

Lung Disease in a Global Context

A Call for Public Health Action

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Abstract

As described in a recently released report of the Forum of International Respiratory Societies, four of the leading causes of death in the world are chronic obstructive pulmonary disease, acute respiratory tract infections, lung cancer, and tuberculosis. A fifth, asthma, causes enormous global morbidity. Not enough progress has been made in introducing new therapies and reducing disease burden for these illnesses in the last few decades, despite generous investments and some notable progress in biomedical research. Four external and modifiable drivers are responsible for a substantial percentage of the disease burden represented by the major lung diseases: tobacco, outdoor air pollution, household air pollution, and occupational exposures to lung toxins. Especially in low- and middle-income countries, but in highly developed economies as well, pressures for economic development and lax regulation are contributing to the continued proliferation of these drivers. Public health approaches to the most

common lung diseases could have enormous effects on reducing morbidity and mortality. There must be increased advocacy from and mobilization of civil society to bring attention to the drivers of lung diseases in the world. The World Health Organization should negotiate accords similar to the Framework Convention on Tobacco Control to address air pollution and occupational exposures. Large increases in funding by government agencies and nongovernmental organizations around the world are needed to identify technologies that will reduce health risks while allowing populations to enjoy the benefits of economic development. This paradigm, focused more on public health than on individual medical treatment, has the best chance of substantial reduction in the burden of lung disease around the world in the next several years.

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A New Paradigm for Lung Disease

As an important new report from the Forum of International Respiratory Societies and an accompanying Perspective in this issue of the *Annals* by Ferkol and Schraufnagel describe (1, 2), lung diseases are a major cause of global morbidity and mortality. To achieve significant reductions in the toll they take, a new approach is required that goes beyond simply developing new treatments for each of the major respiratory

disorders. We propose a new framework in which we consider major lung diseases, which include lung cancer, chronic obstructive pulmonary disease (COPD), tuberculosis (TB), asthma, and acute respiratory infections, as primarily stemming from only a few extrinsic drivers, primarily tobacco, indoor and outdoor air pollution, and occupational exposures. We assert that by modifying these drivers, we can profoundly affect the incidence, morbidity, and mortality of diseases that affect large percentages of the world's

population. This approach is likely to be more efficient and effective than current strategies for addressing these illnesses.

The Global Burden of Lung Disease

COPD

COPD is an umbrella term used to describe chronic lung diseases, such as emphysema and chronic bronchitis, that cause limitations in airflow. It is estimated that

there are at least 210 million persons in the world with COPD and that this group of conditions causes 3 million deaths annually (3). The disease burden from COPD, in contrast to TB, appears to be growing, despite the development of new therapeutics such as long-acting antimuscarinic agents, long-acting β -agonists, inhaled corticosteroids, and phosphodiesterase inhibitors. COPD is the third leading cause of death in the world, and the burden of COPD is projected to increase substantially in Asia and Africa in the coming decades, mostly as a result of increased tobacco use in those regions.

Asthma

Approximately 235 to 300 million people in the world suffer from asthma (4). Globally, about 200,000 people die of asthma every year, with over 80% of these deaths occurring in low- and middle-income countries (5, 6). Asthma prevalence is increasing worldwide as communities adopt modern lifestyles and become urbanized, perhaps through increasing obesity (7, 8), interactions with common environmental microorganisms, and exposure to outdoor air pollution (8–11). It is estimated that an additional 100 million people will have asthma by 2025, corresponding to the projected increase in the proportion of the world's population living in urban areas.

Acute Respiratory Infections

Acute respiratory infections—mainly pneumonia and influenza—result in over 4 million deaths worldwide each year (12). They are the leading causes of illness in children and the leading killer among children under 5 years of age (13). Acute respiratory infections are responsible for at least 6% of the world's disability and death and for 20 to 40% of all hospitalizations among children (3, 14). In parts of the developing world, the death rate from acute respiratory infections alone is 10 times higher than the global median death rate from all causes.

Tuberculosis

For 2013, The World Health Organization (WHO) estimates that there will be approximately 8.7 million new cases of active TB and 1.4 million deaths (15). This places TB as the tenth leading cause of death in the world (3). These numbers reflect some progress in controlling TB around the world, and recent analyses by

the WHO put the rate of decline of TB cases at roughly 2% per year for the past several years (16, 17). However, the WHO has recently called for a rapid increase in the rate of decline of the global TB burden if the goal of elimination is to be met by 2050 (18). According to their projection, it would take a dramatic increase to at least a 15% annual decrease in cases to achieve elimination by 2050. Although the pipeline for new drugs is longer than it has been in decades and a new drug, bedaquiline, has successfully been registered for use in treatment of multidrug-resistant TB, many more novel agents will be needed to effect radical transformation in the way TB is treated. Furthermore, the worldwide emergence of multidrug-resistant TB threatens TB control efforts globally and endangers the lives of hundreds of thousands of people (15, 19).

Lung Cancer and Other Cancers of the Respiratory Tree

Since 1985, respiratory tract malignancies have been the most common cancers in the world, with 1.45 million new cases in 2004, representing 12.7% of all new cancers (3). They are the most common cause of death from cancer, resulting in 1.4 million deaths in 2008, or 18.3% of the world total deaths due to cancer. Approximately half of these cases occur in developing countries, where cases are increasing (20–22).

Aggressive efforts to control tobacco use have been promoted in many regions of the world (discussed in more detail below), but the tobacco industry is a resilient and extraordinarily wealthy and politically sophisticated foe. Emerging markets in the developing world represent rich targets, and the struggle to reduce the burden of respiratory tract cancers will be prolonged, despite some notable successes in New York City and elsewhere.

Lung Disease in a Global Context

Over the last several decades, a great deal of time, attention, and money has been spent understanding the cellular, molecular, and genetic bases of these illnesses, and this work has led to a greater understanding of their pathogenesis. Although some exciting new therapies have been developed, these newer therapeutic modalities are expensive and out of the reach of a large

percentage of the world's population. As a result, for most patients the treatment of COPD relies mostly on the use of bronchodilators and inhaled steroids, medications that have been in use for more than 30 years (23). The same is true for asthma (24). Only one new class of medications has been introduced in the United States for the treatment of TB in the last 40 years, and this drug (bedaquiline) has extremely limited indications (25); the same is true for delamanid, which was recently approved in Europe. Antibacterial and antiviral product development for acute respiratory infections has slowed to a crawl (although there has been better progress in vaccines for these illnesses) (26). Although many new chemotherapeutic agents have been introduced for lung cancer recently, overall survival remains dismal (27). Relying on exciting and novel but expensive therapeutic approaches to these disorders is unlikely to result in major reductions in global disease burden from respiratory illnesses in the near- or medium term.

A new paradigm is needed. Although lung diseases have varied pathogeneses—cancer, inflammation, infection, and immune dysregulation—the drivers of these illnesses are mainly factors extrinsic to the human body and related to environmental exposures that can be modified. These drivers are common to most of these illnesses, and changes in any of them could lead to significant reduction in the burden of disease of all of them. Furthermore, the drivers are governed by higher-level processes that are similar across many regions of the globe. We propose a framework for thinking about this hierarchy of causes of lung disease in hopes that such a framework will lead to progress in reducing the burden of morbidity and mortality of lung disease around the world.

Drivers of the Major Causes of Lung Disease around the World

There is a large evidence base supporting the idea that four drivers—tobacco, indoor air pollution (largely from biomass fuel burning in cookstoves), outdoor air pollution, and occupational exposures to lung toxins and/or irritants—play a significant role in creating or worsening the lung diseases described above (Tables 1 and 2).

Table 1. Four drivers of chronic lung disease: global burden

	Indoor/Household Air Pollution	Outdoor Air Pollution	Occupational-Related Illness	Tobacco-Related Illness
Overview	<p>Roughly half of the world's population relies on inefficient and highly polluting solid fuels for its everyday household energy needs, most of which is coal and biomass (wood, animal dung, crop wastes). Burning these fuels in open fires or simple stoves releases smoke into the home resulting in IAP (smoke contains many health-damaging pollutants such as particulate matter and CO).</p> <p>These pollutants mainly affect the lungs by causing inflammation, reduced ciliary clearance, and impaired immune response.</p> <p>IAP is a major threat to health, particularly for women and young children, who tend to spend more time in the home.</p> <p>Approximately 3 billion people rely on solid fuels: 2.4 billion on biomass and the rest on coal (most of which are in China) with variation across regions from < 20% in Europe and Central Asia to > 80% in Sub-Saharan Africa and South Asia.</p>	<p>Industries, households, cars, and trucks emit complex mixtures of air pollutants, many of which are harmful to health.</p> <p>Air pollutants are usually classified into suspended particulate matter (dusts, fumes, mists, and smokes), gaseous pollutants (gases and vapors), and odors.</p> <p>Of these pollutants, fine particulate matter has the greatest effect on human health. Most fine particulate matter comes from fuel combustion from mobile sources (e.g., vehicles) and from stationary sources (e.g., power plants, industry, households, or biomass burning).</p> <p>Middle-income and developing countries disproportionately experience the disease burden due to pollution.</p>	<p>The workforce that resides in the developing world disproportionately shares in the global burden of occupational disease and injury.</p> <p>The health of a country's workforce, even more than the health of the country's overall population, is critical to its economic and national security.</p> <p>Compared with industrial countries, where single-digit percentages prevail, developing countries employ about 70% of their economically active population in the agricultural sector.</p> <p>Workers in developing countries face different risks in the health transition than do their counterparts in industrialized countries by being exposed to the combined and often synergistic risks of traditional and emerging hazards as well as facing unregulated and unprotected exposures to known hazards such as silica and asbestos.</p>	<p>Tobacco use in any form is dangerous and is the single most preventable cause of death in the world.</p> <p>Cigarette smoking and other forms of tobacco use impose a large and growing global public health burden. More than 1.1 billion people worldwide smoke, with 82% of smokers residing in low- and middle-income countries.</p> <p>Smoking prevalence continues to increase in many low- and middle-income countries, although many high-income countries have witnessed decreases, mostly in men.</p> <p>Smoking cigarettes has been scientifically proven to harm nearly every organ in the body and to increase morbidity and mortality.</p> <p>Nicotine is the major agent in tobacco responsible for addiction and is on par with other powerfully addictive drugs, such as heroin and cocaine.</p> <p>Quitting tobacco use greatly reduces illness by immediately providing short-term benefits and lowering the risk of all diseases caused by smoking.</p>
Disease burden/mortality	<p>Three main health outcomes are included in the burden of IAP: acute lower respiratory infections in children under 5 yr, COPD in adults over 30 yr, and lung cancer due to coal exposure in adults over 30 yr.</p>	<p>Worldwide, pollution by fine particulate matter is estimated to cause 9% of lung cancer deaths, 5% of cardiopulmonary deaths, and ~1% of respiratory infection deaths, adding up to 7.9 million DALYs based on mortality only. This mortality occurs primarily in developing countries.</p>	<p>According to a recent estimate by the International Labor Organization among the world's 2.7 billion workers, at least 2 million deaths per year are attributable to occupational diseases and injuries.</p>	<p>In 2011, tobacco use killed almost 6 million people, with nearly 80% of these deaths occurring in low- and middle-income countries.</p> <p>By the year 2030, 8 million people will die annually from tobacco use.</p>

(Continued)

The first three of these drivers share a common mechanism of producing inhaled toxins through incomplete combustion. Because these drivers are pervasive, interventions to reduce their impact will undoubtedly have greater impact than individual treatments for the various diseases they cause or worsen. Recent data from the Global Burden of Disease Project indicate that these four drivers are among the leading risk factors for global

mortality overall (28). For men, smoking, household air pollution, and ambient air pollution are among the top six risks for overall mortality in the world. For women, household air pollution and smoking are among the top five risks for death globally. Extrinsic drivers act together with host genetic factors to exert a large influence on disease occurrence and manifestations in any given individual. However, only extrinsic drivers are modifiable and thus

are excellent targets for global public health policies.

Tobacco

Tobacco is the leading preventable cause of death in the world (29–32). The link to lung cancer and COPD is well known, but in recent years solid evidence has emerged that smoking increases the risk of acute respiratory infections and TB (33–39). One recent clinical trial found that cigarette

Table 1. (CONTINUED)

Indoor/Household Air Pollution	Outdoor Air Pollution	Occupational-Related Illness	Tobacco-Related Illness
<p>About 32% of the burden occurs in Sub-Saharan Africa, 37% in South Asia, and 18% in East Asia and Pacific.</p> <p>The poorest regions of the world carry by far the greatest burden, particularly for acute lower respiratory infections, which accounts for more than half of all deaths attributable to solid fuel use.</p>	<p>Researchers have linked asthma to urban air pollution; ozone exposure as a trigger of asthma attacks is a particular concern.</p> <p>Total daily exposure to air pollution is determined by people's time and activity patterns, and it combines indoor and outdoor exposures.</p>	<p>WHO estimates that occupational exposures to workplace lung carcinogens (e.g., asbestos, diesel exhaust, and silica) and leukeogens (e.g., benzene, ionizing radiation, and ethylene oxide) account for about 9% of all cancers of the lung, trachea, and bronchus.</p> <p>Occupational exposures account for about 13% of all COPD-related morbidity and mortality (318,000 deaths per year and about 3.7 million DALYs) and about 11% of asthma morbidity and mortality (38,000 deaths per year and 1.6 million DALYs).</p>	<p>Up to half of all lifetime smokers will die of a disease caused by smoking.</p> <p>Smoking causes almost 80% of male and nearly 50% of female lung cancer deaths.</p> <p>Smoking increases the risk of TB infection and disease, and 40 million smokers with TB are expected to die between 2010 and 2050.</p> <p>Worldwide, approximately 600,000 nonsmokers died in 2011 from involuntary exposure to second-hand smoke.</p>

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; DALY = disability adjusted life-year; IAP = indoor/household air pollution; TB = tuberculosis.

smoking was the single strongest predictor of the development of active TB in persons with latent infection (40). Recent analyses estimate that abstinence from smoking is worth 10 years of life (29–32). Simply put, eliminating tobacco from the world would benefit health more than any other intervention. More than 1.1 billion people worldwide smoke, with 82% of smokers residing in low- and middle-income countries (41). Although many high-income countries have witnessed decreases in smoking rates, overall smoking prevalence has continued to increase in many low- and middle-income countries. WHO has succeeded in negotiating a landmark treaty, the Framework Convention for Tobacco Control, which has been signed by over 171 countries, and its provisions have been implemented in a number of them. Measures such as restrictions on tobacco advertising, restrictions on sale of cigarettes to minors, limits on smoking in public places, and increasing the cost of cigarettes through taxation are effective in reducing tobacco use and are far more effective than secondary prevention measures (e.g., smoking cessation) in reducing the burden of disease from tobacco (42–46). New York

City, where aggressive measures taken to reduce smoking include raising taxes and severely limiting smoking in public places, has the lowest lung cancer death rates in New York State (47). Political corruption remains a significant hurdle in implementing these measures in many countries around the world (48).

Outdoor Air Pollution

Industries, households, cars, and trucks emit complex mixtures of air pollutants, many of which are harmful to health. Air pollutants are usually classified as suspended particulate matter (dusts, fumes, mists, and smokes), gaseous pollutants (gases and vapors), and odors (49). Of these pollutants, fine particulate matter has the greatest effect on human health (50). Most fine particulate matter comes from fuel combustion from mobile sources (e.g., vehicles) and from stationary sources (e.g., power plants, industry, households, or biomass burning). Indoor sources also contribute to outdoor pollution, and in heavily populated areas, the contribution from indoor sources can create extremely high levels of outdoor air pollution.

Worldwide, pollution by fine particulate matter (PM₁₀ and PM_{2.5}) is estimated to cause 9% of lung cancer deaths, 5% of

cardiopulmonary deaths, and about 1% of respiratory infection deaths, adding up to 7.9 million disability-adjusted life years (DALYs) based on mortality only. This mortality occurs primarily in poor populations and in developing countries (51–56).

Outdoor air pollution is likely to become an even more serious concern in the coming years. As the global trend toward urbanization continues, issues related to outdoor air pollution that have been problems for developed countries will become growing problems in developing countries (57–61).

Technologies to reduce pollution at its source are plentiful, as are technologies that reduce pollution by filtering it away from the emission source. These include vehicle-specific interventions such as mandating the use of lead-free gasoline, encouraging the use of more fuel-efficient vehicles, and/or policies that manage traffic demand or reduce “unnecessary” driving. Power plants and industrial plants that burn fossil fuels may use a variety of filtering methods to reduce particles and scrubbing methods to reduce gases.

Indoor Air Pollution

Over half of the world's population relies on inefficient and highly polluting solid fuels

Table 2. Four drivers of chronic lung disease: current interventions and recognized issues

	Indoor/Household Air Pollution	Outdoor Air Pollution	Occupational-Related Illness	Tobacco-Related Illness
Current intervention models	<p>Poverty reduction tends to be a key element of IAP policy, and household energy interventions are important factors in several of the United Nation's Millennium Development Goals.</p> <p>Three general types of interventions are those acting on the source of pollution (e.g., cooking devices, alternative fuels), those improving the living environment (e.g., improved ventilation, kitchen design), and those causing changes in user behaviors (e.g. change in operation of source, smoke avoidance).</p> <p>Policy instruments typically used: information, education, and communication; taxes and subsidies; regulation and legislation; direct expenditures; and research and development</p>	<p>Technologies to reduce pollution at its source are plentiful, as are technologies that reduce pollution by filtering it away from the emission source. However, getting these technologies applied in practice requires government or corporate policies that guide technical decision-making in the right direction in the form of outright bans, guidance on desirable technologies, or economic instruments that make using more polluting technologies more expensive than using less polluting technologies.</p> <p>Vehicle-specific interventions include mandating the use of lead-free gasoline, encouraging the use of more fuel-efficient vehicles, and/or policies that manage traffic demand or reduce "unnecessary" driving.</p> <p>Power plants and industrial plants that burn fossil fuels use a variety of filtering methods to reduce particles and scrubbing methods to reduce gases.</p> <p>Power plants and industrial plants that burn fossil fuels use a variety of filtering methods to reduce particles and scrubbing methods to reduce gases.</p>	<p>Strategies for controlling occupational disease, developed by industrial hygienists and others over many decades in industrial countries, are as fully applicable in developing countries.</p> <p>Strategies include a hierarchy of controls in the following decreasing order of preference: (1) substituting major hazards for less hazardous materials or processes, (2) applying engineering controls to separate workers from hazards that remain, (3) using administrative controls to minimize contact uncontrollable by engineering, and (4) using personal protective equipment (e.g., respirators).</p> <p>Interventions can exist at the international level (ILO-WHO Joint Committee on Occupational Health to provide guidance), the national level (government-established workplace rules and system of enforcement), the workplace level (training, use of safer materials/equipment), or the individual level (use of personal protective equipment).</p>	<p>Most WHO member states have ratified the main treaty on tobacco, the WHO Framework Convention on Tobacco Control (WHO FCTC).</p> <p>Surveillance is essential to support sound policy, and almost half of all countries have monitoring systems enhanced by research initiatives such as GYTS, GATS, and STEPS.</p> <p>Tobacco taxation is widely used, but significant differences exist across countries and range from specific or per unit taxes to percentage of wholesale or retail prices. A significant number of studies demonstrate that increases in taxes on cigarettes and other tobacco products lead to significant reductions in cigarette smoking and other tobacco use.</p> <p>Smoke-free areas: levels of smoke exposure are 90% lower than they are where smoking is permitted; public support is high for smoking bans in public places, including indoor and outdoor areas. A smoking ban is relatively inexpensive to implement and can produce immediate economic benefits.</p> <p>Sustained use of health information and mass media campaigns contributes to population-level decreases in smoking prevalence by increasing knowledge about the harm of tobacco use.</p> <p>Health warnings on product packaging ranging from text to strong graphic warnings</p> <p>Bans or restrictions on tobacco marketing: Only comprehensive bans on all forms of tobacco advertising, marketing, sponsorship, and promotion are effective at reducing population smoking rates.</p> <p>Smoking cessation treatments</p>

(Continued)

Table 2. (CONTINUED)

	Indoor/Household Air Pollution	Outdoor Air Pollution	Occupational-Related Illness	Tobacco-Related Illness
Identified needs and issues	<p>There is a lack of substantive evidence on the effect of reducing IAP exposure on the incidence of acute lower respiratory infections or the course of COPD in adults.</p> <p>It is difficult to assess the amount of disease directly attributed for IAP, especially for chronic diseases like COPD.</p> <p>There is limited understanding of the true exposure–disease relationship due to challenges in exposure measurement: it is very difficult to get personal exposure measurements, and pollutant readings in the house are typically used as a proxy.</p> <p>There is a lack of information on the relative dangers of the smoke from different types of biomass fuels.</p> <p>There is limited understanding of how clean an alternative fuel needs to be or how much more efficient a new cookstove needs to be to cause a change in outcomes.</p> <p>It is difficult to manage cultural needs.</p>	<p>Further research is needed to guide regulations and interventions. The issues that were problems for developed countries are still major problems in developing countries; however, direct application of experiences from developed countries may not be appropriate because exposed populations in developing countries may have a different burden of preexisting diseases, malnutrition, and other factors related to poverty.</p> <p>Research on specific vulnerabilities and on relevant dose-response relationships for different levels of economic development and for various geographic conditions would be valuable for assessing risks and targeting interventions.</p> <p>There is a need to clearly define the long-term health effects of exposure to air pollution as existing literature indicates more adverse effects due to long-term exposure.</p> <p>The health sector needs to be involved in urban planning, in planning the location of industries, and in planning the development of transportation systems and needs to encourage those designing public transportation and housing to ensure that new sources of air pollution are not being built into cities.</p>	<p>Effective intervention strategies will be those based on a comprehensive approach to the overall burden rather than those addressing the individual burdens of specific exposures, recognizing that organizational or institutional interventions (e.g., eliminating asbestos from the workplace) are far more effective than those targeting individual behaviors (e.g., smoking cessation).</p> <p>Inadequate data and reporting systems make capturing the effect of workplace risks problematic.</p> <p>In general, attempts to derive evidence-based estimates of the burden of disease related to occupational exposures are likely to systematically and significantly underrepresent the extent of the problem.</p> <p>Although the WHO model is fairly comprehensive, the absence of data in much of the developing world has limited the range of occupational risk factors that WHO could measure, and the available data excluded children under age 15 who work.</p> <p>What differs in developing countries is the context in which the paradigm used for controlling occupational disease must be applied. Options are often sharply limited, and knowledge of them is even more so.</p>	<p>Needed now is a coherent public health strategy designed to reduce tobacco consumption, involving international, regional, national, and local actors involved in strategic planning, policy-oriented research, capacity building, funding enforcement, and evaluation.</p> <p>We must identify the problem and scale of the problem through monitoring and surveillance, including prevalence, health, economic impact, actions taken, experience, and lessons learned from other countries.</p> <p>Current challenges with smoking reduction include how to decrease smoking in the home and how to regulate smoking in multifamily homes and in vehicles with small children.</p> <p>Most countries should be doing more to inform their citizens adequately about the illnesses and deaths caused by tobacco.</p> <p>World Bank data reveal that ample room exists to increase tobacco taxes.</p> <p>Some evidence shows that improved national capacity and local needs assessment could increase the likelihood that tobacco-control measures will be adopted.</p> <p>Tobacco-control budgets are only a fraction of what is required.</p>

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; DALY = disability-adjusted life-year; GATS = Global Adult Tobacco Survey; GYTS = Global Youth Tobacco Survey; IAP = indoor/household air pollution; ILO = International Labor Organization; STEPS = WHO STEPwise Approach to Chronic Disease Risk Factor Surveillance; TB = tuberculosis; WHO = World Health Organization.

for its everyday household energy needs (62). These fuels include coal and biomass (wood, animal dung, and crop wastes). Burning these fuels in open fires or simple stoves releases smoke into the home, resulting in indoor air pollution. Indoor air pollution is a major threat to health, particularly for women and young children,

who tend to spend more time in the home. Although the evidence base linking biomass fuel burning and indoor air pollution to specific lung diseases is accumulating, there is convincing evidence that biomass smoke exposure is a major driver of acute respiratory infections in children and of COPD in adults (63–65).

Globally, burning of solid fuels is estimated to account for nearly 3.5 million deaths annually from indoor air pollution and an additional 0.5 million deaths owing to the contribution of indoor air pollution to ambient air pollution. Indoor air pollution contributes substantially to DALY lost as well. About 32% of the burden occurs in

Sub-Saharan Africa, 37% in South Asia, and 18% in East Asia and Pacific (66–72).

Three general types of interventions have been proposed to ameliorate lung disease due to indoor air pollution: those that act on the source of pollution (e.g., novel cooking devices, alternative fuels), those that improve the living environment (e.g., improved ventilation, kitchen design), and those that cause changes in user behaviors (e.g., smoke avoidance). The evidence base for assessing the effectiveness of these various interventions is still being developed, and only one randomized, controlled trial examining the health benefits of interventions aimed at reducing indoor air pollution has been conducted, with mixed results (73). There is a limited understanding of how clean an alternative fuel needs to be or how much more efficient a new cookstove needs to be to cause a change in health outcomes. In addition, there is a challenge in managing cultural needs. Cooking tends to be a deeply embedded part of the culture in many regions, making it difficult to motivate individuals to change their cooking methods. However, given the large number of people affected, investments in identifying ways to reduce indoor air pollution, even if large, are likely to have a tremendous impact on morbidity and mortality. An excellent discussion of health risks and research priorities related to household air pollution has recently been published (74), and this report emphasizes the need to build a solid evidence base before new stoves are introduced on a widespread scale.

Occupational Exposures

Occupational exposure remains a major cause of lung disease around the world, even as, and perhaps because, a good deal of the global manufacturing base has shifted to developing countries where there is often less regulation of workplace hazards. In the United States, lung disease among firefighters responding to the attack on the World Trade Center in 2001 was a grim reminder of the consequences of exposure to inorganic dust, fumes, and smoke (75–77). WHO has estimated that occupational exposures to workplace lung carcinogens (e.g., asbestos, diesel exhaust, and silica) account for about 9% of cancers of the lung, trachea, and bronchus (78). Occupational exposures account for about 13% of cases of COPD (318,000

deaths per year and about 3.7 million DALYs) and about 11% of cases of asthma (38,000 deaths per year and 1.6 million DALYS) (79–82).

Strategies for reducing lung disease from occupational exposures include a hierarchy of controls in the following order of preference: replacing major hazards with less hazardous materials or processes, applying engineering controls to separate workers from hazards that remain, using administrative controls to minimize contact uncontrollable by engineering, and using personal protective equipment (e.g., respirators) (83, 84).

Public Health Action to Reduce the Drivers of Mortality and Morbidity from Lung Disease around the World

The lung diseases that account for the greatest global morbidity and mortality are preventable to a very significant degree. Although the pathogenesis of the most important lung diseases in the world are quite varied, most of them are linked by common drivers. Although some of those drivers are primary causes of these lung diseases and some exert their effect secondarily by worsening the course or severity of existing disease, all are important (Figure 1). Thus, it is likely that efforts to

reduce exposure to tobacco, indoor air pollutants, outdoor air pollutants, and occupational toxins will have a greater impact in reducing illness and death from respiratory infections, asthma, COPD, and lung cancer than will individual therapies provided to patients. In cities such as New York, aggressive antitobacco measures have reduced smoking rates to 14% of the population, and this will result in more lives saved from lung cancer and COPD than will any medical therapy currently in hand.

We do not underestimate the difficulty in reducing the impact of the important drivers of lung disease in the world. These drivers arise to a great degree because of poverty (e.g., due to a lack of access to clean burning fuels and efficient stoves for cooking) because of a lack of government oversight and regulation (regarding the sale of tobacco products or worker safety), or a combination of both (Figure 1). Additionally, the tobacco industry has tenaciously fought every effort to reduce the use of its product. Slowly but surely, however, in more and more countries, the tide is turning, but continuous action is still required. We believe that the same is possible in the areas of pollution and occupational exposures. Education of the public is crucial to mobilize sentiment against these dangers. Advocacy at local, regional, national, and international levels is critical. Insistence that industries be

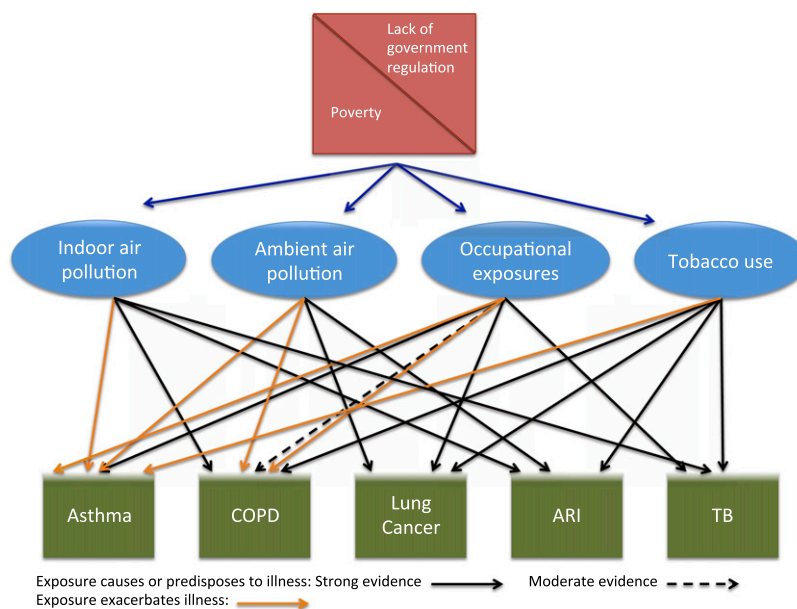


Figure 1. The world's five leading lung diseases and their environmental drivers.

accountable for the health of those who use their products must be unceasing. In circumstances where complete removal of a particular exposure is not a realistic goal (it is hard to imagine a world without cars or factories), funders of all sorts should support research that will identify the best way to reduce exposure as much as possible and to protect citizens from what cannot be eliminated completely. Governments must be held accountable as well for protecting the lives of their citizens at least as much as they protect the commercial interests of large industries. Monitoring and surveillance of the burden of disease and of actions to reduce or eliminate the various drivers of lung disease must be constant. This cannot be entrusted to industry or governments alone but should be performed with partners from civil society. Rapidly developing countries are especially vulnerable because the pressure to industrialize to improve the economic lot of citizens often trumps the responsibility to regulate industries and activities whose activities create unhealthy living conditions. The air pollution problem in Beijing is an example of this (85), and the recent

worldwide attention given to air pollution in Harbin, China, where $PM_{2.5}$ concentrations reached levels of over $1,000 \mu m/m^3$ and visibility decreased to 10 m, also focused attention on this problem, which is not unique to China (86).

We call for action in the following areas: (1) There must be increased advocacy from and mobilization of civil society to bring attention to the drivers of lung diseases in the world. Tobacco advocacy is an excellent model to follow. Civil society groups, including nongovernmental organizations, must monitor and hold accountable governments and industries that are not addressing these problems of indoor and outdoor air pollution and occupational causes of lung disease. (2) The WHO should negotiate accords similar to the Framework Convention on Tobacco Control to address air pollution and occupational exposures. These accords would commit governments to identify specific measures that they would take to reduce airborne pollutants and toxins. Two of the drivers of lung disease are the result of energy policies that place vulnerable populations at unique risks for respiratory

diseases. In light of this, WHO should ensure that the proposed convention should be in harmony with the 2011 United Nations Sustainable Energy for All initiative. (3) Large increases in funding by government agencies and nongovernmental organizations around the world are needed to identify technologies (e.g., cleaner cookstoves, cleaner cars, and cleaner factories) that will reduce health risks while allowing populations to enjoy the benefits of economic growth and development.

Failure to protect vulnerable populations from preventable illnesses is an abrogation of societal responsibility. We hope that the framework we have proposed will help focus on actions that can be taken to reduce lung diseases by addressing their root cause. ■

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References

- 1 FIRS. Respiratory disease in the world: realities of today—opportunities for tomorrow. Sheffield, UK: European Respiratory Society; 2013.
- 2 Ferkol T, Schraufnagel D. The global burden of respiratory disease. *Ann Am Thorac Soc* 2014;11:404–406.
- 3 Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, Abraham J, Adair T, Aggarwal R, Ahn SY, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2095–2128.
- 4 Masoli M, Fabian D, Holt S, Beasley R. Global burden of asthma [cited 2013 Apr 4]. Available from: http://www.ginasthma.org/local/uploads/files/GINABurdenReport_1.pdf.
- 5 Pawankar R, Canonica GW, Holgate ST, Lockey RF. Allergic diseases and asthma: a major global health concern. *Curr Opin Allergy Clin Immunol* 2012;12:39–41.
- 6 Anandan C, Nurmatov U, van Schayck OC, Sheikh A. Is the prevalence of asthma declining? Systematic review of epidemiological studies. *Allergy* 2010;65:152–167.
- 7 Boulet LP. Asthma and obesity. *Clin Exp Allergy* 2013;43:8–21.
- 8 Kattan M, Kumar R, Bloomberg GR, Mitchell HE, Calatroni A, Gergen PJ, Kercsmar CM, Visness CM, Matsui EC, Steinbach SF, et al. Asthma control, adiposity, and adipokines among inner-city adolescents. *J Allergy Clin Immunol* 2010;125:584–592.
- 9 Clark NA, Demers PA, Karr CJ, Koehoorn M, Lencar C, Tamburic L, Brauer M. Effect of early life exposure to air pollution on development of childhood asthma. *Environ Health Perspect* 2010;118:284–290.
- 10 Baek HS, Kim YD, Shin JH, Kim JH, Oh JW, Lee HB. Serum leptin and adiponectin levels correlate with exercise-induced bronchoconstriction in children with asthma. *Ann Allergy Asthma Immunol* 2011;107:14–21.
- 11 Gilstrap DL, Kraft M. Asthma and the host-microbe interaction. *J Allergy Clin Immunol* 2013;131:1449–1450, e1443.
- 12 Schluger NW, Feiden K, Sebek K. The acute respiratory infections atlas. New York: World Lung Foundation; 2010.
- 13 Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, Rudan I, Campbell H, Cibulskis R, Li M, et al.; Child Health Epidemiology Reference Group of WHO and UNICEF. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet* 2012;379:2151–2161.
- 14 Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2197–2223.
- 15 World Health Organization. Global tuberculosis report 2013. Geneva, Switzerland: WHO; 2013.
- 16 Dye C, Lönnroth K, Jaramillo E, Williams BG, Raviglione M. Trends in tuberculosis incidence and their determinants in 134 countries. *Bull World Health Organ* 2009;87:683–691.
- 17 Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. *Soc Sci Med* 2009;68:2240–2246.
- 18 World Health Organization. Countdown to 2015: global tuberculosis report 2013 supplement. Geneva, Switzerland: World Health Organization; 2013.
- 19 Zignol M, van Gemert W, Falzon D, Sismanidis C, Glaziou P, Floyd K, Raviglione M. Surveillance of anti-tuberculosis drug resistance in the world: an updated analysis, 2007–2010. *Bull World Health Organ* 2012;90:111D–119D.
- 20 Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011;61:69–90.
- 21 McCormack VA, Boffetta P. Today's lifestyles, tomorrow's cancers: trends in lifestyle risk factors for cancer in low- and middle-income countries. *Ann Oncol* 2011;22:2349–2357.
- 22 Bello B, Fadahun O, Kielkowski D, Nelson G. Trends in lung cancer mortality in South Africa: 1995–2006. *BMC Public Health* 2011;11:209.

- 23 Niewoehner DE. Clinical practice: outpatient management of severe COPD. *N Engl J Med* 2010;362:1407–1416.
- 24 Fanta CH. Asthma. *N Engl J Med* 2009;360:1002–1014.
- 25 Avorn J. Approval of a tuberculosis drug based on a paradoxical surrogate measure. *JAMA* 2013;309:1349–1350.
- 26 Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, Rice LB, Scheld M, Spellberg B, Bartlett J. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clin Infect Dis* 2009;48:1–12.
- 27 Petrosyan F, Daw H, Haddad A, Spiro T. Targeted therapy for lung cancer. *Anticancer Drugs* 2012;23:1016–1021.
- 28 Institute for Health Metrics and Evaluation. Global burden of disease [accessed 25 Feb 2014]. Available from: <http://www.healthmetricsandevaluation.org/gbd/visualizations/gbd-arrow-diagram>.
- 29 Jha P, Ramasundarahettige C, Landsman V, Rostron B, Thun M, Anderson RN, McAfee T, Peto R. 21st-century hazards of smoking and benefits of cessation in the United States. *N Engl J Med* 2013;368:341–350.
- 30 Schroeder SA. New evidence that cigarette smoking remains the most important health hazard. *N Engl J Med* 2013;368:389–390.
- 31 Thun MJ, Carter BD, Feskanich D, Freedman ND, Prentice R, Lopez AD, Hartge P, Gapstur SM. 50-year trends in smoking-related mortality in the United States. *N Engl J Med* 2013;368:351–364.
- 32 Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, Amann M, Anderson HR, Andrews KG, Aryee M, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2224–2260.
- 33 Farr BM, Bartlett CL, Wadsworth J, Miller DL; British Thoracic Society Pneumonia Study Group. Risk factors for community-acquired pneumonia diagnosed upon hospital admission. *Respir Med* 2000;94:954–963.
- 34 Farr BM, Woodhead MA, Macfarlane JT, Bartlett CL, McCracken JS, Wadsworth J, Miller DL. Risk factors for community-acquired pneumonia diagnosed by general practitioners in the community. *Respir Med* 2000;94:422–427.
- 35 Nuorti JP, Butler JC, Farley MM, Harrison LH, McGeer A, Kolczak MS, Breiman RF; Active Bacterial Core Surveillance Team. Cigarette smoking and invasive pneumococcal disease. *N Engl J Med* 2000;342:681–689.
- 36 O'Dempsey TJ, McArdle TF, Morris J, Lloyd-Evans N, Baldeh I, Laurence BE, Secka O, Greenwood BM. A study of risk factors for pneumococcal disease among children in a rural area of west Africa. *Int J Epidemiol* 1996;25:885–893.
- 37 den Boon S, van Lill SW, Borgdorff MW, Verver S, Bateman ED, Lombard CJ, Enarson DA, Beyers N. Association between smoking and tuberculosis infection: a population survey in a high tuberculosis incidence area. *Thorax* 2005;60:555–557.
- 38 Lin HH, Ezzati M, Murray M. Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis. *PLoS Med* 2007;4:e20.
- 39 Gajalakshmi V, Peto R, Kanaka TS, Jha P. Smoking and mortality from tuberculosis and other diseases in India: retrospective study of 43000 adult male deaths and 35000 controls. *Lancet* 2003;362:507–515.
- 40 Sterling TR, Villarino ME, Borisov AS, Shang N, Gordin F, Bliven-Sizemore E, Hackman J, Hamilton CD, Menzies D, Kerrigan A, et al.; TB Trials Consortium PREVENT TB Study Team. Three months of rifapentine and isoniazid for latent tuberculosis infection. *N Engl J Med* 2011;365:2155–2166.
- 41 WHO. Who report on the global tobacco epidemic: warning about the dangers of tobacco. Geneva, Switzerland: World Health Organization; 2011.
- 42 Mackay J. Implementing tobacco control policies. *Br Med Bull* 2012;102:5–16.
- 43 Henriksen L. Comprehensive tobacco marketing restrictions: promotion, packaging, price and place. *Tob Control* 2012;21:147–153.
- 44 Goodman PG, Haw S, Kabir Z, Clancy L. Are there health benefits associated with comprehensive smoke-free laws. *Int J Public Health* 2009;54:367–378.
- 45 Wipfli H, Samet JM. Global economic and health benefits of tobacco control: part 1. *Clin Pharmacol Ther* 2009;86:263–271.
- 46 Wipfli H, Samet JM. Global economic and health benefits of tobacco control: part 2. *Clin Pharmacol Ther* 2009;86:272–280.
- 47 Carrascal A, Sciandra R, Horner H. The cancer burden in New York State. New York: American Cancer Society of New York and New Jersey; 2012.
- 48 Bogdanovica I, McNeill A, Murray R, Britton J. What factors influence smoking prevalence and smoke free policy enactment across the European Union Member States. *PLoS ONE* 2011;6:e23889.
- 49 Sava F, Carlsten C. Respiratory health effects of ambient air pollution: an update. *Clin Chest Med* 2012;33:759–769.
- 50 Brunekreef B, Holgate ST. Air pollution and health. *Lancet* 2002;360:1233–1242.
- 51 Deguen S, Zmirou-Navier D. Social inequalities resulting from health risks related to ambient air quality: a European review. *Eur J Public Health* 2010;20:27–35.
- 52 Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr, Speizer FE. An association between air pollution and mortality in six U.S. cities. *N Engl J Med* 1993;329:1753–1759.
- 53 Samet JM, Zeger SL, Dominici F, Currier F, Coursac I, Dockery DW, Schwartz J, Zanobetti A. The national morbidity, mortality, and air pollution study. Part II: morbidity and mortality from air pollution in the United States. *Res Rep Health Eff Inst* 2000;94:5–70; discussion 71–79.
- 54 Samet JM, Dominici F, Zeger SL, Schwartz J, Dockery DW. The national morbidity, mortality, and air pollution study. Part I: methods and methodologic issues. *Res Rep Health Eff* 2000;5–14; discussion 75–84.
- 55 Katsouyanni K, Zmirou D, Spix C, Sunyer J, Schouten JP, Ponka A, Anderson HR, Le Moulec Y, Wojtyniak B, Vigotti MA, et al. Short-term effects of air pollution on health: a European approach using epidemiological time-series data. The APHEA project: background, objectives, design. *Eur Respir J* 1995;8:1030–1038.
- 56 Hart JE, Garshick E, Dockery DW, Smith TJ, Ryan L, Laden F. Long-term ambient multipollutant exposures and mortality. *Am J Respir Crit Care Med* 2011;183:73–78.
- 57 Romieu I, Gouveia N, Cifuentes LA, de Leon AP, Junger W, Vera J, Strappa V, Hurtado-Diaz M, Miranda-Soberanis V, Rojas-Bracho L, et al. Multicity study of air pollution and mortality in Latin America (the Escala study). *Res Rep Health Eff Inst* 2012:5–86.
- 58 Dong GH, Zhang P, Sun B, Zhang L, Chen X, Ma N, Yu F, Guo H, Huang H, Lee YL, et al. Long-term exposure to ambient air pollution and respiratory disease mortality in Shenyang, China: a 12-year population-based retrospective cohort study. *Respiration* 2012;84:360–368.
- 59 Mustapha BA, Blangiardo M, Briggs DJ, Hansell AL. Traffic air pollution and other risk factors for respiratory illness in schoolchildren in the Niger-Delta region of Nigeria. *Environ Health Perspect* 2011;119:1478–1482.
- 60 Nandasena YL, Wickremasinghe AR, Sathikumar N. Air pollution and health in Sri Lanka: a review of epidemiologic studies. *BMC Public Health* 2010;10:300.
- 61 Kan H, London SJ, Chen G, Zhang Y, Song G, Zhao N, Jiang L, Chen B. Season, sex, age, and education as modifiers of the effects of outdoor air pollution on daily mortality in Shanghai, China: The Public Health and Air Pollution in Asia (PAPA) Study. *Environ Health Perspect* 2008;116:1183–1188.
- 62 WHO. World health statistics, 2010. Geneva, Switzerland: World Health Organization; 2010.
- 63 Torres-Duque C, Maldonado D, Pérez-Padilla R, Ezzati M, Viegi G; Forum of International Respiratory Studies (FIRS) Task Force on Health Effects of Biomass Exposure. Biomass fuels and respiratory diseases: a review of the evidence. *Proc Am Thorac Soc* 2008;5:577–590.
- 64 Perez-Padilla R, Schilman A, Riojas-Rodriguez H. Respiratory health effects of indoor air pollution. *Int J Tuberc Lung Dis* 2010;14:1079–1086.

- 65 Sood A. Indoor fuel exposure and the lung in both developing and developed countries: an update. *Clin Chest Med* 2012;33:649–665.
- 66 Hulin M, Simoni M, Viegi G, Annesi-Maesano I. Respiratory health and indoor air pollutants based on quantitative exposure assessments. *Eur Respir J* 2012;40:1033–1045.
- 67 Po JY, FitzGerald JM, Carlsten C. Respiratory disease associated with solid biomass fuel exposure in rural women and children: systematic review and meta-analysis. *Thorax* 2011;66:232–239.
- 68 Kaplan C. Indoor air pollution from unprocessed solid fuels in developing countries. *Rev Environ Health* 2010;25:221–242.
- 69 Fullerton DG, Bruce N, Gordon SB. Indoor air pollution from biomass fuel smoke is a major health concern in the developing world. *Trans R Soc Trop Med Hyg* 2008;102:843–851.
- 70 Fullerton DG, Semple S. Air pollution and health: indoor air pollution in the developing world is the real key to reducing the burden of ill health. *Thorax* 2008;63:288, author reply 288.
- 71 Dherani M, Pope D, Mascarenhas M, Smith KR, Weber M, Bruce N. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. *Bull World Health Organ* 2008;86:390C–398C.
- 72 Emmelin A, Wall S. Indoor air pollution: a poverty-related cause of mortality among the children of the world. *Chest* 2007;132:1615–1623.
- 73 Smith KR, McCracken JP, Weber MW, Hubbard A, Jenny A, Thompson LM, Balmes J, Diaz A, Arana B, Bruce N. Effect of reduction in household air pollution on childhood pneumonia in Guatemala (RESPIRE): a randomised controlled trial. *Lancet* 2011;378:1717–1726.
- 74 Martin WJ II, Glass RI, Araj H, Balbus J, Collins FS, Curtis S, Diette GB, Elwood WN, Falk H, Hibberd PL, *et al*. Household air pollution in low- and middle-income countries: health risks and research priorities. *PLoS Med* 2013;10:e1001455.
- 75 Rom WN, Reibman J, Rogers L, Weiden MD, Oppenheimer B, Berger K, Goldring R, Harrison D, Prezant D. Emerging exposures and respiratory health: World Trade Center dust. *Proc Am Thorac Soc* 2010;7:142–145.
- 76 Webber MP, Gustave J, Lee R, Niles JK, Kelly K, Cohen HW, Prezant DJ. Trends in respiratory symptoms of firefighters exposed to the world trade center disaster: 2001–2005. *Environ Health Perspect* 2009;117:975–980.
- 77 Aldrich TK, Gustave J, Hall CB, Cohen HW, Webber MP, Zeig-Owens R, Cosenza K, Christodoulou V, Glass L, Al-Othman F, *et al*. Lung function in rescue workers at the World Trade Center after 7 years. *N Engl J Med* 2010;362:1263–1272.
- 78 WHO. Environmental and occupational cancers: fact sheet no. 350, March 2011 [cited 2013 Apr 15]. Available from: <http://www.who.int/mediacentre/factsheets/fs350/en/>.
- 79 Weinmann S, Vollmer WM, Breen V, Heumann M, Hnizdo E, Villave J, Doney B, Graziani M, McBurnie MA, Buist AS. COPD and occupational exposures: a case-control study. *J Occup Environ Med* 2008;50:561–569.
- 80 Blanc PD, Iribarren C, Trupin L, Earnest G, Katz PP, Balmes J, Sidney S, Eisner MD. Occupational exposures and the risk of COPD: dusty trades revisited. *Thorax* 2009;64:6–12.
- 81 Melville AM, Pless-Mulloli T, Afolabi OA, Stenton SC. COPD prevalence and its association with occupational exposures in a general population. *Eur Respir J* 2010;36:488–493.
- 82 Govender N, Laloo UG, Naidoo RN. Occupational exposures and chronic obstructive pulmonary disease: a hospital based case-control study. *Thorax* 2011;66:597–601.
- 83 Nicholson PJ, Cullinan P, Taylor AJ, Burge PS, Boyle C. Evidence based guidelines for the prevention, identification, and management of occupational asthma. *Occup Environ Med* 2005;62:290–299.
- 84 de Groene GJ, Pal TM, Beach J, Tarlo SM, Spreeuwiers D, Frings-Dresen MH, Mattioli S, Verbeek JH. Workplace interventions for treatment of occupational asthma. *Cochrane Database Syst Rev* 2011;5:CD006308.
- 85 Chen Y, Ebenstein A, Greenstone M, Li H. Evidence on the impact of sustained exposure to air pollution on life expectancy from China's Huai River policy. *Proc Natl Acad Sci USA* 2013;110:12936–12941.
- 86 Wong E. Response to a city's smog points to a change in Chinese attitude. *The New York Times*. October 24, 2013:A12.