The Global Asthma Report 2014

Global Asthma Network

Asthma may affect as many as 334 million people.*

*For explanation see Chapter 2 "How many people have asthma?"

ISBN: 978-0-473-29125-9 (PRINT) | 978-0-473-29126-6 (ELECTRONIC)

Suggested citation: The Global Asthma Report 2014. Auckland, New Zealand: Global Asthma Network, 2014.

www.globalasthmanetwork.org

Global Asthma Network

GLOBAL ASTHMA REPORT 2014

Foreword

The Global Asthma Report 2014 has been prepared by the Global Asthma Network (GAN) Steering Group and invited authors with additional expertise. It provides substantial up-to-date information about asthma: each chapter is a state-of-the-art summary of what is known and where the gaps lie, and each makes recommendations to authorities on required actions. Included are findings from new GAN surveys on asthma guidelines, national asthma strategies and access to quality-assured, affordable asthma medicines.

Designed for government ministers, policy-makers, health authorities, health professionals, patient support organisations and people living with asthma, this report gives an update of what is known about the global burden of asthma, management of asthma and capacity building, and ways of making asthma a global priority.

It is encouraging to see that recognition of asthma as a global problem has increased since the first Global Asthma Report 2011 was published by the International Union Against Tuberculosis and Lung Disease (The Union) and International Study of Asthma and Allergies in Childhood (ISAAC).

GAN was established in 2012, building on the work pioneered and achieved by the ISAAC programme over the preceding 20 years and the asthma management work of The Union in low- and middle-income countries. The people involved in founding GAN, from each organisation, were largely those involved in publishing the Global Asthma Report 2011.

GAN is a worldwide collaboration, involving more than half the world's countries. It will undertake global surveys of asthma in children and adults to measure and monitor asthma and its burden, providing the essential data called for by the World Health Organization. No one else is currently doing this work. GAN aims to reduce asthma suffering by improving asthma care globally, with a focus on low-and middle-income countries, achieving this through research, capacity building, and access to effective asthma management and care including quality–assured essential asthma medicines.

Elsewhere, there have been other developments increasing the visibility of asthma. On 19 September 2011, the General Assembly of the United Nations (UN) made a political declaration on the prevention and control of non-communicable diseases (NCDs), focussing world attention on the increasing threat of asthma and other NCDs to global health, social welfare and economic development, especially in low- and middle-income countries. This was followed in 2013 by two reports from the World Health Organization (WHO) on NCDs: A Global Action Plan 2013-2020 and Global Monitoring Framework. In July 2014 the UN held a review meeting. In his opening address the UN Secretary General, Ban Ki-moon, said

> *"…The global epidemic of NCDs is a major and growing challenge to development. Each year, in developing countries alone, strokes, heart attacks, cancer, diabetes or asthma kill more than 12 million people between the ages of 30 and 70…".*

While estimating the number of people in the world with asthma remains difficult due to the many gaps in the data, the Global Burden of Diseases Study (GBD) published in 2012 gave us the latest estimate of asthma prevalence, indicating that as many as 334 million people in the world have asthma, and that the related burden is high.

Since 2012, WHO has published guidelines for the prevention and control of asthma in primary health care in low-resource settings. Guidelines on asthma from other organisations, including the Global Initiative on Asthma (GINA), have been updated. The European Academy of Allergy and Clinical Immunology (EAACI) has published a Global Atlas of Asthma. The Forum of International Respiratory Societies (FIRS) has published its report "Respiratory diseases in the world. Realities of today – opportunities for tomorrow", which highlights asthma as one of the top 5 respiratory diseases in the world.

All these activities, concerns, developments and knowledge inform contents of the Global Asthma Report 2014 and its recommendations. We hope you will find it useful. We will continue to work together to increase the worldwide understanding of this disease, and to reduce the burden and suffering from asthma, over the next few years.

Innes Asher
Chair
The Global Asthma Network

Executive Summary

With good long-term management, the burden of asthma can be reduced.

In the Global Asthma Report 2014, the Global Asthma Network (GAN) has brought together an up-to-date overview of the key issues regarding asthma globally.

When examining the burden of asthma today, there is much to be concerned about.

Asthma is a common chronic non-communicable disease that affects as many as 334 million people of all ages in all parts of the world. It is a cause of substantial burden to people, often causing a reduced quality of life, not only due to its physical effects, but also its psychological and social effects. The various estimates of its economic burden, mostly due to productivity loss, are all significant. Further, avoidable asthma deaths are still occurring due to inappropriate management of asthma, including over-reliance on reliever medication rather than preventer medication. Asthma is a particularly serious burden in low- and middle-income countries least able to afford the costs.

While our knowledge has increased, the remaining gaps in the data are significant.

While hospital admissions save lives during acute asthma attacks, there are many places where the number of hospital admissions is too high, and the reasons for this need more research. The factors affecting asthma also require further research. New surveys are needed to update asthma trends, assess the burden of asthma and access to effective management. Meanwhile, GAN is working towards closing the data gaps.

But much of this burden of disease and lack of information is avoidable.

Asthma which is well controlled imposes far less of an economic and personal burden than non-controlled asthma. Strategies towards improving access and adherence to evidence-based therapies can therefore be effective in reducing the personal and economic burden of asthma in all countries. Implementation of relatively simple measures within a systematic national or local strategy can improve early detection of asthma and provide effective preventive treatment. Asthma management guidelines are an essential part of successfully managing asthma and promoting the delivery of quality asthma care; these are widely available.

Political commitment and action are required to make the burden of asthma a thing of the past.

The Global Asthma Report 2014 makes many recommendations to the World Health Organization (WHO), governments, health authorities and health professionals, which, if followed, will transform asthma globally from a burden to an inconvenience.

As part of their asthma strategy, every country needs:

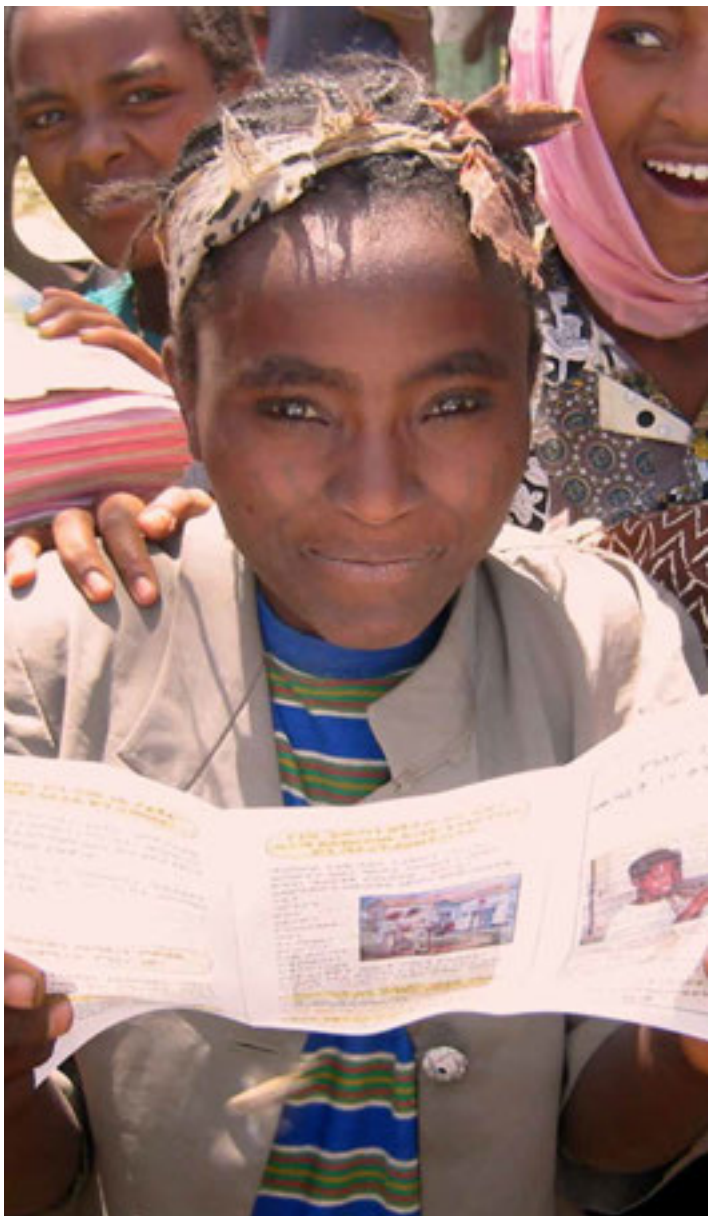
- **An up-to-date approach to the diagnosis and management of wheezing in young children.** This is an evolving field. This report includes a review of recurrent wheezing in infants including information from a recent international study. If an infant presents with frequent and/or severe episodes of recurrent wheezing they should be diagnosed and managed as asthma, unless there is evidence to the contrary.
- **Guaranteed access to quality-assured essential asthma medicines.** This is vital to improving asthma outcomes. Essential asthma medicines need to be on all national lists of essential medicines and reimbursed medicines; this is not yet the case. Essential asthma medicines are inhalers which are complex devices, requiring accurate manufacturing to produce a reliable dose with particles of an inhalable size. Many devices on the market are substandard or unaffordable. WHO has a key role in setting standards for these medicines, and all parties must working to make them affordable.
- **Effective policy action on known, remediable causes of asthma** such as parental smoking (for children) and occupational exposures (for adults).
- **Capacity building of trained health professionals.** This is vital and can be enabled by participation in research. Short courses in research generally, or asthma research in particular, provide opportunities for 'upskilling' in research for those with limited time and resources.

In low- and middle-income countries, efforts should be accelerated to make asthma a lung health priority. Asthma management and control is feasible even in low-income countries, and it should be on everyone's agenda. In 2012 WHO published guidelines for asthma management in low-income settings.

GAN will work with others to achieve better asthma outcomes through undertaking global surveys of asthma in children and adults, research, capacity building, improving access to effective asthma management and care, including quality-assured essential medicines, and through advocacy activities.

Together, we can ensure that asthma is managed so that its associated disability, death, and economic drain is massively reduced – even if prevalence rises.

Key Recommendations



The World Health Organization (WHO) should

- add essential asthma medicines to their Prequalification Programme, promote the standardisation of the dosages of active ingredients in combined inhalers and the harmonisation of quality requirements for inhalers across international reference documents such as the pharmacopoeias.

Governments should

- commit to research, intervention, and monitoring to reduce the burden of asthma in the world. Global surveillance of asthma requires standardised measures of asthma implemented in large scale surveys of both children and adults in diverse settings worldwide;
- include asthma in all their actions arising from the WHO Global Action Plan for the Prevention and Control of Non-communicable Diseases (NCDs) 2013-2020, and the WHO NCD Global Monitoring Framework;
- ensure that they have a list of essential medicines for asthma which includes both inhaled corticosteroids and bronchodilator in dosages recommended by WHO, and that these are available, quality-assured, and affordable for everyone in their countries;
- ensure all asthma inhalers procured, distributed and sold in their countries meet international quality standards;
- particularly in low-income countries, make commitments to ensure that the supply of quality-assured, affordable essential asthma medicines is uninterrupted, health professionals are appropriately trained, and health services are organised to manage asthma;

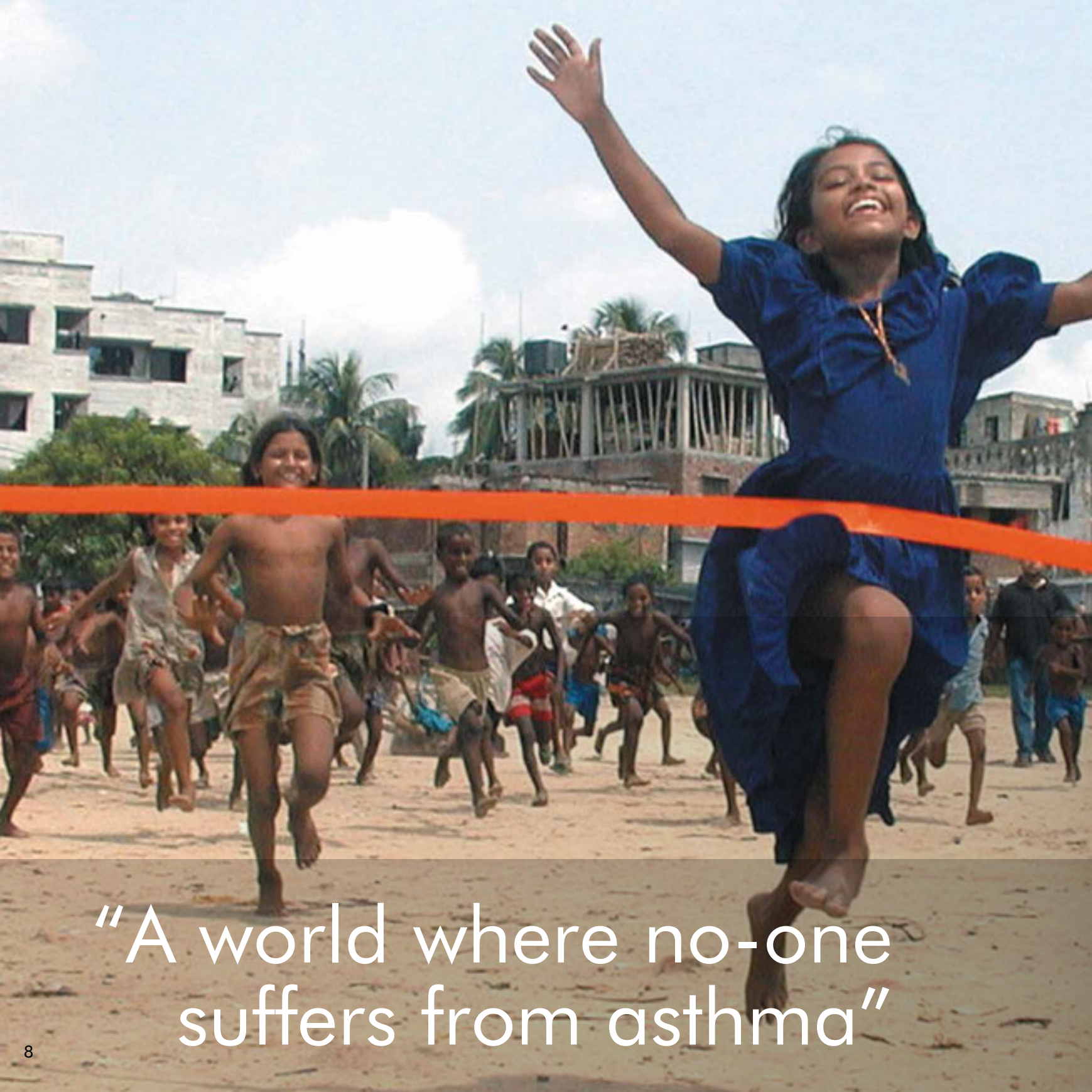
- particularly in low- and middle-income countries make asthma a health priority, in order to more quickly invest in asthma research relevant to their populations, integrate care at community and primary health care levels with appropriate referral procedures, and develop capacity in standard case management of asthma;
- strengthen policies to reduce tobacco consumption, encourage healthy eating and reduce exposure to potentially harmful chemicals, smoke and dust. Funders need to support further research to identify causes of asthma;
- measure and monitor the economic costs of asthma in their countries, including health care costs and productivity losses.

Health authorities in all countries should

- develop national strategies and action plans to improve asthma management and reduce costs;
- ensure the availability of nationally approriate asthma management guidelines and provide access for everyone to the quality-assured, affordable essential asthma medicines those guidelines recommend;
- encourage their health professionals to attend short courses relevant to asthma research and policy;
- collect counts of hospital admissions in children and adults, from defined catchment populations, to monitor trends in asthma over time;
- report rates of asthma deaths in children and adults to monitor progress in asthma care and as an early warning of epidemics of fatal asthma.

Health professionals in all countries should

- regard frequent or severe recurrent wheezing in infancy as part of the spectrum of asthma;
- ensure that their country is represented in the Global Asthma Network (GAN).



"A world where no-one suffers from asthma"

THE GLOBAL ASTHMA NETWORK

1. Global Asthma Network

Innes Asher, Nils Billo, Karen Bissell, Chiang Chen-Yuan, Philippa Ellwood, Asma El Sony, Luis García-Marcos, Javier Mallol, Guy Marks, Neil Pearce, David Strachan

The Global Asthma Network (GAN) has grown out of the International Study of Asthma and Allergies in Childhood (ISAAC) and the International Union Against Tuberculosis and Lung Disease (The Union). It aims to reduce asthma suffering by improving asthma care globally with a focus on low- and middle-income countries. GAN will achieve this through undertaking global surveys of asthma in children and adults, research, capacity building, improving access to effective asthma management and care, including quality-assured essential medicines, and through regular advocacy activities.

Closing the world data gaps for asthma in children and adults will be a key activity of the Global Asthma Network.

GAN plays a crucial role in collecting asthma data on adults and children globally; this data is not being obtained by any other group. In 2012 the leader of the World Health Organization (WHO), Dr Margaret Chan, said

"Accurate assessment of the global, regional and country health situation and trends is critical for evidence-based decision making in public health…. The real need is to close the data gaps, especially in low-and middle-income countries".

For asthma this is exactly what GAN is doing – closing the data gaps.

GAN was established in 2012 to improve asthma care globally (www.globalasthmanetwork.org). GAN is a new collaboration between individuals from ISAAC - isaac.auckland.ac.nz/ (now wound up) and The Union - www.theunion.org.

GAN is building on the work achieved by the ISAAC programme (1991-2012), which has an impressive track record of undertaking surveys which have contributed extensive data on asthma and allergies in children, monitoring these diseases over time, and researching possible causes. GAN is operating on the same principles used in ISAAC of collaborative and systematic application of standardised methodologies able to be used in all settings in the world. In addition to asthma in children, GAN will study asthma in adults. Surveys will be conducted and repeated as resources allow.

GAN is led by an 11-member international Steering Group responsible for developing and overseeing its work programme. Long-term targets have been developed (Figure 1). The GAN Data Centre is located in Auckland, New Zealand. The Data Centre leads the surveys, communicates methodologies,

analyses data, oversees publications, and develops and maintains the GAN website.

Methods

GAN welcomes participation from centres in all countries in the world. In August 2014 there were 276 centres in 119 countries that had expressed an interest in participating in GAN (Figure 2).

Principal Investigators in each centre complete surveys about asthma in their centre and country. Surveys are of two types: on-line surveys of GAN Principal Investigators about specific topics, and questionnaire surveys undertaken through schools. High participation rates are sought in all surveys. In 2013/14, GAN surveys of the first type were completed, on national asthma strategies, asthma management guidelines and access to quality-assured, affordable asthma medicines; the findings are summarised in Chapters 8, 9 and 10.

Surveys of the second type are planned to start in 2015. Each centre will be invited to undertake a survey using the GAN protocol and questionnaires. Two age groups of children will be involved (13-14 year olds and 6-7 year olds), as well as parents/caregivers of each child. The adolescents and the parents of the children will be asked to complete questionnaires based on ISAAC, including additional questions on asthma management and the environment; for the adults, questions will be based on the European Community Respiratory Health Survey.

Participants will be selected from randomly sampled schools within a specified geographical area (or all schools) around each study centre. Within each country at least one urban and one rural centre will be sought so that the different influences of these environments on asthma can be explored. A sample size of 3000 per age group per centre will be used to give sufficient power to detect differences in the severity of asthma. For smaller populations, such as a small island nation, all pupils (and their parents/caregivers) of the age group will be selected.

Figure 1:

Targets of the Global Asthma Network

Decrease severe asthma by 50% by 2025

- **proportion of symptomatic people with asthma not on inhaled corticosteroids**
- **time off work/school because of asthma**
- **unplanned visits for asthma**
- **hospital admissions for asthma**
- **severity of asthma**
- **mortality from asthma**

Increase the access to quality-assured essential asthma medicines by 2018:

- **On the WHO prequalification list - 2014**
- **On National Essential Medicines Lists - 2015**
- **Available in all countries - 2018**
- **Affordable in all countries - 2018**

Tools to enable centres to follow and use the methodology will be available on the GAN website.

Impact

GAN is currently the only global study of asthma in populations (following on from the ISAAC programme) and will contribute new information on adult as well as childhood asthma. GAN connects with others who strive for a world where no-one suffers from asthma and has established communication with worldwide organisations concerned with respiratory health and non-communicable diseases (NCDs), especially in low-and middle-income countries.

ISAAC demonstrated that asthma and allergies are global health problems and that environmental factors are key. GAN is continuing this work. The value of GAN is attested to by the large number of centres that have expressed an interest in participating, and the fact that major international respiratory and NCD advocacy organisations involved in monitoring and preventing chronic respiratory disease have expressed their support for GAN.

GAN has set ambitious targets to decrease severe asthma by 50% by 2025 and to increase the access to quality-assured essential asthma medicines (Figure 1). If these targets are achieved, then the burden of, and suffering from, asthma in

Mission of the Global Asthma Network:

To prevent asthma and improve asthma care globally with a focus on low- and middle-income countries.

The network will achieve this through enhanced surveillance, research, capacity building, and access to effective asthma care, including quality-assured essential medicines.

Vision of the Global Asthma Network:

A world where no-one suffers from asthma.

ASPIRATIONS OF THE GLOBAL ASTHMA NETWORK

- Strive for a world where no-one suffers from asthma.
- Be the asthma surveillance hub for the world.
- Raise the profile of asthma as a non-communicable disease.
- Stimulate and encourage capacity building in low- and middle-income countries.
- Promote access to appropriate management of asthma.
- Research ways of reducing the burden of asthma.

VALUES OF THE GLOBAL ASTHMA NETWORK

Empowerment

Solidarity

Independence

Quality

Accountability

Figure 2:

Global Asthma Network participating centres, August 2014

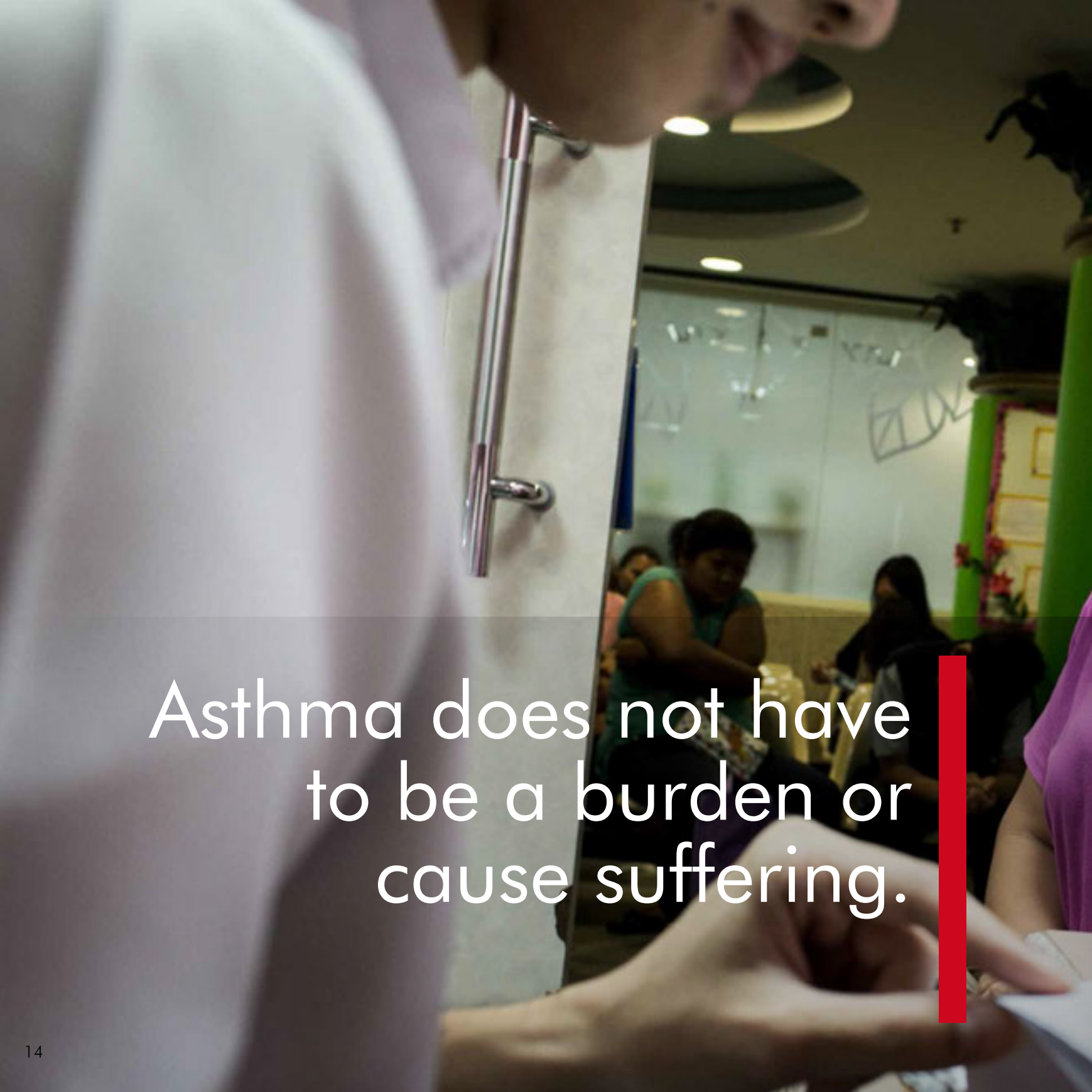
the world will be markedly reduced.

Conclusion

GAN seeks to build on the work of ISAAC and The Union to lessen the suffering from asthma in the world through surveillance of asthma, research, capacity building, improving access to effective asthma management and care, including quality-assured essential medicines, and to advocate for asthma to be high on the public health agenda.

Key Recommendation

Health professionals in all countries should ensure that their country is represented in the Global Asthma Network.


Asthma does not have
to be a burden or
cause suffering.

PART ONE:

THE BURDEN OF ASTHMA

2. Global Burden of Disease due to Asthma

Guy Marks, Neil Pearce, David Strachan, Innes Asher

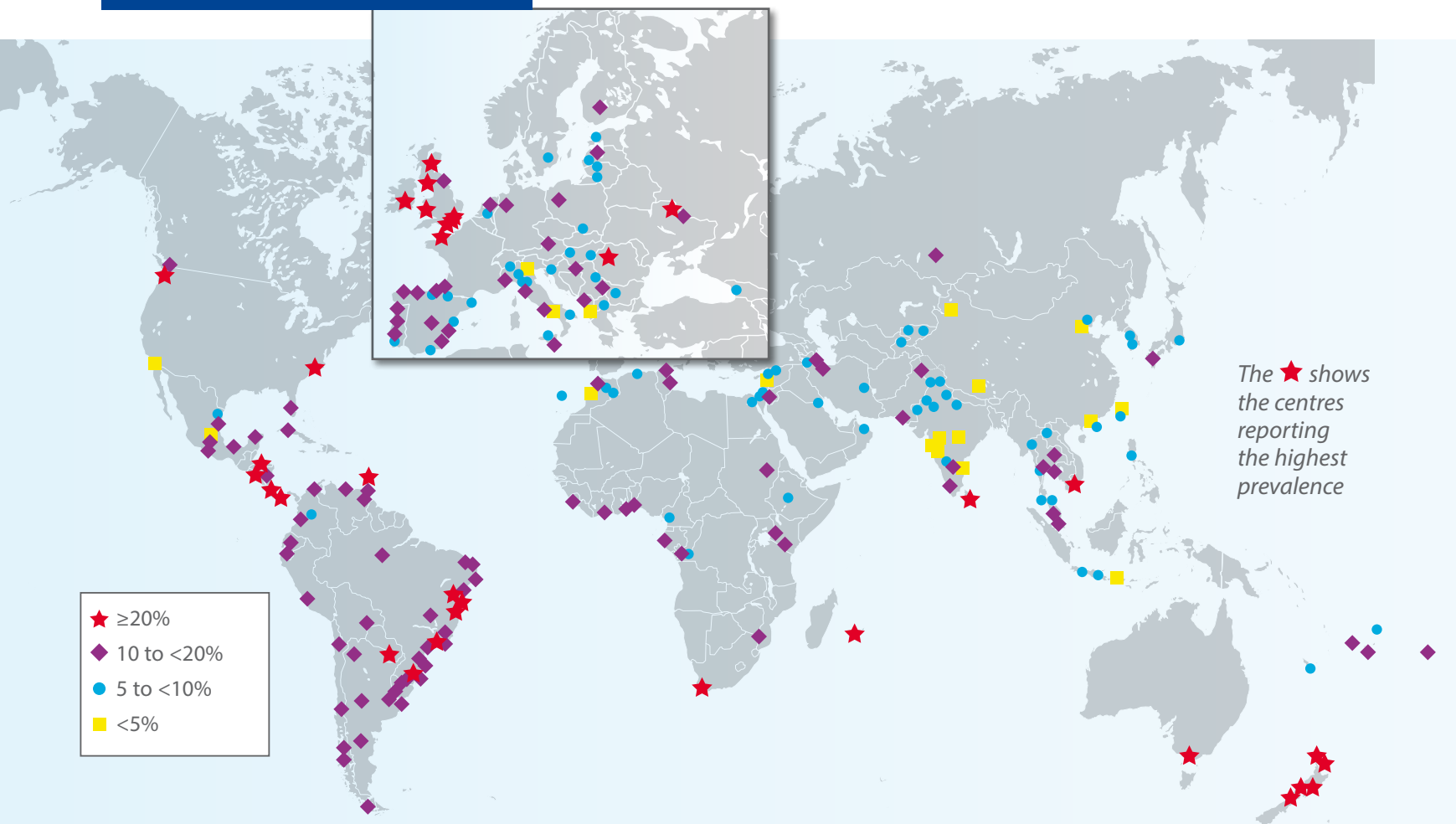


Figure 1: Prevalence of asthma symptoms among 13-14 year olds (ISAAC).

Source: Lai CKW, et al. Thorax 2009

Asthma, a disease of the airways, occurs in people of all ages, and wheeze is the most common symptom. The most recent revised global estimate of asthma suggests that as many as 334 million people have asthma, and that the burden of disability is high. The historical view of asthma being a disease of high-income countries no longer holds: most people affected are in low- and middle-income countries, and its prevalence is estimated to be increasing fastest in those countries. Ongoing monitoring is needed to follow the epidemic of asthma and its management.

What is asthma?

Asthma is a disease of the bronchial tubes in the lungs (the "airways"). People with asthma typically experience "wheezing", a high-pitched whistling sound heard during breathing, especially when breathing out. However, wheezing does not always occur, and asthma can also involve breathlessness, chest tightness or coughing. The underlying process includes chronic inflammation of the airways, reversible obstruction of the flow of air in and out of the

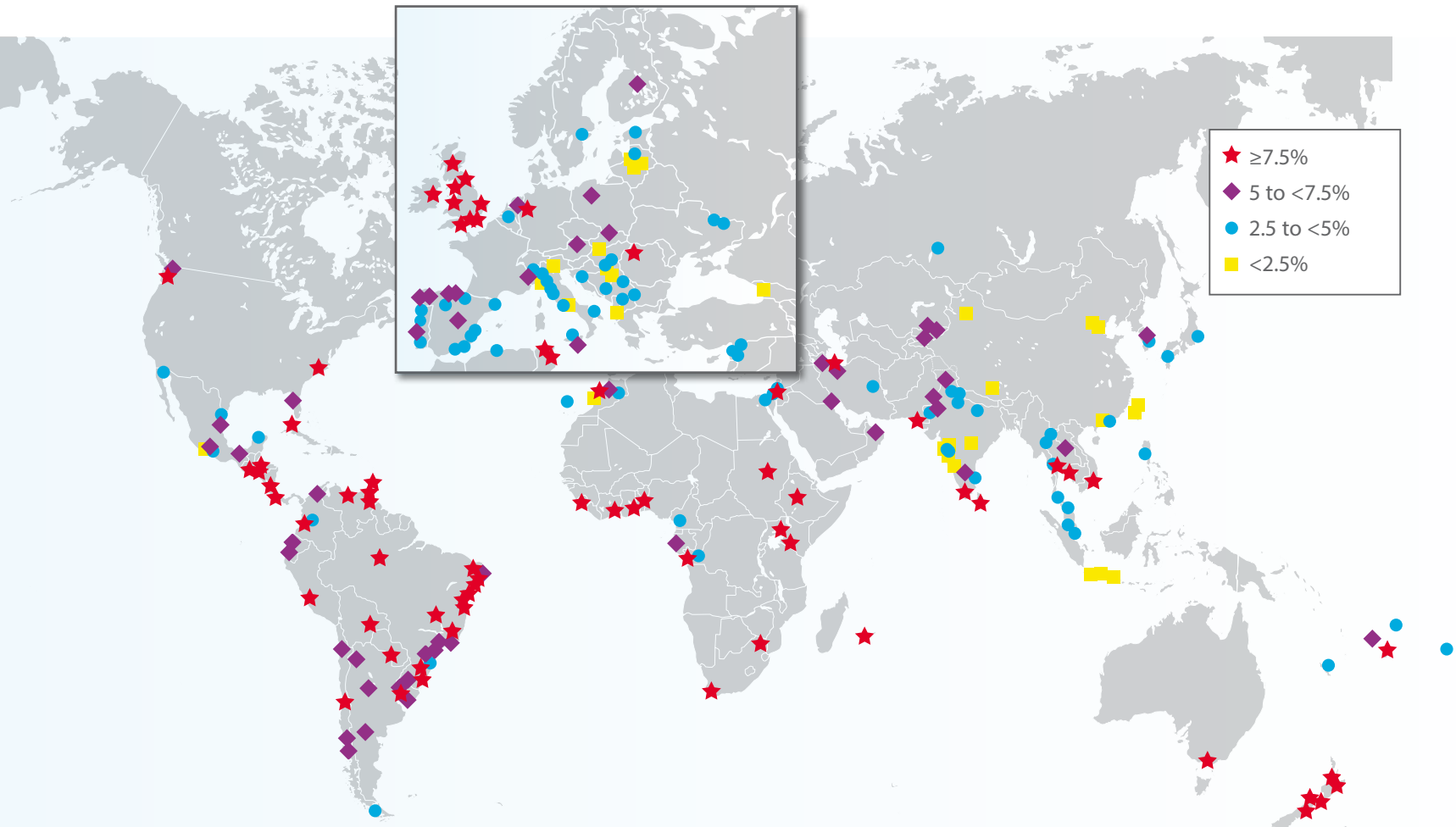


Figure 2: Prevalence of severe asthma among 13-14 year olds (ISAAC).

Source: Lai CKW, et al. Thorax 2009

airways, and the tendency of the airways to over-react to stimuli. 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.

How many people have asthma?

The number of people with asthma in the world may be as high as 334 million. This figure comes from the most recent comprehensive analyses of the Global Burden of Disease Study (GBD) undertaken in 2008-2010. A lower figure of 235 million used in the Global Asthma Report 2011 came from the most up-to-date GBD information available at that time based on

Asthma is a common chronic disease that affects millions of people of all ages in all parts of the world. It is a cause of substantial burden, often causing a reduced quality of life. New surveys are needed to update asthma trends.

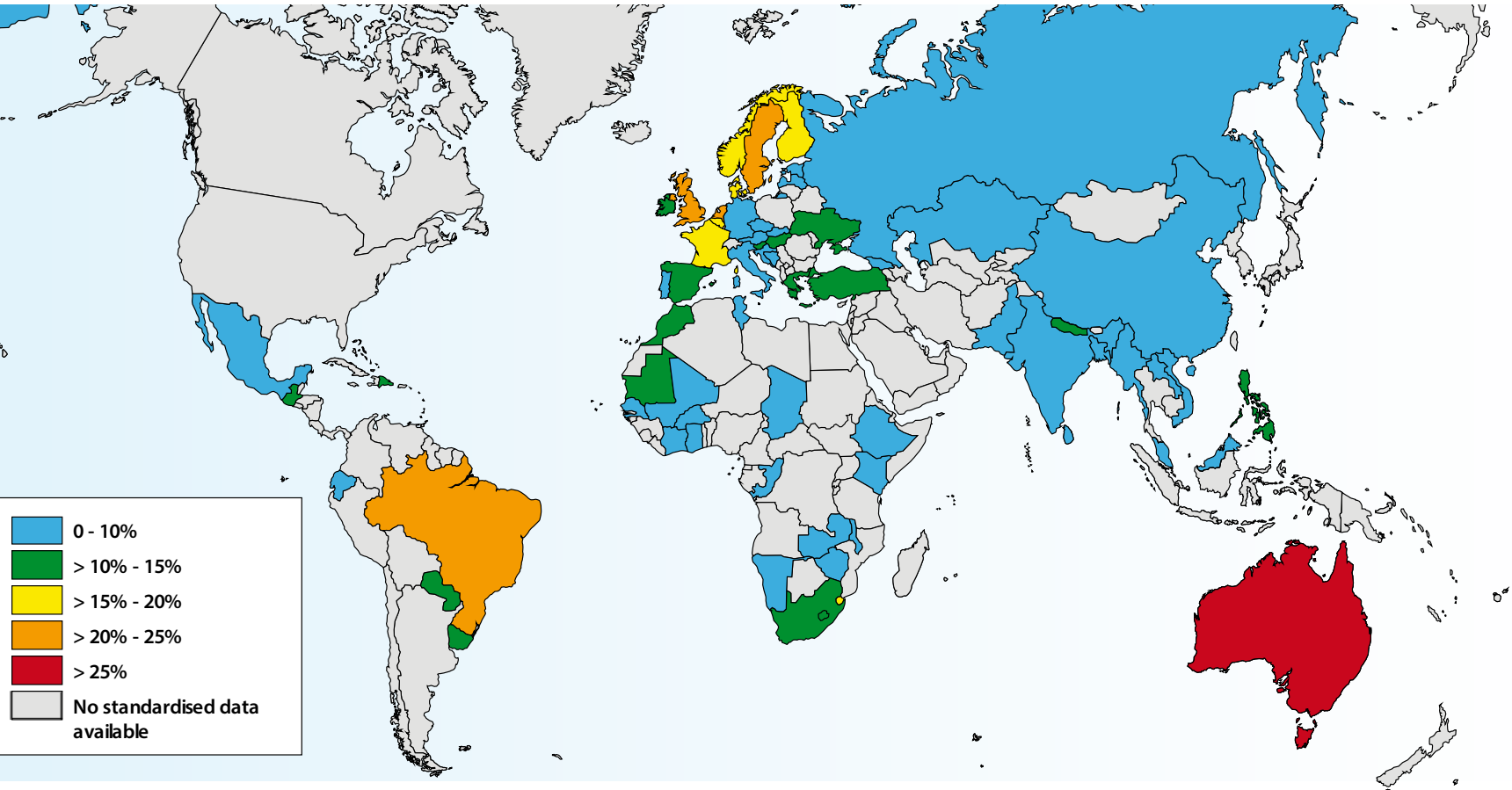


Figure 3: Prevalence of symptoms of asthma in the past 12 months among persons aged 18 to 45 years in 70 countries, World Health Survey 2002-2003.

Source: To T, et al. BMC Public Health 2012.

analyses from 2000-2002. These numbers are not precise, rather they are estimated from the best data available. However, as the following paragraphs illustrate, there are many gaps in asthma statistics. There is no evidence that the number of people with asthma in the world has increased from 235 to 334 million between our 2011 and 2014 reports; rather this situation illustrates the need for high quality data on asthma to be collected in an ongoing way.

Much of the information on which the later estimate is based is already out of date, as the last global surveys of the proportion of the population who have asthma (that is, prevalence) were carried out about 10 years ago. Unfortunately the World Health Organization (WHO) is not undertaking any future global asthma monitoring work; however the Global Asthma Network (GAN) plans to continue this work with worldwide studies to find out how the pattern of asthma is changing in children and adults (See Chapter 1).

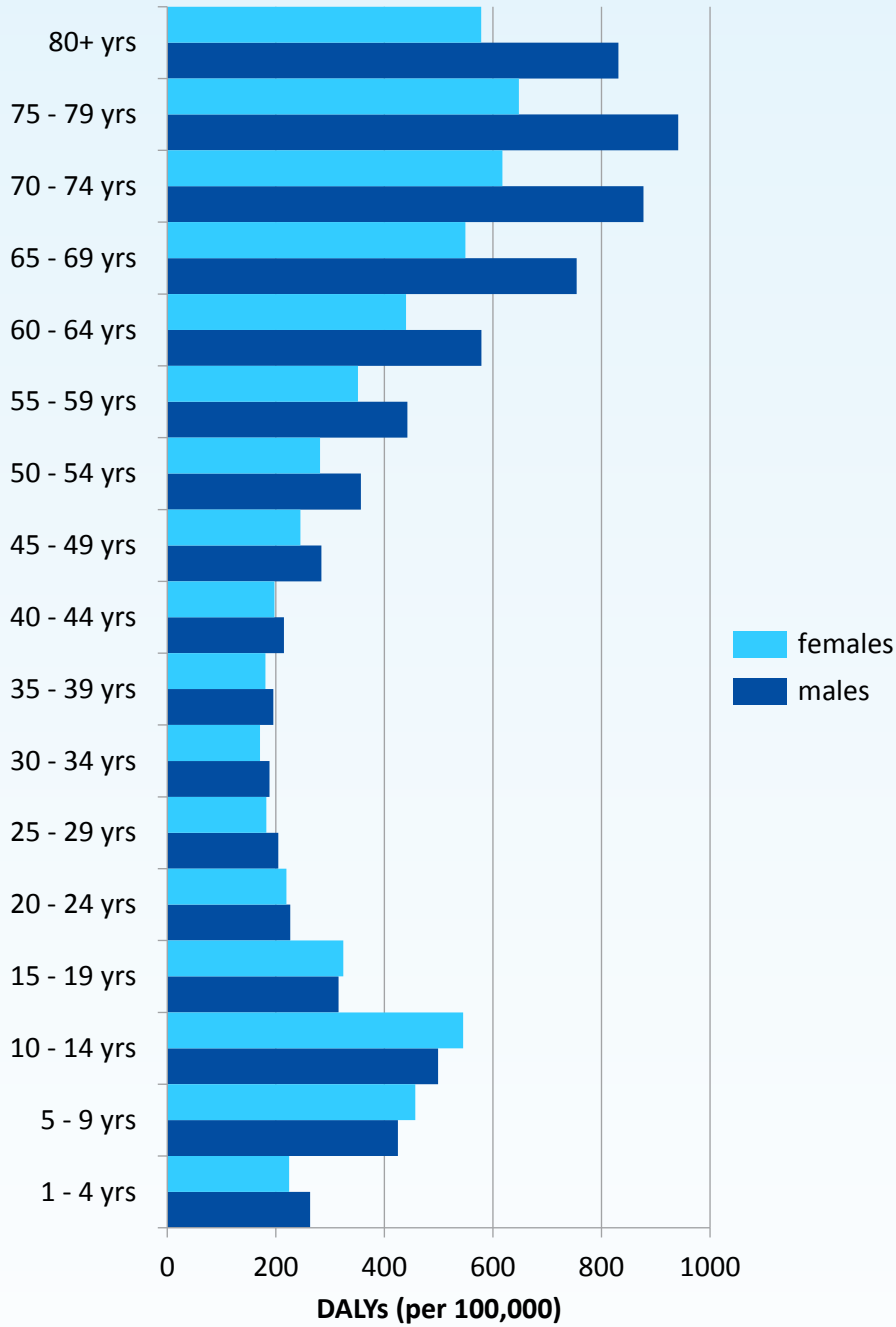
To make comparisons of the prevalence of asthma between different parts of the world, and changes over a period of time, standardised measurements are needed (that is, measurements done in the same way at different places and times). The most common way of doing this is by questionnaire, which is feasible for large scale surveys. Using this approach The International Study of Asthma and Allergies in Childhood (ISAAC) undertook its latest survey between 2000 and 2003.

ISAAC found that about 14% of the world's children were likely to have had asthmatic symptoms in the last year and, crucially, the prevalence of childhood asthma varies widely between countries, and between centres within countries studied (Figure 1). These conclusions resulted from ISAAC's ground-breaking survey of a representative sample of 798,685 children aged 13-14 years in 233 centres in 97 countries. (A younger age group of children (6-7 years) was also studied by ISAAC and the findings were generally similar to the older children). These adolescents were asked whether they

Figure 4:

Burden of disease, measured by disability adjusted life years (DALYs see explanation p20) per 100,000 population attributed to asthma by age group and sex. Global population, 2010.

Source: Institute for Health Metrics and Evaluation (IHME).



had experienced wheeze in the preceding 12 months. Prevalence of recent wheeze varied widely (Figure 1). The highest prevalence (>20%) was generally observed in Latin America and in English-speaking countries of Australasia, Europe and North America as well as South Africa. The lowest prevalence (<5%) was observed in the Indian subcontinent, Asia-Pacific, Eastern Mediterranean, and Northern and Eastern Europe. In Africa, 10-20% prevalence was mostly observed.

In this same survey, the prevalence of symptoms of severe asthma in the preceding 12 months, defined as 4 or more attacks of wheeze, waking at night with asthma symptoms one

or more times per week, and/or any episodes of wheeze severe enough to limit the ability to speak, also varied substantially, but was > 7.5% in many centres (Figure 2).

The prevalence of asthma in younger adults varies widely as it does in children. Overall, 4.3% of respondents to WHO's World Health Survey aged 18-45 in 2002-2003 reported a doctor's diagnosis of asthma, 4.5% had reported either a doctor's diagnosis or that they were taking treatment for asthma, and 8.6% reported that they had experienced attacks of wheezing or whistling breath (symptoms of asthma) in the preceding 12 months (Figure 3). The highest prevalence was observed in Australia, Northern and Western Europe and Brazil. The World Health Survey, which was conducted about the same time as ISAAC, used a different survey method which may contribute to some of the differences in the findings within a region. The prevalence of asthma was measured by questionnaire administered to 177,496 persons aged 18 to 45 years living in 70 countries.

Much less is known about the prevalence of asthma in middle-aged and older adults. This reflects both a paucity of survey data and the greater difficulty of distinguishing asthma from other respiratory conditions, such as chronic obstructive pulmonary disease (COPD) in older age groups. There are no internationally standardised comparisons of asthma prevalence in the elderly.

Is asthma becoming more or less common?

Asthma symptoms became more common in children from 1993 to 2003 in many low- and middle-income countries which previously had low levels, according to ISAAC. However, in most high-prevalence countries, the prevalence of asthma changed little and even declined in a few countries. Factors responsible for increasing asthma rates are not fully understood, but environmental and lifestyle changes play the key roles (see Chapter 7). What has happened to the prevalence and severity of asthma since 2003? We do not know because there have been no surveys.

What is the impact of asthma on rates of disability and premature death?

The burden of asthma, measured by disability and premature death, is greatest in children approaching adolescence (ages 10-14) and the elderly (ages 75-79) (Figure 4). The lowest impact is borne by those aged 30-34. The burden is similar in males and females at ages below 30-34 years but at older ages the burden is higher in males. This sex difference increases with increasing age. Figure 4 shows the GBD's measure of health loss attributable to specific diseases, for asthma. The GBD used mortality statistics and health survey data, where available, to estimate, for many countries of the world, two components of disease burden: years of life lost due to premature death, and years of life lived with disability. The latter quantifies both the extent of disability and its duration. The years of life prematurely lost, and the years of life lived with disability are added together and expressed as disability adjusted life years (DALYs), which is the measure of burden of disease.

Among people aged less than 45 years, most of the burden of disease is disability. The GBD estimated that asthma was the 14th most important disorder in terms of global years lived with disability. However, for people in older age groups, premature death due to asthma contributes more to the burden of disease (Figure 5).

Asthma has a global distribution with a relatively higher burden of disease in Australia and New Zealand, some countries in Africa, the Middle East and South America, and North-Western Europe (Figure 6).

Conclusion

The global burden of disease due to asthma has become better understood through standardised measurement of the proportion of the population who have asthma, severe asthma, disability due to asthma and/or who have died from asthma. Little is known about asthma in the many countries where it has not been studied, and little information is available about asthma in adults over the age of 45.

THE GLOBAL BURDEN OF ASTHMA: CURRENT ESTIMATES

- 334 million people have asthma.
- 14% of the world's children experience asthma symptoms.
- 8.6% of young adults (aged 18-45) experience asthma symptoms.
- 4.5% of young adults have been diagnosed with asthma and/or are taking treatment for asthma.
- The burden of asthma is greatest for children aged 10-14 and the elderly aged 75-79.
- Asthma is the 14th most important disorder in the world in terms of the extent and duration of disability.

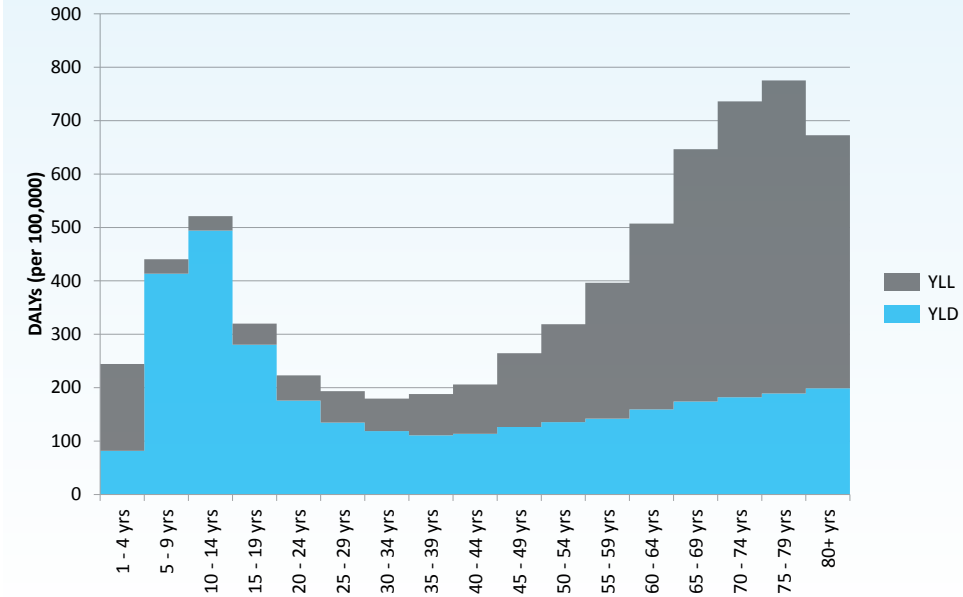
Key Recommendation

Governments should commit to research, intervention, and monitoring to reduce the burden of asthma in the world. Global surveillance of asthma requires standardised measures of asthma implemented in large scale surveys of both children and adults in diverse settings worldwide.

Figure 5:

Components of disability adjusted life years (DALYs): years lived with disability (YLD) and years of life lost (YLL) per 100,000 population attributed to asthma by age group. Global population, 2010. (see DALY explanation on p20)

Source: Institute for Health Metrics and Evaluation (IHME).



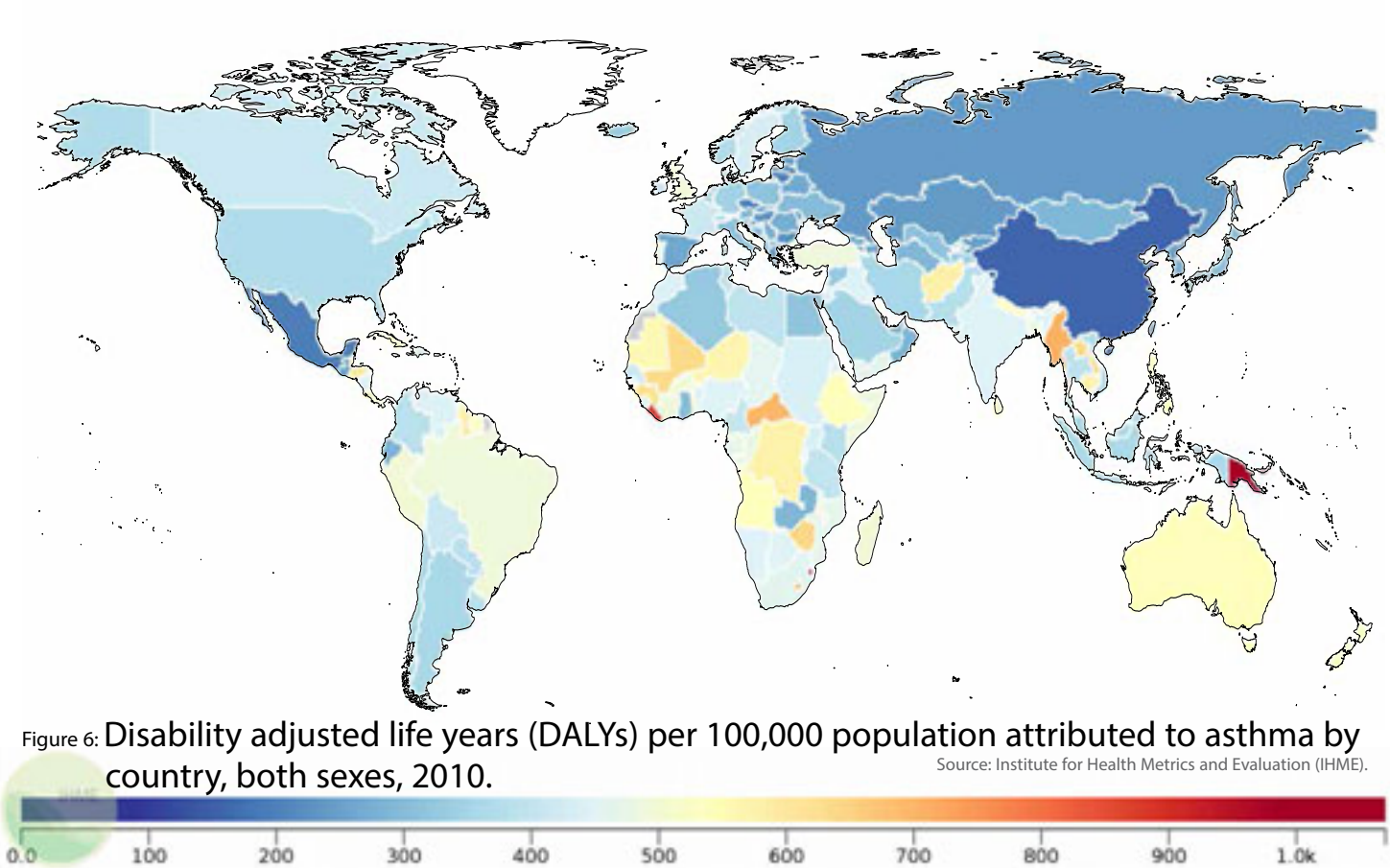


Figure 6: Disability adjusted life years (DALYs) per 100,000 population attributed to asthma by country, both sexes, 2010.

Source: Institute for Health Metrics and Evaluation (IHME).

3. Hospital Admissions for Asthma

David Strachan, Ramyani Gupta, Luis García-Marcos

Hospital admissions for asthma have been proposed as a target indicator of improvements in asthma care, but the factors underlying variations in hospital admission rates are poorly understood. Admission to hospital during an asthma attack may indicate the first episode in the disease or a failure of preventive care for established asthma. Hospital care may be important to prevent a fatal outcome in severe or troublesome asthma. Historically, the relationship between asthma prevalence, severity, admissions, and mortality rates in high-income countries has been complex. Changes in the admission rate over time correlate (albeit imperfectly) with changes in the prevalence and severity of childhood asthma. However, the relative ranking of national admission rates for asthma is not consistent between children and adults.

Hospital admissions for asthma may be used as an indirect indicator of the burden of more severe asthma and the efficacy of care. However the factors underlying variations in hospital admission rates are poorly understood and need more research.

International Comparisons

Many attacks of asthma are mild and self-limiting and never present for hospital treatment. The proportion of acute episodes which result in hospital admission varies greatly between countries, depending upon the accessibility and affordability of the health care system, the local thresholds for referral from community to hospital, and from outpatient or emergency visits to inpatient care.

National hospital admission statistics are mainly limited to high-income countries in Europe, North America and Australasia. Data are lacking for most low- and middle-income countries. In European countries, among all age groups, asthma contributes 0.6% of hospital admissions and 0.4% of all inpatient bed-days. Figure 1 shows an almost tenfold variation in age-standardised admission

Figure 1:

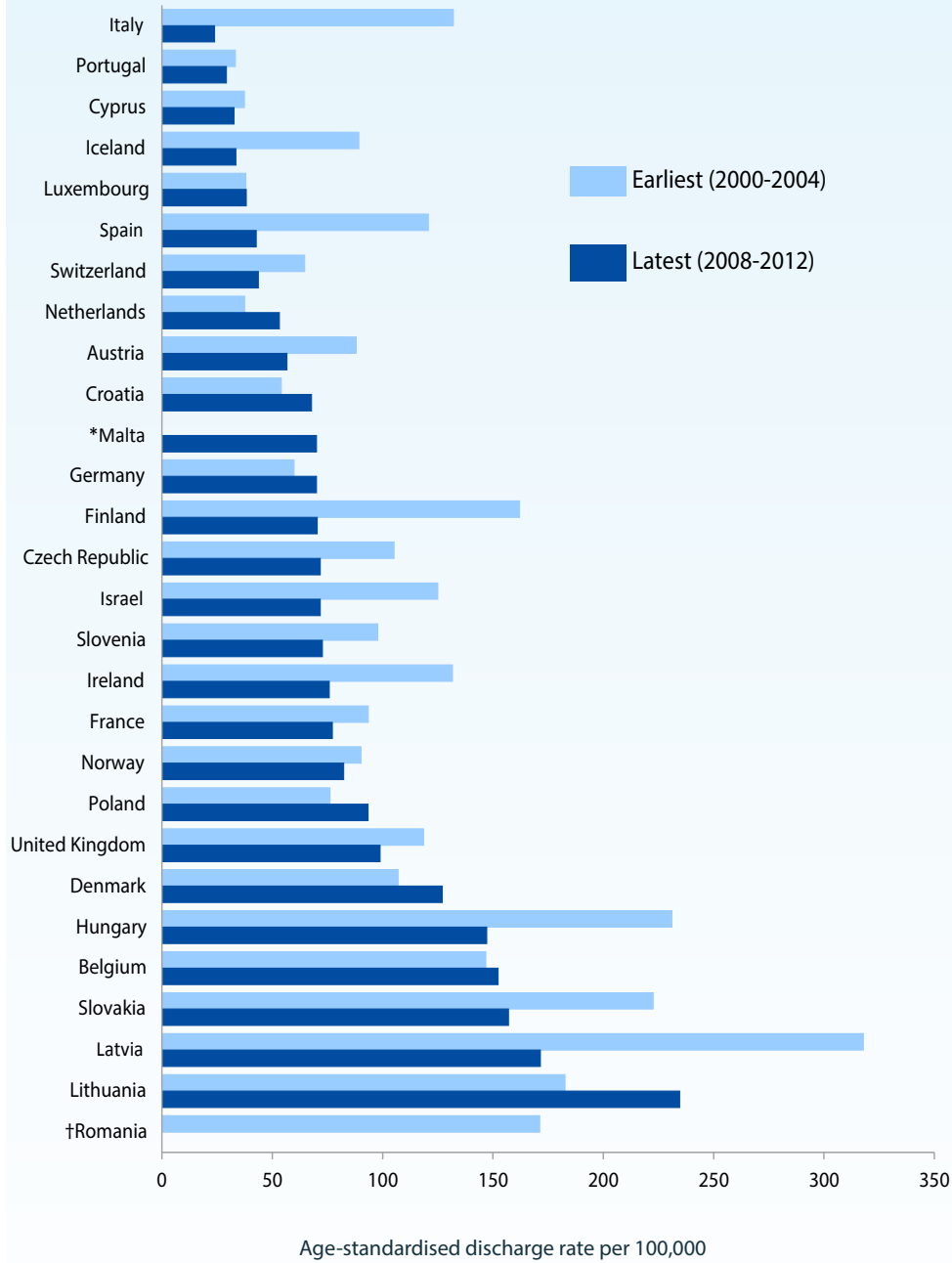
Age-standardised admission rates for asthma for earliest and latest available year in European countries ordered by latest admission rate.

Source: WHO Hospital Morbidity Database, accessed November 2013, plus Eurostat (for some earlier data).

Note: earlier data corresponds approximately to the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three study period.

* No data available for earliest time period.

† No data available for latest time period.



rates for asthma between European countries in recent years.

These all-ages rates conceal considerable variation in hospital admission rates between children (where rates are generally higher) and adults. Caution should be exercised when interpreting geographical differences and trends over time in asthma admission rates for pre-school children (where diagnostic overlap with acute bronchitis and bronchiolitis may occur) and for older adults (where chronic obstructive pulmonary disease may be confused with asthma).

Among 23 European countries, in recent years, there were close correlations between the national admission rates for younger and older children, and between younger and older adults (see Appendices Figures 1-3), but the correlations between rates for adults and children are less impressive (Figure 2).

Trends over time

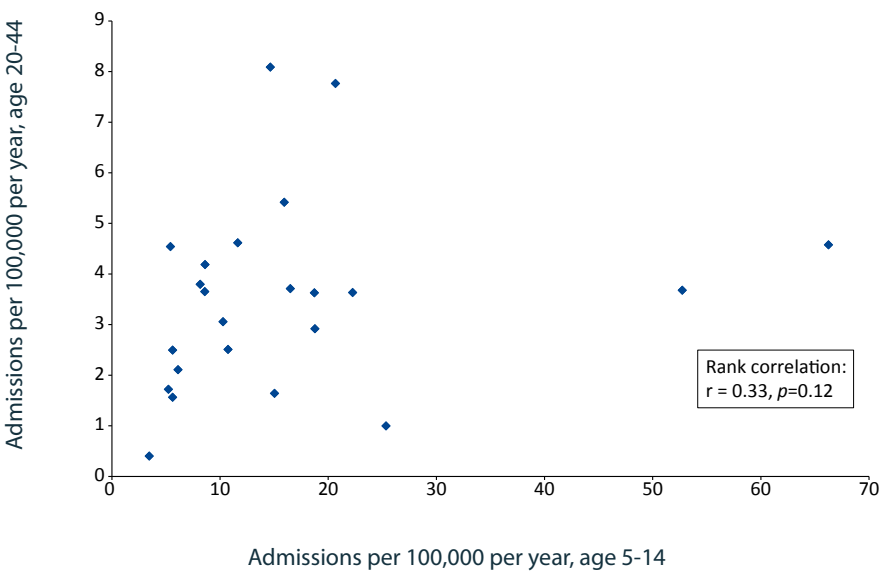
In most, but not all, European countries, age-standardised asthma admission rates declined through the last decade (Figure 1). In some countries, the reduction was two-fold or greater, a larger change than has been proposed as a target indicator of improvements in asthma care, for example by the Global Initiative for Asthma (GINA) and the Global Asthma Network. This recent decline is largely due to a reduction in admission rates among children, which is part of a longer-term rise and fall, peaking in the early 1990s. This is shown schematically in Figure 3 (based on data from several European countries, the United States of America, Canada, Australia, New Zealand, Hong Kong and Singapore).

Taking a 50-year perspective, the "epidemic" of asthma admissions bears no temporal relationship to two epidemics of asthma mortality (in the 1960s and the 1980s, related to the use of older asthma relievers with potentially toxic side effects), nor to time trends for self-reported asthma prevalence (Figure 3). However, data from the United Kingdom show a peak of primary care contacts for acute asthma, particularly among children, in the early 1990s, similar to that of asthma hospital admissions. This suggests a rise and fall in the incidence of asthma attacks in the community, rather than simply a change in patterns of referral to secondary care, or a reduction in the severity threshold for admission to the hospital ward.

An international comparison of time trends in asthma admissions and asthma drug sales in 11 countries during the 1990s found that increased sales of inhaled corticosteroids ("preventer" medication) were associated with a decline in rates of hospital admissions for asthma. However, inhaled corticosteroids became more widely used for asthma during the 1980s, a period of increasing hospital admission rates among children. Thus, it is not possible to draw firm conclusions about the extent to which uptake of effective "preventer" medication has reduced hospital admission rates for asthma in high-income countries.

Figure 2:

Asthma admission rates for European countries, age 5-14 v 20-44 years.



Source: WHO Hospital Morbidity Database, accessed November 2013.

Relationship of hospital admissions to other measures of the burden of asthma

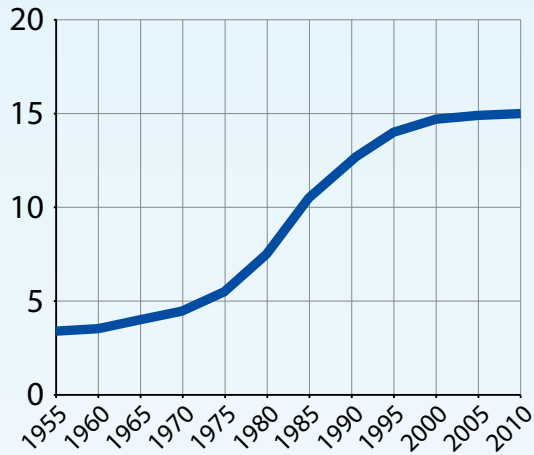
When national asthma admission rates for children were compared with the asthma symptoms prevalence and severity data for centres (but not whole countries) participating in the International Study of Asthma and Allergies in Childhood (ISAAC) Phase One study around 1995, a highly significant positive correlation was found between national admission rates and the prevalence of more severe asthma symptoms in 13-14 year olds (14 countries), but not in 6-7 year olds (11 countries). However, a similar analysis (prepared for this chapter) of ISAAC Phase Three data (collected around 2002) for 15 European countries with data in the older age-group, and 11 European countries in the younger age-group, found no statistically significant correlations between how the countries ranked against each other for national admission rates in children and how they ranked for any measure of wheeze or asthma prevalence, including more severe symptoms.

Figure 3:

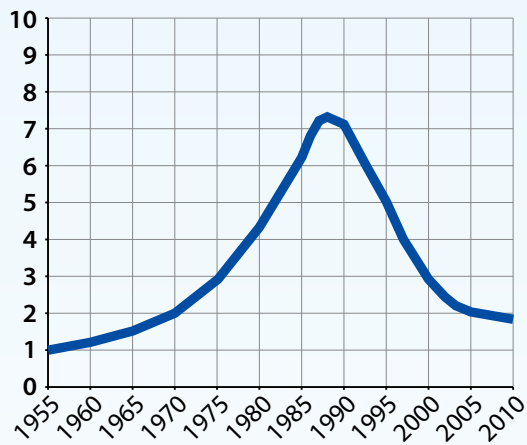
Long-term time trends in self-reported asthma prevalence, hospital admission rates and mortality rates for asthma among children in high-income countries.

Source: Chawla J, et al. Pediatric Pulmonology 2012.

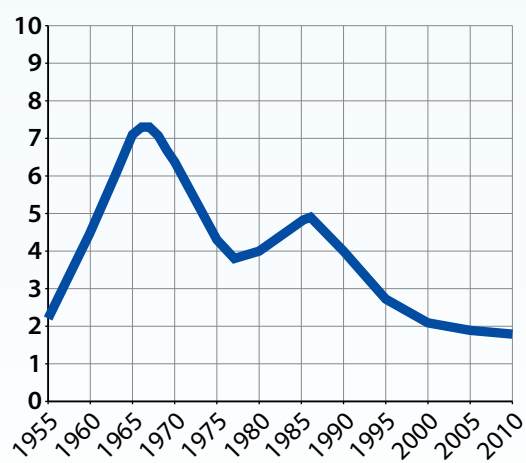
Self-reported asthma per 100 children



Asthma admissions per 1,000 children



Asthma mortality per 1,000,000 children

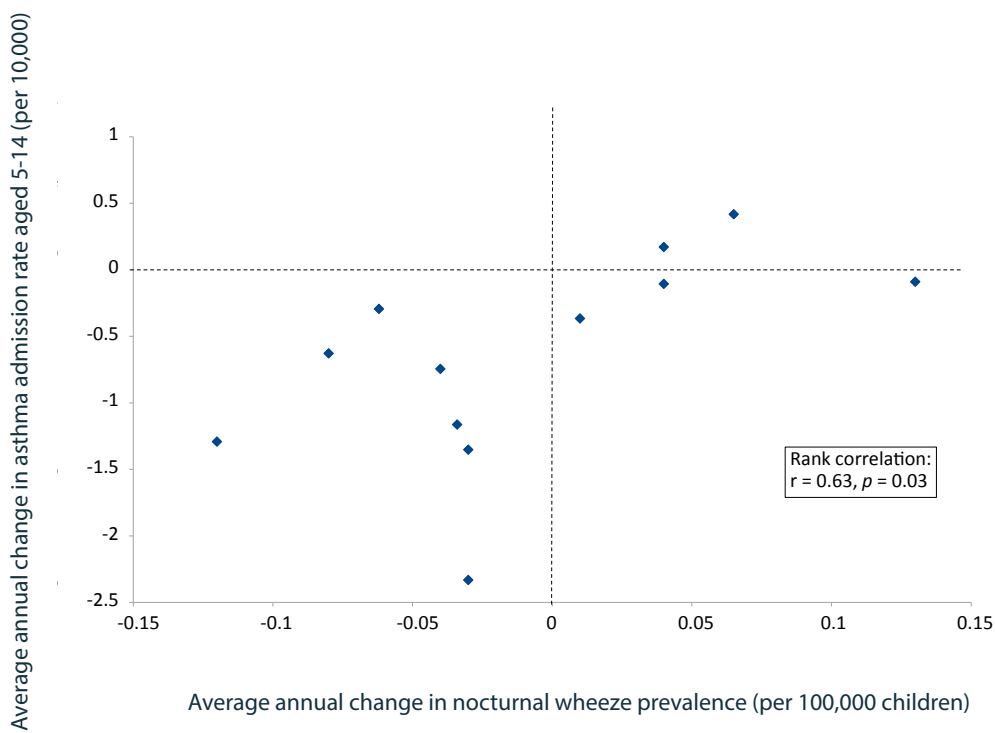


Such comparisons need to be interpreted with caution, because ISAAC centres are self-selected and are not necessarily representative of the countries in which they are located. Additionally, between-country comparisons at a single point in time are potentially biased in many ways. However, some of these biases become less relevant if within-country changes are examined over time.

For countries with ISAAC study centres participating in both Phase One and Phase Three, Figure 4 plots the annual change in childhood hospital admission rates (~1995-2002) against the change in the prevalence of wheeze causing 13-14 year old children to wake at night at least once a week. Over this period, admission rates declined in all these countries except Hong Kong and Poland. There was a significant positive correlation between the decline in prevalence of severe asthma symptoms between Phase One and Phase Three and the decline in the corresponding national admission rates for childhood asthma over a similar period.

Figure 4:

Annual change in hospital admission rates for childhood asthma (ages 5-14) by change in prevalence of nocturnal wheezing among 13-14-year-olds in countries with one or more ISAAC centres providing prevalence data for both ISAAC Phase One (around 1995) and ISAAC Phase Three (around 2002).



Sources: National admissions data from Anderson HR et al. IJE 2008; (updated by WHO Hospital Morbidity Database). Prevalence data fom Pearce NE et al. Thorax 2007.

Conclusion

Asthma admission rates have been proposed as a target indicator for monitoring progress towards improved asthma care. Large reductions in admissions have occurred already over the last decade in several countries.

However, currently routinely collected information is almost entirely restricted to high-income countries, limiting the value of admission rates for surveillance of the global burden of asthma. Large unexplained changes in admission rates have occurred over the past 25 years, particularly for childhood asthma, but international correlations of within-country change in prevalence versus within-country change in admission rates provide some support for the concept that changes in hospital admission rates can be used as an indirect indicator of the burden of more severe asthma in the community.

In countries which routinely collect admissions data, changes in hospital admissions over time may be used as an indirect indicator of the burden of more severe asthma. Before admission rates can be used as an indirect indicator of the global burden of severe asthma, more countries need to collect admissions data.

Key Recommendation

Health authorities in all countries should collect counts of hospital admissions in children and adults from defined catchment populations, to monitor trends in asthma over time.

4. Asthma Mortality

David Strachan, Elizabeth Limb, Neil Pearce, Guy Marks

Deaths due to asthma are uncommon but are of serious concern because many of them are preventable. Most deaths certified as caused by asthma occur in older adults, although comparisons of mortality rates have tended to focus upon children and younger adults. Over the past 50 years, mortality rates in these younger age groups have fluctuated markedly in several high-income countries, attributed to changes in medical care for asthma, especially the introduction of new asthma medications.

Avoidable asthma deaths are still occurring due to inappropriate management of asthma, including over-reliance on reliever medication rather than preventer medication.

International comparisons

Asthma is a rare cause of mortality, contributing to less than 1% of all deaths in most countries worldwide. Rates of death from asthma rise almost exponentially from mid-childhood to old age, so the majority of asthma deaths occur after middle age. However, there is considerable potential for diagnostic confusion with other forms of chronic respiratory disease in the older age groups, so comparisons of mortality rates have tended to focus on children and younger adults.

International mortality statistics for asthma are limited to those countries reporting a full set of causes of death. Figure 1 compares the mortality rates (age-standardised) for asthma among countries reporting asthma separately in recent years (around 2010). For some of the less populous countries with few asthma deaths, there is a substantial range of uncertainty around the published rate. However, among the more populous countries there is a 100-fold variation in age-adjusted rates, for instance between the Netherlands (low) and South Africa (high).

When the comparisons are limited to 5-34 year olds (Figure 2), numbers of deaths are fewer and margins of error are larger, but the disparities persist.

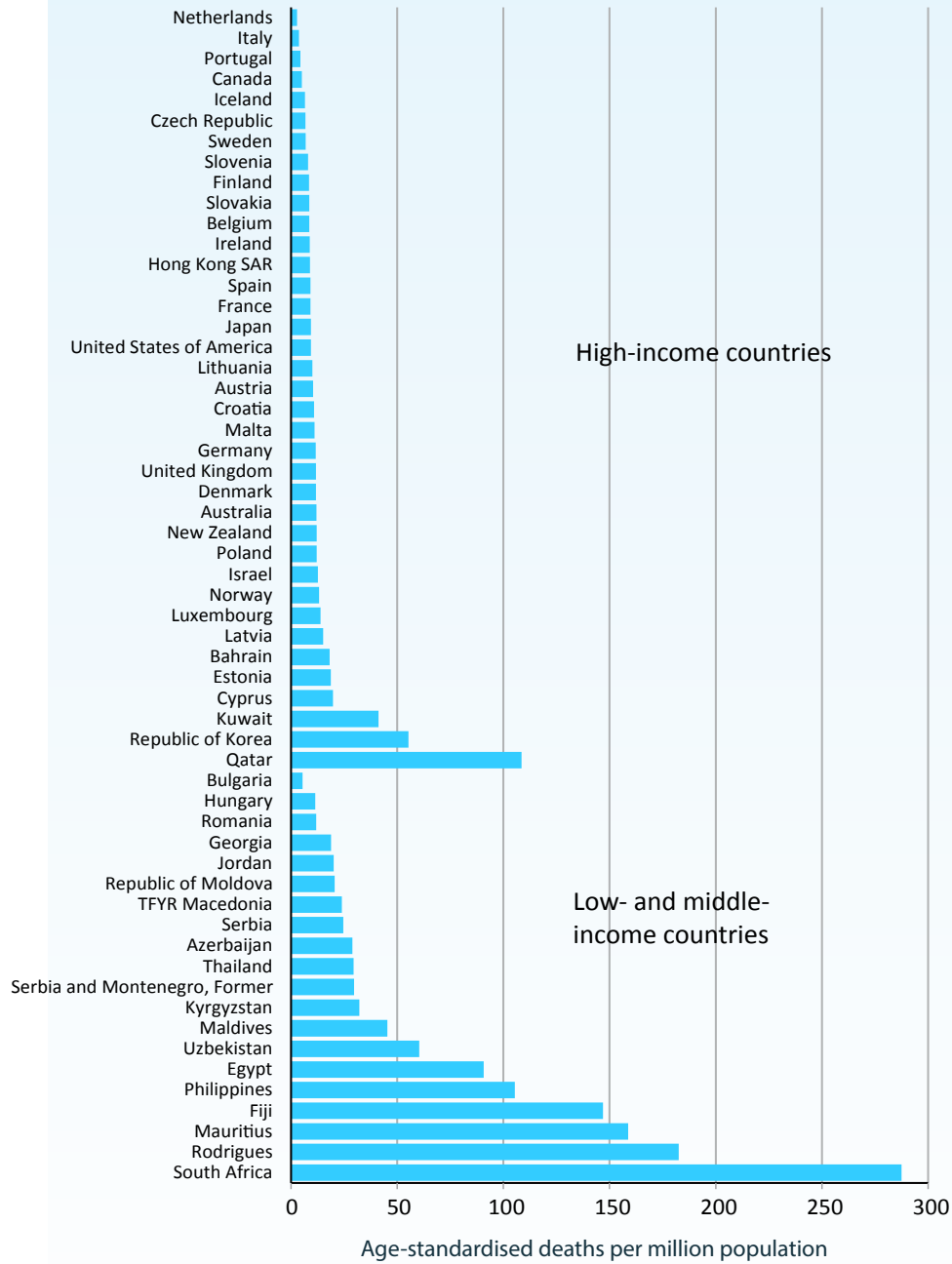
Trends over time

The Global Burden of Disease (GBD) Study estimates that age-standardised death rates from

Figure 1:

Age-standardised asthma mortality rates for all ages 2001-2010 from countries where asthma is separately coded as a cause of death, ordered by mortality rate and country income group.*

Source: WHO Detailed Mortality Database, February 2014 update.

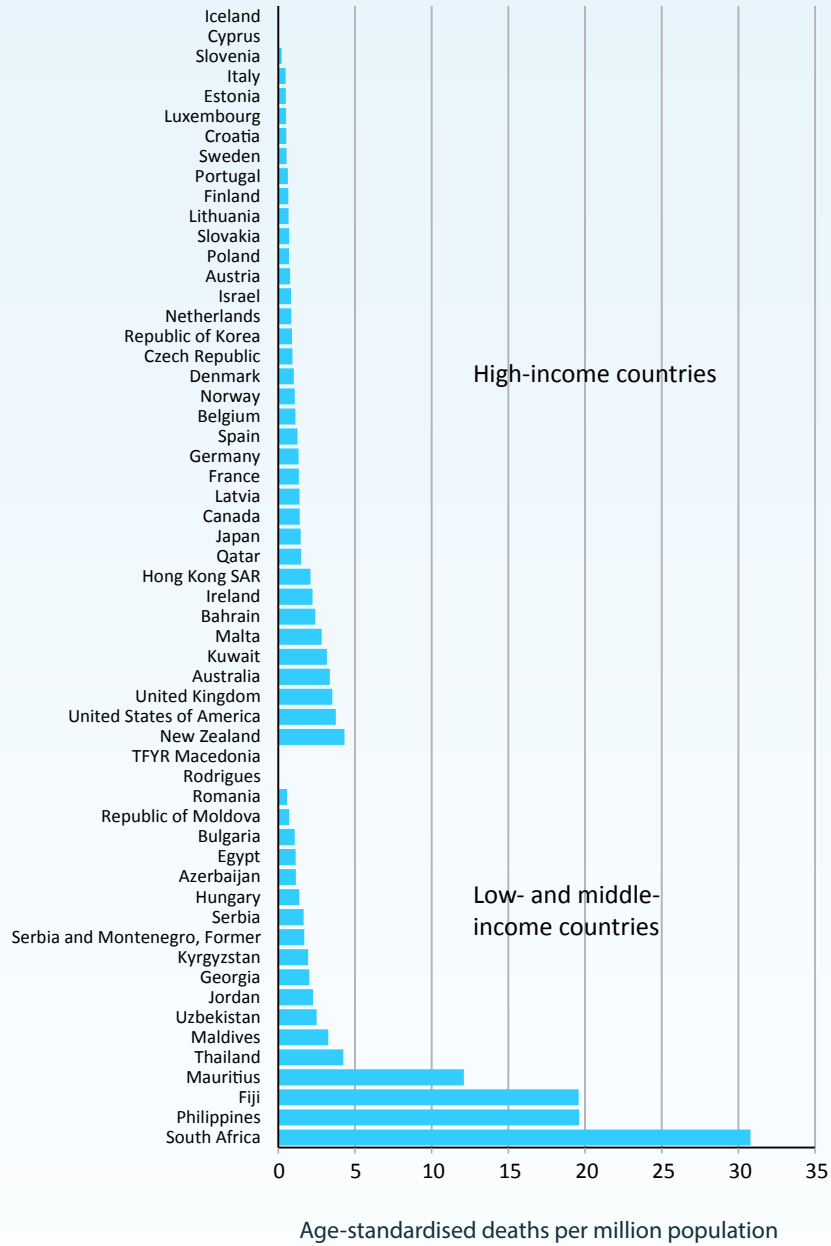


*Data standardised to the World Standard Population. Calculated from the average number of deaths and average population for each 5-year age-group over the period 2001-2010, using all available data for each country (the number of available years over this period ranged from 1 to 10).

Figure 2:

Age-standardised asthma mortality rates for ages 5-34 years only, 2001-2010 from countries where asthma is separately coded as a cause of death, ordered by mortality rate and country income group.*

Source: WHO Detailed Mortality Database, February 2014 update.



*Data standardised to the World Standard Population. Calculated from the average number of deaths and average population for each 5-year age-group over the period 2001-2010, using all available data for each country (the number of available years over this period ranged from 1 to 10).

asthma fell by about one-third between 1990 and 2010: from 250 per million to 170 per million among males, and from 130 per million to 90 per million among females. These worldwide figures include all ages.

More detailed comparisons have been made over a longer time period in high-income countries, focussing on younger age groups. Over the past half-century, there have been two distinct peaks in asthma mortality in a number of high-income countries (Chapter 3, Figure 3).

The first, during the mid-to-late 1960s, represented an approximately 50% increase in asthma death rates among 5-34 year olds. It is generally attributed to the introduction of high-dose isoprenaline inhalers as an asthma reliever medication, which can have toxic effects on the heart during acute asthma attacks. When these medications were withdrawn, the 1960s epidemic of asthma deaths subsided.

The second epidemic, during the mid-1980s, represented an increase of approximately 38% in asthma death rates among 5-34 year olds. In at least some of the affected countries, it was probably due to the widespread use of fenoterol, another inhaled asthma medication with potential cardiac toxicity. However, this second epidemic was also observed in some countries, such as the United States of America, where fenoterol was never approved or widely used.

Relationship of mortality to other measures of the burden of asthma

Taking a 50-year perspective, the epidemics of asthma mortality (related to the use of older asthma relievers with potentially toxic side effects) understandably bear little relationship to the time trends for asthma prevalence or hospital admission rates for asthma. In several high-income countries, asthma admission rates among children rose to a peak in the 1990s, after the 1980s peak in asthma mortality. However, both hospital admission rates and asthma mortality rates among children have been declining since 2000 in countries where they have been measured, whereas asthma prevalence has been stable or rising in many countries (Chapter 3, Figure 3).

When national asthma mortality rates for children were compared with the asthma symptoms prevalence and severity data for the International Study of Asthma and Allergies in Childhood (ISAAC) Phase One centres in the same countries, a significantly positive correlation was found between childhood asthma mortality and the prevalence of more severe asthma symptoms in both 6-7 year olds (29 countries) and 13-14 year olds (38 countries).

Such comparisons need to be interpreted with caution, because ISAAC centres are not necessarily representative of the countries in which they are located. However, when comparing mortality and hospital admission rates, national data can be used in both instances. Figure 3 shows this comparison for

24 European countries which have reported recent data for both outcomes. There is a significantly positive correlation between mortality and admission rates for asthma at all ages.

Avoidable factors in asthma deaths

Although asthma mortality rates have declined in many high-income countries, confidential enquiries in the United Kingdom have suggested that avoidable factors still play a part in the majority of asthma deaths.

The most recent comprehensive review, of 195 asthma deaths in the United Kingdom during 2012-2013, found that nearly half died without seeking medical assistance or before emergency medical care could be provided, and the majority were not under specialist medical supervision during the year prior to death. Only one-quarter had been provided with a personal asthma action plan, acknowledged to improve asthma care, and there was evidence of excessive prescribing of short-acting reliever medication, under-prescribing of preventer medication, and inappropriate prescribing of long-acting beta-agonist bronchodilator inhalers as the sole form of treatment.

These observations, from a high-income country with a tradition of evidence-based medicine and a national health service which is free at the point of use, suggest that improved access to appropriate asthma medication is a key goal in reducing asthma mortality worldwide.

Conclusion

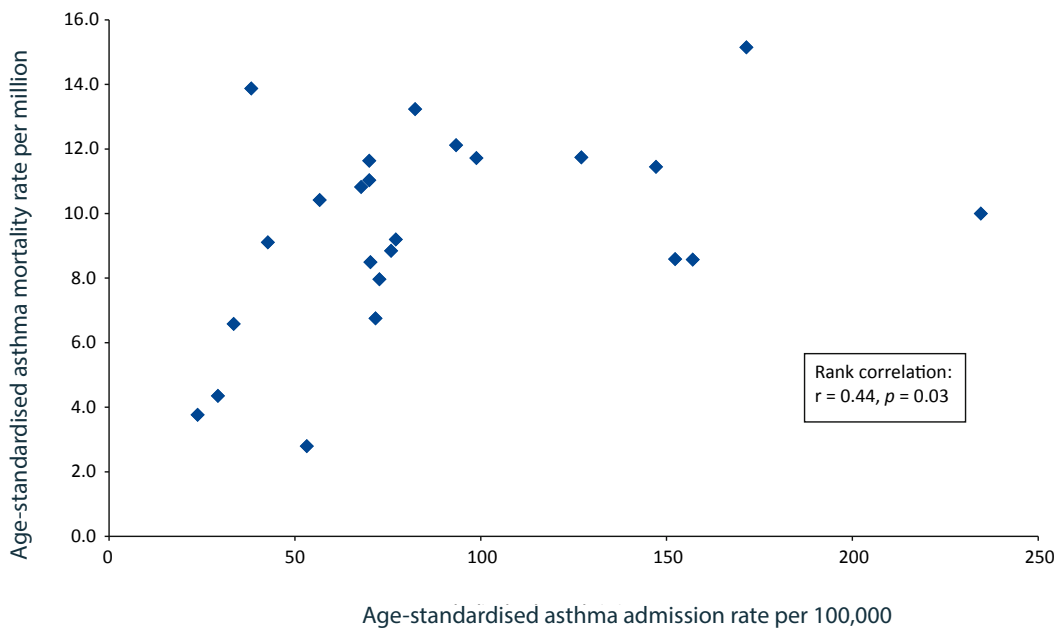
Asthma deaths represent the "tip of the iceberg" with respect to the global burden of asthma. Although the risk of any individual asthmatic patient dying of their disease is thankfully very low, continued surveillance of asthma mortality rates is essential to monitor progress in asthma care, and as an early warning of epidemics of fatal asthma, as have occurred in the past half-century.

Key Recommendation

Health authorities in all countries should report rates of asthma deaths in children and adults to monitor progress in asthma care and as an early warning of epidemics of fatal asthma.

Figure 3:

Age-standardised asthma mortality rates and age-standardised hospital admission rates for asthma, in European countries providing recent data for both (2001-2010).



Sources: WHO Detailed Mortality Database, February 2014 update, WHO Hospital Morbidity Database, accessed November 2013.

5. Wheezing in Infants

Javier Mallol, Luis García-Marcos, Paul Brand

Recurrent wheezing in infants is the most common clinical expression of asthma at that age. It should no longer be considered a benign condition that disappears later in childhood, particularly because many of these infants develop frequent and severe episodes. Early diagnosis and effective management of troublesome recurrent wheezing may decrease the high proportion of infants with recurrent wheezing who have severe episodes as well as visits to the Emergency Department and admissions for wheezing during the first year of life.

International Study on Wheezing in Infants

The largest multi-centre study of wheezing in the first year of life, the International Study on Wheezing in Infants (Estudio Internacional de Sibilancias en Lactantes, EISL), has contributed new information about therapeutic approaches to recurrent wheezing (RW). Data from this cross-sectional study including 30,093 children in 17 centres: 25,030 in 12 centres in Latin America and 5,063 from 5 centres in Europe were published in 2010 (Figure 1). RW in the first year of life, defined as having three or more episodes of wheezing during that time, is common (20%), with a high proportion of these infants suffering from frequent and severe episodes. EISL found that 32.2% of infants with RW have 7 or more episodes (32.3% in Latin America and 31.8% in Europe); 71% reported visits to the Emergency Department (ED) due to wheezing (74% in Latin America and 55% in Europe); and 26.8% reported admission for wheezing during the first year of life (28.4% in Latin America and 14.2% in Europe) (Figure 2). Overall, these figures imply a high burden of health costs for countries and parents in terms of use of health facilities and medications.

The Common Cold

EISL found a strong association between RW during the first year of life (both in affluent and non-affluent countries) and: common viral respiratory illnesses (the symptoms of such illnesses are that of a cold) during the first 3 months of life; attending day-care; wheezing in the first three months of life; male gender; the mother smoking during pregnancy; and family history of asthma or rhinitis. Breast feeding for >3 months and high maternal education showed a protective effect. Thus, avoiding smoking during pregnancy, delaying day-care attendance, breastfeeding babies for at least 3 months, and improving maternal education could be effective strategies for decreasing the prevalence of RW.

Recurrent wheezing in infants, particularly if they are presenting with frequent and/or severe episodes, should be diagnosed and managed as asthma, unless there is evidence to the contrary.

There is increasing evidence that having a cold in the first year of life plays an important role in the commencement and/or maintenance of wheezing and asthma in early life. Wheezing illnesses in infants, caused by human rhinovirus and respiratory syncytial virus (RSV) among other things, are robust predictors of subsequent development of asthma, decreased lung function, and increased bronchial responsiveness in school age children. Common cold viruses are by far the most frequent cause of asthma exacerbations at any age.

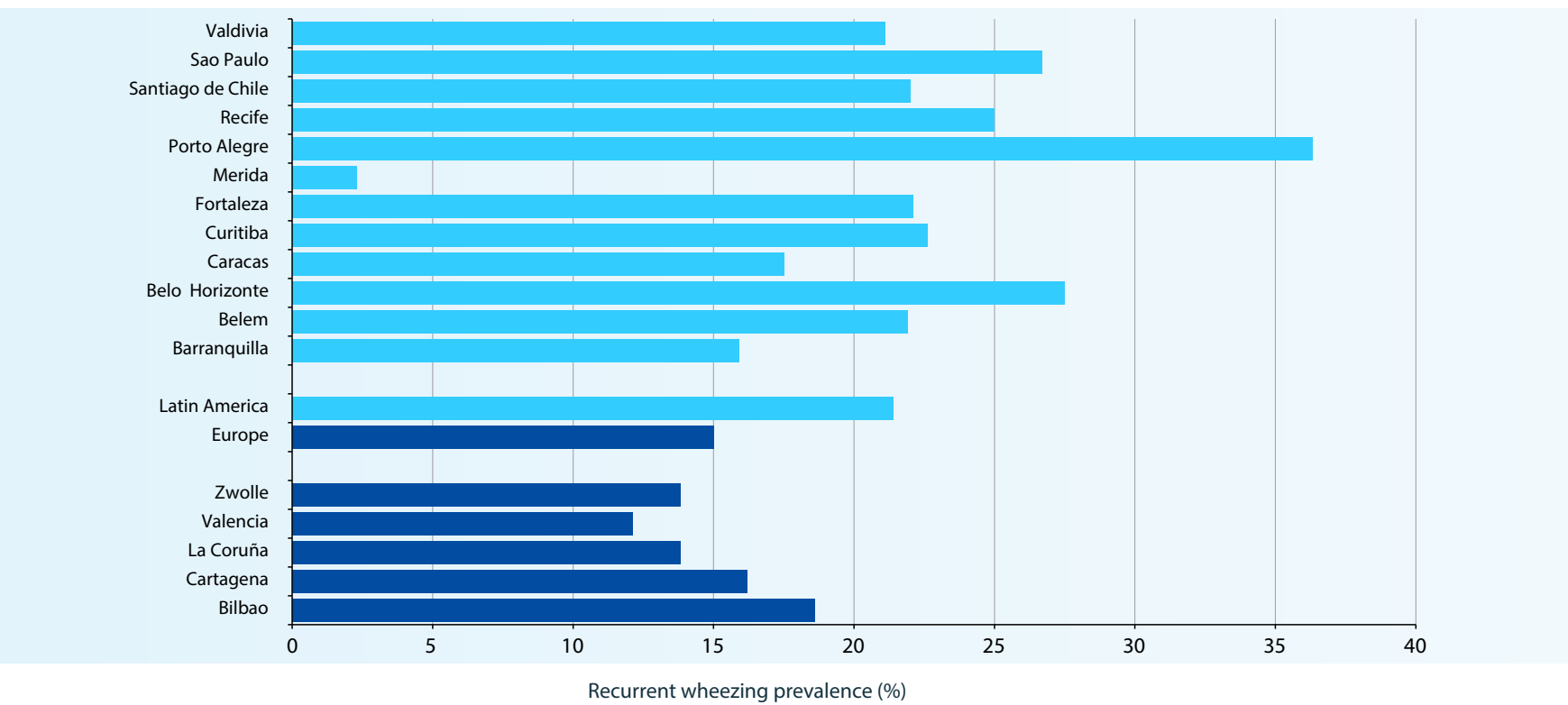
While there is no consensus on the effectiveness of medical interventions for RW in the first year of life, these infants - particularly if episodes are frequent and/or severe - are frequently treated with asthma medicines, both in hospitals and in primary care. Ninety-one percent of infants with RW used inhaled bronchodilators and 46% used inhaled corticosteroids (ICS) with differences between regions (Figure 2). Evidence-based guidelines also suggest using clinical severity signs (higher frequency and severity of wheezing episodes) as key indicators for starting therapy with ICS in preschool wheeze, with the aim of decreasing the number and severity of wheezing exacerbations. The ways that wheezing is classified in preschool children in clinical and epidemiological studies do not reliably predict the outcome of wheeze over time or the response to ICS treatment. In addition, these classifications of wheezing are difficult to identify in clinical practice and can even change within the first year of life. Thus these classifications of wheeze are not helpful for clinicians when they are deciding treatment for infants with RW.

Management

The effectiveness of ICS in treating children with more severe or persistent symptoms of preschool wheeze in children over 12 months of age is well established. In EISL the high proportion of infants with severe symptoms of RW leading to ED visits, hospital admissions, sleep disturbance, and impaired quality of life, may be partly explained by poor recognition and management of infants with troublesome recurrent asthma symptoms. Contributing factors may include a reluctance to diagnose asthma in young children, a delay in starting proper treatment, prescription of medicines with doubtful efficacy (antileukotrienes) or proven absence of efficacy (antibiotics, cough syrups, antihistamines, among others), or poor education of parents about how to use inhalers and spacers. We suggest outcomes for infants with RW would be improved if the use of ICS could be improved, i.e. a sufficient dose taken over a sufficient time with good adherence.

Figure 1: Prevalence of recurrent wheezing during the first year of life in European and Latin American centres.

Source: Mallol J, et al. Thorax. 2010.



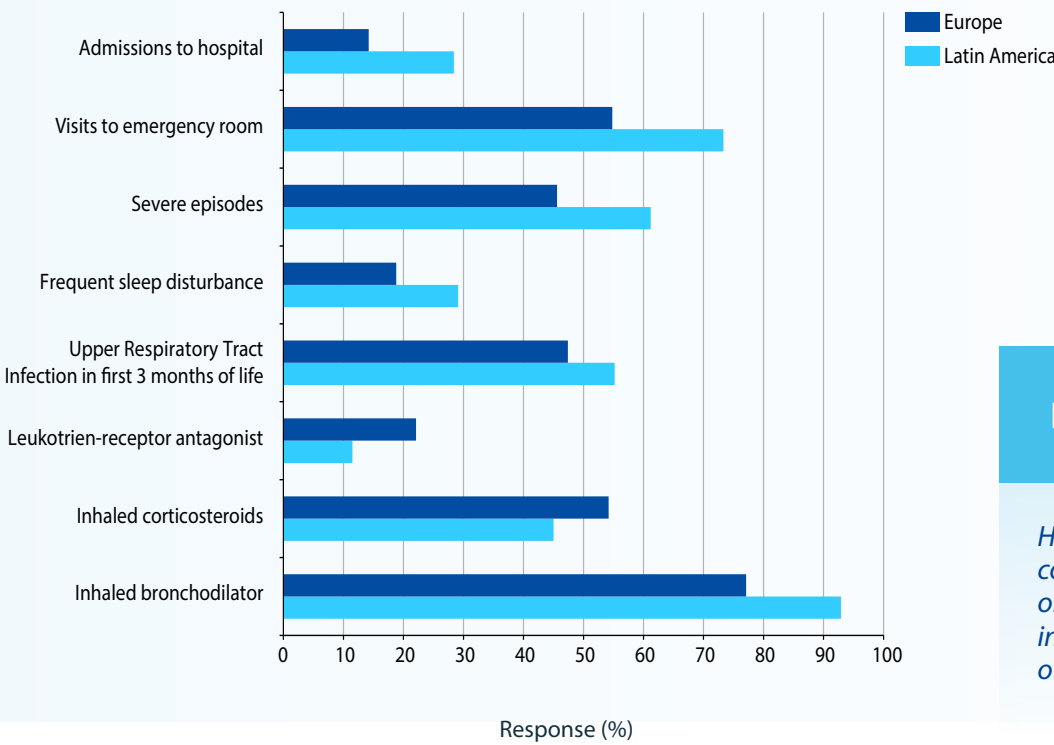
Conclusion

The EISL data strongly supports the need for efficient, realistic, and easy-to-implement strategies for the education and management of infants with recurrent asthma symptoms, directed at both parents and health care workers, especially in developing countries. Early identification and proper management of infants with recurrent troublesome asthma symptoms is likely to decrease the prevalence of severe episodes, ED visits and hospital admissions, use of inappropriate medications, and other complications. This requires a paradigm shift: health care workers and authorities should no longer consider RW in infancy, especially when frequent and/or severe episodes are present, as a benign condition.

Figure 2:

Reported severity, medications and other variables in infants with recurrent wheezing during the first year of life.

Source: Mallol J, et al. Thorax. 2010.



Key Recommendation

Health professionals in all countries should regard frequent or severe recurrent wheezing in infancy as part of the spectrum of asthma.

6. The Economic Burden of Asthma

Mohsen Sadatsafavi, J Mark FitzGerald

It is difficult to quantify the global economic burden of asthma, but estimates for separate countries and regions are tremendously high. The indirect costs of asthma, especially its negative impact on productivity, is at least as large as its direct costs. Attempts to reduce the economic burden of asthma should move towards better management of asthma. Improving access to care and adherence to evidence-based treatment can reduce the economic burden of asthma, even in locations where prevalence is rising.

Controlled asthma imposes far less of an economic burden than non-controlled asthma. Strategies towards improving access and adherence to evidence-based therapies can therefore be effective in reducing the economic burden of asthma in both developed and developing countries.

Challenges in estimating the global economic burden of asthma

Diseases can cause economic loss in a number of ways. They can impose direct costs through consumption of resources (e.g., hospitalisations, physician visits, and medications), as well as indirect costs through loss of productivity. Globally, as a major non-communicable disease, asthma creates a tremendous economic burden, although the exact quantification of this burden is challenging. What is clear is that the economic burden of asthma is high, adding to the need for it to be recognised as a public health priority.

Attaching numbers to the economic burden of asthma is fraught with several challenges. One challenge is how to attribute resources to asthma. For example, it is difficult to tease out the contribution of asthma to depression in a patient with both conditions, or to attribute how many days of sick leave are due to asthma. Even estimating the prevalence of asthma, a key factor in estimating the burden at the regional and national level, is difficult, as seen in Chapter 2, given the inconsistencies in definition, as well as under-diagnosis and over-diagnosis of asthma in different subgroups of individuals.

What we know about the global burden of asthma

Most studies on the burden of asthma are from developed countries, where national surveys of diseases and large, administrative databases, can be interrogated to provide a broad picture of the burden. The one systematic review (2009) illustrates the variation within countries and the relative lack of information from low-and middle-income countries. A recent study in the United States of America estimated that the total cost of asthma to society was $56 billion in 2007, or $3,259 per person per year (in 2009 US dollars).

A further European study in 2011 has estimated the total cost of asthma in that year to be €19.3 billion among Europeans aged from 15 to 64 years (in 2011 Euros). In a separate study in the Asia-Pacific region, the sum of direct and indirect costs of asthma per person per year ranged from $184 in Vietnam to $1,189 in Hong Kong (in 2000 US dollars). Furthermore, there is a significant variation in cost estimates even among the studies from the same country. For example, US-based estimates of the cost of asthma per person vary up to five-fold. Despite the heterogeneous settings and different numbers, many studies have pointed towards the fact that the indirect cost of asthma is at least as large as its direct costs. This is not a surprising finding: disability from asthma affects individuals who are often at the most productive phase of their working lives, and parents of dependent children with asthma are also often in the workforce. Research also suggests that the contribution of "presenteeism" (individual loss of function when at work) is larger than absenteeism (inability to come to work) in patients with asthma. A recent Canadian study has shown that, compared with controlled asthma, uncontrolled asthma results in a $184 (in 2012 Canadian dollars) loss of productivity during a week for such a person, 90% of which is attributable to presenteeism.

The preventable burden of asthma: the importance of clinical control

Currently, asthma cannot be cured, and there are limited evidence-based options to prevent its development. The emphasis of asthma management is therefore focused on achieving clinical control with an added priority of preventing the future risk of exacerbations. Strategies which result in well-controlled asthma are associated with a significant reduction in economic burden compared to uncontrolled disease, as shown by programmes implemented in Salvador (Brazil) and Finland (for more examples see Chapter 8). Despite the wide availability of effective medications for several decades, asthma remains uncontrolled in a substantial proportion of the population. Thus, the incremental economic burden of uncontrolled asthma is of particular relevance to decision makers as it represents the aspect of the burden that is preventable.

Low adherence as a major cause of preventable burden

Research in diverse jurisdictions, including both developed and developing countries, has consistently shown that adherence to controller medications is poor. The evidence linking adherence to controller medications with better asthma outcomes is strong, making adherence a modifiable factor and a potential target for reducing the economic burden of asthma.

Improving access to care and adherence to evidence-based medication

Given the proven benefit of existing essential asthma medicines for most asthma patients, improving access and adherence to such treatments should be a major global priority (see chapter 12). In developing countries, additional barriers to delivering effective management may include poverty, poor education, and poor infrastructure, indicating that a more comprehensive approach is required, including political commitment to better asthma care (see Chapter 12). In both developing and developed countries, improving adherence to controller treatment requires education of both care providers and patients about its long-term benefits. Developing interventions such as shared care models for asthma management, or the use of communication technologies to facilitate interaction between patients and care providers,

can be beneficial. The role of health literacy and the socio-cultural context in which the patients find themselves are also important.

A small fraction (less than 10%) of patients with asthma which is difficult to control (refractory asthma) do not respond to conventional controller therapies and depend on treatments that are currently very expensive and only accessible in certain parts of the world. Reducing the cost of these treatments and making them accessible across the world will help reduce the burden due to refractory asthma. This requires the coordinated efforts of industry, government, non-governmental organisations (NGOs), and international organisations such as the World Health Organization (WHO).

Conclusion

Most countries have not yet estimated the costs of asthma. Where it has been estimated, the economic burden of asthma is great because of direct healthcare costs, and indirect costs, as a result of loss of productivity due to people being absent from work, or working less effectively while at work. The impact of these indirect costs would be diminished by improving asthma control, through improving access to good management including medicines.

Key Recommendation

Governments should measure and monitor the economic costs of asthma in their countries, including health care costs and productivity losses.

7. Factors Affecting Asthma

Neil Pearce, David Strachan

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 process or trait (about which much less is known). Both groups of factors may contribute to the severity and persistence of asthma.

Parental smoking (for children) and occupational exposures (for adults) are the clearest examples of remediable causes of asthma.

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.

The role of allergy?

Asthma used to be thought of as an allergic disease, where allergen exposure causes sensitisation to allergens and continued exposure leads to the processes in the airway which lead to asthma symptoms. While allergy is a potential underlying factor for up to half of the people with asthma, the remainder have no allergic features. In low- and middle-income countries the proportion of people with non-allergic asthma is greater than in high-income countries. Furthermore, some occupational causes of asthma do not appear to involve allergy. These non-allergic mechanisms are currently not well understood.

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 tobacco smoke exposure, 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), and medicines (including aspirin).

Causes of the underlying asthma trait - environmental factors: Facts and theories

Environmental factors are much more likely than genetic factors to have caused the large increase in the numbers of people in the world with asthma, but we still do not know all the factors which may be important and how they interact with each other.

Secondhand smoke is a confirmed risk

Secondhand tobacco smoke has been confirmed as a risk for asthma both in childhood and adulthood (see references at the end of the report). 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, such as cooking on an indoor open fire, 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, inviting further research. Few people with asthma are demonstrably allergic to fungal moulds. Dampness in homes 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?

Asthma 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 asthma symptoms, but this may also be "reverse causality"; people with asthma symptoms may avoid using aspirin, since it is a known trigger of wheezing attacks in a small proportion of asthmatics, who use paracetamol instead.

Occupational exposures

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.

Preventive and remedial measures

Eat a balanced diet

Prolonged exclusive breastfeeding was once thought to protect against allergic diseases, including asthma, but extensive research has shown that this is not 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 diets that are widely recommended to prevent cardiovascular diseases and cancer may slightly reduce the risk of asthma. A link has been established between obesity and asthma, although the mechanisms are not clear.

Avoid exposure to causal agents

Occupational exposures provide some of the clearest examples of remediable causes of asthma. Special care is required in high-risk occupations (baking, woodworking, farming, exposure to laboratory animals, and use of certain chemicals, notably paints containing isocyanates) to minimise inhalation of potentially harmful substances, and care to reduce exposure to chemical cleaning agents in the home is also needed.

Don't smoke or go near second hand smoke

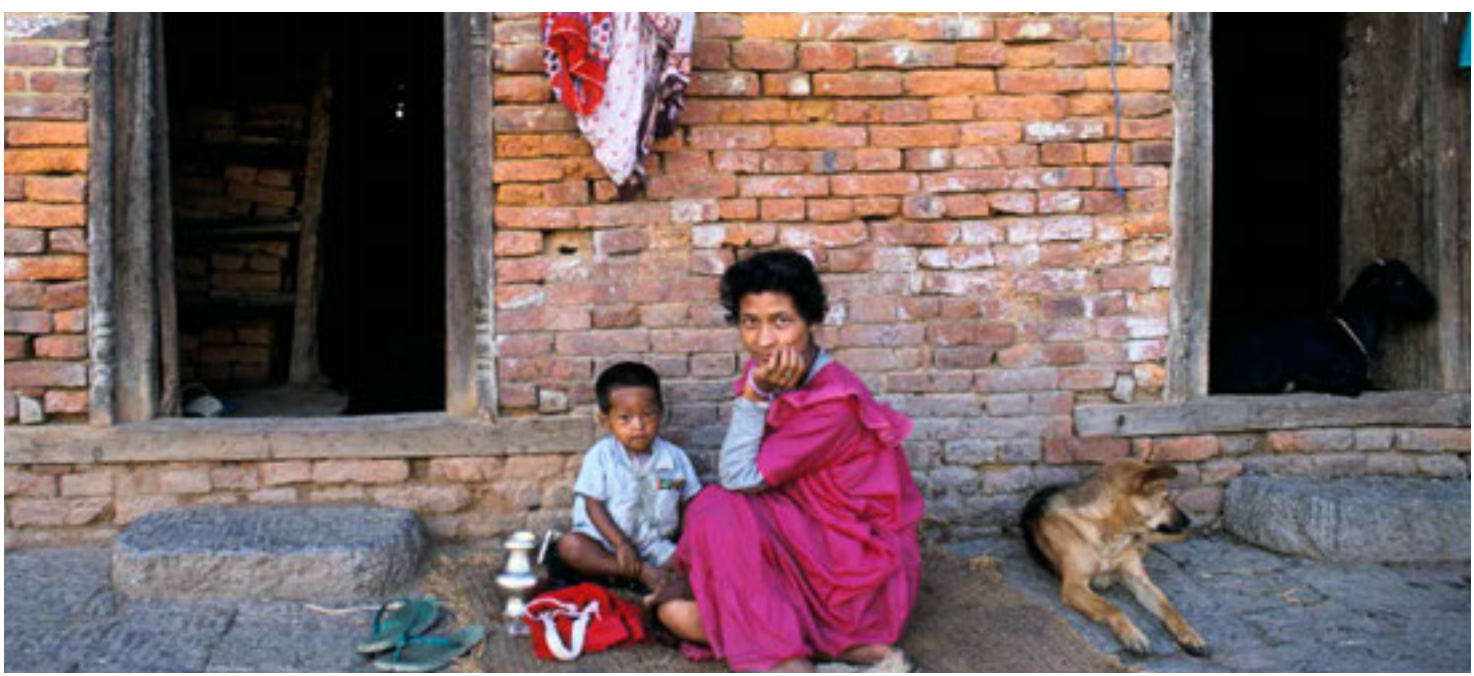
Smokefree environments are important for people of all ages. Little is known about the factors affecting asthma after middle age, when there is substantial overlap between the reversible airflow obstruction, which is typical of asthma, and the irreversible airflow obstruction of chronic obstructive pulmonary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

Conclusion

Environmental factors are much more likely than genetic factors to have caused the large increase in the numbers of people in the world with asthma. Tobacco smoking and secondhand tobacco smoke are avoidable by the individual. Occupational exposure is a risk diminishable by both workplace practices and government policies. These and other factors require further research.

Key Recommendation

Governments should strengthen policies to reduce tobacco consumption, encourage healthy eating, and reduce exposure to potentially harmful chemicals, smoke, and dust. Funders need to support further research to identify causes of asthma.



Quality-assured asthma medicines need to reach everyone with asthma.

PART TWO:

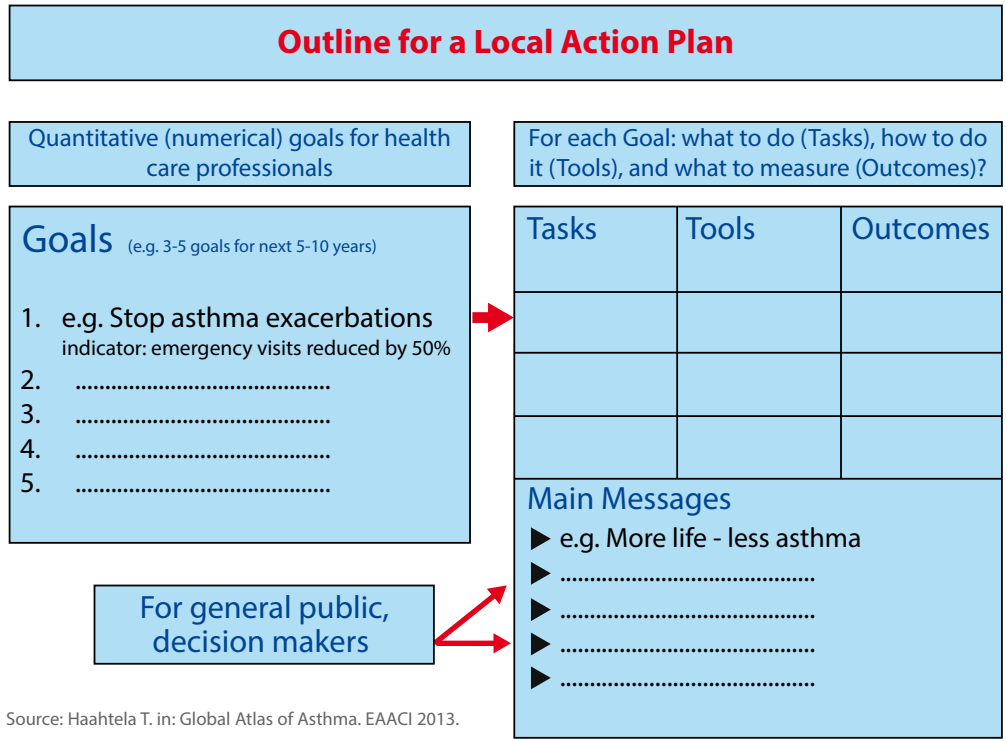
MANAGEMENT OF ASTHMA AND CAPACITY BUILDING

8. National Asthma Strategies

Tari Haahtela, Olof Selroos Philippa Ellwood, Nadia Aït-Khaled

There are many examples worldwide of systematic strategies which have successfully reduced the burden of asthma, in low-, middle- and high-income contexts. Properly implemented strategies have been proven repeatedly to work. From the public health perspective, the key issue in reducing the burden of asthma is to implement the best standards of care in everyday practice. The benefits can be remarkable; systematic implementation of the best standards of care can reduce both human suffering and the associated societal costs. It is the responsibility of asthma experts and healthcare professionals to collaborate with national public health authorities and international organisations to improve efficiency in management and care. In 2013, roughly 1 in 4 countries had national asthma strategies in place, for children and/or adults.

Figure 1: Generic template for a local action plan.



Source: Haahtela T. in: Global Atlas of Asthma. EAACI 2013.

Successfully managed asthma

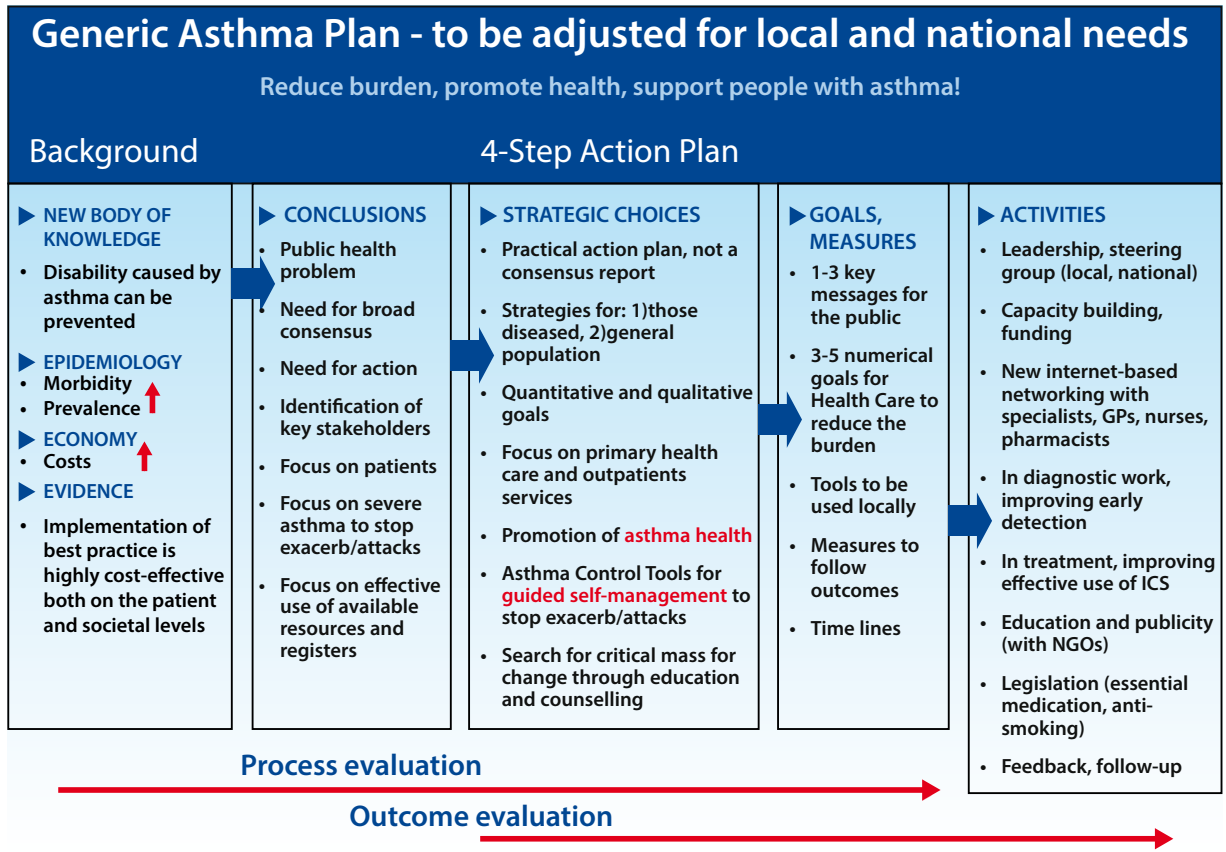
When asthma is successfully managed, the person with asthma will have no symptoms or only very mild symptoms, no attacks, no emergency department visits, no limitation of exercise or activities, no loss of sleep due to asthma, minimal use of an asthma reliever medicine(<2 times/week), and the least side effects possible of asthma medicines. The person will have no impediments to their lifestyle due to asthma, and will be able to attend their place of education or work with no time off due to asthma. National asthma strategies are aimed at achieving successful management for all people with asthma.

Examples of successful strategies

In Finland, patients and society have benefitted from the systematic and consistent development and implementation of asthma management. A comprehensive nationwide Asthma Programme was undertaken from 1994 to 2004 to lessen the burden of asthma on individuals and society. In 2010, it was estimated that the total asthma costs (healthcare, drugs, disability, and productivity loss) would have been €500-800 million annually by then, if nothing had been done and if 1990s trends had continued. However, the realised costs in 2010 were less than half of that, around €200 million. This implied a potential cost saving from €300-600 million every year, depending on the scenario used.

Figure 2:

Strategic flow for an asthma plan.



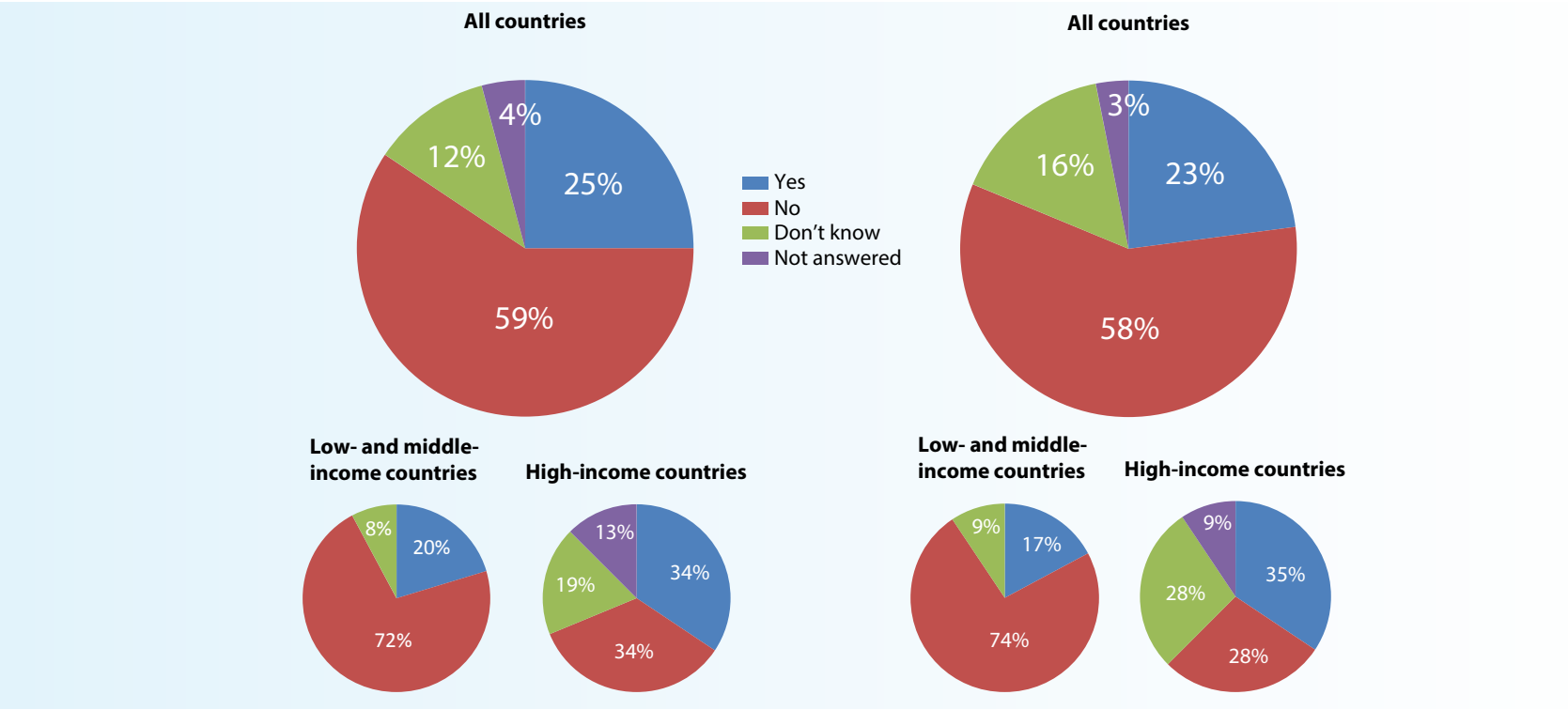
Source: Haahtela T, et al. Allergy 2008.

Several other encouraging examples now exist, e.g. in Poland, Portugal, Brazil, and recently in Costa Rica. As not all such programmes are reported, we encourage publication of strategies and outcomes. The problems to be addressed are different in high-income compared to low- and middle-income countries, and the solutions need to be tailored according to local needs and resources. There is, however, no question that the burden of asthma can be markedly reduced using strategies that have been adapted to the local societal, economic and health care environments.

Patients from a low resource setting in Salvador, Brazil, received free medication for asthma and rhinitis in accordance with international guidelines. The outcome was impressive. The costs for asthma care were reduced on average by US$ 733 per patient per year for the families and by US$ 387 per patient per year for the public health system. In the entire Salvador population a 74% reduction in asthma hospitalisation rates occurred after the implementation of the programme. The educational effort targeting both patients and professionals was paid back in a few years. In Benin, in 2008 a pilot study of asthma management was conducted. The cohort analysis after one year of standardised management (see Chapter 12) demonstrated a dramatic decrease in asthma severity, the number of exacerbations and hospitalisations (see Chapter 14).

Asthma burden can be rapidly reduced by the implementation of relatively simple measures within a systematic strategy to improve early detection and provide effective anti-inflammatory treatment.

Figure 3: National asthma strategies for children and adults in countries responding to the Global Asthma Network survey, 2013.



Inhaled corticosteroids are essential to success

Asthma projects and programmes in Argentina, Australia, Brazil, China, Japan, Mexico, the Philippines, Russia, South Africa, and Turkey were discussed in 2009 in Berlin by a group of experts in asthma care, the Advancing Asthma Care Network. Their report "Asthma programmes in diverse regions of the world: challenges, successes and lessons learnt" concluded that the major barriers for all programmes are: 1) low rates of dissemination and implementation of treatment guidelines, 2) low levels of continuing medical education and training of primary health care professionals, and 3) poor access to and distribution of inhaled corticosteroids. Additionally, under-diagnosis and inadequate treatment further limit the success of less developed programmes.

All successful asthma programmes seem to have the following characteristics: 1) improving early diagnosis and the introduction of first-line treatment with anti-inflammatory medication (mainly inhaled corticosteroids), 2) improving long-term disease control, 3) introducing simple means for guided self-management to proactively prevent exacerbations/attacks, and 4) effective education and networking with general practitioners, nurses and pharmacists. A systematic approach is required and must aim to motivate and organise. Improvements can be achieved with relatively simple means. All the main stakeholders should be represented when multidisciplinary actions are being planned.

Especially important is the involvement of the non-governmental patient organisations, which are aware of the grass-root problems. Any programmes should set 3-5 goals, preferably accompanying each with at least one quantifiable indicator and target. For example, one goal could be to reduce asthma exacerbations, measured by the number of emergency visits, with the target of reducing emergency visits by 50% over the next 3-5 years. For each goal, more specific targets (what to do?), tools (how to do it?) and outcomes (what to follow and measure?) should be defined (Figure 1). The strategic flow for a programme is indicated in Figure 2.

Regardless of the health care system and its coverage, experience gained from national and local interventions should be brought

Key Recommendation

Health authorities in all countries should develop national strategies and action plans to improve asthma management and reduce costs.

together. A major change for the better can be achieved by local efforts, systematic planning, and networking to implement the best possible asthma management practice. The gains can be remarkable, both in reducing human suffering as well as associated societal costs. The asthma burden can be tackled, and it is the responsibility of asthma experts and healthcare professionals to collaborate with national public health authorities and international organisations to improve efficiency in management and care.

Following in the successful footsteps of the Asthma Programme in Finland 1994-2004, an Allergy Programme 2008–2018 was launched there to combat the allergy epidemic, and to further assist the asthma epidemic. This new activity aims to increase immunological tolerance and improve management of severe allergy phenotypes, including asthma. The early results are promising and, in addition, economic costs for all allergy and asthma are declining.

Global Asthma Network survey 2013-2014: national asthma strategies

A short survey for Global Asthma Network (GAN) centres was carried out in 2013. One of the questions was: "Has a national asthma strategy been developed in your country for the next five years? For children, for adults?" Of the 96 countries that answered, 25% had a programme for children and 23% had one for adults. Of the high-income countries (n=64), 34% reported a programme for children and 35% reported one for adults, while the corresponding figures were 20% and 17% for the low- and middle-income countries (n=32) (Figure 3). The details of the programmes are quite variable and would need further evaluation. Only a few countries have reported results of any nationwide, comprehensive programme.

Conclusion

Generally, asthma responds favourably to effective drug treatment. The earlier the correct diagnosis is obtained, the better the response. Patients should adhere to long-term management, use inhalers correctly, and proactively prevent exacerbations by themselves after receiving education. In Europe, improved management has resulted in a remarkable decline in mortality (6287 asthma deaths in 1980 and 1164 in 2012). Asthma mortality, however, is the tip of the iceberg when considering the overall asthma burden. Systematic national and regional asthma plans (programmes) have been employed in many countries to tackle emergency visits, hospitalisations, disability, costs, and loss of productivity. When programmes involve community stakeholders and are tailored to the characteristics of the community, they work successfully. Benchmarking against specific indicators of asthma outcomes would improve implementation of best practices.

9. Asthma Management Guidelines

Philippa Ellwood, Innes Asher, Karen Bissell, Guy Marks, Asma El Sony, Eamon Ellwood

Asthma management guidelines were first created in the 1980s, with many being commercially sponsored consensus statements. Now, asthma management guidelines are most commonly independent of pharmaceutical industry support and are evidence-based. The Global Asthma Report 2011 undertook the first worldwide survey on the use of National Asthma Management Guidelines and this survey was repeated by the Global Asthma Network (GAN) in 2013. Use of asthma management guidelines is increasing in countries around the world, particularly in low- and middle-income countries, and most of the guidelines in use were developed without financial assistance from the pharmaceutical industry.

Asthma management guidelines are an essential part of successfully managing asthma and promoting the delivery of quality asthma care.

The role of guidelines

Asthma management guidelines play an important role in standardising timely and correct assessment of asthma symptoms and severity, and effective case management, thus potentially lessening the burden of asthma. More recently, asthma management guidelines have become evidence-based guidelines initiated by governments or non-profit bodies. In 2012 the World Health Organization (WHO) published guidelines for the management of asthma for children and adults in their report "Prevention and Control of Noncommunicable Diseases: Guidelines for primary health care in low resource settings."

Key components of asthma guidelines are recommendations about what asthma medicines to use, and when to use them. It follows that the development of guidelines which are free of the influence, and thus potential bias, of the developers and manufacturers of asthma medicines (the pharmaceutical industry) is preferred.

The Global Asthma Report survey 2011

Chapter 8 of the Global Asthma Report 2011 reported a survey of asthma guidelines use in ISAAC centres. Of 92 countries responding (88% response rate), 74 countries (80%) used asthma management guidelines. Of these 74 countries, 67 (73%) had their own national guidelines, 45 (49%) used guidelines developed without support from the pharmaceutical industry, and 31 (34%) had pharmaceutical industry support.

The Global Asthma Network survey 2013

In 2013, 105 GAN centres were asked to undertake a similar survey about asthma guidelines, completed on-line. The survey questions are in Appendix A, Figure 6. The survey was completed by investigators in 96 countries (93%). Asthma management guidelines were used in 89% of the 96 countries (Figure 1). Most (63%) of the responding countries used their own national asthma guidelines.

The use of guidelines prepared with support of the pharmaceutical industry varied around the world (Figure 2). Of the 96 countries that completed the survey, 42% used guidelines sponsored by the pharamaceutical industry. Of the 63% of countries that had their own national guidelines, 15% were sponsored by the pharmaceutical industry, 30% did not provide information about whether pharmaceutical sponsorship was involved or not, and 8% used a combination of pharmaceutical sponsored and non-pharmaceutical sponsored guidelines (see Appendix A, Table 2 and Figure 7).

Type of guideline

40% of countries used their own national guidelines exclusively. The Global Initiative for Asthma (GINA) guidelines (supported by unrestricted educational grants from non pharmaceutical and pharmaceutical companies) were exclusively used in 17% of countries, 7% used other international guidelines, and 25% of countries used several types of guidelines. 11% did not have any guidelines and, of these, 8% said they would use the recently released WHO guidelines and 3% did not intend to use the recently released WHO guidelines (Figure 1).

Use of guidelines in low-, middle-, and high-income countries

There were some different patterns of use of guidelines according to country income. Of the 96 countries, 32 (33%) were high-income countries and 64 (67%) were low- and

Figure 1:

Asthma management guidelines in countries responding to the Global Asthma Network survey, 2013.

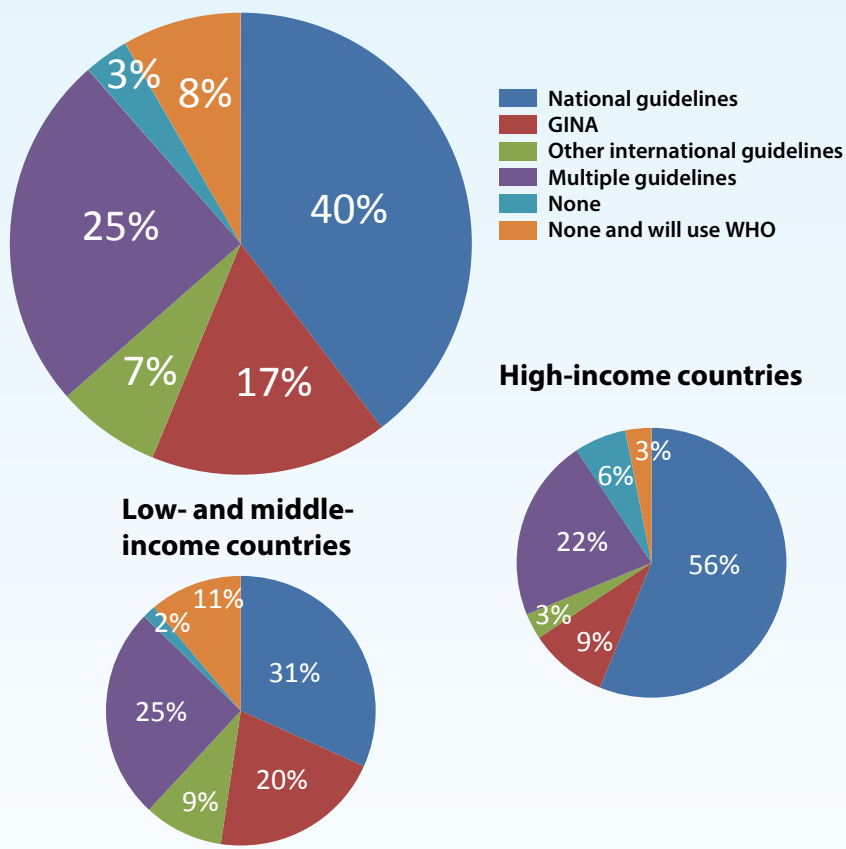


Table: Comparison of 2011 and 2013 asthma guideline usage for those 72 countries participating in both surveys.

	2011	2013
Not using guidelines	14 (19%)	5 (7%)
Using guidelines	58 (81%)	67 (93%)
Using a national guideline	55 (76%)	52 (72%)
Multiple guidelines	1 (1%)	11 (15%)
*Guidelines with no industry support**	31 (43%)	33 (46%)
*Guidelines with industry support**	26 (36%)	35 (49%)
Guidelines with industry not specified	5 (7%)	10 (14%)

*Includes countries with multiple guidelines

middle-income countries. Exclusive use of their own national guidelines was greater in high-income countries than in low- and middle-income countries (78% and 55%, respectively). Use of GINA and other international guidelines was higher in low- and middle-income countries; The International Union Against Tuberculosis and Lung Disease (The Union) guideline was used in three of these. Of low- and middle-income countries, 11% intended to use the recently released WHO guidelines while only one high-income country intended to. A similar proportion of low- and middle-income countries and high-income countries had similar figures for use of multiple guidelines, or no guidelines.

Time Trends

Most (72) countries participated in both the 2011 and 2013 surveys. Comparisons for some of the variables are shown in the Table. The proportion of countries using guidelines increased over the two years, as did the number using multiple guidelines.

Key Recommendation

Health authorities in all countries should ensure the availability of nationally appropriate asthma management guidelines, and provide access for everyone to the quality-assured, affordable essential asthma medicines those guidelines recommend.

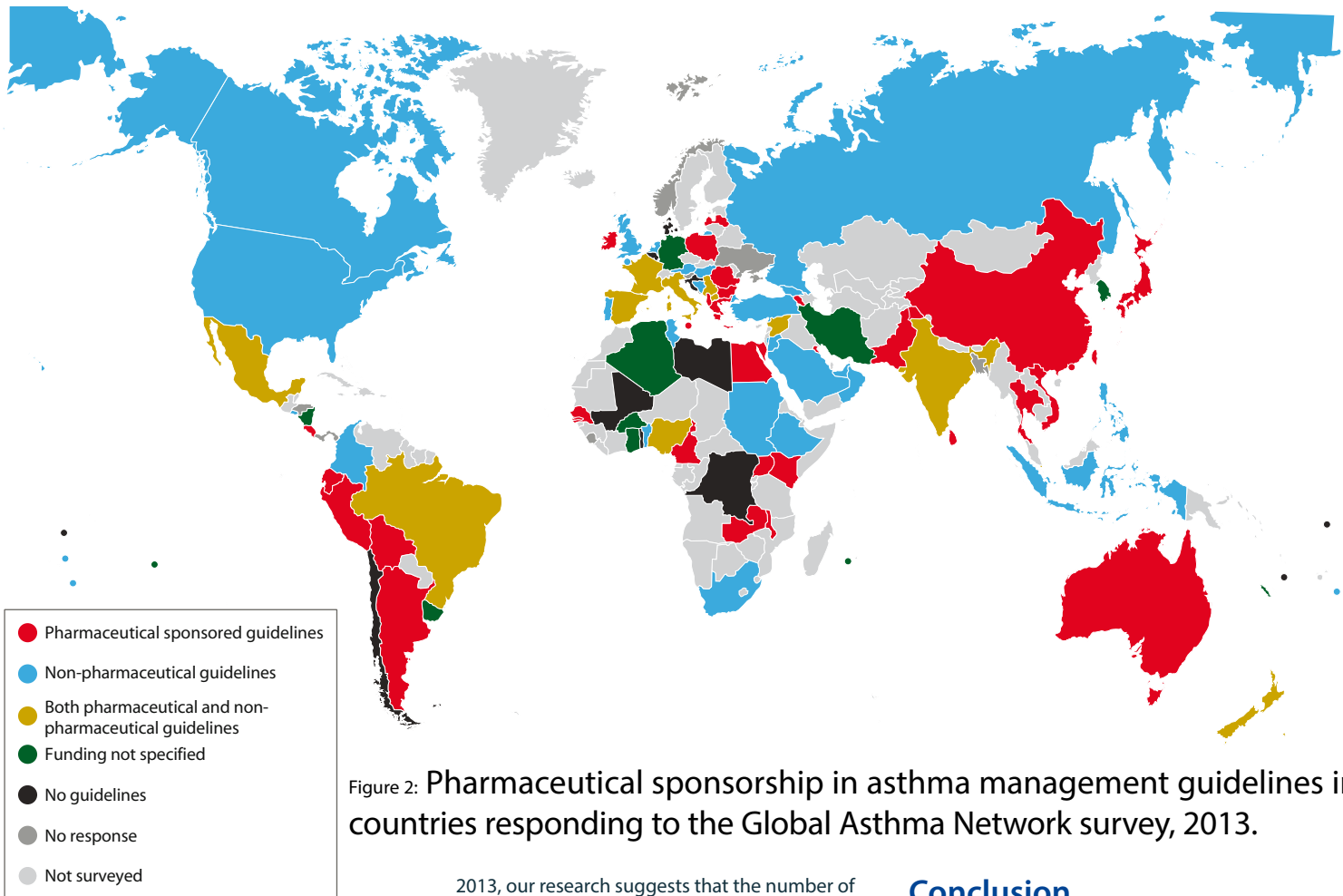


Figure 2: Pharmaceutical sponsorship in asthma management guidelines in countries responding to the Global Asthma Network survey, 2013.

The proportion of guidelines with specified pharmaceutical industry support increased from 36% to 49%. This increase was in part caused by the number of countries using GINA guidelines increasing from 6 to 22 from 2011 to 2013.

Summary of surveys

These surveys fill a global data gap on guideline use by providers within countries. It is encouraging that the majority of countries use management guidelines, and that most of these were developed without financial assistance from the pharmaceutical industry. Between 2011 and 2013, our research suggests that the number of countries using a guideline has increased. More than one guideline was used in one quarter of the countries. This is not surprising given the availability of guidelines through the internet. However guidelines which are not tailored to the health care system in the country where they are used will be more difficult to implement.

Most investigators were not aware of the recently released WHO guidelines, and at the time of the 2013 survey these guidelines were not widely used. They should be considered for primary health care in low-resource settings, especially where national guidelines free of pharmaceutical industry support are unavailable.

Conclusion

National guidelines are an important tool for the management of asthma. International guidelines free of pharmaceutical industry support are freely available, including the WHO guidelines for low-resource settings. They can be used directly or, with permission, as a model for countries to modify for their own national guidelines. Guidelines should promote access for everyone to quality-assured, affordable essential medicines within the countries they are used.

10. Access to Quality-Assured, Affordable Asthma Medicines

Karen Bissell, Christophe Perrin

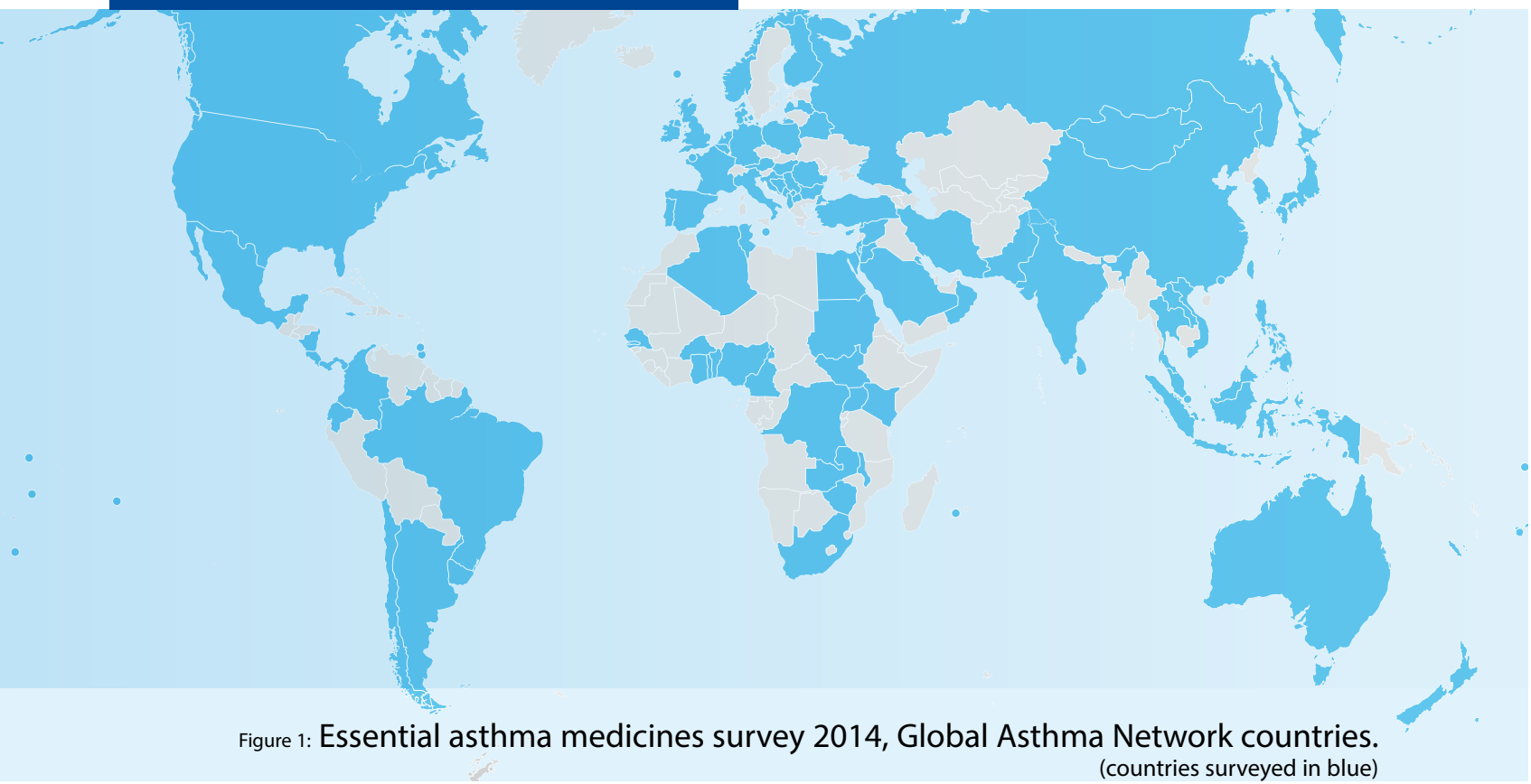


Figure 1: Essential asthma medicines survey 2014, Global Asthma Network countries.
(countries surveyed in blue)

The World Health Organization (WHO) Essential Medicines List includes two inhaled corticosteroids (preventer inhalers) and one bronchodilator (a reliever inhaler) for asthma. A Global Asthma Network (GAN) survey shows that many countries do not have these WHO-recommended medicines on their national Essential Medicines List (EML), and many are not providing them free or subsidised for patients, especially in low-and middle-income countries. A number of medicine-related measures should be urgently addressed at a global and country level.

Adding essential asthma medicines onto national Essential Medicines Lists and lists of reimbursed medicines will improve access to these medicines and reduce the burden of asthma.

Targets for essential asthma medicines

WHO defines essential medicines as those that satisfy the priority health care needs of the population. They are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford. An EML is a government-approved selective list of medicines that guides: the procurement and supply of medicines in the public sector; schemes that reimburse medicine costs; medicine donations; and local medicine production. When properly resourced, it is a cost-effective means of providing safe, effective treatment for the majority of communicable and non-communicable diseases.

The WHO EML includes two inhaled corticosteroids: beclometasone 50 micrograms (µg) and 100µg, and budesonide 100µg and 200µg, as well as one bronchodilator: salbutamol 100µg. Corticosteroids are called 'preventers' because they act to prevent the chronic inflammation of the airways and reduce the twitchiness of the airways. They are recommended for persistent asthma, and are effective at reducing the number of attacks and severity of asthma symptoms. They need to be taken once or twice a day every day even when a person is free of symptoms, and reach peak effect after two weeks. Bronchodilators are called relievers because they relieve the spasm of airway smooth muscle which occurs when asthma symptoms appear. Salbutamol starts to work straight after inhalation and reaches a peak of effect after 20 minutes which lasts for about 4 hours.

Patients with a chronic condition such as asthma need a reliable uninterrupted supply of quality-assured medicines. They also need to be able to afford these medicines over the long term,

WHO NCD TARGET NUMBER 9

An 80% availability of the affordable basic technologies and essential medicines, including generics, required to treat major NCDs in both public and private facilities by 2025.

Source: World Health Organization (WHO) "Global monitoring framework and targets for non-communicable diseases (NCDs)".

Table:

Inclusion of inhalers on the WHO Essential Medicines List (EML) in National EML and National Reimbursement Lists (NRL), by country, in 99 Global Asthma Network countries, 2014.

		Beclometasone 50 µg		Beclometasone 100 µg		Budesonide 100 µg		Budesonide 200 µg		Salbutamol 100 µg	
		EML	NRL	EML	NRL	EML	NRL	EML	NRL	EML	NRL
High-Income Countries	Australia	n/a	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes
	Austria	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes
	Belgium	No	Yes	No	No	No	No	No	Yes	Yes	Yes
	Canada	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes
	Channel Islands	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Chile	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Croatia	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes
	Cyprus	n/a	No	n/a	Yes	n/a	No	n/a	No	n/a	Yes
	Denmark	No	No	Yes	No	No	No	Yes	No	No	No
	Faroe Islands	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Finland	n/a	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes
	France	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes
	French Polynesia	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes
	Germany	n/a	yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes
	Hong Kong	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes
	Ireland	n/a	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes
	Israel	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No
	Italy	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Japan	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a
	Korea, South	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a
	Kuwait	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Latvia	No	No	No	No	No	No	No	No	Yes	Yes
	Malta	n/a	Yes	n/a	No	n/a	No	n/a	Yes	n/a	Yes
	Netherlands	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes
	New Caledonia	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes
	New Zealand	n/a	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes
	Norway	n/a	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes
	Oman	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes	n/a
	Poland	No	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes
	Portugal	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
	Reunion Island	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes
	Russia	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes
	Saudi Arabia	Yes	n/a	No	n/a	No	n/a	Yes	n/a	Yes	n/a
	Singapore	Yes	Yes	No	No	No	No	No	No	Yes	Yes
	Spain	n/a	Yes	n/a	No	n/a	Yes	n/a	Yes	n/a	Yes
	Trinidad and Tobago	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes
	United Kingdom	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes
	United States	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
	Uruguay	No	n/a	No	n/a	No	n/a	No	n/a	Yes	n/a
	Vatican City	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Low- and Middle-Income Countries	Albania	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Algeria	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes
	Argentina	No	No	No	No	No	Yes	No	Yes	No	Yes
	Belarus	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Benin	No	n/a	No	n/a	No	n/a	No	n/a	No	n/a
	Bosnia and Herzegovina	No	No	No	No	No	No	No	No	Yes	Yes
	Brasil	Yes	No	No	No	No	No	No	No	Yes	No
	Bulgaria	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Burkina Faso	Yes	No	No	No	No	No	Yes	No	Yes	No
	Cameroon	No	n/a	No	n/a	No	n/a	No	n/a	No	n/a
	China	Yes	Yes	No	No	No	No	No	No	Yes	Yes

No — Not on list

Yes — Included on list

n/a — No list

	Beclometasone 50 µg		Beclometasone 100 µg		Budesonide 100 µg		Budesonide 200 µg		Salbutamol 100 µg	
	EML	NRL	EML	NRL	EML	NRL	EML	NRL	EML	NRL
Colombia	Yes	n/a	No	n/a	No	n/a	No	n/a	Yes	n/a
Congo Dem Rep	No	n/a	Yes	n/a	No	n/a	No	n/a	Yes	n/a
Costa Rica	No	No	Yes	Yes	No	No	No	No	Yes	Yes
Ecuador	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes
Egypt	No	No	No	No	No	No	No	No	No	No
Gambia	No	n/a	No	n/a	No	n/a	No	n/a	No	n/a
Ghana	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Grenada	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes	n/a
Hungary	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes
India	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Indonesia	No	No	No	No	Yes	No	Yes	No	Yes	Yes
Iran	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Jamaica	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Jordan	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes
Kenya	No	n/a	No	n/a	No	n/a	No	n/a	No	n/a
Kosovo	No	No	No	No	No	No	No	No	Yes	No
Lao PDR	No	No	No	No	No	No	No	No	Yes	No
Macedonia	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes
Malawi	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes	n/a
Malaysia	No	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a
Mexico	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mongolia	Yes	No	Yes	No	No	No	No	No	Yes	Yes
Nicaragua	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes
Nigeria	Yes	n/a	No	n/a	No	n/a	No	n/a	Yes	n/a
Pakistan	No	n/a	No	n/a	No	n/a	No	n/a	No	n/a
Palestine	No	n/a	No	n/a	No	n/a	Yes	n/a	Yes	n/a
Panama	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes
Philippines	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Romania	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Samoa	No	No	Yes	No	No	No	No	No	Yes	No
Senegal	No	No	No	No	No	No	No	No	No	No
Serbia	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
South Africa	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sri Lanka	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes	n/a
Sudan	Yes	No	No	No	No	No	No	Yes	Yes	Yes
Syrian Arab Republic	No	Yes	No	Yes	No	Yes	No	Yes	Yes	Yes
Taiwan	n/a	No	n/a	No	n/a	No	n/a	Yes	n/a	Yes
Thailand	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Togo	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes
Tokelau	Yes	n/a	No	n/a	No	n/a	No	n/a	Yes	n/a
Tonga	No	n/a	Yes	n/a	No	n/a	No	n/a	Yes	n/a
Tunisia	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes
Turkey	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes	n/a	Yes
Tuvalu	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes	n/a
Uganda	Yes	n/a	No	n/a	No	n/a	No	n/a	Yes	n/a
Vietnam	No	No	No	No	No	No	No	No	Yes	Yes
Zambia	Yes	n/a	No	n/a	No	n/a	No	n/a	Yes	n/a
Zimbabwe	Yes	n/a	Yes	n/a	No	n/a	No	n/a	Yes	n/a
Total (Yes) n=99	**49**	**50**	**42**	**46**	**24**	**31**	**33**	**42**	**68**	**64**
Total (Yes) %	**49%**	**51%**	**42%**	**46%**	**24%**	**31%**	**33%**	**42%**	**69%**	**65%**

Low- and Middle-Income Countries

not just for a one-time or short-term expenditure as for many communicable diseases. To provide for these patients, countries need to add essential asthma medicines onto national EMLs and/or reimbursement lists. Global targets have been established by WHO to encourage countries to improve access to quality-assured, affordable medicines for non-communicable diseases, including asthma (see Box), and GAN has created specific targets for asthma (see Chapter 1).

Global Asthma Network survey about essential asthma medicines 2014

GAN Principal investigators were surveyed in May 2014 with a brief questionnaire about the inclusion of WHO essential asthma medicines in two lists their countries may have: a national EML and a type of national reimbursement list (NRL) or similar, which lists medicines that are either fully or partially reimbursed by the government. Data were returned from 99 of 118 countries surveyed. The results are presented in the Table, with countries grouped as high-income countries (HICs) or low- and middle-income countries (LMICs). Results presented here should not be considered definitive. Some results may reflect a difficulty for health services to access and interpret information about these lists; some results would benefit from explanations about the specificities of individual health systems. Mostly, however, the outcome for the patient is the same – if the essential medicines they need have not been prioritised at national level, the patients will have difficulty accessing them and affording them.

Of the 99 responding countries, 79 (80%) have an EML, with an impressive 57 (97%) of the LMICs having an EML. However, the results show that the asthma medicines on WHO EML are not systematically included by all countries in their EMLs. Of the 79 countries that reported having an EML, 62 (78%) had one or more inhaled corticosteroid on their EML, and 68 (86%) had the bronchodilator salbutamol on their EML. However, a range of doses of inhaled corticosteroid is needed so that the appropriate dosage can be prescribed, for each level of disease severity. It is therefore of concern that only 16 (40%) HICs and 33 (56%) LMICs have the corticosteroid beclometasone 50µg on their EML, and only 16 (40%) HICs and 26 (44%) LMICs have beclometasone 100µg. The inclusion of budesonide was even lower: 9 (23%) HICs and 15 (25%) LMICs had the 100µg dosage; 12 (30%) HICs and 21 (36%) LMICs had the 200µg.

Of 73 countries that reported having a National Reimbursement List (NRL), 60 (82%) had one or more inhaled corticosteroid on the NRL. There was a marked difference between country income level regarding inclusion of corticosteroids on the NRL: 31 (94%) of the HICs versus 29 (73%) of the LMICs. There were 28 (70%) HICs but only 21 (36%) LMICs that included 50µg beclometasone; similarly, 27 (68%) HICs but only 19 (32%) LMICs included 100 µg beclometasone. Best reimbursed was salbutamol: 64 (88%) of the countries with an NRL included it; 31 (78%) of the HICs and 33 (56%) of the LMICs. Patients in HICs with some kind of national reimbursement scheme for improving access to medicines are faring best – for HICs with an NRL, 94% included both an inhaled corticosteroid and salbutamol.

In conclusion, although countries may have other dosages or formulations of these medicines, and other asthma medicines, in circulation, this survey shows that many countries do not have the WHO-recommended essential asthma medicines on their lists, and many are not providing them free or subsidised for patients, especially in LMICs. This situation is detrimental for patient access to medicines. It requires urgent attention and ongoing monitoring.

Key Recommendation

Governments in all countries should ensure that they have a list of essential medicines for asthma which includes both inhaled corticosteroids and a bronchodilator in dosages recommended by WHO, and that these are available, quality-assured, and affordable for everyone in their countries.

Measures to improve access

People often speak about high prices being a barrier to accessing medicines. However, there are in fact many factors that can affect the availability and affordability of quality-assured essential asthma medicines. Countries may need to work on how asthma medicines are addressed in their national policies, programmes, guidelines, budgets and teaching curricula, for example, as well as how medicines are procured and made available to patients. The following measures would improve access to quality-assured medicines:

1. Include the essential asthma medicines in national EMLs and NRLs, and stop reimbursing inappropriate, unnecessary, and very expensive asthma medicines.
2. Ensure EMLs and NRLs include products only propelled by hydrofluoroalkanes (HFA) , and that product strengths have been updated where appropriate (HFA propellants replaced chlorofluorocarbons, as required by the 1987 Montreal Protocol on Substances that Deplete the Ozone Layer).
3. Check that national asthma management guidelines are based on medicines that are available and affordable, and that the guidelines explicitly address the need to ensure access to medicines at all levels of health care, and especially among poor and marginalised populations.
4. Add essential asthma medicines to the list of the WHO Prequalification Programme (a centralised quality assessment initiative that has achieved greater access for millions of patients to quality-assured medicines for selected diseases).
5. Standardise the dosages of active ingredients in combined inhalers marketed in both high- and low- and middle-income countries to facilitate quality assessment, procurement, prescribing practices and the achievement of affordable prices globally (see chapter 11 for more).
6. Harmonise quality requirements across the international reference documents such as the pharmacopoeias (see chapter 11 for more).
7. Facilitate the development of independent laboratories for the testing of generic products that are not already approved by a stringent regulatory authority or relevant global mechanism.
8. Encourage low- and middle-income populations to demand quality-assured, affordable essential medicines for asthma as part of the health care provided by the government.
9. Support in-country implementation of sustainable cost recovery programmes such as Revolving Drug Funds (after an initial capital investment, medicine supplies are replenished with monies collected from the sales of medicines). Such funds become self-financing and build demand for quality-assured, affordable essential asthma medicines.
10. Monitor and strengthen country capacity in pharmaceutical policy and procurement.
11. Monitor and publish on factors that influence availability, affordability, and access to essential asthma medicines.

Conclusion

Most countries have not included the essential medicines recommended by the WHO on their EMLs and most do not reimburse these asthma medicines. The main type of asthma preventer medicines which lead to improved asthma control (inhaled corticosteroid inhalers) are less commonly supported by governments than the short term reliever inhaler, even though reliance solely on the reliever does not reduce the burden of asthma in the long term (see chapter 12).

11. Quality of Inhalers

Christophe Perrin, Luis García-Marcos, Javier Mallol, Karen Bissell

Asthma inhalers are among the most complex pharmaceutical industry manufactured medical devices in widespread use. To be safe and efficacious, they need to comply with international quality standards. Inhalers of the original brand (innovator) and subsequent products produced by different manufacturers (generics) may meet these standards, but many asthma inhalers in the marketplace do not. Low-resource settings would benefit greatly if the World Health Organization (WHO) Prequalification Programme could include essential asthma medicines and provide its technical support to countries. WHO should promote standardised dosages for combination inhalers and harmonise the quality requirements for inhalers across all the international reference pharmacopoeias.

Inhalers are complex devices

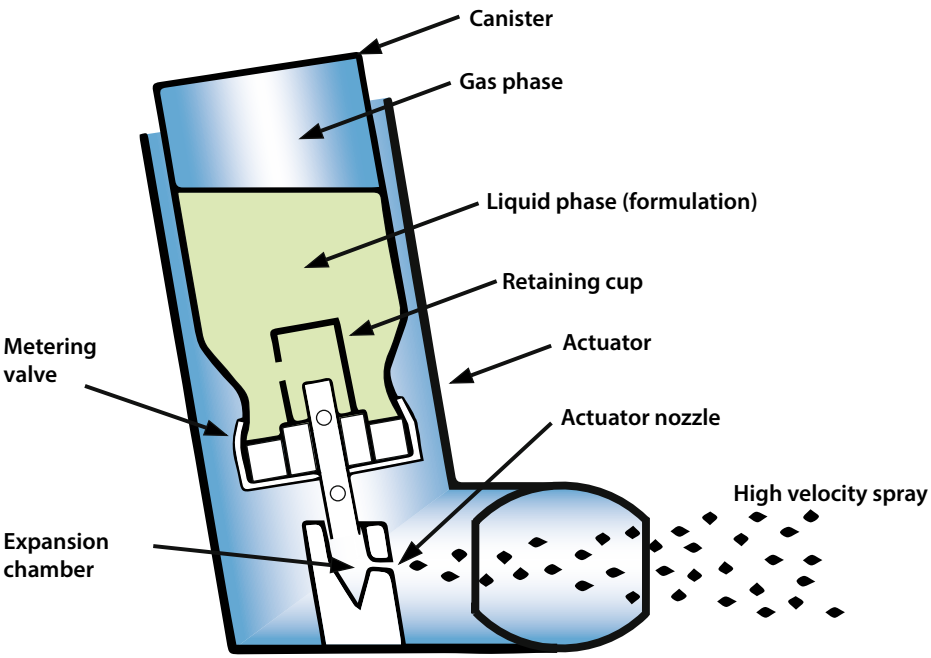
Asthma inhalers, also called 'pressurised Metered Dose Inhalers' (pMDI), are among the most complex medical devices manufactured by the pharmaceutical industry. Active ingredients, such as salbutamol or beclometasone, are mixed with a propellant in a canister. When a person presses upwards on the actuator, a standardised dose of the active ingredients is pushed by the metering valve into the mouthpiece (Figure 1). The person then inhales the active ingredients into his/her airways, where they should stay and thus be "deposited". Children, the elderly, and others who have trouble coordinating their movements, should always use pMDI with a spacer or holding chamber attached to optimise delivery of the aerosol into the lungs.

It is important that a high deposition rate is achieved in the lungs and the periphery of the lungs, and that as little medication as possible deposits in the mouth or throat, or gets swallowed into the gastrointestinal tract. This is so the active ingredients can achieve the intended effect on the airways (reliever or preventer). For these reasons, the amount deposited in the lung (pulmonary deposition rate) of a pMDI needs to be measured against internationally agreed standards of efficiency and safety. For adults, the particles of the active ingredient have to be less than 5 micrometres in order to travel efficiently into the patient's lungs. Only particles between 1 and 3 micrometres will manage to be deposited deep in the lungs. Particles of less than 0.5 micrometres are automatically exhaled and thus have no effect. In children, and particularly in infants and preschoolers, the "breathable" particle size is considerably lower.

Both innovator and generic products have met international standards

A further key requirement for inhalers is to deliver the same quantity of active ingredients (e.g. 100 micrograms of salbutamol) for each of the 200 doses contained in a canister. The fine particle size distribution in the puff, or cloud of the spray, has to conform to strict calibration

Figure 1:
Pressurised metered dose inhaler.



curves that will allow efficient deposition in the lungs. Manufacturing hundreds of thousands of pMDIs that conform to these strict requirements, batch after batch, year after year, represents a significant technical challenge for pharmaceutical companies. It is no surprise then that only a limited number of manufacturers worldwide have the capacity to produce innovator or generic pMDIs that meet international quality standards. Furthermore, there is a wide variability in the size of the particles in an aerosol generated by pMDIs made by different manufacturers, even for the same medication (e.g. for budesonide). Therefore, manufacturers should be required to specify particle size distribution, so that clinicians can correctly select the best aerosol for each patient.

Nevertheless, innovator and generic single ingredient pMDIs supplied by manufacturers based in the United Kingdom, Spain, India, and Bangladesh have successfully gone through three consecutive qualification processes conducted by the Asthma Drug Facility (ADF) (a project of The Union) between 2008 and 2013, after public and international invitations for Expressions of Interest. These qualifications were based on international quality standards set by the WHO and stringent National Medicine Regulatory Agencies (NMRAs). In addition, generic companies have started to register some of their pMDIs with stringent NMRAs, such as the NMRA in the United Kingdom.

Despite the challenge for generic companies to develop a formulation with the required characteristics, as well as to define the right combination of diameters of the metering valve and the actuator nozzle to dispense the right size of fine particles, several of them have managed to demonstrate the bio-equivalence of their generic products with innovator products. Bio-equivalence means the efficiency and safety of a generic medicine is the same as that of the innovator product and is in compliance with international quality standards. It is one of the fundamental requirements for generics.

In all countries, an NMRA is responsible for ensuring the quality of medicines marketed on their territory. However, according to WHO surveys, 30% of NMRAs, principally those in low-income countries, have limited capacity to perform regulatory functions and 50% have variable capacity to do so, whereas stringent NMRAs are found mainly in wealthier countries. Thus, many NMRAs have major difficulty assessing the innovator and generic pMDIs they want to supply to their populations. This may lead to some treatment failure and/or safety issues.

International measures to support countries

Considering the great global burden of asthma, and that effective medicines for it are available, having quality-assured effective asthma pMDIs is vital. An important step is to have pMDIs added to the WHO Prequalification Programme, which is a centralised quality assessment initiative capable of qualifying products which meet the strict technical criteria discussed above. Since 2001, the centralised quality assessment of

Asthma inhalers are complex devices which require accurate manufacturing. Quality should never be compromised in the search for affordably-priced medicines.

medicines for HIV/AIDS, tuberculosis, malaria and reproductive health has achieved greater access for millions of patients to quality-assured medicines for these diseases, even in the least affluent countries. If asthma pMDIs were added to the list, the WHO Prequalification Programme could provide technical assistance to NMRAs in how to assess the inhalers, as well as guidance for manufacturers in how to upgrade their production of asthma inhalers.

The WHO could also contribute to improving the quality of pMDIs circulating globally by promoting the standardisation of the dosages of active ingredients in combined inhalers that are marketed in both high- and low- and middle-income countries. Combined inhalers are made of a bronchodilator (short or long acting β2 agonists) and a corticosteroid. Together they reverse the inflammation in the lungs and have a bronchodilatory (airway-opening) effect. However, there is great variation in the dosages available globally today, especially those including long acting β2 agonists. Such variation is not justified by objective clinical data and creates unnecessary confusion for prescribers, dispensers, patients, and their families.

It would also be greatly beneficial if WHO could promote the harmonisation of quality requirements across current international references, such as the pharmacopoeias (reference books containing directions for the identification of compound medicines) of the United States, the United Kingdom and Europe. These would assist the pharmaceutical industry and NMRAs by having clearer quality standards to work with for the production and assessment of pMDIs. In addition, WHO should modify the requirements for becoming a WHO-prequalification laboratory. These should include the ability to analyse particle size distribution using a cascade impactor. If WHO-prequalified laboratories could provide this service, complemented by a network of qualified university-based laboratories that specialise in analysing aerosols, then NMRAs from low- and middle-income countries would have independent places to test any generic products not already approved by a stringent regulatory authority or a global mechanism such as an Asthma Drug Facility.

Conclusion

The manufacture of asthma inhalers requires accuracy and reliability so that their quality is assured for each dose, and from one inhaler to another. Non-quality-assured asthma inhalers may be ineffective.

Key Recommendation

The WHO should add essential asthma medicines to their Prequalification Programme, promote the standardisation of the dosages of active ingredients in combined inhalers and the harmonisation of quality requirements for inhalers across international reference documents such as the pharmacopoeias. Governments in all countries should ensure all asthma inhalers procured, distributed, and sold in their countries meet international quality standards.

12. Asthma Management in Low-Income Countries

Karen Bissell, Chiang Chen-Yuan, Nadia Aït-Khaled, Christophe Perrin

Low-income countries face extra challenges to achieve good asthma management compared with other countries. They have more difficulty achieving an uninterrupted supply of quality-assured, affordable essential asthma medicines, well-trained health professionals, well-organised health services to provide long-term care, standardised management of asthma with appropriate use of inhaled corticosteroids, and information systems for monitoring and improving quality of care. To achieve all these vital components of asthma care, commitments are needed from governments, and such commitments may be harder to achieve where resources are scarce, making the contributions of national non-governmental organisations (NGOs) and global governmental agencies such as the World Health Organization (WHO) vital.

Asthma can be effectively and affordably managed in low-resource countries. In 2012 WHO published guidelines for asthma management in low-income settings.

Goals for successfully managed asthma

The goals for successfully managed asthma (Chapter 8) are the same in low- as in middle- and high-income countries – people with asthma will have minimal symptoms and minimal side effects of any medicines, and have no limitations on their lifestyle due to asthma.

Inhaled corticosteroids are essential to success

Inhaled corticosteroids (asthma preventer medicines) are essential for achieving these goals and managing patients with persistent asthma over the long term. However, studies in low-income countries 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 (reliever medicines) instead.

Patients may be inclined to 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. These beliefs are understandable, and common in people throughout the world, resulting in the need for active asthma education as part of good asthma care. In low-income countries where these medicines are less well known, the education task is harder. Further, in low-income countries the cost of inhaled corticosteroids is usually much higher than bronchodilators and may not be affordable. Consequently patients are likely to over-use bronchodilators and under-use inhaled corticosteroids.

Projects undertaken with the International Union Against Tuberculosis and Lung Disease (The Union) in Benin and Sudan evaluated asthma treatment outcomes after one year of follow-up. They found that asthma severity and symptom frequency reduced significantly when patients took preventer treatment regularly. However there were challenges: practitioners demonstrated only moderate adherence to guidelines when grading the severity of their patients' asthma and prescribing inhaled corticosteroids. A substantial proportion of patients also stopped taking their inhaled corticosteroids.

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

The under-use of inhaled corticosteroids is resulting in inadequate asthma control, frequent unplanned visits to the emergency room or hospitalisations, and an unnecessary reduction in quality of life for those who live with asthma which, in low-income countries, places a disproportionate burden on the people with asthma and society at large. There are several reasons for the failure of health systems to provide appropriate asthma care. To turn this situation around requires action on several fronts:

Countries need to apply guidelines for standard case management of asthma

The term 'standard case management' encompasses diagnosis of asthma, standardisation of treatment according to severity based on asthma guidelines, and patient education, coupled with a simple system for monitoring patient outcomes. Appropriate training of health care workers and availability of essential asthma medicines are key to the effectiveness of standard case management. 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. In four

recent asthma projects that involved The Union, in Benin, China, El Salvador and Sudan, the training of clinicians in guideline implementation and outcome evaluation was combined with the procurement of affordable essential medicines for asthma. All countries observed a substantial reduction in the severity of asthma for the majority of enrolled patients and the almost complete disappearance of visits to emergency services and hospitalisations in patients that were adhering well to treatment.

Clinicians and health care workers need to be trained 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 β-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. What this project suggested was both that asthma may be a hidden disease in rural China and that it is feasible to train health workers to provide standardised case management of asthma.

Quality-assured essential asthma medicines need to be accessible and affordable to all who need them

In low-income countries, essential asthma medicines are more likely to be unavailable than in more affluent countries (see Chapter 10). They are more likely to be of inadequate quality (see Chapter 11) due to inadequate government regulation. They are also more likely to be unaffordable, in that an inhaled corticosteroid inhaler may cost as much as the equivalent of two weeks wages. Such high costs are a major obstacle to the person with asthma receiving the medicine they need.

A situation analysis in Benin prior to the project there revealed that only 11% of asthma patients were prescribed inhaled corticosteroids. In both El Salvador and Sudan, inhaled corticosteroids were not available in the pilot sites before the project. The Union, through its Asthma Drug Facility (ADF) 2008-2013, worked with several countries running pilot projects which demonstrated that the price of essential

asthma medicines could be markedly reduced through negotiation with suppliers of quality-assured medicines so that they could be procured at affordable prices. In Benin, the price of the inhaled corticosteroid beclometasone was €4.27 per inhaler before this process and was reduced to €1.98 when procured through the ADF. Similar price reductions were achieved for El Salvador and Sudan. Benin also established a financial mechanism to ensure an uninterrupted supply of essential medicines for asthma. Known as a Revolving Drug Fund, this mechanism works because, after an initial capital investment, medicine supplies are replenished with monies collected from the sales of medicines. Such funds become self-financing and build demand for quality-assured, affordable essential asthma medicines.

Health services need to serve chronic patients effectively

In many low-income countries 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.

Collecting and monitoring data helps to assure quality of care

Information systems are less likely to be well developed in low-income countries than in more affluent countries. 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.

Patient education is needed to overcome fears and encourage self-management

Patient education is essential to prevent unnecessary concerns about asthma and asthma medicines, especially in low-income countries where there has been little experience with asthma. Patients need to learn that inhaled corticosteroid inhalers 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 quality-assured, affordable essential asthma medicines, organised services and trained human resources are the minimum requirements for the health services to manage asthma. These are harder to achieve in low-income countries. Political commitment is critical for establishing and maintaining the long-term management of asthma, especially in resource-limited settings.

Conclusion

In low-income countries, where asthma is not as well recognised and effective asthma management has not been commonplace, carefully planned programmes can be introduced to improve management. The components include access to quality-assured essential asthma medicines, asthma management guidelines, health service organisation, patient education and political commitment.

Key Recommendation

Governments in low-income countries should make commitments to ensure that the supply of quality-assured, affordable essential asthma medicines is uninterrupted, health professionals are appropriately trained, and health services are organised to manage asthma.

13. Short Courses Relevant to Asthma Research and Policy

Neil Pearce, Nils Billo, Karen Bissell

Brief History

The Global Asthma Network (GAN), established in 2012, brought together a global network of asthma researchers from the International Study of Asthma and Allergies in Childhood (ISAAC) and the International Union against Tuberculosis and Lung Disease (The Union). Over the years, ISAAC and The Union have provided many opportunities for further research collaboration and training. In many instances this has involved researchers from low- and middle-income countries doing a higher degree (e.g. MPH, MSc, PhD) in universities in high-income countries. However, this is often not an option because of the cost and time involved. Short courses in research generally, or asthma research in particular, provide opportunities for 'upskilling' in research for those with limited time and resources.

Typical courses, who should go and why

Typical short courses on asthma research and policy range from one to three weeks, and may include a range of clinicians, epidemiologists, public health professionals, statisticians, and professionals from other disciplines. The opportunity to interact with researchers from other disciplines and with other interests is often a strength of such short courses. They may also involve a range of levels (PhD students, post-doctoral fellows, and more experienced researchers who need a 'refresher') and may include lectures, exercises, discussion sessions, and practical experience in the design of a research proposal.

Some recommended courses

There are many such short courses available in different parts of the world. Some highly recommended courses in which GAN Steering Group members are involved include:

- The European Educational Programme in Epidemiology; this is a three-week residential course which has been held every June/July in Florence since 1990 (www.eepe.org/).
- The International Epidemiological Association International Course on Epidemiological Methods; this is a two-week residential course which has been held every April/May in various parts of the world since 2009 (www.iea-course.org/).
- Operational research courses conducted by The Union; participants design their own research questions and are guided through the research process right through to preparing a paper to report the results. These Operational Research courses are made up of 3 one week blocks of course work which are spread out over a time period of 10 months (www.theunion.org/).
- Issues in Global Non-communicable Disease: From Research to Policy; this is an annual one week course run in London by the London School of Hygiene and Tropical Medicine Centre for Global Non-communicable Disease. It integrates research and policy for NCDs in general, including asthma (www.lshtm.ac.uk/study/cpd/issues_ncd.html).

Key Recommendation

Health authorities in all countries should encourage their health professionals to attend short courses relevant to asthma research and policy.

PART THREE:

ASTHMA - A GLOBAL PRIORITY

14. Asthma as a Lung Health Priority in Low- and Middle-Income Countries

Asma El Sony , Nadia Aït-Khaled, Javier Mallol

It is essential that asthma becomes an explicit global health priority, alongside and complementary to other non-communicable diseases (NCDs) including chronic obstructive pulmonary disease (COPD), and lung infections such as pneumonia and tuberculosis. Asthma, because it causes such a burden of disease, should be one of the top priorities of governments, development partners and partners in lung health, yet at the present time it has little profile with them. We must accelerate our efforts to overcome the operational bottlenecks that are preventing patients from receiving care in low-income settings. Implementing standard case management (see Chapter 12), strengthening health systems at all levels, starting from the community level, and using appropriate technologies efficiently are the way to go.

Asthma is already an epidemic

It is concerning that the global burden of asthma, which is already substantial in terms of both morbidity and economic costs, seems to be increasing rapidly as the world becomes more westernised. Low- and middle-income countries shoulder most of the asthma-related deaths. The recent Global Burden of Disease (GBD) study estimated that asthma was the 14th most important disorder in terms of global years lived with disability. Therefore when assessing health priorities, allocating resources, and evaluating the potential costs and benefits of public health interventions, asthma should be among the top priorities of Ministries of Health in low- and middle-income countries.

Underprivileged settings and fragile health systems are characteristics of Low- and Middle-income countries

Within low- and middle-income countries poverty has a larger effect on the quality of life of communities, and on health system preparedness for disease, compared with high-income countries. Poverty is a vicious cycle that may deprive people of their basic human rights. Poverty affects both systems and people: it constrains education and health systems as well as people's ability to seek education and health care. Poverty also exacerbates risk factors, such as indoor air pollution and tobacco consumption, and increases the burden of communicable and non-communicable diseases.

How far are we from welfare and equity?

Access to and affordability of asthma management and control:

Disparities in health coverage within low- and middle-income countries are huge and expenditure on health and development is generally very low. Barriers to accessing health services are many, so when combined with the low coverage of health insurance, families may face catastrophic out-of-pocket expenditure when a family member has asthma. Absence of guidelines (see Chapter 9) and non-standardisation of asthma management increases the cost and has the potential to force families into poverty due to direct and indirect costs to themselves. This can lead to disastrous events for individuals and society - children may be stopped from attending school so that their treatment can be purchased and breadwinners may be unable to work on their farms and feed their families because of severe asthma symptoms.

In low- and middle-income countries, there are various operational bottlenecks facing asthma management and control. The reasons for these include: a lack of consensus around asthma as a priority; lack of training of health care workers; lack of patient education in chronic disease management; lack of diagnostic equipment such as peak flow meters and mouthpieces; lack of access to essential asthma medicines; the high cost of these inhalers and delivery devices (holding chambers or spacers); and the effect of international agreements such as Trade-Related aspects of Intellectual Property Rights (TRIPS) on the costs of, and access to, essential asthma inhalers.

These problems can be addressed successfully. For example, studies in 2007-8 in Sudan (Figure 1) and Benin (Figure 2) trained health workers and delivered standard case management of asthma. Among patients present at the one year follow-up visit, 50% improved in Benin and 82.6% improved in Sudan, with a huge reduction in emergency room visits and economic costs.

Asthma and Stigma:

Asthma symptoms, especially breathlessness, can cause fear and other psychological and emotional suffering. Stigma within communities is noticeable; it can delay health seeking and case detection, and it hinders adherence to long-term management.

The stigma hinders everyday life including the ability to socialise. In some places there is a reluctance to marry a person with asthma to avoid passing the disease on to future offspring. Some refuse to use preventive inhalers as they see it as a declaration of having asthma for the rest of their life.

Slow progress getting asthma high on the political agenda:

The High Level Meeting of the 66th Session of the United Nations General Assembly held in September 2011 issued a Political Declaration that focused the attention of world leaders and the global health community on the prevention and control of NCDs. Asthma is included in the global NCD agenda under "chronic respiratory diseases",

Asthma is a serious burden in low- and middle-income countries and we should accelerate efforts to make asthma a lung health priority. Asthma management and control is feasible and it should be on everyone's agenda.

Figure 1: The reduction in emergency room visits from one year of enrolment in the asthma standard case management project in Sudan 2007-08.

Source: El Sony A, et al. Public Health Action. 2013.

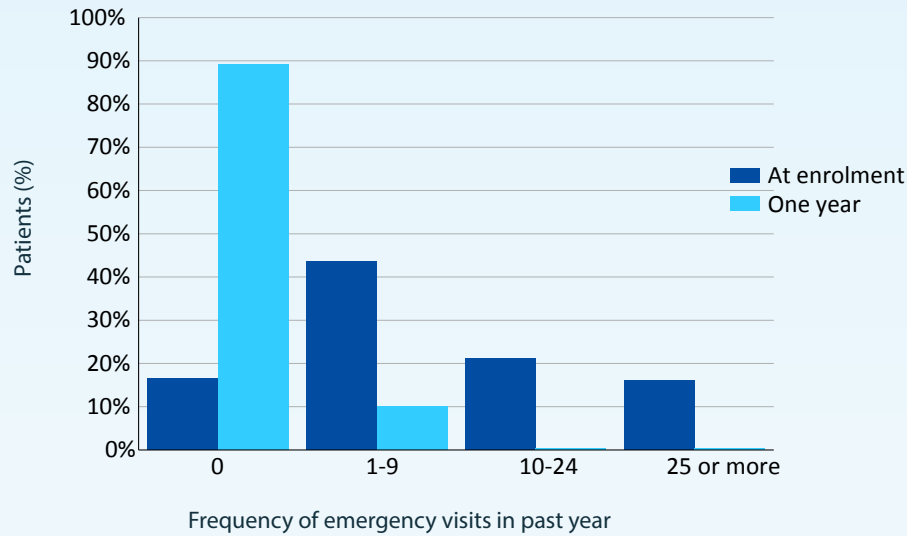
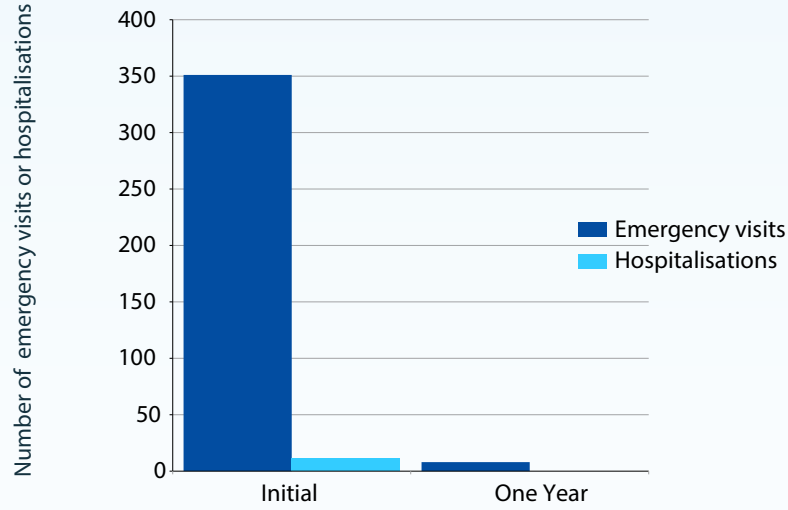


Figure 2: Number of emergency visits and hospitalisations in Benin: initial at enrolment versus one year 2007-08.

Source: Ade G, et al. Public Health Action. 2013.



yet the proposed interventions will do little to prevent or control it - unless the declaration is backed-up with national and international political commitment, support and resources.

Following the Declaration, low- and middle-income countries committed themselves to developing national action plans to control these chronic conditions. However, strategic and collaborative action has been slow. Technical and financial assistance should be given to low- and middle-income countries so that they can build a responsive health infrastructure, capable of tackling the physical, social and economic conditions that affect the burden of asthma on their populations.

Efforts should be speeded up collectively by:

- Investing in research to measure asthma trends in relation to geographic location, socio-economic status and marginalised populations.
- Developing pro-poor strategies in which asthma is a "lung health priority" and developing guidelines that integrate asthma care at community and primary health care levels.
- Developing the capacity of human resources to diagnose and manage asthma, through standardised case management, and to respond to patients' needs.
- Procuring a regular supply of quality-assured, affordable asthma medicines and equipment through a regular supplier that is linked to an asthma management programme (see Chapters 10 and 12)
- Strengthening referral procedures for asthma patients within the health system.
- Adopting The Union's innovative application of the Directly Observed Treatment Short-course (DOTS) strategy for treatment of tuberculosis in the community in low- and middle-income countries to asthma and lung health. Integrating asthma management with DOTS has already shown success in improving treatment outcomes and reducing the burden of asthma in resource-poor settings.
- Strengthening community systems, such as informal health providers, in order to increase access to care and case detection, and to reduce stigma.
- Establishing "patients networks" to empower patients as central partners in the efforts to manage asthma and to advocate for greater political commitment.
- Utilising innovations and appropriate technologies in a sustainable manner to support standard case management; by improving awareness, case detection, adherence and long-term follow-up. For example, a Sudan pilot project using rapid mobile asthma Short Message Service (SMS) texts showed that such SMS use was feasible, reduced rates of loss to follow up, and supported standard case management by improving awareness, case detection, adherence, and long-term follow-up.

Conclusion

Asthma has a low profile in the health priorities of low- and middle-income countries. The identification of asthma as a lung health priority would give it attention along with COPD, pneumonia, and tuberculosis.

Key Recommendation

Governments in low- and middle-income countries should make asthma a health priority, in order to more quickly invest in asthma research relevant to their populations, integrate care at community and primary health care levels with appropriate referral procedures, and develop capacity in standard case management of asthma.

15. Asthma as an NCD Priority

Neil Pearce, Javier Mallol

The asthma epidemic experienced by high-income countries over the past 30 years is now an increasing problem in low- and middle-income countries as they become more urbanised. Non-communicable diseases (NCDs) are emerging as a major global public health problem and asthma is an important component of this group of diseases, particularly with regard to morbidity, but its importance is being ignored and neglected. This chapter provides a summary of the current challenges facing asthma management worldwide and suggests several approaches addressing these issues.

Asthma is an important NCD in all regions of the world, affecting people in non-affluent as well as affluent countries.

Asthma is a global concern

Asthma has become an issue of international development. The asthma epidemic experienced by developed nations over the last 30 years is now hitting developing countries in a big way as they become more urbanised. Whilst it is true that communicable diseases such as malaria are still a major health problem for many developing countries, NCDs including asthma, allergic rhinitis, and eczema are now emerging as serious additional problems in these countries and authorities believe that they will be responsible for tomorrow's pandemics. The majority of people with these conditions live in the developing world, and in some of those countries asthma has become more common than in some western countries.

Asthma is one of the significant NCDs

Asthma is now recognised as one of the most important NCDs in all regions of the world, affecting people in non-affluent as well as affluent countries. NCDs now outstrip communicable diseases as the leading causes of death in the world - 60% among people of all ages, most (80%) of these deaths occurring in non-affluent countries. Chronic respiratory diseases (CRDs) cause 15% of the world's deaths, and many of these have their origins in childhood influences including asthma, which may be aggravated by tobacco use in pregnancy, exposure to second hand smoke in childhood, and taking up smoking in adolescent or adult years. The burden and suffering caused by CRDs has been identified by the World Health Organization (WHO) as a priority issue.

NCD priority actions will help asthma

Asthma symptoms will be helped by two of the five priority interventions for the NCD crisis - tobacco control and access to essential medicines. The reduction in obesity that will be achieved through a third priority of improved diets and physical activity is likely to be beneficial as a relationship between obesity and asthma is becoming more evident.

Asthma surveillance needs to be extended

We know that asthma has become a serious global health issue because health researchers (paediatricians, respiratory physicians, and epidemiologists) in 306 centres in 105 countries, wanting to estimate how large the problem was for children in their locality, joined the International Study of Asthma and Allergies in Childhood (ISAAC) research programme; it was found that asthma affects about one in seven of the world's children. Through that information from ISAAC (children) and the European Community Respiratory Health Survey (ECRHS) (adults), and with the recent estimates from the Global Burden of Disease Study (GBD), we now know that asthma is an important NCD. The WHO has 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 using simple instruments which can be widely used around the world and repeated at regular intervals, such as those used in ISAAC and including younger age groups, such as preschool children.

Economic prosperity will be helped by treating asthma well….

The GBD found that asthma affects approximately 334 million people worldwide, causing an estimated 345,736 deaths annually (1 in 150 deaths worldwide). Around 22 million disability-adjusted life years (DALYs) are lost annually, and children with untreated asthma miss much of their primary school education, resulting in reduced educational opportunities and increased time off work for the parents/ guardians which then impacts on the economy through loss of productivity. People with asthma are less able to work or look after their families, which causes huge financial and emotional stress. Emergency visits, hospitalisation, and inappropriate treatments are a great financial drain on struggling health systems.

….especially in non-affluent countries

The burden of severe asthma symptoms (frequent attacks, waking at night, or breathing difficulty affecting speech) disproportionately falls among children with wheeze in low- and middle-income countries. These children especially need access to affordable asthma medicines to help reduce attacks and relieve symptoms.

More asthma research is needed

Asthma research is decades behind cardiovascular research, and needs further investment. A key challenge now is to identify modifiable environmental risk factors suitable for public health interventions which have the

ability to reduce the morbidity and severity of this increasing global problem. An important emerging problem is asthma or recurrent wheeze in infants, which was found, in a large international multi-centre study in 2008, to be highly prevalent and associated with greater severity in developing countries (see Chapter 5).

Universal access to quality-assured and affordable asthma drugs

Universal access to good-quality affordable drugs for NCDs is an important issue. For everyone with asthma, access to affordable medicines is needed, appropriate to the severity of their asthma – a β2 agonist reliever for all people with asthma, and an inhaled corticosteroid preventer for those with more frequent symptoms. These essential medicines, particularly inhaled corticosteroids, are not available or affordable to patients, or to the health service in many developing countries, and as a consequence people become disabled or die from asthma. Thus, asthma is a factor in increasing the poverty of individuals and countries, especially low- and middle-income countries. The International Union Against Tuberculosis and Lung Disease (The Union) developed a process to provide access to quality-assured, affordably priced asthma inhalers in resource-constrained settings (see Chapter 12). Such an approach must be continued. It must be added that quality-assured and affordable holding chambers or spacers attached to inhalers are critical for the success of inhaled asthma therapy in childhood.

Organisation of health services for long term treatment

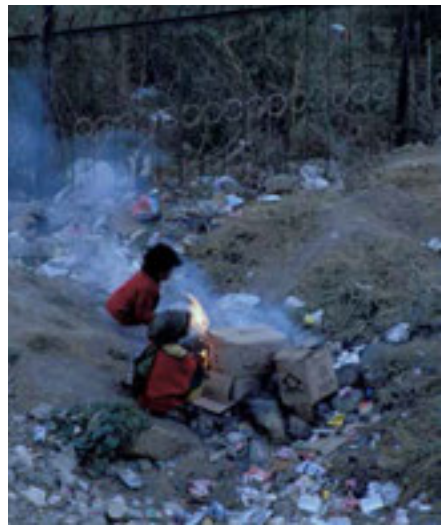
In addition to the difficulty of accessing affordable essential medicines, the other main obstacle for management of NCDs, including asthma, is the lack of organisation of health services for long term management of patients with regular follow-up. Usually these diseases are treated only in an emergency. Training of health personnel and organisation of health services are needed. The Union has provided training material for health care workers; and, for regular monitoring and evaluation, an EpiData programme has been designed for registration and follow-up of patients.

Conclusion

Asthma is an NCD which causes a high burden of disease and economic impact throughout the world. The reasons for the increasing prevalence of asthma have not yet been clarified. Many people with asthma are not receiving effective treatment, often because quality-assured essential medicines are unavailable or unaffordable, or health care is not delivered well. There is a great deal that can be done to address all these issues, monitor their impact, and reduce the suffering of people with asthma in the world.

Key Recommendation

Governments should include asthma in all their actions arising from the WHO Global Action Plan for the Prevention and Control of NCDs 2013-2020, and the WHO NCD Global Monitoring Framework.



ACTIONS REQUIRED TO ENSURE ASTHMA BECOMES A GLOBAL PRIORITY:

Asthma is a major global health problem.

We know it is – world leaders please action all the recommendations in this report.

Asthma is one of the most significant NCDs globally and NCD priority actions will help prevent asthma.

Keep asthma highlighted among NCDs.

Asthma monitoring needs to be ongoing.

Asthma needs to be studied in all countries, and the trends updated.

Asthma data need to be obtained for nearly half the world's countries, which have not yet been surveyed.

Economic prosperity will be helped by correctly treating asthma, especially in non-affluent countries.

Measure the economic impacts of asthma, and the impact of adequate asthma management.

More asthma research is needed.

This includes research to identify the causes of asthma, especially in low- and middle-income countries; definition and management of asthma in infants and preschool children; and links between asthma in children and adolescents, and the development of COPD.

Universal access to quality-assured, affordable asthma medicines, delivery devices, and medical care is required.

Develop and implement policies to enable access to affordable good medical care and asthma medicines for all people with asthma in every country.

Appendices

Glossary of Abbreviations

ADF	*Asthma Drug Facility*
COPD	*Chronic Obstructive Pulmonary Disease*
CRDs	*Chronic Respiratory Diseases*
DALYs	*Disability Adjusted Life Years*
DOTS	*Directly Observed Treatment Short-course*
EAACI	*The European Academy of Allergy and Clinical Immunology*
ECRHS	*European Community Respiratory Health Survey*
ED	*Emergency Department*
EISL	*Estudio Internacional de Sibilancias en Lactantes (International Study on Wheezing in Infants)*
EML	*Essential Medicines List*
FIRS	*Forum of International Respiratory Societies*
GAN	*Global Asthma Network*
GBD	*Global Burden of Disease Survey*
GINA	*Global Initiative on Asthma*
HFA	*Hydrofluoroalkanes*
HICs	*High-Income Countries*
ICS	*Inhaled Corticosteroids*
ISAAC	*International Study of Asthma and Allergies in Childhood*
LMICs	*Low- and Middle-Income Countries*
NCDs	*Non-Communicable Diseases*
NGO	*Non-Governmental Organisation*
NMRAs	*National Medicine Regulatory Agencies*
NRL	*National Reimbursement List*
pMDI	*Pressurised Metered Dose Inhalers*
RSV	*Respiratory Syncytial Virus*
RW	*Recurrent Wheezing*
SMS	*Short Message Service*
The Union	*The International Union Against Tuberculosis and Lung Disease*
TRIPS	*Trade-Related aspects of Intellectual Property Rights*
UN	*United Nations*
WHO	*World Health Organization*
YLD	*Years Lived with Disability*
YLL	*Years of Life Lost*

Chapter 2, Appendix 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*

Sources: ISAAC Steering Committee. European Respiratory Journal 1998; Lai et al. Thorax 2009.

Chapter 9, Appendix Table 2:

National asthma guidelines in countries responding to the Global Asthma Network survey, 2013.

KEY TO TABLE

1. Will use WHO Guidelines
2. National guidelines with no pharmaceutical company involvement
3. National guidelines with pharmaceutical company involvement
4. National guidelines with pharmaceutical company involvement not specified
5. Pharmaceutical company sponsored International guidelines
6. International guidelines with no pharmaceutical company involvement

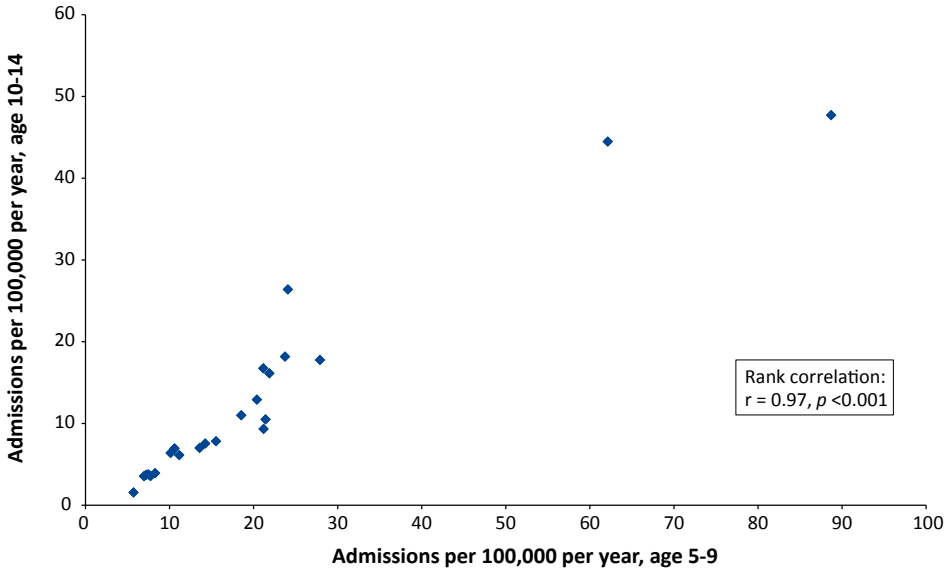
	CountryName	1	2	3	4	5	6
High-income countries	Australia			Yes[15]		Yes[1]	Yes[2]
	Austria		Yes[16]				
	Belgium						
	Canada		Yes[15]				
	Channel Islands						Yes[2]
	Croatia	Yes					
	Denmark						
	France	Yes	Yes[14,16]		Yes[17]	Yes[1]	
	French Polynesia				Yes[17]		
	Germany				Yes[17]		
	Greece	Yes				Yes[1]	
	Hong Kong				Yes[17]	Yes[1]	
	Hungary		Yes[17]				
	Ireland				Yes[17]	Yes[1]	
	Italy	Yes	Yes[15,16]	Yes[17]		Yes[1]	
	Japan			Yes[14,16]			
	Korea, South				Yes[17]		
	Kuwait					Yes[1]	
	Malta					Yes[1]	
	Netherlands		Yes[16]				
	New Caledonia				Yes[17]		
	New Zealand		Yes[14,15,16]		Yes[17]	Yes[1]	Yes[2,3]
	Oman		Yes[15]				
	Poland			Yes[17]			
	Portugal		Yes[15,16]				
	Reunion Island				Yes[17]		
	Saudi Arabia		Yes[15]				
	Singapore		Yes[17]			Yes [1]	
	Spain	Yes	Yes[15,16]	Yes[14]	Yes[17]		
	United Arab Emirates		Yes[17, 12]				
	United Kingdom		Yes[15]				
	United States		Yes[15]				
Low- and middle-income countries	Albania				Yes[15]	Yes[1]	
	Algeria				Yes[16,17]		
	Argentina				Yes[16]	Yes[1]	
	Armenia					Yes[1]	
	Benin	Yes					Yes[8]
	Bolivia				Yes[17]	Yes[1]	
	Bosnia and Herzegovina		Yes[16,17]				Yes[2,4]
	Brasil	Yes	Yes[15]	Yes[17]		Yes[1]	Yes[3]
	Bulgaria	Yes				Yes[1]	
	Burkina Faso				Yes[17]		
	Cameroon					Yes[1]	
	Chile	Yes					
	China			Yes[17]	Yes[16]	Yes[1]	
	Colombia		Yes[16]		Yes[17]		
	Congo Dem Rep	Yes					
	Costa Rica					Yes[1]	

CountryName	1	2	3	4	5	6
Ecuador			Yes[15]			
Egypt				Yes[17]	Yes[1]	
El Salvador						Yes[8]
Ethiopia	Yes	Yes[15]				
Gambia					Yes[1]	
Georgia		Yes[17]				
Ghana	Yes			Yes[17]		
India	Yes	Yes[16]	Yes[17]	Yes[17]	Yes[1]	Yes[2]
Indonesia		Yes[17]				
Iran	Yes			Yes[17]		
Jordan		Yes[17]				
Kenya	Yes		Yes[15]			
Kosovo					Yes[1]	
Latvia					Yes[1]	
Libya	Yes					
Macedonia					Yes[1]	Yes[7]
Malawi			Yes[17]			
Mali	Yes					
Mexico	Yes	Yes[16]	Yes[15]	Yes[16]	Yes[1]	Yes[3]
Nicaragua				Yes[17]		
Nigeria		Yes[17]		Yes[17]	Yes[1]	Yes[6]
Niue						Yes[9]
Pakistan					Yes[1]	
Palestine	Yes	Yes[15,17]				
Peru			Yes[15,16]			Yes[3,4,5]
Philippines		Yes[10,14,16]				
Romania					Yes[1]	
Russia	Yes	Yes[16,17]		Yes[16]		
Samoa	Yes					Yes[9]
Senegal					Yes[1]	
Serbia		Yes[15,16]			Yes[1]	
South Africa		Yes[14,16]				
Sri Lanka					Yes[1]	
Sudan	Yes					Yes[8]
Syrian Arab Republic	Yes				Yes[1]	Yes[4,5]
Taiwan	Yes		Yes[15]	Yes[17]		
Thailand	Yes			Yes[15]	Yes[1]	Yes[3]
Togo	Yes					
Tokelau	Yes					
Tonga		Yes[17]				Yes[2]
Tunisia						Yes[5]
Turkey		Yes[14]				
Tuvalu	Yes					
Uganda					Yes[1]	
Uruguay				Yes[17]		
Vanuatu						
Vietnam	Yes				Yes[1]	
Zambia				Yes[17, 11]	Yes[1]	Yes[2]

[1] Global Initiative for Asthma (GINA) guidelines
[2] British Thoracic Society (BTS Sign) guidelines
[3] National Asthma Education and Prevention Program (NAEPP) guidelines
[4] World Health Organization (WHO) Package of Essential Noncommunicable (PEN) Disease Interventions for Primary Health Care in Low-resource Settings
[5] WHO Practical approach to Lung Health (PAL)
[6] South African guidelines
[7] International consensus on (ICON) pediatric asthma
[8] The Union guidelines
[9] Starship Auckland Children's Hospital guidelines
[10] Printing and dissemination
[11] Submitted
[12] Partial funding
[13] In progress
[14] Adult
[15] Both ages
[16] Child
[17] Age unspecified

Chapter 3, Appendix Figure 1:

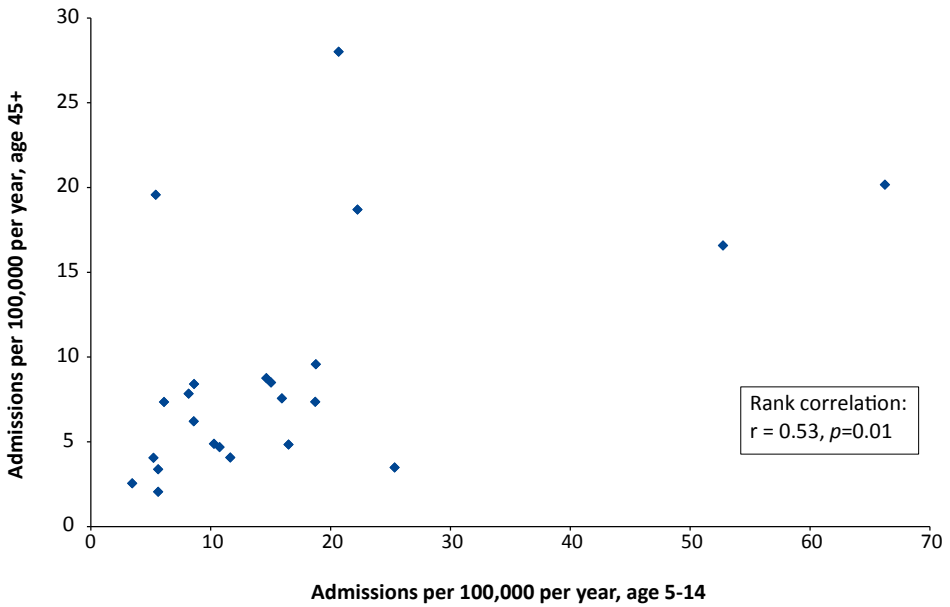
Asthma admission rates for European countries, age 5-9 v 10-14 years.



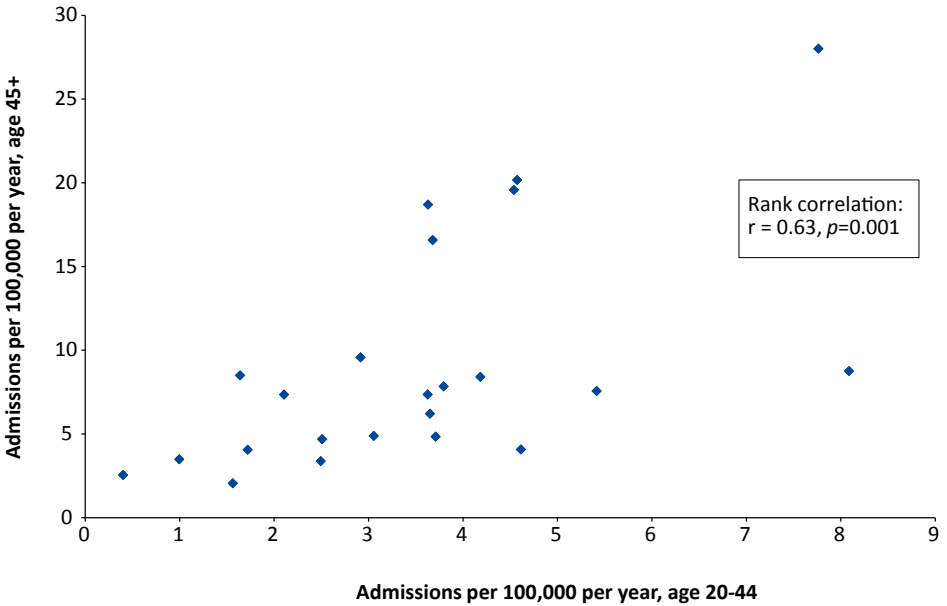
Source: WHO Hospital Morbidity Database. Accessed November 2013.

Chapter 3, Appendix Figure 2:

Asthma admission rates for European countries, age 5-14 v 45+ years.



Source: WHO Hospital Morbidity Database. Accessed November 2013.



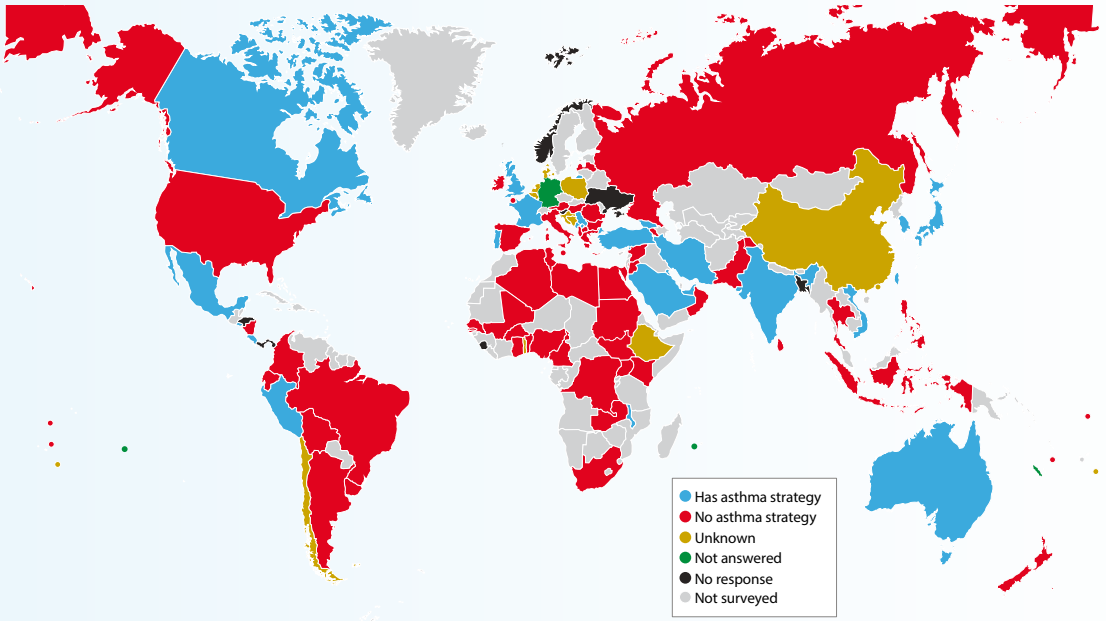
Chapter 3, Appendix Figure 3:

Asthma admission rates for European countries, age 20-44 v 45+ years.

Source: WHO Hospital Morbidity Database. Accessed November 2013.

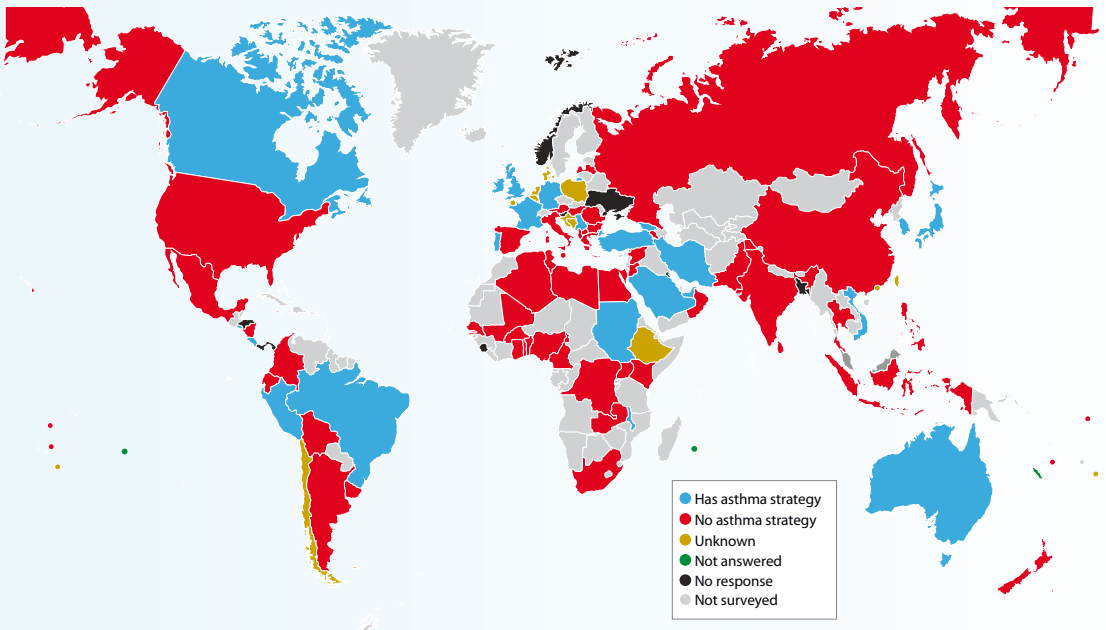
Chapter 8, Appendix Figure 4:

National asthma strategies for children in countries responding to the Global Asthma Network survey, 2013.



Chapter 8, Appendix Figure 5:

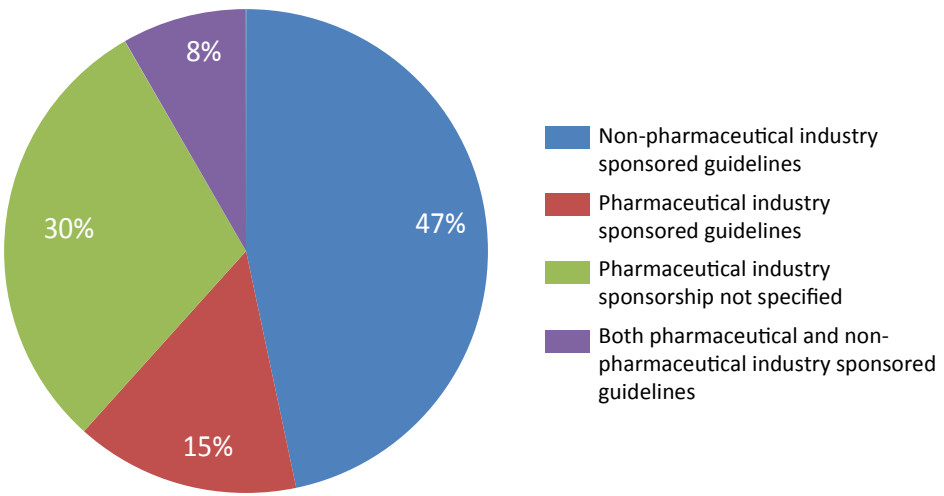
National asthma strategies for adults in countries responding to the Global Asthma Network survey, 2013.



Chapter 9, Appendix Figure 6:

Questions asked in the Global Asthma Network asthma guidelines survey 2013.

Q1.	Did you know that WHO has recently released guidelines for the management of asthma for children and adults?
Q2.	If Yes to Q1: Do you have a copy of the WHO guidelines?
Q3.	If No to Q2: Are you interested in having a copy of these guidelines for your use? (Link below) apps.who.int/iris/bitstream/10665/76173/1/9789241548397_eng.pdf
Q4.	Does your country intend to use the WHO guidelines for the management of asthma in children and adults?
Q5.	Do you have other guidelines that you use?
Q6.	If Yes to Q5: Would you send us a copy of your guidelines for children and adults to put on the Global Asthma Network website as a resource?
Q7.	Does your centre or country have any short courses for asthma?



Chapter 9, Appendix Figure 7:

Pharmaceutical industry involvement in National Asthma Guidelines in countries responding to the Global Asthma Network survey, 2013.

1. Global Asthma Network

The International Union Against Tuberculosis and Lung disease, The International Study of Asthma and Allergies in Childhood (ISAAC), editors. *The Global Asthma Report 2011*. Paris, France: The International Union Against Tuberculosis and Lung Disease; 2011.

Douwes J, Pearce N. *Epidemiology of Respiratory Allergies and Asthma.* In: Ahrens W, Pigeot I, (eds). Handbook of Epidemiology. 2nd ed. New York: Springer Science+Business Media; 2014.

Ellwood P, Asher MI, Beasley R, et al. *The International Study of Asthma and Allergies in Childhood (ISAAC): Phase Three rationale and methods.* International Journal of Tuberculosis and Lung Disease. 2005;9(1):10-6.

Enarson DA. *Fostering a spirit of critical thinking: the ISAAC story.* International Journal of Tuberculosis and Lung Disease. 2005;9(1):1.

Global Asthma Network Steering Group. *The Global Asthma Network Website:* The Global Asthma Network; 2012. Available from: www.globalasthmanetwork.org.

Horton R. *GBD 2010: understanding disease, injury, and risk.* Lancet. 2012;380(9859):2053-4.

ISAAC Steering Committee. *The ISAAC Story: The International Study of Asthma and Allergies in Childhood.* Asher M, Strachan D, Pearce N, et al., editors. Auckland, New Zealand: The International Study of Asthma and Allergies in Childhood; 2011.

2. Global Burden of Disease due to Asthma

Institute for Health Metrics and Evaluation (IHME). *Global Burden of Disease (GBD) Cause Patterns.* Seattle, WA: University of Washington; 2013 [8th May 2014]. Available from: www.healthmetricsandevaluation.org/gbd/visualizations/gbd-cause-patterns.

Institute for Health Metrics and Evaluation (IHME). *Global Burden of Disease (GBD) Compare.* Seattle, WA: University of Washington; 2013 [8th May 2014]. Available from: viz.healthmetricsandevaluation.org/gbd-compare/.

Lai CKW, Beasley R, Crane J, 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):476-83.

Murray CJ, Vos T, Lozano R, et al. *Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010.* Lancet. 2013;380(9859):2197-223.

To T, Stanojevic S, Moores G, et al. *Global asthma prevalence in adults: findings from the cross-sectional world health survey.* BMC Public Health. 2012;12:204.

3. Hospital Admissions

Anderson HR, Gupta R, Kapetanakis V, et al. *International correlations between indicators of prevalence, hospital admissions and mortality for asthma in children.* International Journal of Epidemiology. 2008;37(3):573-82.

Anderson HR, Gupta R, Strachan DP, et al. *50 years of asthma: UK trends from 1955 to 2004.* Thorax. 2007;62(1):85-90.

Chawla J, Seear M, Zhang T, et al. *Fifty years of pediatric asthma in developed countries: how reliable are the basic data sources?* Pediatric Pulmonology. 2012;47(3):211-9.

Gupta R, Anderson HR, Strachan DP, et al. *International trends in admissions and drug sales for asthma.* International Journal of Tuberculosis and Lung Disease. 2006;10(2):138-45.

Hasegawa K, Tsugawa Y, Brown DF, et al. *Childhood asthma hospitalisations in the United States, 2000-2009.* The Journal of Pediatrics. 2013;163(4):1127-33 e3.

4. Asthma Mortality

Anderson HR, Gupta R, Kapetanakis V, et al. *International correlations between indicators of prevalence, hospital admissions and mortality for asthma in children.* International Journal of Epidemiology. 2008;37(3):573-82.

Chawla J, Seear M, Zhang T, et al. *Fifty years of pediatric asthma in developed countries: how reliable are the basic data sources?* Pediatric Pulmonology. 2012;47(3):211-9.

Chatenoud L, Malvezzi M, Pitrelli A, et al. *Asthma Mortality and Long-Acting Beta2-Agonists in Five Major European Countries, 1994–2004.* Journal of Asthma. 2009;46(6):546-51.

Royal College of Physicians (UK). Why asthma still kills. *The National Review of Asthma Deaths Confidential Enquiry Report, May 2014.* London: Royal College of Physicians, 2014.

Wijesinghe M, Weatherall M, Perrin K, et al. *International trends in asthma mortality rates in the 5- to 34-year age group: a call for closer surveillance.* Chest. 2009;135(4):1045-9.

5. Wheezing in Infants

Guidelines for the diagnosis and management of asthma (August 2007). National Asthma Education and Prevention Program (NAEPP), National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH). 2007.

Busse WW, Lemanske RF, Jr., Gern JE. *Role of viral respiratory infections in asthma and asthma exacerbations.* Lancet. 2010;376(9743):826-34.

García-Marcos L, Mallol J, Solé D, et al. *International study of wheezing in infants: risk factors in affluent and non-affluent countries during the first year of life.* Pediatric Allergy and Immunology. 2010;21(5):878-88.

Mallol J, García-Marcos L, Solé D, et al. *International prevalence of recurrent wheezing during the first year of life: variability, treatment patterns and use of health resources.* Thorax. 2010;65(11):1004-9.

Schultz A, Brand PL. *Episodic viral wheeze and multiple trigger wheeze in preschool children: a useful distinction for clinicians?* Paediatric Respiratory Reviews. 2011;12(3):160-4.

Ducharme FM, Tse SM, Chauhan B. *Diagnosis, management, and prognosis of preschool wheeze.* Lancet. 2014;383(9928):1593-604.

6: The Economic Burden of Asthma

Accordini S, Corsico AG, Braggion M, et al. *The cost of persistent asthma in Europe: an international population-based study in adults.* Int ernational Archives of Allergy and Immunology. 2013;160(1):93-101.

Bahadori K, Doyle-Waters MM, Marra C, et al. *Economic burden of asthma: a systematic review*. BMC Pulmonary Medicine. 2009;9:24.

Barnett SB, Nurmagambetov TA. *Costs of asthma in the United States: 2002-2007.* Journal of Allergy and Clinical Immunology. 2011;127(1):145-52.

Bender B, Boulet L, Chaustre L, et al. *Adherence to long-term therapies: evidence for action [Internet].* Geneva: World Health Organzation; 2003 [cited 2013 Aug 11]. Available from: www.who.int/chp/knowledge/publications/adherence_report/en/.

Lai CKW, Kim Y-Y, Kuo S-H, et al. *Cost of asthma in the Asia-Pacific region.* European Respiratory Review. 2006;15(98):10-6.

Sadatsafavi M, Rousseau R, Chen W, et al. *The preventable burden of productivity loss due to suboptimal asthma control: a population-based study.* Chest. 2014;145(4):787-93.

Zafari Z, Lynd LD, FitzGerald JM, et al. *Economic and health effect of full adherence to controller therapy in adults with uncontrolled asthma: A simulation study.* Journal of Allergy and Clinical Immunology. 2014; Epub ahead of print.

7. Factors Affecting Asthma

Asher MI, Stewart AW, Mallol J, et al. *Which population level environmental factors are associated with asthma, rhinoconjunctivitis and eczema? Review of the ecological analyses of ISAAC Phase One.* Respiratory Research. 2010;11:8.

Douwes J, Boezen M, Pearce N. *Chronic obstructive pulmonary disease and asthma.* In: Detels R, Beaglehole R, Lansang MA, et al., (eds). Oxford textbook of public health. Vol.3. 5th ed. Oxford: Oxford University Press; 2009. p. 1021-45.

Pearce N, Douwes J, Beasley R. *Asthma.* In: Detels R, McEwen J, Beaglehole R, et al., (eds). Oxford textbook of public health. Vol.3. 4th ed. Oxford: Oxford University Press; 2002. p. 1255-77.

Strachan DP. *The role of environmental factors in asthma.* British Medical Bulletin. 2000;56(4):865-82.

U.S. Dept of Health and Human Services. *The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General.* Atlanta: U.S. Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2006.

8. National Asthma Strategies

Ade G, Gninafon M, Tawo L, et al. *Management of asthma in Benin: the challenge of loss to follow-up.* Public Health Action. 2013;3(1):76-80.

Ellwood P, Ellwood E, Asher MI, et al. *Asthma Management Guidelines and Strategies - who has them? (Abstract).* ATS Conference; San Diego 2014.

Haahtela T, Tuomisto LE, Pietinalho A, et al. *A 10 year asthma programme in Finland: major change for the better.* Thorax. 2006;61(8):663-70.

Haahtela T, von Hertzen L, Makela M, et al. *Finnish Allergy Programme 2008-2018--time to act and change the course.* Allergy. 2008;63(6):634-45.

Hanski I, von Hertzen L, Fyhrquist N, et al. *Environmental biodiversity, human microbiota, and allergy are interrelated.* Proceedings of the National Academy of Sciences of the United States of America. 2012;109(21):8334-9.

Kupczyk M, Haahtela T, Cruz AA, et al. *Reduction of asthma burden is possible through National Asthma Plans.* Allergy. 2010;65(4):415-9.

Lalloo UG, Walters RD, Adachi M, et al. *Asthma programmes in diverse regions of the world: challenges, successes and lessons learnt.* International Journal of Tuberculosis and Lung Disease. 2011;15(12):1574-87.

Reissel E, Herse F, Väänänen J, et al. *Asthma costs in Finland 1987–2005 (in Finnish, Abstract in English).* Finnish Medical Journal. 2010;65:811-6.

9. Asthma Management Guidelines

FitzGerald JM, Quon BS. *The impact of asthma guidelines.* Lancet. 2010;376(9743):751-3.

Rabe KF, Decramer M, Siafakas N. *The year of the lung.* Lancet. 2010;376(9743):753-4.

The International Union Against Tuberculosis and Lung disease, The International Study of Asthma and Allergies in Childhood (ISAAC), editors. *The Global Asthma Report 2011*. Paris, France: The International Union Against Tuberculosis and Lung Disease; 2011.

World Health Organization. *Prevention and Control of Noncommunicable Diseases: Guidelines for primary health care in low resource settings.* Geneva, Switzerland: World Health Organization; 2012.

10. Access to Quality-Assured, Affordable Asthma Medicines

Babar ZU, Lessing C, Mace C, Bissell K. *The availability, pricing and affordability of three essential asthma medicines in 52 low- and middle-income countries.* Pharmacoeconomics 2013; 31:1063-82.

Cameron A, Ewen M, Ross-Degnan D, et al. *Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis.* Lancet. 2009 Jan 17;373(9659):240-9.

WHO. *Medicines prices, availability and affordability. The World Medicines Situation 2011*. Geneva, Switzerland: World Health Organization, 2011 WHO/EMP/MIE/2011.2.1.

Chiang C-Y, Bissell K, Perrin C. *Are national asthma programmes needed in resource-limited settings?* International Journal of Tuberculosis and Lung Disease 2012; 16: 572.

Hogerzeil HV. *The concept of essential medicines: lessons for rich countries.* British Medical Journal 2004; 329(7475):1169-1172.

11. Quality of Inhalers

Azatyan S. Roles of National Medicines Regulatory Authorities. WHO/Global Fund joint meeting on Quality Assurance of Essential Medicines; 30-31 August Geneva2011.

Committee for medicinal products for human use. *Guideline on the requirements for clinical documentation for orally inhaled products (OIP) including the requirements for demonstration*

of therapeutic equivalence between two inhaled products for use in the treatment of asthma and chronic obstructive pulmonary disease (COPD) in adults and for use in the treatment of asthma in children and adolescents. London: European Medicines Agency, 2009.

WHO. *WHO Prequalification Programme: progress report June 2013.* Geneva, Switzerland: World Health Organization, 2013.

12. Asthma Management in Low-Income Countries

Ade G, Gninafon M, Tawo L, et al. *Management of asthma in Benin: the challenge of loss to follow-up.* Public Health Action. 2013;3(1):76-80.

Aït-Khaled N, Enarson DA, Chiang C-Y, et al. *Management of Asthma: A guide to the essentials of good clinical practice.* Paris, France: International Union Against Tuberculosis and Lung Disease, 2008.

El Sony AI, Chiang C-Y, Malik E, et al. *Standard case management of asthma in Sudan: a pilot project.* Public Health Action. 2013;3(3):247-52.

Global Initiative for Asthma (GINA). *Global Strategy for Asthma Management and Prevention (Updated 2014).* Global Initiative for Asthma (GINA) 2014.

Kan XH, Chiang C-Y, Enarson DA, et al. *Asthma as a hidden disease in rural China: opportunities and challenges of standard case management.* Public Health Action. 2012;2(3):87-91.

World Health Organization. *Prevention and Control of Noncommunicable Diseases: Guidelines for primary health care in low resource settings.* Geneva, Switzerland: World Health Organization; 2012.

14. Asthma as a Lung Health Priority in LMICs

Ade G, Gninafon M, Tawo L, et al. *Management of asthma in Benin: the challenge of loss to follow-up.* Public Health Action. 2013;3(1):76-80.

El Sony AI, Chiang C-Y, Malik E, et al. *Standard case management of asthma in Sudan: a pilot project.* Public Health Action. 2013;3(3):247-52.

Asthmasms Sudan: *An asthma follow up system using rapidsms:* UNICEF; 2013 [updated 10 September; cited 2014]. Available from: unicefstories.org/2013/09/10/asthmasms-sudan-an-asthma-follow-up-system-using-rapidsms/.

The Impact of Involving Informal Health Providers for Tuberculosis Control in Sudan (TriagePlus): National Institutes of Health; 2013 [cited 2014]. Available from: clinicaltrials.gov/show/NCT01841541.

Brooks C, Pearce N, Douwes J. *The hygiene hypothesis in allergy and asthma: an update.* Current Opinion in Allergy and Clinical Immunology. 2013;13(1):70-7.

Pearce N, Asher I, Billo N, et al. *Asthma in the global NCD agenda: A neglected epidemic.* Lancet Respiratory Medicine. 2013;1(2):96-8.

Seita A, Harries AD. *All you need to know in public health we can learn from tuberculosis care: lessons for non-communicable disease.* International Journal of Tuberculosis and Lung Disease, 2013, 17:429–430

Vos T, Flaxman AD, Naghavi M, et al. *Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010.* Lancet. 2012;380(9859):2163-96.

15. Asthma as a NCD priority

Mallol J, García-Marcos L, Sole D, et al. *International prevalence of recurrent wheezing during the first year of life: variability, treatment patterns and use of health resources.* Thorax. 2010;65(11):1004-9.

Pearce N, Asher I, Billo N, et al. *Asthma in the global NCD agenda: A neglected epidemic.* Lancet Respiratory Medicine. 2013;1(2):96-8.

Pearce N, Ebrahim S, McKee M, et al. *The road to 25x25: how can the five-target strategy reach its destination?* Lancet Global Health. 2014;2:e126.

TABLES AND FIGURES

2. Global Burden of Disease

Figures 1 and 2. Prevalence of asthma symptoms among 13-14 year olds (ISAAC); Prevalence of severe asthma among 13-14 year olds (ISAAC). From: Lai CKW, Beasley R, Crane J, 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 3. Prevalence of "attacks of wheezing or whistling breath" (symptoms of asthma) in the last 12 months among persons aged 18 to 45, 70 countries, World Health Survey 2002-2003. From: To T, Stanojevic S, Moores G, et al. *Global asthma prevalence in adults: findings from the cross-sectional world health survey*. BMC Public Health. 2012; 12:204.

Figure 4. Burden of disease, measured by disability adjusted life years (DALYs, see explanation p20) per 100,000 population attributed to asthma by age group and sex. Global population, 2010. From: Institute for Health Metrics and Evaluation (IHME). *Global Burden of Disease (GBD) Cause Patterns.* Seattle, WA: University of Washington; 2013 [8th May 2014]. Available from: www.healthmetricsandevaluation.org/gbd/visualizations/gbd-cause-patterns.

Figure 5. Components of disability adjusted life years (DALYs), Years lived with disability (YLD) and Years of life lost (YLL) per 100,000 population attributed to asthma by age group. Global population, 2010 (see DALY explanation on p20). From: Institute for Health Metrics and Evaluation (IHME). *Global Burden of Disease (GBD) Cause Patterns.* Seattle, WA: University of Washington; 2013 [8th May 2014]. Available from: www.healthmetricsandevaluation.org/gbd/visualizations/gbd-cause-patterns.

Figure 6. Disability adjusted life years (DALYs) per 100,000 population attributed to asthma by country, both sexes, 2010. From: Institute for Health Metrics and Evaluation (IHME). *Global Burden of Disease (GBD) Compare.* Seattle, WA: University of Washington; 2013 [8th May 2014]. Available from: viz.healthmetricsandevaluation.org/gbd-compare/

3. Hospital Admissions

Figure 1. Age-standardised admission rates for asthma for earliest and latest available year in European countries ordered by latest admission rate. From: WHO Hospital Morbidity Database, November 2013 download, plus Eurostat (for some earlier data).

Figure 2. Asthma admission rates for European countries, age 5-14 v 20-44 years. From: WHO Hospital Morbidity Database, November 2013 download.

Figure 3. Long-term time trends in self-reported asthma prevalence, hospital admission rates and mortality rates for asthma among children in high income countries. From: Chawla J, Seear M, Zhang T, et al. *Fifty years of pediatric asthma in developed countries: how reliable are the basic data sources?* Pediatric Pulmonology 2012;47:211-219.

Figure 4. Annual change in hospital admission rates for childhood asthma (ages 5-14) in countries with one or more ISAAC centres providing prevalence data for both ISAAC Phase One (around 1995) and ISAAC Phase Three (around 2002), by change in prevalence of nocturnal wheezing among 13-14-year-olds. Adapted from: Anderson HR, Gupta R, Kapetanakis V, et al. I*nternational correlations between indicators of prevalence, hospital admissions and mortality for asthma in children.* International Journal of Epidemiology 2008; 37(3):573-82. (National admissions data from updated by WHO Hospital Morbidity Database) and Pearce N, Aït-Khaled N, Beasley R, et al. *Worldwide trends in the prevalence of asthma symptoms: Phase III of the International Study of Asthma and Allergies in Childhood (ISAAC).* Thorax 2007; 62(9): 758-66. (Prevalence data)

4. Mortality

Figure 1. Age-standardised asthma mortality rates for all ages 2001-2010 from countries where asthma is separately coded as a cause of death, ordered by mortality rate and country income group. Calculated from the average number of deaths and average population for each 5-year age-group over the period 2001-2010, using all available data for each country (the number of available years over this period ranged from 1 to 10). Source: WHO Detailed Mortality Database, February 2014 update.

Figure 2. Age-standardised asthma mortality rates for ages 5-34 years only, 2001-2010 from countries where asthma is separately coded as a cause of death, ordered by mortality rate and country income group. Data standardised to the World Standard Population. Calculated from the average number of deaths and average population for each 5-year age-group over the period 2001-2010, using all available data for each country (the number of available years over this period ranged from 1 to 10). Source: WHO Detailed Mortality Database, February 2014 update.

Figure 3. Age-standardised asthma mortality rates and age-standardised hospital admission rates for asthma, in European countries providing recent data for both (2001-2010). Sources: WHO Detailed Mortality Database, February 2014 update, WHO Hospital Morbidity Database, November 2013 download.

5. Wheezing in Infants

Figure 1. Prevalence of recurrent wheezing in infants during the first year of life in European and Latin American centres. From: Mallol J, García-Marcos L, Sole D, et al. *International prevalence of recurrent wheezing during the first year of life: variability, treatment patterns and use of health resources*. Thorax. 2010;65(11):1004-9.

Figure 2. Reported severity, medications and other variables in infants with Recurrent Wheezing during the first year of life. Source: Mallol J, García-Marcos L, Sole D, et al. *International prevalence of recurrent wheezing during the first year of life: variability, treatment patterns and use of health resources.* Thorax. 2010;65(11):1004-9.

8. National Asthma Strategies

Figure 1. Generic template for a local action plan. Adapted from: Haahtela T. *Evidence for asthma control – zero tolerance to asthma with the Finnish Programmes*. In: Global Atlas of Asthma. Eds.C.A. Akdis, I. Agache. EAACI 2013.

Figure 2. Strategic flow for an asthma plan Adapted from: Haahtela T, von Hertzen L, Makela M, et al. *Finnish Allergy Programme 2008-2018--time to act and change the course.* Allergy. 2008;63(6):634-45.

Figure 3. National asthma strategies for children and adults in countries responding to the Global Asthma Network survey, 2013. Global Asthma Network survey; 2013.

9. Asthma Management Guidelines Update

Figure 1. Asthma management guidelines in countries responding to the Global Asthma Network survey, 2013. Global Asthma Network survey; 2013.

Figure 2. Pharmaceutical sponsorship in asthma management guidelines in countries responding to the Global Asthma Network survey, 2013. Global Asthma Network survey; 2013.

Table: Comparison of 2011 and 2013 asthma guideline usage for those 72 countries participating in both surveys. Global Asthma Network surveys 2011 and 2013.

10. Access to Quality-Assured, Affordable Asthma Medicines

Figure 1. Essential asthma medicines survey 2014, Global Asthma Network countries. Global Asthma Network survey; 2014.

Table 1. Inclusion of inhalers on the WHO Essential Medicines List (EML) in National EML and National Reimbursement Lists (NRL), by country, in 99 Global Asthma Network countries, 2014. Global Asthma Network survey; 2014.

11. Quality of Inhalers

Figure 1. Schematic diagram of a pressurised metered dose inhaler.

14. Asthma as a lung health priority in LMICs

Figure1. The reduction in emergency room visits from one year of enrolment in the asthma standard case management project in Sudan 2007-2008. From: El Sony AI, Chiang C-Y, Malik E, et al. *Standard case management of asthma in Sudan: a pilot project*. Public Health

Action. 2013;3(3):247-52.

Figure 2. Number of emergency visits and hospitalisations in Benin:initial at enrolment versus one year 2007-2008. From: Ade G, Gninafon M, Tawo L, et al. *Management of asthma in Benin: the challenge of loss to follow-up*. Public Health Action. 2013;3(1):76-80.

Tables and Figures in appendices

Table 1. ISAAC world map data, symptoms of asthma. Adapted from: ISAAC Steering Committee. *Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC)*. European Respiratory Journal 1998; 12(2): 315-35. And: Lai CKW, Beasley R, Crane J, 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.

Table 2. National asthma management guidelines in countries participating in the Global Asthma Network, 2013. Global Asthma Network survey; 2013.

Figures 1-3. Scatter plots of national admission rates for asthma among children (aged 5-14) and adults (aged 20-44 and 45+) in European countries, latest available data (around 2010). From: WHO Hospital Morbidity Database, November 2013 download.

Figure 4. National asthma strategies for children in countries responding to the Global Asthma Network survey, 2013. Global Asthma Network survey; 2013.

Figure 5. National asthma strategies for adults in countries responding to the Global Asthma Network survey, 2013. Global Asthma Network survey; 2013.

Figure 6. Questions asked in the Global Asthma Network asthma guidelines survey 2013.

Figure 4. Pharmaceutical involvement in national asthma management guidelines in countries responding to the Global Asthma Network survey, 2013. Global Asthma Network survey; 2013.

GLOBAL ASTHMA REPORT: AUTHORS

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

Professor M Innes Asher
Dept of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, University of Auckland
New Zealand

Dr Nils E Billo
Public Health Consulting, Bern
Switzerland

Dr Karen Bissell
Dept of Research
International Union Against Tuberculosis and Lung Disease (The Union)
France

Professor Paul L P Brand
Princess Amalia Children's Center, Isala Hospital, Zwolle and UMCG Postgraduate School of Medicine, University Medical Center and University of Groningen, the Netherlands.

Dr Chiang Chen-Yuan
Dept of Lung Health and NCDs, International Union Against Tuberculosis and Lung Disease (The Union)
France

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

Mr Eamon Ellwood
Dept of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, University of Auckland, New Zealand

Mrs Philippa Ellwood
Dept of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, University of Auckland, New Zealand

Professor J Mark FitzGerald
Institute for Heart and Lung Health, Faculty of Medicine, the University of British Columbia, Canada

Professor Luis García-Marcos
Respiratory and Allergy Units, Arrixaca University Children's Hospital, University of Murcia, Spain

Ms Ramyani Gupta
Division of Community Health Sciences
St Georges, University of London, United Kingdom

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

Ms Elizabeth Limb
Division of Community Health Sciences
St Georges, University of London, United Kingdom

Professor Javier Mallol,
Department of Pediatric Respiratory Medicine, Hospital El Pino, University of Santiago de Chile, Chile

Professor Guy Marks,
Woolcock Institute of Medical Research, University of Sydney and South Western Sydney Clinical School, UNSW, Sydney, Australia

Professor Neil Pearce
Dept of Medical Statistics, Epidemiology and Public Health
London School of Hygiene and Tropical Medicine, United Kingdom

Mr Christophe Perrin
Médecins sans Frontières
France

Dr Mohsen Sadatsafavi
Institute for Heart and Lung Health, Faculty of Medicine, the University of British Columbia, Canada

Professor Olof Selroos
Selroos Medical Consulting (Semeco AB), Ängelholm, Sweden

Professor David Strachan
Division of Community Health Sciences
St Georges, University of London, United Kingdom

GLOBAL ASTHMA NETWORK STUDY GROUP*

Steering Group

MI Asher, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

NE Billo,
Public Health Consulting, Bern, Switzerland

K Bissell, International Union Against Tuberculosis and Lung Disease (The Union), Paris, France

C-Y Chiang, International Union Against Tuberculosis and Lung Disease (The Union), Paris, France

A El Sony, The Epidemiological Laboratory (Epi-Lab), Khartoum, Sudan

P Ellwood, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

L García-Marcos, University of Murcia, Pabellon Docente Universitario, Murcia, Spain

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

G Marks, Woolcock Institute of Medical Research, Sydney, NSW, Australia

N Pearce, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, United Kingdom

D Strachan, St George's, University of London, London, United Kingdom.

Principal Investigators

Africa

Algeria
Bab El Oued, Professor Samya Taright
Blida, Professor Rachida Boukari
Wilaya of Algiers, Professor Badia Benhabylès

Benin
Cotonou, Professor Martin Gninafon
Sèmè Podji, Dr Hervé Lawin

Burkina Faso
Bobo-Dioulasso, Dr Emile Birba

Cameroon
Douala, Dr Bertrand Hugo Mbatchou Ngahane
Yaounde, Dr Eric Walter Pefura Yone

Congo, Dem. Rep.
Kinshasa, Professor Dr Jean-Marie Kayembe

Egypt
Alexandria, Dr Alaa Mokhtar
Cairo, Professor Mona El Falaki

Ethiopia
Mekelle, Amanuel Berihu

Gambia
Fajara, Dr Suzanne Anderson

Ghana
Accra, Dr Henry N. Nagai
Kumasi, Dr Emmanuel OD Addo-Yobo

Kenya
Eldoret, Professor Fabian O Esamai
Nairobi, Dr Evans I. Amukoye

Libya
Tripoli, Dr Mohamed Shenkada

Malawi
Blantyre, Dr Kevin Mortimer

Mali
Bamako, Dr Yacouba Toloba

Nigeria
Enugu, Dr Adaeze Ayuk
Gusau, Dr Bilkisu Garba Ilah
Ibadan, Professor Adegoke Falade
Ife, Professor Gregory E. Erhabor
Lagos, Dr Ngozi Onyia
Maiduguri, Dr Ahmed Hamman Gabdo

Reunion Island
Reunion Island, Dr Isabella Annesi-Maesano

Senegal
Dakar, Associate Professor Nafissatou O. Toure

South Africa
Cape Town, Professor Heather J Zar
Ekurhuleni, Polokwane, Professor Kuku Voyi
Pretoria, Professor Refiloe Masekala

Sudan
Gadarif, Sara Azeim
Khartoum, Professor Asma El Sony

Togo
Lome, Professor Osseni Tidjani

Tunisia
Ariana, Professor Agnès Hamzaoui

Uganda
Kampala, Dr William Worodria

Zambia
Lusaka, Dr Somwe Wa Somwe

Zimbabwe
Zimbabwe, Dr Portia Manangazira

Asia-Pacific

China
Beijing, Professor Yu-Zhi Chen
Hefei, Dr Xiaohong Kan
Tayuan, Professor Yan Lin

Hong Kong
Hong Kong, Dr Christopher K W Lai

Indonesia
Bandung, Professor Dr Cissy B Kartasasmita
North Sumatera, Dr Wisman Dalimunthe

Japan
Fukuoka, Dr Hiroshi Odajima
Tochigi, Professor Shigemi Yoshihara

Korea, South
Seoul, Professor Dr Soo-Jong Hong

Lao PDR
Lao PDR, Associate Professor Dr Kongsap Akkhavong

Malaysia
Kota Bharu, Dr Mariana Daud

Mongolia
Ulaanbaatar, Professor Sonomjamts Munkhbayarlakh

Philippines
Metro Manila, Professor Felicidad Cua-Lim†

Singapore
Singapore, Associate Professor Daniel Yam Thiam Goh

Taiwan
Tainan, Professor Y Leon Guo
Taipei, Professor Jing-Long Huang

Thailand
Bangkok, Dr Pakit Vichyanond
Chantaburi, Dr Sintra Phumethum
Chiang Mai, Professor Muthita Trakultivakorn
Khon Kaen, Associate Professor Jamaree Teeratakulpisarn

Vietnam
Ho Chi Minh, Associate Professor Lan Thi Tuyet Le

Eastern Mediterranean

Iran
Ahwaz, Dr Maria Cheraghi
Birjand, Bushehr, Rasht, Tehran, Zanjan, Dr Mohammed-Reza Masjedi
Yazd, Associate Professor Mehran Karimi

Jordan
Amman, Professor Faisal Abu-Ekteish
Jerash, Professor Omar Al Omari

Kuwait
Kuwait, Dr Jawad A al-Momen

Malta
Malta, Professor Stephen Montefort

Oman
Al-Khod, Professor Omar Al-Rawas

Pakistan
Islamabad, Dr Mohammad Osman Yusuf

Palestine
North Gaza, Ramallah, Associate Professor Nuha El Sharif

Saudi Arabia
Abha, Dr Badr Rashed Al-Ghamdi
Alkhobar, Dr Abdullah Yousef
Madinah, Dr Mahmoud A. Nahhas
Riyadh, Dr Ziad A Memish

Syrian Arab Republic
Lattakia, Professor Yousser Mohammad

United Arab Emirates
Sharjah, Assistant Professor Bassam Mahboub

Indian Sub-Continent

India
Bangalore, Dr Bharath Kumar Reddy
Bikaner, Professor Mohammed Sabir
Chandigarh, Professor Meenu Singh
Chennai, Dr RP Ilangho
Jaipur, Professor Virendra Singh
Kolkata (10), Dr Anirban Maitra
Kolkata (14), Dr Mausumi Mukherjee
Kottayam, Professor T U Sukumaran
Lucknow, Professor Shally Awasthi
Mumbai (11), Dr Asha Vijaykumar Pherwani
Mumbai (7), Dr Uday Ananth Pai
New Delhi, Professor S K Sharma
Vellore, Dr Sneha Varkki

Sri Lanka
Colombo, Dr Kirthi D Gunasekera
Peradeniya, Dr Sanathusara T Kudagammana

Latin America

Argentina
Buenos Aires, Dr Natalio Salmun
Mendoza, Dr Fabian Alejandro Castracane
Salta, Dr Maximiliano Gómez

Bolivia
Santa Cruz, Dra Rosario Pinto-Vargas

Brazil
Belo Horizonte, Professor Paulo Augusto M Camargos
Curitiba, Professor Nelson Rosário
Feira de Santana, Professora Heli Viera Brandão
Passo Fundo, Dr Arnaldo Carlos Porto Neto
Pelotas, Professor Ana Maria Menezes
Porto Alegre, Professor Gilberto B Fischer
Recife, Professor Murilo de Britto
Rio de Janeiro, Professor Fábio Chigres Kuschnir
Santo André, Assistant Professor Neusa Falbo Wandalsen
Sao Paulo South, Professor Dirceu Solé

Chile
Santiago, Dra Viviana Aguirre
Valdivia, Professor Mario A Calvo Gil

Colombia
Bogota, Dr Elizabeth Garcia
Bucaramanga, Dr Jürg Niederbacher
Cali, Dr Gustavo A Ordoñez

Costa Rica
Costa Rica, Professor Manuel E Soto-Quirós

Ecuador
Esmeraldas, Professor Phillip Cooper
Guayaquil, Dr César Bustos
Quito, Dr Sergio Barba

El Salvador
San Salvador, Dr Margarita Figueroa Colorado

Grenada
Grenada, Associate Professor Muge Akpinar-Elci

Jamaica
Kingston, Dr Eulalia Kahwa

Mexico
Ciudad de Mexico, Dra Blanca E Del-Río-Navarro
Ciudad Victoria, Dr Roberto García-Almaráz
Guadalajara, Mr Dante Hernández-Colín
Mexicali Valley, Dr Valente Merida-Palacio
Monterrey, Professor Sandra Nora González-Díaz
Querétaro, Dr Rafael Francisco Páramo-Arroyo
San Luis Potosí, Dr Carlos A. Jiménez González

Nicaragua
Matagalpa, Marcia Zulema Cordero Rizo

Panama
David-Panamá, Dr Gherson Cukier

Peru
Lima, Dr Pascual Chiarella
Puno, Tumbes, Assistant Professor William Checkley

Trinidad and Tobago
Trinidad and Tobago, Dr Darren Dookeeram

Uruguay
Montevideo, Dra Dolores Holgado

North America

Canada
Montréal, Dr Sze Man Tse
Ontario, Professor Teresa To
Saskatoon, Professor Donna C. Rennie

United States
Chicago, Assistant Professor Harsha Kumar
Fort Wayne, Dr Riddhi Prakash Doshi
North Carolina, Professor Karin Yeatts
Seattle, Professor Gregory J Redding

Northern and Eastern Europe

Albania
Tiranë, Professor Alfred Priftanji

Armenia
Yerevan, Liana Kostanyan

Belarus
Grodno, Dr Andrei Shpakou

Bosnia and Herzegovina
Prijedor, Dr Sanela Domuz

Bulgaria
Sofia, Dr Tihomir B Mustakov

Croatia
Rijeka, Professor Vojko Rožmanic

Denmark
Copenhagen, PhD Fellow Lene Lochte

Finland
Helsinki, Professor Mika Mäkelä

Georgia
Kutaisi, Tbilisi, Professor Maia Gotua

Hungary
Szeged, Professor Zoltán Novák

Kosovo
Prishtina, Luljeta Neziri Ahmetaj

Latvia
Riga, Assistant Professor Vija Svabe

Macedonia
Skopje, Associate Professor Emilija Vlaski

Norway
Oslo, Tromsø, Dr Wenche Nystad

Poland
Krakow, Associate Professor Grzegorz Lis
Poznan, Associate Professor Anna Brêborowicz

Romania
Cluj-Napoca, Professor Diana Deleanu

Russia
Novosibirsk, Professor Dr Elena G Kondiourina
Tomsk, Professor Elena Kamaltinova

Serbia
Belgrade, Professor Zorica Zivkovic
Indjija, Dr Danilo Višnjevac
Novi Sad, Dr Mila Hadnadjev

Turkey
Ankara, Professor Arzu Yorgancioglu

Oceania

Australia
Adelaide, Dr Andrew Tai
Brisbane, Dr Scott Burgess
Newcastle, Professor Joerg Mattes
Sydney, Professor Guy Marks

French Polynesia
Polynésie française, Dr Isabella Annesi-Maesano

New Caledonia
Nouvelle-Calédonie, Dr Isabella Annesi-Maesano

New Zealand
Auckland, Professor Innes Asher
Bay of Plenty, Dr Chris Moyes
Christchurch, Associate Professor Philip Pattemore
Hawke's Bay, Dr Sarah Currie
Marlborough, Karen Vis
Northland, Kataraina Harawira
Otago, Associate Professor Robert Hancox
Waikato, Dr David Graham
Wellington, Dr Sunia Foliaki

Niue
Niue Island, Dr Marina Pulu

Samoa
Apia, Dr Litara Esera-Tulifau

Tokelau
Tokelau, Dr Tekie Iosefa

Tonga
Nuku'alofa, Dr George Aho

Tuvalu
Funafuti, Dr Nese Ituaso-Conway

Vanuatu
Port Vila, Dr Griffith Harrison

Western Europe

Austria
Salzburg, Professor Josef Riedler
Urfahr-umgebung, Associate Professor Gerald Haidinger

Belgium
Antwerp, Professor Joost Weyler

Channel Islands
Guernsey, Dr Peter Standring

Cyprus
Nicosia, Dr Panayiotis Yiallouros

France
Bordeaux, Professor Chantal Raherison
Créteil, West Marne, Dr Isabella Annesi-Maesano
Marseille, Professor Denis Charpin

Germany
Munich, Professor Dr med. Erika von Mutius

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

Ireland
Ireland, Dr Patrick Manning

Italy
Ascoli Piceno, Professor Sergio Bonini
Empoli, Dr Maria Grazia Petronio
Palermo, Dr Stefania La Grutta
Roma, Dr Francesco Forastiere
Trento, Dr Silvano Piffer

Netherlands
Utrecht, Professor Bert Brunekreef

Portugal
Lisboa, Dr José Rosado Pinto

Spain
Asturias, Dr Ignacio Carvajal-Urueña
Barcelona, Professor Rosa M Busquets
Bilbao, Dr Carlos González Díaz
Cádiz, Dr Andrés Rabadán-Asensio
Cartagena, Professor Luis García-Marcos
Castellón, Dr Alberto Arnedo-Pena
La Coruña, Dr Angel López-Silvarrey Varela
Madrid, Professor Gloria García-Hernández
Málaga, Dr Julia Wärnberg
San sebastián, Professor Eduardo G Pérez-Yarza
Sevilla, Professor Manuel Praena-Crespo
Valencia, Professor Maria M. Morales Suárez-Varela

United Kingdom
Birmingham, Dr Adel H Mansur

Vatican City
Vatican City, MD Alessandro Fiocchi

* The Global Asthma Network Study Group consists of centres that contributed data to this report through the surveys in chapters 8-10. For the full list of Global Asthma Network centres see www.globalasthmanetwork/about/centres.php
† Deceased

ACKNOWLEDGEMENTS

The Global Asthma Network (GAN) Steering Group would like to thank The Union for its generous support of the Global Asthma Reports 2011 and 2014, and all the activities of GAN to date. We also appreciate the support of the University of Auckland, which has provided facilities for GAN.

We would like to thank all of the authors who contributed to the chapters, and all of those around the world who collected data for this second Global Asthma Report. In particular we would like to acknowledge Eamon Ellwood, Website Manager, for the development and production of the report. The editing group were Innes Asher, Philippa Ellwood, Karen Bissell, David Strachan, Neil Pearce, Janet McAllister and Catherine Gilchrist.

We also acknowledge the enormously valuable contributions of our colleagues, participants and funders of ISAAC and The Union which underpin our work and this report.

Photographs were provided by Matthieu Zellweger on location in Thailand (Bangkok), Vietnam (Ho-Chi-Minh City), and India (New Delhi), enabled by Professor Pakit Vichyanand (Thailand), Associate Professor Lan Thi Tuyet Lee (Vietnam), and Professor S K Sharma and Dr Ragesh R Nair (India). Matthieu Zellweger is represented and distributed by Haytham Pictures, Paris.

The design of the Global Asthma Report 2014 was undertaken by Eamon Ellwood in Auckland based on the Global Asthma Report 2011 designed by Gilles Vérant in Paris.

PHOTOGRAPHY:

Matthieu Zellweger: ©2014, Thailand: cover, pages 1, 7, 14-15, 27, 28, 33, 35, 38, 42-43, 48, 53, 58, 62, 65, 66-67; ©2014, Vietnam: pages 10, 12, 36, 39, 57; ©2014, India: pages 22, 27, 31, 47, 56, 60, 63, 64, 68, 72, 73, 75.
Courtesy of the World Lung Foundation: Gary Hampton: ©2004, India: pages 4, 61, ©2007, India: pages 5, 92-93; Jan van den Hombergh: ©2009, Ethiopia: page 6; Damien Schumann: ©2009, South Africa: page 40; Jad Davenport: ©1997, Bangladesh: page 69.
Courtesy of the World Health Organization:
Christopher Black: ©2008 France: page 3. 2008
Courtesy of Worldbank:
Scott Wallace: ©2009, Tanzania: page 25; Curt Carnemark: ©1992, Nepal: page 41, ©2003, Bhutan: page 75; Tran Thi Hoa, ©2002, Vietnam: page 74; Shehzad Noorani: ©2002, Bangladesh: pages 76-77
Courtesy of Photoshare: Roobon, The Hunger Project, ©2004, Bangladesh: pages 8-9.
Courtesy of The New Zealand Asthma Foundation: ©2011, New Zealand: pages 50,79, ©2012, New Zealand: page 50.
Courtesy of stargazette.com: ©2007, United States of America: page 26.
Courtesy of UNESCO: Karel Prinsloo: ©2013, Kenya: page 71.

DESIGN:

Gilles Vérant, Paris
Eamon Ellwood, New Zealand

Global Asthma Network

Visit our website www.globalasthmareport.org

ISBN: 978-0-473-29125-9