

# Respiratory diseases in the world. Realities of today – opportunities for tomorrow

Forum of International Respiratory Societies (FIRS)

Experts from the world's leading lung organisations have come together for the first time to call for a world-wide effort to improve healthcare policies, systems, and care delivery to make a positive difference to the lung health of the world.

Their report features five major disease areas that are of immediate and greatest concern. These include acute respiratory infections, tuberculosis asthma, COPD, and lung cancer, which are the leading causes of death or morbidity worldwide.

We here reproduce a selection from the report.

## Foreword

When we are healthy we take our breathing for granted, never fully appreciating that our lungs are essential organs for life. But when our lung health is impaired, nothing else but our breathing really matters. That is the painful reality for those suffering from lung disease, which affects people of all ages in every corner of the world. Lung diseases kill millions and causes suffering to millions more. Threats to our lung health are everywhere, and they start at an early age, when we are most vulnerable. Fortunately, many of these threats are avoidable and their consequences treatable. By acting now, we can save lives and prevent suffering worldwide.

The Forum of International Respiratory Societies (FIRS) is comprised of the leading international respiratory societies in the world. The goal of FIRS is to unify and enhance efforts to improve lung health throughout the world. The purpose of this document is to inform, raise awareness, and assist those who advocate for protecting and improving respiratory health. It tells of the magnitude of respiratory diseases and the threats to lung health across the globe. It is not a comprehensive textbook, but a guide emphasizing the diseases of greatest and immediate concern. It outlines practical approaches to combat threats to respiratory health, and proven strategies to improve significantly the care we provide for individuals around the world afflicted with respiratory diseases. It calls for improvements in healthcare policies, systems, and care delivery, as well as provides direction for research. In brief, it outlines ways to make a positive difference in the respiratory health of the world.

We would like to thank everyone involved in the development of this work, especially Don Enarson and his colleagues who comprised the Writing Committee. We would also like to express our sincere appreciation to Dean Schraufnagel for his careful and expert review. We intend to update this document regularly, and are seeking feedback and suggestions for ways to improve it.

On behalf of those suffering from respiratory disease and those who are at risk of respiratory disease in the future, from around the world, we ask for your help in making a difference and a positive impact on the respiratory health of the world.

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## Introduction

Respiratory disease causes an immense worldwide health burden. *It is estimated that 235 million people suffer from asthma;<sup>1</sup> more than 200 million people have chronic obstructive pulmonary disease (COPD); 65 million endure moderate to severe COPD;<sup>2</sup> 1% to 6% of the adult population (more than 100 million people) experience sleep-disordered breathing;<sup>3</sup> 8.7 million people develop tuberculosis annually<sup>4</sup> millions live with pulmonary hypertension;<sup>3</sup> and more than 50 million people struggle with occupational lung diseases, totaling more than one billion persons suffering from chronic respiratory conditions.<sup>5</sup>* At least two billion people are exposed to the toxic effects of biomass fuel consumption; one billion are exposed to outdoor air pollution; and one billion are exposed to tobacco smoke. *Each year, 4 million people*

die prematurely from chronic respiratory disease.<sup>5</sup>

Infants and young children are particularly susceptible. Nine million children under 5 years of age die annually, and lung diseases are the most common causes for these deaths. Pneumonia is the world's leading killer of young children.<sup>6</sup> Asthma is the most common chronic disease, affecting about 14% of children globally and rising.<sup>7</sup>

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death worldwide, and the numbers are growing.<sup>8</sup> The most common lethal cancer in the world is lung cancer, which kills more than 1.4 million people each year (2008 statistics),<sup>9</sup> and the numbers are growing. Respiratory tract infections caused by influenza kill 250,000 to 500,000 people and costs 71 to 167 billion US dollars annually.<sup>10</sup>

*"Respiratory infections" ranks number one as the greatest single contributor to the overall burden of disease in the world, as measured in disability-adjusted life-years lost (DALY), which estimate the amount of active and productive life lost due to a condition.\**

No organ is more vital and no organ is more vulnerable than the lung. Being unable to breathe is one of the most distressing feelings one can have. The lungs are the largest internal organ in the body, and the only internal organ that is exposed constantly to the external environment. *Everyone who breathes is vulnerable to the infectious and toxic agents in the air.* While respiratory disease causes death in all regions of the globe and in all social classes, certain people are more vulnerable to environmental exposures than others are.

In recent decades, modern medicine has advanced the length and quality of life in most countries, although changing life styles and infections, such as with human immunodeficiency virus (HIV), have created new challenges. At the same time, increasing health care costs have threatened many nations' financial health, and the effort needed to care for the ill and dying affects national productivity. It has become abundantly clear that the economic development of countries is tightly linked to the health of its citizens. Poor health, both individual and public, along with lack of education and lack of an enabling political structure are major impediments to a country's development and the roots of poverty. *Poor health impoverishes nations, and poverty causes poor health,* in part related to inadequate access to quality health care. Even more distressing is the enormous suffering that living with illness causes. Those who are most disadvantaged suffer most due to poor health. With this awareness, the United Nations convened a high-level meeting on noncommunicable diseases to develop a global plan for their prevention and control.<sup>11</sup> The Forum

\* DALY is composed of two measures, *years of life lost* (YLL), which is the potential years of life lost if the person had not died prematurely, and *years lived with disability* (YLD), to take into account the years of life with disability. *Disability-Adjusted Life Years* (DALY) is calculated by summing the two:  $DALY=YLL+YLD$ . This measure is sometimes referred to as the burden of disease.

of International Respiratory Societies (FIRS) has been part of this effort. It strongly believes that investing in public health pays dividends many times in many ways.

Health care cost for respiratory diseases is increasingly burdening economies of all countries. For example, the annual cost of asthma in the United States is estimated to be \$18 billion.<sup>12</sup> If one considers the lost productivity of family members and others caring for these individuals, the cost to society is far greater.

## The Big Five

Five respiratory conditions account for the greatest burden to society: 1. chronic obstructive pulmonary disease (COPD), 2. asthma, 3. acute respiratory infections, 4. tuberculosis, and 5. lung cancer.

### 1. Chronic Obstructive Pulmonary Disease Scope of the disease

Chronic obstructive pulmonary disease (COPD) affects more than 200 million people and is the fourth leading cause of death in the world.<sup>5</sup> *COPD is the only major disease that is increasing in prevalence and it is increasing on all continents.*<sup>13-15</sup> Furthermore, studies show that underdiagnosis ranges from 72% to 93%, which is higher than reported for hypertension, hypercholesterolemia, and similar disorders. Misdiagnosis is also common.<sup>16</sup> The most important factor leading to the development of COPD is tobacco smoking. Tobacco smoke causes destruction of lung tissue and obstruction of the small airways leading to emphysema and bronchitis, which are the main diseases of COPD.

Indoor smoke, inhaled occupational exposures through farming, mining, construction, transportation, and manufacturing pose risks for COPD throughout the world. Other risks for COPD include genetic syndromes, such as  $\alpha$ 1-antitrypsin deficiency, outdoor air pollution, and other diseases that involve the airways, such as chronic asthma and tuberculosis.<sup>17</sup> Smoke exposure in childhood may predispose to the development of chronic lung disease in adult life.<sup>18</sup>

### Prevention

Reduction of smoking is the first and most important priority in preventing COPD. This measure also will greatly reduce the morbidity and mortality of other lung diseases. Chimney cook stoves and other devices to decrease indoor smoke exposure lessen the risk of respiratory infections in children and potentially the incidence of COPD in non-smokers, especially women. Controlling occupational exposure to dust and fumes will have important benefits in reducing the burden of COPD.

### Treatment

Identification and reduction of exposure to risk factors are essential to prevent and treat COPD. All individuals who smoke should be encouraged and enabled to quit. Spirometry is required for the clinical diagnosis of

COPD, to avoid misdiagnosis, and to evaluate the severity of the airflow limitation. Inhaled bronchodilators are the main medicines that help these patients. Long-term treatment with inhaled corticosteroids added to long-acting bronchodilators can help patients with frequent exacerbations and severe airflow obstruction.

Avoiding other precipitating factors and air pollution is important. Persons with low levels of oxygen in their blood may require supplemental oxygen. Maintaining physical fitness is central because difficulty breathing may lead to a lack of activity and subsequent deconditioning. Therefore, exercise-based pulmonary rehabilitation is important for most people with COPD. Treating coexisting illnesses can extend life in many patients. Vaccination against seasonal influenza may reduce the risk of severe exacerbations triggered by influenza.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) is an organization that has developed recommendations on the management of COPD and has guided many national and international programs.<sup>5</sup> Despite the availability of guidelines, several studies have showed that COPD is undertreated in its early as well as advanced stages. In Latin America, only about one fourth of persons with COPD were treated according to these standards.<sup>19</sup>

## Control or elimination

The key element of reducing and controlling chronic obstructive pulmonary disease is reducing and controlling tobacco use. This is best addressed through political and public health initiatives. Public health and societal efforts are needed to reduce indoor smoke exposure and develop cost-effective management protocols for COPD in low-income settings. Research could lead to better understanding how risk factors and comorbidities interact to affect the severity of disease and what other factors cause COPD in smokers and non-smokers. Other research questions include how to identify and treat early COPD, how to manage it in the context of concomitant conditions, such as sleep apnea, cardiovascular disease, depression, osteoporosis, diabetes, lung cancer, aging, and frailty.

## 2. Asthma

### Scope of the disease

Asthma afflicts about 235 million people worldwide<sup>1</sup> and it has been increasing during the past three decades in both developed and developing countries. Although it strikes all ages, races, and ethnicities, wide variation exists in different countries and in different groups within the same country. It is the most common chronic disease in children and is more severe in children in nonaffluent countries. In these settings, under-diagnosis and under-treatment are common, and effective medicines may not be available or affordable. The burden of asthma is also greater in urban settings. It is one of the most frequent reason for preventable hospital admissions among chil-

dren.<sup>20,21</sup> Asthma causes about 180 000 deaths worldwide each year.<sup>22</sup> In some studies, asthma accounts for over 30% of all pediatric hospitalizations and nearly 12% of readmissions within 180 days of discharge.<sup>21</sup>

The cause for the increase in global prevalence of asthma is not well understood. Genetic predisposition, exposure to environmental allergens, air pollution, dietary factors, and abnormal immunological responses all promote the development of asthma. The timing and level of exposure to allergens and irritants may be crucial factors leading to the development of disease. Early viral infections and passive tobacco smoke exposure has been associated with the development of asthma in young children. Airborne allergens and irritants associated with asthma occur in the workplace and can lead to chronic and debilitating disease if the exposure persists.

### Prevention

The cause of most asthma is unknown and thus its prevention is problematic. People who smoke and have asthma have a much more rapid decline in lung function than those who do not smoke. Avoidance of smoking during pregnancy and avoidance of passive smoke exposure after birth can reduce asthma severity in children. Occupational asthma has taught us that removing allergens or irritants early may ablate or reduce the disease.

### Treatment

Asthma is a generally a lifelong disease that is not curable, but effective treatment can alleviate the symptoms. Inhaled corticosteroids are the cornerstone of effective asthma treatment. When used appropriately, that is, taken regularly with a spacer or other device to assist inhalation, these medicines can decrease the severity and frequency of symptoms of asthma. They also reduce the need for reliever inhalers (rapid-acting bronchodilators) and the frequency of severe episodes ("exacerbations") requiring urgent medical care, emergency room visits, and hospitalizations. Inhaled bronchodilators are important to give quick relief from asthma symptoms.

Unfortunately, many people suffering from asthma do not have access to effective asthma medicines. Even though inhaled corticosteroids and inhaled bronchodilators are on the World Health Organization's essential drug list they are either unavailable or unaffordable in many low-income countries. Universal access to effective, proven therapies for controlling asthma and treating exacerbations is an essential requirement to combat this disease.

Lack of availability of medicines is not the only reason that people with asthma do not get effective care. Widespread misconceptions about the nature of the disease and its treatment often prevent people using the most appropriate treatments. Educational campaigns to encourage the use of inhaled corticosteroids and avoidance of exposures that trigger asthma attacks are an important part of effective asthma control programs.

### Control or elimination

Research is critical to understand better the origins of asthma, the causes of exacerbations, and the reasons for its rising worldwide prevalence. The International Study of Asthma and Allergies in Childhood (ISAAC) has provided insights into the disease and facilitated standardized research on asthma in children that has helped define the prevalence, trends and determinants of asthma and allergies worldwide.<sup>23</sup>

The Global Initiative for Asthma (GINA) has developed an evidence-based strategy for the management of asthma. Dissemination and implementation of this strategy will improve asthma control. Making inhaled corticosteroids, bronchodilators, and spacer devices widely available at an affordable price and educating people with asthma about the disease and its management are key steps to improve outcomes for people with asthma. Policy-makers should develop and apply effective means of quality-assurance within health services for respiratory diseases at all levels. Strategies to reduce indoor air pollution, smoke exposure, and respiratory infections will enhance asthma control.

## 3. Acute respiratory infections

### Scope of the disease

Respiratory infections account for more than four million deaths annually and are the leading cause of death in developing countries.<sup>24</sup> Because these deaths are preventable with adequate medical care, a much higher proportion of them occur in low-income countries. Pneumonia is the most common serious respiratory infection. *In children under 5 years of age, pneumonia accounts for 18% of all deaths, or more than 1.5 million annually;<sup>6</sup> pneumonia kills far more than human immunodeficiency virus (HIV) or malaria.*<sup>24</sup> Risk factors for pneumonia include living in crowded conditions, malnutrition, lack of immunization, HIV, and exposure to tobacco or indoor smoke.

In Africa, pneumonia ranks among the most frequent reasons for adults being admitted to hospitals; one in ten of these patients die of their disease. There is one episode of pneumonia for every 100 adults under 60 years of age. It is several-fold higher in the elderly and HIV-infected individuals. *Streptococcus pneumoniae* remains the most frequent bacterial cause of pneumonia; HIV infection increases the risk of pneumonia caused by this organism twenty-fold.<sup>25</sup> Pneumonia can also lead to chronic respiratory disease, such as bronchiectasis.

Viral respiratory infections can occur in epidemics and can spread rapidly within communities across the globe. Every year influenza causes respiratory tract infections in 5 to 15% of the population and severe illness in three to five million people.<sup>10</sup> In 2003, the severe acute respiratory syndrome (SARS), caused by a previously unrecognized coronavirus, rapidly spread throughout the world. Its lethality mobilized international efforts that rapidly identified the cause and the method of spread. Stringent

infection control measures reduced its spread and were so effective that no further cases were identified.<sup>26</sup> This is in stark contrast to the 1918 influenza pandemic that claimed the lives of between 30 and 150 million persons.

### Prevention

Vaccination is one of the greatest achievements of public health. Primary prevention strategies for respiratory infections are based on immunization programs that have been developed for both viruses and bacteria. Bacteria are the most common cause of pneumonia; *Streptococcus pneumoniae* and *Haemophilus influenzae* type b most frequently cause severe pneumonia in children. Vaccines are effective against these agents as well as measles and pertussis (whooping cough). The influenza vaccine is effective in preventing influenza in adults and children. *The S. pneumoniae conjugate vaccine is highly effective in reducing pneumonia in children, but this vaccine is still not available as part of the national expanded program on immunization in many low-income countries.*

Childhood respiratory disease can be prevented or ameliorated by several basic measures—improving childhood nutrition, promoting breastfeeding, comprehensive immunization, improving living conditions to prevent crowding, avoidance of tobacco smoke exposure, reduction of indoor air pollution, and measures to treat HIV and prevent of mother-to-child HIV transmission.

### Treatment

*Most bacterial respiratory infections are treatable with antibiotics and most viral infections are self-limited. Yet, millions of people die of pneumonia.* The failure to prevent these deaths largely results from lack of access to health care or the inability of the health care system to care for these individuals.

The most effective way to manage these diseases is through *standard case management*. Case management is defined as “a collaborative process of assessment, planning, facilitation, care coordination, evaluation, and advocacy for options and services to meet an individual’s and family’s comprehensive health needs through communication and available resources to promote quality cost-effective outcomes.”<sup>27</sup>

For childhood pneumonia this involves a standard approach to diagnosis and treatment as has been well developed by the WHO in the Integrated Management of Childhood Illness program. The contribution of case management is well illustrated in the Child Lung Health services developed in Malawi in collaboration with The Union. In this resource-limited country, adopting a standardized case management program, training health workers, and developing the infrastructure to implement the program steadily improved the outcome for children under 5 years of age with pneumonia.<sup>28</sup> The cornerstone of pneumonia management is appropriate diagnosis and use of antibiotics.

## Control or elimination

Vaccines are essential for the control and elimination of disease. The new conjugate vaccines must be available as part of the expanded program on immunization in all countries. Development of improved vaccines with broader coverage are needed to control or eliminate specific infections.

Antibiotics have made most bacterial pneumonia easily curable. As with other diseases in which the causes are known and cures are available, the key efforts must be in improving the availability and delivery of quality health care and medicine. Diagnosis must be made earlier, which entails more awareness in the community. Better diagnostic tests include more effective sampling procedures and better methods for rapid laboratory detection of the infectious agents or microbial molecules in sputum, blood, and urine.

Improved diagnosis enables targeted therapy. More intelligent use of antibiotics will decrease the huge problem of antimicrobial drug resistance. Misuse of antibiotics leads to the emergence and selection of resistant bacteria. Physicians worldwide now face situations where infected patients cannot be treated adequately because the responsible bacterium is totally resistant to available antibiotics. Three strategic areas of intervention include: (a) prudent use of available antibiotics, giving them only when they are needed, with the correct diagnosis and in the correct dosage, dose intervals, and duration; (b) hygienic precautions to control of transmission of resistant strains between persons, including hand hygiene, screening for carriage of resistant strains, and isolation of positive patients, and (c) research and development of effective antibiotics with new mechanisms of action [29].

## 4. Tuberculosis

### Scope of the disease

In 2011, there were about 8.7 million new cases of tuberculosis; 13% were also infected with HIV.<sup>30</sup> Tuberculosis killed 1.4 million people and took an extraordinary high toll in parts of Africa. About 80% of global HIV-TB cases occurred in Africa where tuberculosis is the leading cause of HIV-related mortality.<sup>31</sup> Tuberculosis is contagious (airborne) and therefore clusters in countries and regions; nineteen countries account for 80% of existing cases of tuberculosis worldwide.<sup>4</sup> Multidrug-resistant tuberculosis is increasing and approached 60 000 cases in 2011.<sup>30</sup> Eastern Europe has been particularly hard hit by drug-resistant disease.

The good news is that the intense multinational efforts for tuberculosis control of the past decade have paid dividends. New cases are falling at a rate of about 2.2% per year and mortality has dropped 41% since 1990.<sup>30</sup> New diagnostic tests and drugs are becoming available and considerable progress is being made in understanding the bacterium and developing vaccines. Unfortunately, this progress masks other persistent serious problems and regional variations.

Individuals become infected by inhaling tuberculous bacteria. Tuberculosis usually develops subtly so that persons at first may not know they are infected. Only about one in ten infected but otherwise healthy persons develop symptomatic disease, although this rate is much higher in young children and people with HIV or certain other illnesses. The disease lies dormant because the infection is contained by the body's immune system, but can become active at any point in the person's lifetime. Active disease usually develops slowly so that individuals may cough and spread the disease without knowing it. With the ease and frequency of international travel, spread to other people is easy. *No one is safe from tuberculosis until the world is safe from tuberculosis.*

Tuberculosis is a particular problem in children where diagnosis is more difficult. Infants and young children are especially susceptible to developing severe or disseminated tuberculosis. Tuberculosis can strain national health care systems because of the effort and cost needed for contact tracing and treatment, especially if the tuberculosis bacteria are resistant to the commonly used drugs.

### Prevention

*In no disease is the phrase "treatment is prevention" truer than with tuberculosis.* The factors promoting the spread of infection relate to the chance that an uninfected individual is exposed to persons with infectious tuberculosis: the more cases in the community, the more likely it is that an individual will become infected. Factors promoting the development of disease in infected individuals relate to the function of the immune system. The most potent factor is infection with HIV, but other conditions that affect immunity, such as certain medications and the presence of poorly controlled diabetes increase the risk of developing active disease.

Comprehensive public health programs that search out cases and contacts and effectively treat tuberculosis reduce the presence of the bacteria in society and thus prevent its spread. Treatment of contacts of patients with active tuberculosis and those with latent tuberculosis that are at high risk for developing active disease, such as those with HIV, reduces the number of cases of active tuberculosis. The treatment of HIV also reduces tuberculosis.

The current vaccine, Bacille-Calmette-Guérin (BCG), is largely ineffective for pulmonary tuberculosis, but offers some protection against disseminated tuberculosis. However, research centers around the world are working on developing new vaccines for tuberculosis.

### Treatment

Most cases of tuberculosis can be cured if diagnosed early and treated appropriately. However, tuberculosis is a complicated disease that can be difficult to diagnose and treat; there are many nuances to its management. Tuberculosis is best managed by a standardized approach that is based on evidence derived from clinical trials. The

long duration of therapy (usually 6 months with three or four drugs in uncomplicated cases) makes adherence to treatment challenging especially in individuals who are taking other drugs for chronic diseases, such as HIV. Failure to take the full course of prescribed drugs may result in relapse with drug-resistant disease, which is more difficult to treat and poses a risk to others who could be infected by that person. For this reason, supervised or directly observed therapy is recommended to ensure adherence throughout the course of treatment for tuberculosis.

To complement the standard case management promoted by the World Health Organization through its Stop TB Department, the Tuberculosis Coalition for Technical Assistance developed a document to engage all providers in the best care for tuberculosis patients wherever they may be found.<sup>32</sup>

### Control or elimination

Many areas of tuberculosis research are producing encouraging results. Diagnosis is often difficult because it has generally relied on seeing bacteria microscopically in the sputum. New diagnostic technologies, such as GeneXpert MTB/RIF® that analyze sputum for mycobacterial DNA, are significantly more sensitive than microscopic sputum smear examination. In addition, DNA technology can detect drug resistance. These tools are becoming available to high prevalence countries where drug resistance is a major problem. Scaling up this technology and enabling treatment for drug resistance are major challenges.

If first-line (standard) antituberculous medicines cannot be used because of drug-resistance, drug-intolerance, or drug-interactions, treatment must extend much longer. Treating drug resistant disease costs much more and the chance for cure is much less. Fortunately, several new drugs are on the horizon for drug-resistant disease. Shorter course therapy for both sensitive and resistant tuberculosis is urgently needed to further reduce the prevalence of this disease. Shorter duration of therapy is also needed for latent tuberculosis. A recent study showed that the treatment with only 12 weekly doses of medicine, directly observed over three months, was as good as the current 9 month daily regimen.<sup>33</sup> Public health efforts to reduce the tuberculosis burden include the World Health Organization's "3Is" initiative (intensified case finding, isoniazid preventive therapy, and improved Infection control).<sup>4</sup>

## 5. Lung cancer

### Scope of the disease

Lung cancer is the most commonly diagnosed cancer in the world, making up 12.7% of the total reported cancers and affecting over 1.61 million people. *Lung cancer is also the most common cause of cancer death, killing 1.37 million, or about 18% of the total cancer deaths.*<sup>9</sup> Lung cancer has the highest fatality rate of all major cancers;

its ratio of mortality to incidence is 0.86.<sup>9</sup> In the United States, lung cancer causes more deaths than breast, colon, and prostate cancer combined.

Tobacco smoke is the cause of most cases of lung cancer. Many components of tobacco smoke mutate DNA and are carcinogenic. These effects correlate with the amount and duration of smoking. Because damage accumulates over time, lung cancer occurs years after people begin smoking. As smoking rates rise, lung cancer rates follow.

Although most lung cancer is associated with smoking, it can occur in non-smokers, especially in those who are passively exposed to the tobacco smoke. Among those who do not smoke and do not live with those who do, exposure to the smoke from biomass fuel is a cause of lung cancer. Exposure to radon, asbestos, and other environmental and workplace elements also cause lung cancer. Although asbestos is now banned in fifty-two countries, it is still in the environment in buildings and previous manufacturing sites. Some countries where its use is banned still produce and market it to poorer countries—this must stop.

### Prevention

Lung cancer is largely preventable by smoking prevention and cessation. At the beginning of the twentieth century, lung cancer and smoking were rare. As the number of smokers grew, the number of lung cancer cases grew about twenty years later. Smoking began to decrease in the last third of the twentieth century in certain countries and lung cancer is now slowly declining in those countries. Public programs that reduce smoking are urgently needed to halt the rise in respiratory cancers in nations where smoking has increased because the incidence of lung cancer will also increase in those countries.

Environmental sources of lung cancer, such as radon and asbestos, can be monitored and reduced. Lung cancer can also occur in nonsmokers without known environmental exposure. Research is needed to determine other causes of lung cancer.

### Treatment

The care of patients with lung cancer is complex. To guide treatment and to determine prognosis, lung cancer patients undergo a staging process. Early stage lung cancer is treated with surgery. More advanced stages may benefit from chemotherapy or radiation therapy or a combination of these interventions. Patients who have advanced stage lung cancer are rarely cured of their disease. Individualized or personalized therapy directed to factors such as specific mutations may improve the results of treatment. Research is ongoing to identify targets in different patients with different lung cancers that can give a greater chance of cure with fewer side effects.

Treatment of lung cancer in the elderly and people with other serious health problems pose a challenge. The benefits of treatment must be balanced against the risks of adverse effects in individual patients. Patients

with lung cancer and HIV infection tend to be relatively young but they usually present with advanced disease and have a poor prognosis. The treatment with chemotherapy in person with HIV may be difficult because of drug interactions and toxicity.

Identifying and treating early cancer is a potential life saving strategy. The national lung cancer screening trial undertaken in the United States was the largest (53,454 participants) randomized trial of a single cancer-screening test in the history of US medicine. The study randomly assigned current and former smokers to plain chest radiography (control) or low-dose chest computed tomography (intervention) yearly for three years and followed them for another 3.5 years. The study showed a 20% reduction in lung cancer specific deaths in the intervention group and a 7% reduction in overall mortality. However, of those screened, a quarter had an abnormal test result, and 96% of these were false positive meaning that many people will need additional investigations as a result of screening and most of these will not derive any benefit from these investigations. Hence, screening is likely to be costly but, as of yet, there have been no cost effectiveness studies with this technology.

## Control or elimination

The first strategy for control and elimination of lung cancer lies with efforts to decrease smoking by helping current smokers stop and developing methods to decrease the number of smokers who start. It is important to limit smoke exposure in the workplace and home. Legislation to regulate tobacco use and its promotion, to eliminate exposure to cigarette smoke in public areas, and to raise taxes on tobacco products are proven techniques that decrease tobacco use. These are particularly important in countries where smoking rates are rising.

Comparative effectiveness research into strategies aimed at tobacco reduction, cessation, and public policy are needed. Research into improving early diagnosis, understanding genetic and molecular mechanisms that influence carcinogenesis, and predicting tumor behavior and genetic predisposition to lung cancer are important. The identification of better screening tools is also important for secondary prevention.

## What can be done to combat respiratory disease

### Prevention

The first step for respiratory health is to prevent illness before it occurs. Identifying and ameliorating the factors that cause or promote respiratory diseases can prevent them, especially because respiratory diseases are often linked to the environment. *More than any other system disease, respiratory conditions are preventable.* The cost of prevention is only a fraction of the cost of treatment. Because preventing and combating respiratory disease is so cost-effective, *targeting respiratory diseases represents a "best buy"* as described by the World Health Organization.<sup>34</sup>

*Breathing unhealthy air is a cause or contributor to most respiratory conditions.* The most common sources of unhealthy air are tobacco smoke, indoor air pollution from burning solid fuels, unhealthy air in the work place, air pollution from traffic and industrial sources, air containing microbes, and air with toxic particles or fumes.

The first step to prevent lung disease is reduction of tobacco use. Smoking was estimated to be responsible for one in seven deaths in men and one in fifteen deaths in women globally in 2004. It is projected that as many as one billion people will die from tobacco smoking in the twenty-first century.<sup>35</sup> Of these deaths, the greatest proportion is due to respiratory diseases, including lung cancers. In the United States, current smokers are twenty-five times more likely to die of lung cancer than those who never smoked.<sup>36</sup> The rate of death from all causes is three times higher in smokers than nonsmokers and life-expectancy is shortened by 10 years in smokers.<sup>37</sup> In Europe, the total health cost of tobacco is about €544 billion annually, which represents about 5% of the European Union GDP.<sup>38</sup> Passive smoke exposure leads to respiratory illness in children including pneumonia and asthma.

*Tobacco smoking is a global problem that can be solved.* Intensive campaigns in Western Europe and North and South America have decreased the number of smokers in several countries, but the tobacco industry moved its target to susceptible populations in Eastern Europe, Asia, and developing countries to increase sales of its products. An estimated 350 million Chinese smoke an average of 11 cigarettes per day, a level of smoking that has not been seen in Western countries in 50 years. Passive smoke exposure also leads to respiratory disease. Children who are exposed to tobacco smoke before birth (from a smoking pregnant mother) or as infants have a greater risk of developing wheezing-associated illnesses, pneumonia, and asthma.

The first international treaty developed for purposes of health was the World Health Organization's Framework Convention on Tobacco Control.<sup>39</sup> It is an important mechanism by which governments can control the tobacco industry by using laws, regulations, administrative decisions, and enforcement measures. Effective strategies, termed MPOWER [35], have been developed by the WHO Tobacco-Free Initiative to support implementation of the Framework to prevent and reduce smoking and the demand for tobacco products. *FIRS calls on all governments, communities, health care practitioners, and individuals to promote these effective preventive measures that have reduced tobacco consumption in many countries.* Much, however, remains to be done, particularly in low and middle-income countries to mitigate the pernicious impact of tobacco smoking.

Poor indoor air quality is an important contributor to respiratory disease. About 50% of all households in the world and 90% of rural households use solid fuels, exposing 2–3 billion people to noxious smoke.<sup>40</sup> The World Health Organization estimates that 1.6 million deaths and 38.5 million DALYs per year can be attributed to indoor smoke. Most disease and death attributable to exposure to poor indoor air quality occurs in women and children, especially in low income families.<sup>41</sup> Exposure to indoor smoke used for heating and cooking leads to COPD, lung cancer and, in children, pneumonia and asthma.<sup>42</sup> People with lung disease are particularly susceptible to the effects of outdoor air pollution. Increased concentrations of airborne fine particles are associated with increased hospital admissions and deaths.<sup>43–45</sup> It is estimated that poor air quality in Europe leads to an average loss of 8.6 months of life expectancy.<sup>46</sup> There is a growing body of evidence that air pollution affects the unborn child leading to enhanced susceptibility to infection, respiratory, and cardiovascular disease.<sup>47</sup> Children, especially those with chronic lung disease, are also more susceptible to the adverse effects of air pollution.<sup>48</sup> The environmental risks are greater in low and middle-income countries and among the disadvantaged and low socio-economic sections of society. *The respiratory societies of the world believe that everyone has the right to breathe clean air.*<sup>46</sup> and we ask lawmakers to enact and enforce clean air standards in all countries. The health benefits of clean air policies are far reaching. In one large urban area, it was estimated that complying with current standards would reduce the annual death toll by 1200 deaths per year, reduce the hospitalizations for heart and lung diseases by 600 per year, reduce the cases of chronic bronchitis in adults by 1,900 per year, reduce the cases of acute bronchitis in children by 12,100 per year, and reduce asthma attacks in children and adults by 18,700 per year.<sup>49</sup> Greater improvements in air quality would yield greater benefits. "Reductions in air pollution over the past two decades have been shown to be associated with increases in life expectancy in the USA and improved respiratory health."<sup>46</sup> Legislation and political action on clean air makes a difference.

Appropriate nutrition and physical activity are critical for health. Both malnutrition and obesity contribute to respiratory diseases. Obesity is linked with obstructive sleep apnea in Western societies and to asthma, heart disease, and diabetes. Malnutrition is an important risk factor for childhood pneumonia and severe illness.

Prevention of respiratory disease entails strengthening health care systems, using established guidelines for health promotion and disease prevention, training medical personnel, and educating the populace.

### Treatment and cure

Once disease occurs, the goal is to lessen its effects and cure it if possible. Reducing its effects is best accomplished by early detection, prompt diagnosis, and early, effec-

tive treatment. Successful treatment is based on sound medical evidence, is cost-effective, and is generally in accordance with standardized guidelines. Patients and health care workers can manage diseases better if they are properly trained and resources are available. The World Health Organization, FIRS members, and other respiratory societies have developed recommendations for standards of care for specific clinical conditions. Unfortunately, effective and uniform implementation, promotion, and adherence to these standards have been lacking. Great medical breakthroughs are not significant if they do not reach the communities and patients that need them. Health care delivery can be readily improved with programmatic research, education, a trained work force, funding, infrastructure, and an efficient system in which to operate.

Economic barriers limit access to care even in many resource-rich settings. *Many people simply cannot afford to obtain good quality care.* In resource-poor settings, many people do not seek care from the public system because it is lacking, of poor quality, or inaccessible. In many countries, public health care systems are seen as a drain on public coffers. They are vulnerable to abrupt change in funding, which depends on the political and economic climate. In some countries, there are health insurance systems that limit medications or services. Elsewhere, governments have defined an essential package of care, but that care may not be adequate. Restrictions on **health-care** should be based on evidence-based standards of care.

### Disease control and global reduction or elimination

The FIRS vision of controlling and eliminating respiratory diseases requires use of the current effective tools coupled with additional research. Antibiotics can cure most pneumonia or tuberculosis and smoking-cessation programs can be effective, yet enormous problems remain in managing these illnesses. In the last few years, application of what is available, bolstered by research, have reduced the rate of pneumonia and tuberculosis worldwide<sup>4</sup> and tobacco use in certain countries. These successes must stimulate the world to consolidate and extend these gains to more countries and regions. It cannot be a shortsighted rationale for reducing effort.

In addition to public health measures, developing health care capacity requires the education of clinicians and researchers. Several FIRS member societies have created training programs. Nearly two decades ago, the *American Thoracic Society* developed the Methods in Clinical and Operational Research (MECOR) program in Latin America to increase the numbers of public health, academic, and clinical leaders to facilitate research and its application to public health and health care related to respiratory diseases. These courses are now available in Asia and Africa, and the program has trained more than 1000 health care workers worldwide. The *Asociación Latinoamericana de Tórax* has taken over the courses in

Latin America. The *Pan African Thoracic Society* has developed similar courses that have operated since 2007. *The Union* has many programs for operational research and management training. Administration is an important component of the health care system that is often ignored. The *European Respiratory Society* has sought to improve respiratory care in Europe by developing a European-wide curriculum and examination, Harmonised Education in Respiratory Medicine for European Specialists (HERMES) that is now used by many jurisdictions as an authorized post-graduate examination in respiratory medicine. The *American College of Chest Physicians* offers dedicated courses, attended by participants from around the world, specifically designed to fortify the skills necessary for subspecialty certification in Pulmonary Medicine.

The other main tool to reduce respiratory diseases lies in research. Public health and clinical research improves and promotes health for a population by improving health care systems' ability to deal with disease and promote health and to set improved guidelines and standards for the care of patients. Basic research aims to uncover the mechanism of disease and develop newer and better diagnostic tools or treatments to alleviate or cure diseases.

*The investment in respiratory research has paid enormous dividends.* People are living longer and healthier, and we are only on the threshold of even greater advances. Many diseases now have genetic profiles, and scientists are working hard to uncover the basic processes that go wrong in disease. The complicated network of cells, signals, and structures is being revealed and used to identify susceptible individuals, to develop better diagnostic tests, and to find new treatments. Equally important is research on how to apply new research findings to help people and to control disease. The results of clinical trials are distilled into guidelines on to how best to manage an illness. These evidence-base recommendations can be powerful tools to secure uniform high quality medical care throughout the world. Respiratory medical research has been shown to represent a six-fold return on investment.<sup>50</sup> Knowledge created through research is cross-cultural and enduring.

## Summary

Respiratory diseases are an enormous challenge to life, health, and productive human activity. Prevention, cure, and control of these diseases and promotion of respiratory health must be the top priority in global decision-making in the health sector. The ability to control, prevent, and cure respiratory diseases make this among the most cost-effective health interventions available. Investment in respiratory health will pay manifold dividends in the longevity, healthy living days, and national economies.

Public awareness and control of the environment are important steps to preventing respiratory diseases. The key controllable factors are reduction in tobacco smoking

and improvement in air quality that includes reduction in second tobacco smoke, smoke from indoor fire, and unhealthy public and workplace air. Strengthening childhood immunization programs and greater availability of the pneumococcal conjugate vaccine must be prioritized in low-income countries. Improved nutrition, especially in pregnant women and children, can have long-term benefits. Prevention and timely treatment of HIV can have major impact in reducing the burden of respiratory illness.

Effective training of health care workers and making available medications and appropriate diagnostics are keys to better lung health. Tuberculosis and pneumonia are two respiratory diseases that can be cured and controlled if the resources devoted to them are increased.

Finally, research in respiratory diseases is the hope for today and the promise for tomorrow. Research must answer many questions: how do lung diseases arise, how do they are spread, who is vulnerable, and what actions can be used control or cure them, to name a few. Research must also help us understand what keeps people healthy. Measures developed from the research must be cost-effective and widely applicable. Increased funding to support respiratory research is needed.

## Recommendations

FIRS calls for these essential actions to reduce the burden of respiratory disease and improve global health:

1. Increase the public and policy makers' awareness that respiratory health is a major component of global health and that improving respiratory health will improve national economies
2. Increase the public and policy makers' awareness that childhood respiratory disease is the major cause of childhood illness and has long-term negative consequences on adult health
3. Urge policy makers to enable universal access to quality health care, including the availability of essential medications for all those with respiratory disease
4. Reduce, and then eliminate, the use of all tobacco products
5. Reduce ambient, indoor, and occupational air pollution
6. Provide universal coverage for childhood and adult immunizations including new conjugate vaccines
7. Improve early diagnosis of respiratory diseases
8. Recognize the impact of malnutrition, obesity, and physical activity on respiratory conditions and implement plans to correct these concerns
9. Increase education and training of health professionals in respiratory disease worldwide
10. Increase respiratory research to develop programs, tools, and strategies to better prevent and treat respiratory diseases

## 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](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/](http://www.who.int/tb/publications/global_report/en/).
- Global Alliance against Chronic Respiratory Disease, W.H.O.; Available from: [http://www.who.int/gard/news\\_events/1-3.GARD-06-07-K1.pdf](http://www.who.int/gard/news_events/1-3.GARD-06-07-K1.pdf).
- Black, R.E., et al., *Global, regional, and national causes of child mortality in 2008: a systematic analysis*. *Lancet*, 2010. **375**(9730): p. 1969-87.
- Pearce, N., 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): p. 758-66.
- World Health Organization *Global surveillance, prevention and control of chronic respiratory diseases, a comprehensive approach*. 2007.
- Ferlay, J., et al., *Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008*. *Int J Cancer*, 2010. **127**(12): p. 2893-917.
- World Health Organization. *Influenza*. 2003; Available from: <http://www.who.int/mediacentre/factsheets/fs211/en/>.
- World Health Organization. *Noncommunicable disease and mental health, United Nations high-level meeting on noncommunicable disease prevention and control*. Available from: [http://www.who.int/nmh/events/un\\_ncd\\_summit2011/en/](http://www.who.int/nmh/events/un_ncd_summit2011/en/).
- Asthma and Allergy Foundation of America.
- Buist, A.S., W.M. Vollmer, and M.A. McBurnie, *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**(7): p. 703-8.
- Menezes, A.M., et al., *Prevalence of chronic obstructive pulmonary disease and associated factors: the PLATINO Study in Sao Paulo, Brazil*. *Cad Saude Publica*, 2005. **21**(5): p. 1565-73.
- Chan-Yeung, M.A.-K., N.; White, N.; Ip, M.S.; Tan, W.C.; , *The burden of COPD in Africa: a literature review and prospective survey of the availability of spirometry for COPD diagnosis in Africa*. *Tropical Medicine and International Health*, 2009. **14**: p. 840-848.
- Talamo, C., et al., *Diagnostic labeling of COPD in five Latin American cities*. *Chest*, 2007. **131**(1): p. 60-7.
- Eisner, M.D., et al., *An official American Thoracic Society public policy statement: Novel risk factors and the global burden of chronic obstructive pulmonary disease*. *Am J Respir Crit Care Med*, 2010. **182**(5): p. 693-718.
- Grigg, J., *Particulate matter exposure in children: relevance to chronic obstructive pulmonary disease*. *Proc Am Thorac Soc*, 2009. **6**(7): p. 564-9.
- Lopez Varela, M.V. and M. Montes de Oca, *Variability in COPD: the PLATINO study viewpoint*. *Arch Bronconeumol*, 2012. **48**(4): p. 105-6.
- Mannino, D.M.H., D.M.; Akinbami, L.J.; Moorman, J.E.; Gwynn, C.; Redd, S.C.;, *Surveillance for asthma – United States, 1980-1999*. *MMWR Surveill Summ*, 2002. **51**: p. 1-13.
- Wallace, J.C., C.E. Denk, and L.K. Kruse, *Pediatric hospitalizations for asthma: use of a linked file to separate person-level risk and readmission*. *Prev Chronic Dis*, 2004. **1**(2): p. A07.
- World Health Organization. *Bronchial asthma Fact sheet 206*. Available from: <http://www.who.int/mediacentre/factsheets/fs206/en/>.
- International Study of Asthma and Allergies in Childhood. Available from: <http://isaac.auckland.ac.nz/>
- World Lung Foundation, *The Acute Respiratory Infections Atlas*. 2010, New York: World Lung Foundation.
- Scott, J.A., et al., *Aetiology, outcome, and risk factors for mortality among adults with acute pneumonia in Kenya*. *Lancet*, 2000. **355**(9211): p. 1225-30.
- Centers for Disease Control and Prevention. Available from: <http://www.cdc.gov/sars>.
- Case Management Society of America *Standards of Practice for Case Management*. 2010.
- Enarson, P.M., et al., *Development and implementation of a national programme for the management of severe and very severe pneumonia in children in Malawi*. *PLoS Med*, 2009. **6**(11): p. e1000137.
- Control, E.C.f.D.P.a. *Antimicrobial resistance*. 2013; Available from: [http://www.ecdc.europa.eu/en/healthtopics/antimicrobial\\_resistance/Pages/index.aspx](http://www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/Pages/index.aspx).
- World Health Organization, *WHO Global Tuberculosis Control, 2010*, World Health Organization: Geneva.
- Getahun, H., et al., *HIV infection-associated tuberculosis: the epidemiology and the response*. *Clin Infect Dis*, 2010. **50** Suppl 3: p. S201-7.
- World Health Organization *International Standards for Tuberculosis Care, Diagnosis, Treatment and Public Health*.
- Sterling, T.R., et al., *Three months of rifapentine and isoniazid for latent tuberculosis infection*. *N Engl J Med*, 2011. **365**(23): p. 2155-66.
- World Health Organization. *From burden to "best buys": reducing the economic impact of non-communicable disease in low- and middle-income countries*. 2011; Available from: [http://www.who.int/nmh/publications/best\\_buys\\_summary.pdf](http://www.who.int/nmh/publications/best_buys_summary.pdf).
- World Health Organization. *Tobacco Free Initiative, MPOWER*. Available from: <http://www.who.int/tobacco/mpower/en/>.
- Thun, M.J.C., B.D.; Pleskanich, D.; Freedman, N.D.; Prentice, R.; Lopez, A.D.; Hartge, P.; Gapstur, S.M.;, *50-year trends in smoking-related mortality in the United States*. *N Engl J Med*, 2013. **368**: p. 351-364.
- Jha, P.R., C.; Landsman, V.; Rostron, B.; Thun, M.; Anderson, R.N.; McAfee, T.; Peto, R.;, *21st-century hazards of smoking and benefits of cessation in the United States*. *N Engl J Med*, 2013. **368**: p. 341-50.
- Jarvis, A.V.M.P.F., B.; Garde, A.; Geber, F.; Daynard, R.; *A study on liability and the health costs of smoking*. 2012.
- World Health Organization. *Framework Convention on Tobacco Control* Available from: <http://www.fctc.org/>.
- 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., et al., *Biomass fuels and respiratory diseases: a review of the evidence*. *Proc Am Thorac Soc*, 2008. **5**(5): p. 577-90.
- Fullerton, D.G., et al., *Wood smoke exposure, poverty and impaired lung function in Malawian adults*. *Int J Tuberc Lung Dis*, 2011. **15**(3): p. 391-8.
- Bell, M.L., et al., *Hospital admissions and chemical composition of fine particulate air pollution*. *Am J Respir Crit Care Med*, 2009. **179**(12): p. 1115-20.
- Katsouyanni, K., et al., *Air pollution and health: a European and North American approach (APHENA)*. *Res Rep Health Eff Inst*, 2009(142): p. 5-90.
- World Health Organization - Europe. *Environment and health risks: A review of the influence and effects of social inequalities*. 2010; Available from: [http://www.euro.who.int/\\_\\_data/assets/pdf\\_file/0003/78069/E93670.pdf](http://www.euro.who.int/__data/assets/pdf_file/0003/78069/E93670.pdf)
- Brunekreef, B., et al., *Ten principles for clean air*. *Eur Respir J*, 2012. **39**(3): p. 525-8.
- Cohen, A.J., et al., *The global burden of disease due to outdoor air pollution*. *J Toxicol Environ Health A*, 2005. **68**(13-14): p. 1301-7.
- Schwartz, J., *Air pollution and children's health*. *Pediatrics*, 2004. **113**(4 Suppl): p. 1037-43.
- (CREAL), E.C.d.R.e.E.A. *The public health benefits of reducing air pollution in the Barcelona metropolitan area*. 2013.
- Society, E.R. *The European Respiratory Roadmap Research*. Health Policy Makers, 2012.

## Erratum

In the article 'Frontline healthcare workers' knowledge of TB in rural south-east Nigeria,' which appeared in the September 2013 issue of *AJRM* the authors' details appeared as U K Nnanna, I Alobu, and O E Mbah. The lead author, Dr Ukwaja Kingsley Nnanna, has requested that the citation be as follows: Ukwaja KN, Alobu I, Onu EM. Frontline healthcare workers' knowledge of TB in rural south-east Nigeria. *Afr J Respir Med* 2013; 9 (1): 7–10.