



Respiratory diseases in the world

Realities of Today – Opportunities for Tomorrow

Forum of International Respiratory Societies



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Print ISBN: 978-1-84984-056-9; e-ISBN: 978-1-84984-057-6

Edited and typeset by the European Respiratory Society publications office, 442 Glossop Road, Sheffield, S10 2PX, UK.

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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 cause 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 composed of the world's leading international respiratory societies. The goal of the 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 intended to be a comprehensive textbook, but instead is a guide emphasising the diseases of greatest and immediate concern. It outlines practical approaches to combat threats to respiratory health, and proven strategies to significantly improve the care we provide for individuals afflicted with respiratory diseases worldwide. The document calls for improvements in healthcare policies, systems and care delivery, as well as providing direction for future 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 seek 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, we ask for your help in making a difference and a positive impact on the respiratory health of the world.

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Preface

FORUM OF INTERNATIONAL RESPIRATORY SOCIETIES (FIRS)

All over the world, medical specialists come together to form societies, pooling their expertise to develop policies, treatment guidelines and best-practice recommendations to combat diseases within their field. At the meetings of their societies, global leaders with the greatest knowledge share and discuss their latest research findings about the nature, prevalence, burden, causes, prevention, control and cure of these diseases.

The world's international respiratory societies formed a collective in 2001, called the Forum of International Respiratory Societies (FIRS), to highlight the importance of respiratory disease for global health and prosperity. The journals of these societies publish the vast majority of respiratory scientific breakthroughs in the world. Their annual meetings provide a forum for nearly all the research in the field. Their educational venues teach or train the majority of respiratory specialists. Their memberships comprise over 70 000 professionals, who devote their working lives to some aspect of respiratory health or disease.

The goal of each of the FIRS societies is to promote respiratory health. The goal of FIRS is to speak with one voice to promote respiratory health worldwide. The member societies of FIRS consist of the world leaders in respiratory health and they speak for the entire field. The members of these societies cover the globe and touch many, or most, persons with serious respiratory disease. FIRS, its societies, their members and the patients they serve, with millions of voices harmonised into one, call out for action to reduce, prevent, cure and control the terrible burden of respiratory disease.

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Introduction

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

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 of these deaths. Pneumonia is the world's leading killer of young children [6]. Asthma is the most common chronic disease, affecting about 14% of children globally and rising [7].

COPD is the fourth leading cause of death worldwide and the numbers are growing [8]. The most common lethal cancer in the world is lung cancer, which kills more than 1.4 million people each year [9], and the numbers are growing. Respiratory tract infections caused by influenza kill 250 000–500 000 people and cost 71–167 billion US dollars annually [10].

Respiratory infections are ranked as the greatest single contributor to the overall burden of disease in the world, as measured in disability-adjusted life-years (DALYs) lost, which estimate the amount of active and productive life lost due to a condition. The DALY burden is composed of two measures: years of life lost (YLL), which is the potential years of life lost to the person through their premature death, and years lived with disability (YLD), to take into account the years of life with disability. DALY is calculated by summing the two: $DALY = YLL + YLD$. This measure is sometimes referred to as the burden of disease.

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.

In recent decades, modern medicine has advanced the length and quality of life in most countries, although changing lifestyles and infections, such as HIV, have created new challenges. At the same time, increasing

healthcare 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 are the roots of poverty. Poor health impoverishes nations and poverty causes poor health, in part related to inadequate access to quality healthcare. Even more distressing is the enormous suffering that living with illness causes. Those who are most disadvantaged suffer most due to poor health.

Many of the biggest causes of the burden of poor health are the so-called "noncommunicable diseases" (NCDs), which include asthma, COPD and cancers. With this awareness, in 2011, the United Nations convened a high-level meeting on NCDs to develop a global plan for their prevention and control [11]. The FIRS has been part of this effort. It strongly believes that investing in public health pays dividends in many ways.

Healthcare costs for respiratory diseases are an increasing burden on the economies of all countries. For example, the annual cost of asthma in the USA is estimated to be \$18 billion [12]. If one considers the lost productivity of family members and others caring for these individuals, the cost to society is far greater.





THE BIG

5

Five respiratory conditions account for a great burden to society. These are: 1) COPD; 2) asthma; 3) acute respiratory infections; 4) TB; and 5) lung cancer.



Scope of the disease

COPD affects more than 200 million people and is the fourth leading cause of death in the world [5]. COPD is the only major disease that is increasing in prevalence worldwide and on all continents [13–15]. Furthermore, studies show that underdiagnosis ranges 72–93%, which is higher than that reported for hypertension, hypercholesterolemia and similar disorders. Misdiagnosis is also common [16].

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 globally. Other risks for COPD include genetic syndromes, such as α_1 -antitrypsin deficiency, outdoor air pollution and other diseases that involve the airways, such as chronic asthma and TB [17]. Smoke exposure in childhood may predispose to the development of chronic lung disease in adult life [18].

Prevention

Reduction of smoking is the first and most important priority in preventing COPD. This measure will also greatly reduce the morbidity and mortality of other lung diseases. Chimney cook stoves and other devices that 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

Spirometry is required for the clinical diagnosis of COPD, to avoid misdiagnosis and evaluate the severity of airflow limitation. Identification and reduction of exposure to risk factors are essential to prevent and treat the disease, and avoiding other precipitating factors and air pollution is important. All individuals who smoke should be encouraged and enabled to quit. 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.

Patients with low levels of oxygen in their blood may require supplemental oxygen. Maintaining physical fitness is key 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 organisation that has developed recommendations on the management of COPD and has guided many national and international programmes [5]. 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 quarter of people with COPD were treated according to these standards [19].

Control or elimination

The key element of reducing and controlling COPD 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 of 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, and how to manage it in the context of concomitant conditions, such as sleep apnoea, cardiovascular disease, depression, osteoporosis, diabetes, lung cancer, ageing and frailty.





Asthma

Scope of the disease

Asthma afflicts about 235 million people worldwide [1] 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 non-affluent countries. In these settings, underdiagnosis 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 reasons for preventable hospital admissions among children [20, 21]. Asthma causes about 180 000 deaths worldwide each year [22]. In some studies, asthma accounts for over 30% of all paediatric hospitalisations and nearly 12% of readmissions within 180 days of discharge [21].


The cause of 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 have 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. Avoiding smoking during pregnancy and avoidance of passive smoke exposure after birth can reduce asthma severity in children. Occupational asthma has taught us that early removal of allergens or irritants 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, *i.e.* 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 hospitalisations. Inhaled bronchodilators are important to give quick relief from asthma symptoms.

A close-up photograph of a person's hands holding a yellow spacer device over a clear plastic inhaler canister. The person is wearing glasses, and their face is partially visible in the background. The background is softly blurred, showing other people in a public setting. The lighting is bright and natural, highlighting the textures of the spacer and the person's skin.

Unfortunately, many people suffering from asthma do not have access to effective asthma medicines. Even though inhaled corticosteroids and inhaled bronchodilators are on the essential drug list of the World Health Organization (WHO), 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 receive effective care. Widespread misconceptions about the nature of the disease and its treatment often prevent people from 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 programmes.

Control or elimination

Research is critical to better understand 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 standardised research on asthma in children that has helped to define the prevalence, trends and determinants of asthma and allergies worldwide [23].

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.



Acute respiratory infections

Scope of the disease


Respiratory infections account for more than 4 million deaths annually and are the leading cause of death in developing countries [24]. Since 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 1.3 million annually [6]; pneumonia kills far more than HIV or malaria [24]. Risk factors for pneumonia include living in crowded conditions, malnutrition, lack of immunisation, HIV and exposure to tobacco or indoor smoke.

In Africa, pneumonia is one of the most frequent reasons for adults being admitted to hospital; one in ten of these patients die from their disease. 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 [25]. 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 5–15% of the population and severe illness in 3–5 million people [10]. In 2003, severe acute respiratory syndrome (SARS), caused by a previously unrecognised coronavirus, rapidly spread throughout the world. Its lethality mobilised 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 [26]. 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 immunisation programmes that have been developed for both viruses and bacteria. Bacteria are the most common cause of pneumonia; *S. 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 a national expanded programme for immunisation in many low-income countries.

Childhood respiratory disease can be prevented or ameliorated by several basic measures: improving childhood nutrition; promoting breastfeeding; ensuring comprehensive immunisation; improving living conditions to prevent crowding; avoiding tobacco smoke exposure; reducing indoor air pollution; and treating HIV and preventing 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 healthcare or the inability of the healthcare 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” [27].

For childhood pneumonia, this involves a standard approach to diagnosis and treatment, as has been developed by the WHO in the Integrated Management of Childhood Illness programme. 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 standardised case management programme, training health workers and developing the infrastructure to implement the programme steadily improved the outcome for children under 5 years of age with pneumonia [28]. 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. New conjugate vaccines must be available as part of expanded programmes for immunisation in all countries. Development of improved vaccines with broader coverage is 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, key efforts must be in improving the availability and delivery of quality healthcare 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 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: 1) 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; 2) hygienic precautions to control transmission of resistant strains between persons, including hand hygiene, screening for carriage of resistant strains and isolation of positive patients; and 3) research and development of effective antibiotics with new mechanisms of action [29].



Tuberculosis

Scope of the disease

In 2011, there were about 8.7 million new cases of TB; 13% were also infected with HIV [4]. TB 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 TB is the leading cause of HIV-related mortality [30]. TB is contagious (airborne) and therefore clusters in countries and regions; 22 countries account for 80% of existing cases of tuberculosis worldwide [4]. Multidrug-resistant TB is increasing and approached 60 000 cases in 2011 [4]. Eastern Europe has been particularly hard-hit by drug-resistant disease.

The good news is that the intense multinational efforts for TB 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 [4]. 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. TB usually develops subtly so that, initially, people may not know they are infected. Only about one in 10 infected but otherwise healthy people 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 TB until the world is safe from TB.

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

Prevention

In no disease is the phrase "treatment is prevention" truer than with TB. The factors promoting the spread of infection relate to the chance that an uninfected individual is exposed to those with infectious TB: 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 programmes that locate cases and contacts and effectively treat TB reduce the presence of the bacteria in society and thus prevent its spread. Treatment of contacts of patients with active TB and those with latent TB that are at high risk for developing active disease, such as those with HIV, reduces the number of cases of active TB. The treatment of HIV also reduces TB.

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

Treatment

Most cases of TB can be cured if diagnosed early and treated appropriately. However, TB is a complicated disease that can be difficult to diagnose and treat; there are many nuances to its management. TB is best managed by a standardised 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 TB.

To complement the standard case management promoted by the WHO through its Stop TB Department, the Tuberculosis Coalition for Technical Assistance developed a document to engage all providers in the best care for TB patients wherever they may be found [31].

Control or elimination

Many areas of TB research are producing encouraging results. Diagnosis is often difficult because it has generally relied on observing bacteria microscopically in the sputum. New diagnostic technologies, such as GeneXpert MTB/RIF[®], which analyse 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 of cure is much less. Fortunately, several new drugs are on the horizon for drug-resistant disease. Shorter-course therapy for both sensitive and resistant TB is urgently needed to further reduce the prevalence of this disease. Shorter duration of therapy is also needed for latent TB. A recent study showed that the treatment with only 12 weekly doses of medicine, directly observed over 3 months, was as good as the current 9-month daily regimen [32]. Public health efforts to reduce the TB burden include the WHO's "3Is" initiative (intensified case finding, isoniazid preventive therapy and improved infection control) [4].





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 annually. Lung cancer is also the most common cause of cancer death, killing 1.37 million per year, or about 18% of the total cancer deaths [9]. Lung cancer has the highest fatality rate of all major cancers; its ratio of mortality to incidence is 0.86 [9]. In the USA, 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. Since 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 tobacco smoke. Among those who do not smoke and do not live with those who do, exposure to smoke from biomass fuel is a cause of lung cancer. Exposure to radon, asbestos and other environmental and workplace elements also causes lung cancer. Although asbestos is now banned in 52 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 through smoking prevention and cessation. At the beginning of the 20th century, lung cancer and smoking were rare. As the number of smokers grew, the number of lung cancer cases grew about 20 years later. Smoking began to decrease in the last third of the 20th century in certain countries and lung cancer is now slowly declining in those countries. Public programmes 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 causes of lung cancer, such as radon and asbestos, can be monitored and reduced. Lung cancer can also occur in non-smokers 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. Individualised or

personalised 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.

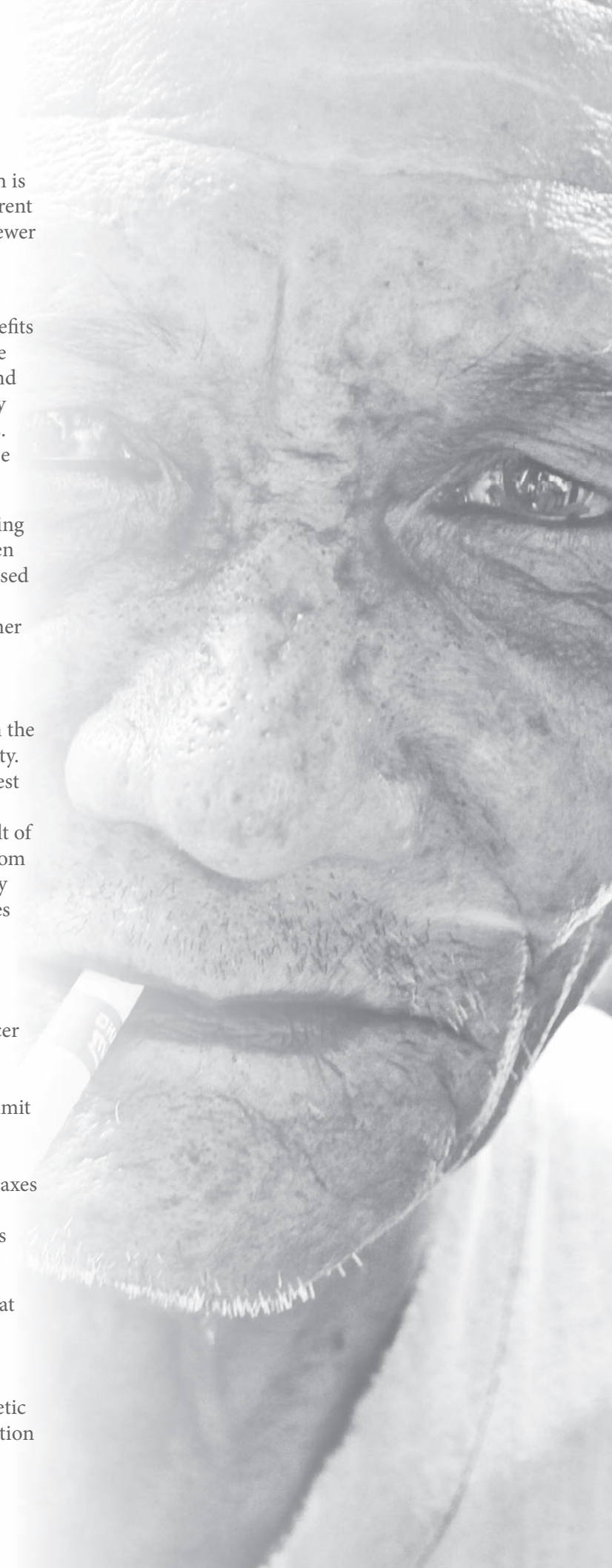
Treatment of lung cancer in the elderly and people with other serious health problems poses a challenge. The benefits of treatment must be balanced against the risks of adverse effects in individual patients. Patients with lung cancer and HIV infection tend to be relatively young but they usually present with advanced disease and have a poor prognosis. Treatment with chemotherapy in people with HIV may be difficult because of drug interactions and toxicity.

Identifying and treating early cancer is a potential lifesaving strategy. A national lung cancer screening trial undertaken in the USA was the largest (53 454 participants) randomised 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 3 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 to stop and developing methods to decrease the number of people who start smoking. 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 is needed. Research into improving early diagnosis, understanding genetic and molecular mechanisms that influence carcinogenesis, and predicting tumour behavior and genetic predisposition to lung cancer is 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. Respiratory conditions are preventable to a greater degree than diseases in any other system. 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 WHO [33].

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 workplace, air pollution from traffic and industrial sources, air containing microbes, and air with toxic particles or fumes.

The first step in preventing lung disease is reduction of tobacco use. Smoking was estimated to be responsible for one in seven deaths in men and one in 15 deaths in women globally in 2004. It is projected that as many as 1 billion people will die from tobacco smoking in the 21st century [34]. Of these deaths, the greatest proportion is due to respiratory diseases, including lung cancers. In the USA, current smokers are 25 times more likely to die of lung cancer than those who never smoked [35]. The rate of death from all causes is three times higher in smokers than non-smokers and life expectancy is shortened by 10 years in smokers [36]. In Europe, the total health cost of tobacco is about €544 billion annually, which represents about 5% of the European Union GDP [37].

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 WHO’s Framework Convention on Tobacco Control [38]. It is an important mechanism through which governments can control the

tobacco industry by using laws, regulations, administrative decisions and enforcement measures. Effective strategies, termed MPOWER [34], 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, healthcare 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 [39]. The WHO 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 [40]. Exposure to indoor smoke used for heating and cooking leads to COPD, lung cancer and, in children, pneumonia and asthma [41].

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 [42–44]. It is estimated that poor air quality in Europe leads to an average loss of 8.6 months of life expectancy [45]. There is a growing body of evidence that air pollution affects the unborn child, leading to enhanced susceptibility to infectious, respiratory and cardiovascular disease [46]. Children, especially those with chronic lung disease, are also more susceptible to the adverse effects of air pollution [47]. The environmental risks are greater in low- and middle-income countries and among the disadvantaged and low socioeconomic sections of society. The respiratory societies of the world believe that everyone has the right to breathe clean air [45] 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 1 200 deaths per year, reduce the hospitalisations 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 [48]. Greater improvements in air quality would yield greater benefits. According to the WHO, “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” [45]. 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. In western societies, obesity is linked with obstructive sleep apnoea, asthma, heart disease and diabetes. Malnutrition is an important risk factor for childhood pneumonia and severe illness.

Prevention of respiratory disease entails strengthening healthcare 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 to cure it, if possible. Reducing its effects is best accomplished by early detection, prompt diagnosis and early effective treatment. Successful treatment is based on sound medical evidence, is cost-effective and is generally in accordance with standardised guidelines. Patients and healthcare workers can manage diseases better if they are properly trained and resources are available. The WHO, 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. Healthcare 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, poor in quality or inaccessible. In many countries, public healthcare 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 medication or services. Elsewhere, governments have defined an essential package of care, but that care may not be adequate. Restrictions on healthcare 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 TB and smoking cessation programmes can be effective, yet enormous problems remain in managing these illnesses. In the last few years, application of what is available, bolstered by research, has reduced the rate of pneumonia and TB worldwide [4] 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 healthcare capacity requires the education of clinicians and researchers. Several FIRS member societies have created training programmes. Nearly two decades ago, the American Thoracic Society developed the Methods in Clinical and Operational Research (MECOR) programme in Latin America to increase the numbers of public health, academic and clinical leaders to facilitate research and its application to public health and healthcare related to respiratory diseases. These courses are now also available in Asia and Africa, and the programme has trained more than 1000 healthcare workers worldwide. The Asociación Latinoamericana de Tórax has now 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 programmes for operational research and management training. Administration is an important component of the healthcare system that is often ignored. The European Respiratory Society has sought to improve respiratory care in Europe by developing a Europe-wide curriculum and examination, Harmonised Education in Respiratory Medicine for European Specialists (HERMES), which is now used by many jurisdictions as an authorised postgraduate 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 the ability of healthcare systems to deal with disease 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 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 identified and used to identify susceptible individuals, develop better diagnostic tests and find new treatments. Equally important is research on how to apply new research findings to help control disease. The results of clinical trials are distilled into guidelines on how best to manage an illness. These evidence-based 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 [49]. 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 priorities in global decision-making in the health sector. Investment in respiratory health will pay manifold dividends in longevity, healthy living days and national economies.

Public awareness and control of the environment are important steps in preventing respiratory diseases. The key controllable factors are reduction in tobacco smoking and improvement in air quality, which includes reduction in second-hand tobacco smoke, smoke from indoor fires, and unhealthy public and workplace air. Strengthening childhood immunisation programmes and greater availability of pneumococcal conjugate vaccine must be prioritised 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 a major impact in reducing the burden of respiratory illness.

Effective training of healthcare workers and making medication and appropriate diagnostics available are keys to better lung health. TB 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 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

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



1. Increase public and policy makers' awareness that respiratory health is essential to global health and that improving it will improve national economies



2. Increase public and policy makers' awareness that childhood respiratory disease is a major cause of childhood illness and has long-term negative consequences on adult health



3. Urge policy makers to enable universal access to quality healthcare, 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 immunisations, including new conjugate vaccines



7. Improve early diagnosis of respiratory diseases



8. Recognise 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 programmes, tools and strategies to better prevent and treat respiratory diseases



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Appendix

INFORMATION ABOUT FIRS MEMBERS AND OBSERVER PARTICIPANTS

FIRS members

American College of Chest Physicians (ACCP)

Website: www.chestnet.org

Headquarters: 3300 Dundee Road, Northbrook, Illinois, 60062-2348, USA

Contact information: Paul Markowski, Executive Vice-President and CEO; pmarkowski@chestnet.org

Number of members: 18 700

Journals/publications: *CHEST*, *Chest Physician*, Board Review Course Textbooks, SEEK

Founded in 1935, the ACCP promotes the prevention, diagnosis and treatment of chest diseases through education, communication and research. By embracing a multidisciplinary membership from over 100 countries and innovative educational techniques, the ACCP is a global leader in providing clinical education in pulmonary, critical care and sleep medicine. The ACCP's premier peer-reviewed publication, *CHEST*, features cutting-edge clinical research and reviews through print, online and mobile editions. The ACCP also publishes *CHEST Physician*, the official ACCP monthly newspaper, and ACCP NewsBrief, a weekly e-newsletter, which offers varied resources for continuing education and practice management. Clinicians also know the ACCP for its clinical guidelines in antithrombotics, cough, lung cancer and more. In addition to the showcase annual CHEST conference, the ACCP also provides board review and simulation education in pulmonary, critical care, sleep, and paediatric pulmonary medicine, all designed to enable clinicians to provide the very best care for their patients.

Asian Pacific Society of Respiriology (APSR)

Website: www.apsresp.org

Headquarters: 2F Hongo Asakaze Bldg, 2-9-8, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Contact information: APSR secretariat office; KYU00671@nifty.com

Number of members: 14 520 members

Journal: *Respirology*

The APSR was established in 1986. The objectives of the Society are the advancement and promotion of knowledge of the respiratory system in health and disease. It strives to encourage research, improve clinical practice through teaching, increase awareness of health problems and promote the exchange of knowledge among respirologists in the Asia-Pacific region. The specific aims of the Society are: promoting and coordinating activities in the field of respiratory medicine; fostering research activities in the field of respiratory medicine; organising and coordinating regular congresses and occasional meetings; and producing regular

publications, including a Newsletter, the APSR Respiratory Updates and *Respirology*.

The APSR has many educational programmes and fellowships including educational seminars of the APSR (ESAP), and scholarships such as the APSR Research Awards, APSR Medal and APSR Travel Awards, especially for young scientists participating at the APSR annual meeting and at annual meetings of other international societies.

Asociación Latinoamericana De Tórax (ALAT)

Website: www.alatorax.org and www.congresosalat.org

Headquarters: Mario Cassinoni 1689, 11200 Montevideo, Uruguay

Contact information: Mariela Rodríguez, ALAT Secretary; secretaria.alat@gmail.com

Number of members: 6 439

Journal: *Archivos de Bronconeumología*

ALAT is a non-profit organisation, founded in 1996. It is an international medical association covering all of Latin America and other Spanish- and Portuguese-speaking countries, including Spain and Portugal. ALAT's mission is to alleviate the suffering of respiratory disease and promote lung health through research, knowledge exchange and continuing medical education. An emphasis is made on control of tuberculosis, a remaining prevalent disease in large areas of Latin America. ALAT promotes the development of science-related chest diseases in Latin America through the following activities: publication of research in its journal, *Archivos de Bronconeumología*; meetings of specialists in respiratory medicine at its biennial conference and other regional events in the specialty; continuing medical education courses and training of young specialists; and development of manuals and guidelines for respiratory health professionals.

American Thoracic Society (ATS)

Website: www.thoracic.org

Headquarters: 25 Broadway, 18th Floor, New York City, New York 10004, USA

Contact information: atsinfo@thoracic.org

Number of members: 15 000

Journals/publications: *American Journal of Respiratory and Critical Care Medicine*, *American Journal of Respiratory Cell and Molecular Biology*, *Annals of the American Thoracic Society*

The mission of the ATS is to improve health worldwide by advancing research, clinical care and public health in respiratory disease, critical illness and sleep disorders. Created in 1905, the ATS is the oldest respiratory society in the world. Its founding philosophy – that disease and suffering can be eliminated faster when discoveries and knowledge are shared – has been expanded to encompass all aspects of pulmonary, critical care and sleep medicine. With its widening mission, the Society's membership has grown increasingly diverse and nearly one-third of the Society's members are international.

The ATS publishes three premier journals that meet the needs of basic, translational and clinical scientists; produces clinical care guidelines; advocates for clean air and tobacco control; works to defeat tuberculosis in developing countries; and trains physicians in Latin America, Africa, and Asia to become researchers through its Methods in Epidemiologic, Operations and Clinical Research (MECOR) programme. Each year, the Society also convenes the world's leading experts in pulmonary, critical care and sleep medicine to present and discuss the latest research in these fields.

European Respiratory Society (ERS)

Website: www.ersnet.org

Headquarters: European Respiratory Society, 4 Avenue St-Luce, 1003 Lausanne, Switzerland

Contact information: info@ersnet.org

Number of members: 10 000

Journals/publications: *European Respiratory Journal*, *European Respiratory Review*, *European Respiratory Monograph*, *Breathe*, ERS Handbook series, *Buyers' Guide*, *European Lung White Book*

The ERS was founded in 1990, with the mission: to alleviate suffering from respiratory disease and to promote lung health through research, knowledge sharing, medical and public education. The ERS Annual Congress is the world's largest scientific gathering in respiratory medicine, bringing together around 20 000 respiratory professionals for cutting-edge science and state-of-the-art education. Through its HERMES projects to harmonise respiratory medical education in Europe, the Society is raising educational standards across the continent. The ERS School also runs a number of educational courses, and maintains a huge online database of material. The ERS office in Brussels is devoted to advocacy at a European level. It has formed alliances with key organisations to push for stronger legislation on tobacco, and for increased recognition of under-diagnosed diseases. The Society takes part in a range of EU-funded scientific projects, taking on a significant educational and patient communication role.

International Union Against Tuberculosis and Lung Disease (The Union)

Website: www.theunion.org

Headquarters: 68, boulevard Saint-Michel, 75006, Paris, France

Contact information: Nils E. Billo, Senior Consultant; union@theunion.org

Number of members: 15 000

Journals: *The International Journal of Tuberculosis and Lung Disease*, *Public Health Action*

The Union was founded in 1920 when 31 national associations decided that a central agency to stop tuberculosis was needed. In 1986, The Union expanded its mission and became The International Union Against Tuberculosis and Lung Disease. The Union has the vision of 'health solutions for the poor' and commits to bring innovation, expertise, solutions and support to address health challenges not only for tuberculosis and lung diseases, but also for non-communicable diseases. With 350 staff/consultants and 15,000 members and subscribers in 152 countries, The Union is a dedicated network of experts with offices in Africa, Asia Pacific, Europe, Latin America, North America and South-East Asia. The annual Union World Conference on Lung Health draws participants from across the globe, and The Union also organises regional conferences. In addition, The Union holds some 100 courses and workshops each year building capacity in technical skills, management and operational research. The Union's journals – *the International Journal of Tuberculosis and Lung Disease* and *Public Health Action* – are highly regarded forums for research; and its technical guides cover subjects such as TB, MDR-TB, TB-HIV, asthma, child lung health, tobacco control, smoking cessation, indoor air pollution and operational research.

Pan-African Thoracic Society (PATS)

Website: www.africanthoracic.org

Headquarters: Virtual society (no fixed headquarters)

Contact information: www.africanthoracic.org

Number of members: 720

Journal: *The African Journal of Respiratory Medicine*

PATS was formed in 2003 to create a representative African respiratory society for the region and to address the high burden of respiratory illness in Africa. The overall aim of PATS is to promote lung health in Africa through education, training, research and advocacy. The society is web based and members currently come from 33 different African countries. PATS has developed several sentinel activities to promote training, education and advocacy. The PATS programme in Methods in Epidemiologic, Clinical and Operations Research (PATS-MECOR) began in 2007 with the aim of developing research capacity in Africa. Highly successful courses have been held annually for trainees from several African countries. *The African Journal of Respiratory Medicine* is closely linked with PATS, including a PATS-elected editorial board and section editors.

Observer participants

Global Initiative for Asthma (GINA)

Website: <http://www.ginasthma.org>

Headquarters: PO Box 65278, Vancouver, Washington 98665, USA

Contact information: Claude Lenfant, Executive Director; Mark FitzGerald, Chair, Board of Directors

Number of members: Committee members: 25; GINA assembly members: ~60 countries

Publication: Global Strategy for Asthma Management and Prevention (2012)

Implemented in 1995, the principal objective of GINA is to form an independent global network of individuals and organisations to: increase awareness of asthma among health professionals, health authorities and the general public; improve diagnosis, management and prevention; stimulate research; and provide evidence-based educational resources concerning asthma for worldwide use.

These goals are achieved in cooperation with professional health organisations, patient organisations/foundations, government agencies, healthcare providers and individuals with interest in asthma research, patient care and health promotion and disease prevention.

Global Initiative for Chronic Obstructive Lung Disease (GOLD)

Website: <http://www.goldcopd.org>

Headquarters: PO Box 65278, Vancouver, Washington 98665, USA

Contact information: Claude Lenfant, Executive Director; Marc Decramer, Chair, GOLD Board of Directors

Number of members: Committee members: 25; GOLD national leaders: ~75 countries

Publication: Global Strategy for Diagnosis, Management and Prevention of COPD (2013)

Implemented in 1998, the principal objective of GOLD is to form an independent global network of individuals and organisations to: increase awareness of COPD among health professionals, health authorities, and the general public; improve diagnosis, management and prevention; stimulate research; and provide evidence-based educational resources concerning COPD for worldwide use.

These goals are achieved in cooperation with professional health organisations, patient organisations/foundations, government agencies, healthcare providers and individuals with interest in COPD research, patient care and health promotion/disease prevention.