

The Global Burden of Respiratory Disease—Impact on Child Health

Heather J. Zar, MD, PhD,^{1*} and Thomas W. Ferkol, MD²

Summary. Respiratory disease is the major cause of mortality and morbidity worldwide, with infants and young children especially susceptible. The spectrum of disease ranges from acute infections to chronic non-communicable diseases. Five respiratory conditions dominate—acute respiratory infections, chronic obstructive pulmonary disease, asthma, tuberculosis (TB), and lung cancer. Pneumonia remains the predominant cause of childhood mortality, causing nearly 1.3 million deaths each year, most of which are preventable. Asthma is the commonest non-communicable disease in children. Pediatric TB constitutes up to 20% of the TB caseload in high incidence countries. Environmental exposures such as tobacco smoke, indoor air pollution, and poor nutrition are common risk factors for acute and chronic respiratory diseases. Pediatric and adult respiratory disease is closely linked. Early childhood respiratory infection or environmental exposures may lead to chronic disease in adulthood. Childhood immunization can effectively reduce the incidence and severity of childhood pneumonia; childhood immunization is also effective for reducing pneumonia in the elderly. The Forum of International Respiratory Societies (FIRS), representing the major respiratory societies worldwide, has produced a global roadmap of respiratory diseases, *Respiratory Disease in the World: Realities of Today—Opportunities for Tomorrow*. This highlights the burden of respiratory diseases globally and contains specific recommendations for effective strategies. Greater availability and upscaled implementation of effective strategies for prevention and management of respiratory diseases is needed worldwide to improve global health and diminish the current inequities in health care worldwide. **Pediatr Pulmonol.** © 2014 Wiley Periodicals, Inc.

Key words: International health; pneumonia; asthma; tuberculosis; child.

Respiratory diseases affect the lives of more than one billion people worldwide and are the predominant cause of mortality and morbidity.^{1–7} Infants and young children are especially susceptible. Five respiratory conditions predominantly contribute to the global burden—acute respiratory infections, chronic obstructive pulmonary disease (COPD), asthma, tuberculosis (TB), and lung cancer. Accounting annually for over four million deaths, respiratory infections are the leading cause of death in

low- or middle-income countries (LMICs).⁷ COPD affecting more than 200 million people, is the fourth leading cause of death in the world and is increasing in prevalence globally.^{5,6} About 235 million people worldwide have asthma,¹ with a rising prevalence reported especially in LMICs. Annually, almost 8.7 million people develop TB, while 1.4 million die from this disease.⁴ Lung cancer is the most common malignancy worldwide, responsible for 1.4 million deaths, or about 18% of all

¹Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital, University of Cape Town, Cape Town, South Africa.

²Department of Pediatrics, Cell Biology, and Physiology, Washington University in St. Louis, St. Louis, Missouri.

Conflict of interest: None.

*Correspondence to: Heather Zar, 5th floor ICH building, Red Cross War Memorial Children's Hospital, Rondebosch 7700, South Africa.
E-mail: heather.zar@uct.ac.za

Received 5 November 2013; Accepted 27 January 2014.

DOI 10.1002/ppul.23030
Published online in Wiley Online Library
(wileyonlinelibrary.com).

cancer mortality.⁸ Respiratory diseases disproportionately affect children; pneumonia is the leading cause of death in infants and children under 5 years.⁹

In this context, *Pediatric Pulmonology* has initiated a focus on global child lung health. This is the first article in this initiative to publish original articles and reviews on global health issues relevant to children. The article highlights the global epidemiology of respiratory illnesses, with special attention to a recent report from the Forum of International Respiratory Societies (FIRS).¹⁰

FORUM OF INTERNATIONAL RESPIRATORY SOCIETIES (FIRS) AND THE GLOBAL ROADMAP OF RESPIRATORY DISEASES

The Forum of International Respiratory Societies (FIRS) is an organization that represents major respiratory societies worldwide, including the American College of Chest Physicians (ACCP), Asociación Latinoamericana de Tórax (ALAT), Asian Pacific Society of Respirology (APSR), American Thoracic Society (ATS), European Respiratory Society (ERS), International Union Against Tuberculosis and Lung Disease (IUATLD), and Pan African Thoracic Society (PATS). For nearly a decade, FIRS has been working for the improvement of global lung health. It is therefore timely that FIRS has released a publication of the global roadmap of respiratory diseases, entitled *Respiratory Disease in the World: Realities of Today—Opportunities for Tomorrow*, which is intended to highlight the burden of respiratory diseases globally and to promote more widespread implementation of effective preventative and management strategies.¹⁰ This publication addresses both infectious and non-communicable respiratory diseases, which have gained rising attention globally.

ENVIRONMENTAL RISK FACTORS

Environmental exposures such as tobacco smoke, indoor air pollution, and poor nutrition are common risk factors for many of these conditions. Tobacco smoke exposure is a major risk factor for respiratory infections, COPD, asthma, TB, and lung cancer.¹¹ Smoking was estimated to be responsible for 12% of deaths in men and 6% of deaths in women globally in 2004.¹² It is projected that as many as one billion people will die from tobacco smoking in the 21st century,¹³ the greatest proportion from respiratory diseases. In the United States, current smokers are 25 times more likely to die of lung cancer than those who never smoked.¹⁴ The life-expectancy is shortened by ten-years in smokers.¹¹ About 50% of all households in the world and 90% of rural households use solid fuels, exposing over two billion people to the toxic effects of biomass fuel.¹⁵ The World Health Organization estimates that 1.6 million deaths can be attributed to indoor smoke each year. Most disease and death

attributable to exposure to poor indoor air quality occurs in women and children, especially in low-income families,¹⁶ predisposing to COPD, lung cancer as well as pneumonia and asthma in children.¹⁷ Socio-economic adversity impacts on lung health, influencing the epidemiology and severity of illness. For example, malnutrition occurs in almost half of all children dying from pneumonia, while lack of breastfeeding is associated with a 15-fold higher risk of developing pneumonia.^{9,18}

THE BURDEN OF CHILDHOOD RESPIRATORY ILLNESS

Great strides have been made in the last 20 years in reducing under 5 mortality from 90 per 1,000 live births in 1990 to 48 per 1,000 in 2012.¹⁸ However, approximately 6.6 million children under 5 years of age still die annually. Pneumonia is the predominant cause of death, leading to nearly 1.3 million childhood deaths each year, most of which are preventable.^{9,18} Further, the reduction in under 5 mortality is inadequate to meet the target for Millenium Development Goal number 4 (MDG4) by 2015, to attain a two-thirds reduction from the 1990 levels. At current rates, MDG4 will only be achieved in 2028, with African countries especially lagging.¹⁸

Infants and young children are particularly vulnerable to respiratory disease. Although data from LMICs are limited, the evidence indicates that more than 90% of respiratory related childhood deaths occur in these regions.^{9,18,19} Amongst these, the burden is heavily skewed towards African nations where half of pneumonia-associated deaths occur.¹⁸ In addition, pneumonia is a major contributor to deaths in children with malnutrition or HIV infection.^{18,20}

Tuberculosis is another respiratory infection associated with much morbidity and mortality, especially in high incidence areas and regions with high HIV prevalence. While the burden of childhood TB is difficult to accurately quantify due to lack of capacity for making a microbiologic diagnosis in children, estimates are that it accounts for 15% to 20% of the TB caseload in high incidence areas.²¹ There are approximately 530,000 new cases of childhood TB and 75,000 deaths annually in children.²¹ The pediatric HIV epidemic is now largely confined to sub-Saharan Africa, where almost 3 million HIV-infected children live.²² Prenatal screening, effective preventative perinatal interventions, and use of antiretroviral therapy (ART) have substantially reduced the incidence of pediatric HIV and of HIV-associated respiratory disease in many countries. ART has enabled long term survival of perinatally infected children, who may develop HIV-associated chronic lung disease.²⁰ However, there are still gaps in access to ART in children with only 28% of eligible children receiving this

compared to 59% of adults.¹⁸ Thus, HIV-associated lung disease remains an important cause of childhood morbidity and mortality in sub-Saharan Africa.

Asthma is the most common non-communicable disease in children, affecting about 14% of children globally, with a rising prevalence worldwide.²³ Though regarded as a disease of higher income societies, data from global comparative studies show that the prevalence of childhood asthma in many LMICs is higher than the global average and that the burden is also increasing in these areas.^{23–25} Furthermore, children living in these countries have more severe symptoms than those in high-income settings.²⁵ In many LMICs nearly 30% of children with severe asthma symptoms have never been diagnosed with asthma.²⁵ Over 80% of asthma-related deaths occur in LMICs. In these areas, under diagnosis is a problem in part due to health systems that are overwhelmed by communicable respiratory diseases.²⁶

While COPD is regarded as an adult disease, increasing evidence suggests that its origins may be in childhood, related to early childhood respiratory tract infection or tobacco smoke exposure.^{27,28} Prenatal tobacco smoke exposure may contribute to COPD, and lead to long-term reductions in lung function and chronic wheezing illness.²⁹

THE IMPACT OF ADULT RESPIRATORY ILLNESS ON CHILD HEALTH

Adult respiratory disease can have a direct negative impact on child health. Children living in households in which an adult with COPD are at increased risk of lower respiratory tract infection such as pneumonia. Passive exposure to tobacco smoke substantially increases the risk of pneumonia, asthma, and greater severity of respiratory illnesses.³⁰ An adult household TB contact is an important risk factor for transmission, especially to infants or young children.²¹ In high HIV prevalence areas, the risk of childhood TB is particularly high. Similarly, a child living in an HIV-infected household will have increased risk of lower respiratory tract infections or TB, even when the child is HIV-negative.²⁰ Conversely, childhood immunization particularly with the new conjugate vaccines can effectively reduce the incidence and severity of childhood pneumonia; further, childhood immunization is effective for reducing pneumonia in the elderly.³¹

Respiratory illness in a parent or caregiver can have important indirect, negative effects on child health. A sick parent who is unable to work, may result in reduced household income and poverty, including childhood malnutrition. Loss of a parent from respiratory illness is devastating for a child with social, psychological, and economic consequences negatively impacting on child health.

PREVENTION AND MANAGEMENT

Most childhood respiratory deaths are preventable.^{9,18} However, implementation of available effective preventive and management interventions is still a real challenge. Scaling up of available, cost-effective interventions can prevent 65% pneumonia deaths by 2025.^{18,32} Improved access to health care, better nutrition, promotion of breast-feeding, improved living conditions and reduced exposure to indoor pollutants may reduce respiratory infections and severity.^{32,33} For HIV-infected children, use of ART early in the course of HIV infection and of cotrimoxazole prophylaxis can substantially reduce the burden of pneumonia and of severe disease.²⁰

Prevention of severe respiratory infections has been advanced by the development of conjugate vaccines against *Haemophilus influenzae* type b (HibCV) and *Streptococcus pneumoniae* (PCV).³³ Combined data from six studies of the effectiveness of HibCV in LMIC indicates a reduction of 18% in radiological pneumonia, of 6% in severe pneumonia, and of 7% in pneumonia-associated mortality.³² Through support from the Global Alliance for Vaccines and Immunization (GAVI), approximately 90% of low-income countries had introduced HibCV in 2011.¹⁸ PCV has resulted in a dramatic decline in pneumonia hospitalization in several countries, especially in children less than 2 years of age. Overall, data from six studies in LMICs estimated a reduction of 29% in radiologically confirmed pneumonia, 11% in severe pneumonia, and 18% in pneumonia-specific mortality.³² Moreover, widespread PCV immunization of infants has also led to a dramatic decline in the rates of hospitalization for pneumonia in adults, especially the elderly due to herd immunity and reduction in transmission of serotypes causing pneumonia.³¹ However, implementation of PCV into national immunization programs is suboptimal, with only 31% of the world's birth cohort currently having access to PCV.³⁴ Only 36% of countries with the highest mortality, and 37% countries in which more than 10% of deaths in children were attributable to pneumonia, had introduced PCV by 2012.³⁴

Effective management strategies include the WHO Integrated management of Childhood Illness (IMCI) program and use of oxygen in cases of severe or very severe pneumonia. The use of case management guidelines for childhood pneumonia can significantly reduce overall and pneumonia-specific mortality in children.³⁵ However, only 60% of children with pneumonia symptoms are taken to a health care provider.¹⁸ Recently, the WHO launched the integrated global action plan for the prevention and control of pneumonia and diarrhea, highlighting common strategies for preventing and treating these illnesses as well as pneumonia-specific strategies.³⁶

Childhood respiratory disease can be prevented by several basic measures—improving nutrition, comprehensive immunization, better living conditions to prevent crowding, avoidance of tobacco smoke and indoor air pollution exposures, and measures to prevent or treat HIV. The roadmap highlights these and other opportunities, and advocates for many improvements that are highly relevant to child health.¹⁰ Legislators and other decision-makers must be informed that respiratory health is a major component of global health, that respiratory disease is the major cause of childhood illness with long-term negative consequences on adult health and that the economic consequences for nations are substantial. Policy makers must ensure universal access to quality health care, including the availability of vaccines and essential medications. Tobacco use and exposure to ambient or indoor air pollution must be reduced. Education and training of health professionals in respiratory diseases worldwide must be strengthened. Further research is essential to develop programs, tools, and strategies to better prevent and treat respiratory diseases. These recommendations provide the framework for the anticipated United Nations high-level summit on non-communicable diseases to assess progress toward a global plan for their prevention and control. Indeed, implementation of these strategies may have a profound effect on child health, reduce economic costs, and diminish current inequities in child health worldwide.

REFERENCES

- World Health Organization. *Chronic respiratory disease, Asthma*. 2013. Available from: <http://www.who.int/respiratory/asthma/en/>
- World Health Organization. *Chronic Respiratory Diseases Burden of COPD*. 2013. Available from: <http://www.who.int/respiratory/copd/burden/en/index.html>
- World Health Organization. *Chronic respiratory diseases*. Available from: http://www.who.int/gard/publications/chronic_respiratory_diseases.pdf
- World Health Organization. *Global Tuberculosis Report 2012*. 2012. Available from: http://www.who.int/tb/publications/global_report/en/
- Global Alliance against Chronic Respiratory Disease, WHO. Available from: http://www.who.int/gard/news_events/1-3_GARD-06-07-K1.pdf
- Buist AS, Vollmer WM, McBurnie MA. Worldwide burden of COPD in high- and low-income countries Part I. The burden of obstructive lung disease (BOLD) initiative. *Int J Tuberc Lung Dis* 2008;12:703–708.
- World Health Organization. *The global burden of disease: 2004 update*. Geneva, Switzerland: WHO Press; 2008. 39–52. Available from: http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf
- Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010;127:2893–2917.
- Walker CL, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, O'Brien KL, Campbell H, Black RE. Global burden of childhood pneumonia and diarrhea. *Lancet* 2013;381:1405–1416.
- Forum of International Respiratory Societies (FIRS). *Respiratory diseases in the world Realities of Today—Opportunities for Tomorrow*. Sheffield, UK: ERS Press; 2013. Available at; <http://www.thoracic.org/global-health/firs-report-respiratory-diseases-in-the-world/resources/firs-report-for-web.pdf>
- Jha PR, Landsman C, Rostron V, Thun B, Anderson M, McAfee RN, Peto T R. 21st-century hazards of smoking and benefits of cessation in the United States. *N Engl J Med* 2013;368:341–350.
- World Health Organization. *Global health risks: mortality and burden of disease attributable to selected major risks*. Geneva, Switzerland: WHO Press; 2009. 21. Available from: http://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_Front.pdf
- World Health Organization. *Tobacco Free Initiative, MPOWER*. Available from: <http://www.who.int/tobacco/mpower/en>
- Thun MJ, Carter BD, Feskanich D, Freedman ND, Prentice R, Lopez AD, Hartge P, Gapstur SM. 50-year trends in smoking-related mortality in the United States. *N Engl J Med* 2013; 368:351–364.
- World Health Organization. *Indoor air pollution and health Fact sheet 292*. 2011. Available from: <http://www.who.int/mediacentre/factsheets/fs292/en/index.html>
- Torres-Duque C, Maldonado D, Pérez-Padilla R, Ezzati M, Viegi G; Forum of International Respiratory Studies (FIRS) Task Force on Health Effects of Biomass Exposure. Biomass fuels and respiratory diseases: a review of the evidence. *Proc Am Thorac Soc* 2008;5:577–590.
- Dherani M, Pope D, Mascarenhas M, Smith KR, Weber M, Bruce N. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. *Bull World Health Organ* 2008;83:390–398.
- United Nations Children's Fund. *Committing to child survival: A promise renewed Progress report*. 2013. UNICEF, 2013. Available at www.apromiserenewed.org
- Nair H, Simões EAF, Rudan I, Gessner BD, Azziz-Baumgartner E, Zhang JS, Feikin DR, Mackenzie GA, Moisi JC, Roca A. et al. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010: a systematic analysis. *Lancet* 2013;381:1380–1390.
- Gray DM, Zar HJ. Community-acquired pneumonia in HIV-infected children: a global perspective. *Curr Opin Pulm Med* 2010;16:208–216.
- World Health Organization, UNICEF, and Centers for Disease Control. "Roadmap for childhood tuberculosis: towards zero deaths." 2013. Available at www.who.int
- UNAIDS. *AIDS epidemic update: Special report on HIV/AIDS*. December 2012. Available from: <http://www.unaids.org>
- Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, Williams H; ISAAC Phase Three Study Group. Worldwide trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis and eczema in childhood: ISAAC phases one and three repeat multicountry cross-sectional surveys. *Lancet* 2006;368:733–737.
- Ait-Khaled N, Odhiambo J, Pearce N, Adjoh KS, Maesano IA, Benhabyles B, Bouhayad Z, Bahati E, Camara L, Catteau C, et al. Prevalence of symptoms of asthma, rhinitis and eczema in 13- to 14-year-old children in Africa: the International Study of Asthma and Allergies in Childhood Phase III. *Allergy* 2007;62:247–258.
- Lai CK, Beasley R, Crane J, Foliaki S, Shah J, Weiland S; International Study of Asthma and Allergies in Childhood Phase Three Study Group. Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2009;64:476–483.
- Zar HJ, Levin ME. Challenges in treating paediatric asthma in developing countries. *Pediatr Drugs* 2012;14:1–7.

27. Svanes C, Sunyer J, Plana E, Dharmage S, Heinrich J, Jarvis D, de Marco R, Norbäck D, Raheison C, Villani S, et al. Early life origins of chronic obstructive pulmonary disease. *Thorax*. 2010;65:14–20.
28. de Marco R, Accordini S, Marcon A, Cerveri I, Antó JM, Gislason T, Heinrich J, Janson C, Jarvis D, Kuenzli N, et al. Risk factors for chronic obstructive pulmonary disease in a European cohort of young adults. *Am J Resp Crit Care Med* 2011;183:891–897.
29. Stocks J, Sonnappa S. Early life influences on the development of chronic obstructive pulmonary disease. *Ther Adv Respir Dis* 2013;7:161–173.
30. US Centers for Disease and Control and Prevention. Smoking and Tobacco Use. Available from: www.cdc.gov/tobacco/data_statistics/fact_sheets/secondhand_smoke/general_facts
31. Griffin MR, Zhu Y, Moore MR, Whitney CG, Grijalva CG. U.S. hospitalizations for pneumonia after a decade of pneumococcal vaccination. *New Eng J Med* 2013;369:155–163.
32. Bhutta ZA, Das JK, Walker N, Rizvi A, Campbell H, Rudan I, Black RE; Lancet Diarrhoea and Pneumonia Interventions Study Group. Interventions to address deaths from childhood pneumonia and diarrhea equitably: what works and at what cost? *Lancet* 2013;381:1417–1429.
33. Zar HJ, Madhi SA, Aston SJ, Gordon SB. Pneumonia in low and middle income countries—progress and challenges. *Thorax* 2013;68:1052–1056.
34. Wang SA, Mantel CF, Gacic-Dobo M. et al. Progress in introduction of pneumococcal vaccine—worldwide 2000–2012. *MMWR Morb Mortal Wkly Rep* 2013;62:308–311.
35. Sazawal S, Black RE, Pneumonia Case Management Trials Group. Effect of pneumonia case management on mortality in neonates, infants, and preschool children: a meta-analysis of community-based trials. *Lancet Infect Dis* 2003;3:547–556.
36. World Health Organization, United Nations Children’s Fund. *Ending preventable child deaths from pneumonia and diarrhea by 2025: The integrated global action plan for the prevention and control of pneumonia and diarrhoea (GAPD)*. Geneva Switzerland: World Health Organisation; 2013. Available at: www.who.int