Bisanti
Palermo, Dr Stefania La Grutta
Roma, Dr Francesco Forastiere*
Siena, Dr Piersante Sestini, Dr Elisabetta Renzoni
Torino, Dr Giovannino Ciccone
Trento, Dr Silvano Piffer
Verona, Professor Attilio Boner
Viterbo, Mr Guiseppe Corbo

Netherlands
Netherlands, Professor Rutger Engels, Professor Bert Brunekreef

Norway
Tromsø, Dr Wenche Nystad

Portugal
Coimbra, Dr M Lourdes Chiera
Funchal, Dr Fernando D Borges, Dra Rita Câmara
Lisbon, Dr José E Rosado Pinto*
Portimao, Dr Carlos Nunes
Porto, Dr José M Lopes dos Santos

Republic of Ireland
Republic of Ireland, Professor Luke Clancy

Spain
A Coruña, Dr Angel López-Silvarrey Varela
Almeria, Dr José Batlles-Garrido
Asturias, Dr Ignacio Carvajal-Urueña
Barcelona, Dr Rosa M Busquets
Bilbao, Dr Alfonso Delgado Rubio, Dr Carlos González Díaz
Cádiz, Dr Andrés Rabadán Asensio
Cartagena, Professor Luis García-Marcos*
Castellón, Dr Alberto Arnedo-Pena
Madrid, Dr Gloria García-Hernández
Pamplona, Professor Francisco Guillén-Grima
San Sebastián, Professor Eduardo G Pérez-Yarza
Valencia, Professor Maria M. Morales-Suárez-Varela
Valladolid, Professor Alfredo Blanco-Quirós

Turkey
Ankara, Dr Yildiz Saraçlar

United Kingdom
Anglia and Oxford, North east and Yorkshire, North Thames, North West, South and West, South Thames, Trent, West Midlands, Professor H Ross Anderson*
Scotland, Professor H Ross Anderson*, Dr Jane B Austin
Sunderland, Dr Mohammad H Shamssain
Surrey/Sussex, West Sussex, Professor David Strachan
Wales, Dr Michael Burr, Professor H Ross Anderson*

Other National Coordinators

Dra Viviana Aguirre (Chile)
Professor Vladimir Ahel (Croatia)
Dr Lepani Waqatakirewa (Fiji)
Professor Dr med Stephan Weiland (Deceased) (Germany)
Mr Roy Otten (Netherlands)
Dr Sylvie Barny (Nouvelle Calédonie)
Dr René Chansin (Polynésie Française)
Dr Patrick Manning (Republic of Ireland)
Dr Etienne Bahati (République Démocratique du Congo)
Mme Christine Catteau (Reunion Island)
Dr Nuualofa Tuuau-Potoi (Samoa)
Dr Lennart Nilsson (Sweden)
Dr Asma El Sony (Sudan)
Dr Tekie Iosefa (Tokelau)
Dr Toakase Fakakovi (Tonga)

About The Union

MORE THAN 90 YEARS OF COLLABORATION AND INNOVATION

The International Union Against Tuberculosis was founded in October 1920 in Paris by 31 national lung associations that saw the need for a central agency to support their efforts to stop TB by organising conferences, offering training, producing publications and disseminating the latest research and information on the disease. These have been core activities of The Union ever since, although it officially expanded its mission and became the International Union Against Tuberculosis and Lung Disease in 1986.

THE UNION'S VISION AND MISSION TODAY

In 2009, The Union redefined its vision as health solutions for the poor and adopted a new mission: to bring innovation, expertise, solutions and support to address health challenges in low- and middle-income populations. These goals reflect the interrelatedness of TB and lung disease with other conditions ranging from HIV/AIDS to non-communicable diseases such as diabetes and the fact that the burden of disease falls most heavily on the poor.

OFFICES AROUND THE WORLD SUPPORT A GLOBAL NETWORK OF EXPERTS

The Union is well-placed to fulfill its mission and vision: With close to 300 staff and consultants and more than 3,300 members from 152 countries, The Union comprises a dedicated network of experts and advocates. Its headquarters are in Paris, and offices serve the Africa, Asia Pacific, Europe, Latin America, Middle East, North America and South-East Asia regions. The Union's scientific departments focus on tuberculosis, HIV, asthma and other non-communicable diseases, child pneumonia and other lung health issues, tobacco control and research.

TECHNICAL ASSISTANCE, EDUCATION AND RESEARCH

Each year The Union provides technical assistance to some 75 countries that request its services. Its research activities include both operational research and clinical trials, with 64 project proposals receiving approval in 2010 alone. Educational activities include the World Conference on Lung Health, which has become the largest annual meeting on lung health issues as they affect low- and middle-income countries, and Union technical and management courses, which attract participants from around the world. In addition, the monthly peer-reviewed *International Journal of Tuberculosis and Lung Disease* (IF: 2.557 in 2010) and other Union publications disseminate the latest developments in research, theory and practice.

25 YEARS OF EXPERIENCE WITH ASTHMA

The Union established an Asthma Division in 1996 to address the rising incidence of asthma in low- and middle-income countries. Using the DOTS model it developed for tuberculosis control, The Union conducted field research to determine how the same principles could apply to managing asthma in limited-resource settings. This led to the publication of the first edition of *Management of Asthma: a guide for low-income countries* in 1997. Based on additional feedback from countries using the guide, revised expanded editions have been published in 2005 and 2008 as *Management of Asthma: a guide to the essentials of good clinical practice.* In its work with numerous countries, The Union repeatedly heard that lack of access to affordable, quality-assured asthma medicines was a major barrier to successful asthma management. The Union's Asthma Drug Facility (ADF) was established to help address this critical issue.

Learn more about The Union 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. It was formed in 1991 to facilitate research into asthma, rhinitis and eczema in children, due to considerable concern that these conditions were increasing not only in high-income countries, but in low- and middle-income countries as well. ISAAC aimed to investigate variations in the prevalence of these conditions at the population level and their potential causes by promoting a standardised methodology that could be used in diverse locations around the world.

In successfully developing a surveillance tool that can be replicated in most places in the world, the ISAAC Steering Committee enhanced research capacity into asthma and allergies throughout the world. The study attracted significant worldwide interest and large-scale participation, becoming the largest worldwide collaborative research project ever undertaken in children.

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. Before ISAAC Phase Three, only five centres in the world had previously studied time trends in all three conditions. ISAAC Phase Three has provided time trend data in two age groups from 110 centres in 56 countries.

ISAAC has been acknowledged for these roles and has established worldwide networks with organisations concerned with health in developing countries, such as the World Health Organization (WHO) and the International Union against Tuberculosis and Lung Disease (The Union) – the leading bodies for respiratory health in low- and middle-income countries.

ISAAC has demonstrated that asthma and allergies are a global health problem, and environmental factors are key. ISAAC findings have been the subject of many editorials in journals such as the *Lancet*, the *American Journal of Respiratory and Critical Care Medicine*, *Thorax* and the *International Journal of Tuberculosis and Lung Disease*. The major effect of the findings has been to stimulate debate concerning the causes of the global variations in asthma, rhinitis and eczema, aided by hypotheses suggested by the findings of ecological analyses of ISAAC data.

ISAAC findings are cited by world organisations involved in monitoring and preventing chronic respiratory diseases (CRDs) and are used to inform global health initiatives. ISAAC findings have been used by the WHO, the Global Alliance against Chronic Respiratory Diseases, the Global Initiative for Asthma (GINA) and the Global Burden of Disease project.

Many international health organisations have stated there is a need for greater emphasis on non-communicable diseases (NCDs), particularly among poor and disadvantaged populations. The Union has joined this call for greater recognition of non-communicable respiratory diseases. ISAAC is uniquely positioned as a global research programme to address the lack of data regarding CRDs in low- and middle-income countries through its existing network of collaborating investigators.

Learn more about ISAAC http://isaac.auckland.ac.nz/

International Union Against Tuberculosis and Lung Disease

Health solutions for the poor

International Union Against Tuberculosis and Lung Disease
68, boulevard Saint-Michel – 75006 Paris – France
Tel: (+33) 1 44 32 03 60 – Fax: (+33) 1 43 29 90 87

ISAAC
The International Study of Asthma and Allergies in Childhood

Visit our website www.globalasthmareport.org