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CHEST

Global Medicine

COPD in Asia*

Where East Meets West

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COPD is a global health concern, and is a major cause of chronic morbidity and mortality worldwide. According to the World Health Organization, it is currently the sixth leading cause of death in the world, and further increases in the prevalence and mortality of the disease is predicted for the coming decades. These increases are mainly linked to the epidemic of tobacco exposure and indoor and outdoor air pollution in Asian countries. The burden of COPD in Asia is currently greater than that in developed Western countries, both in terms of the total number of deaths and the burden of disease, as measured in years of life lost and years spent living with disability. The types of health-care policies and the practice of medicine vary considerably among the regions of Asia and have an impact on the burden of disease. Treatment aims in Asian countries are based on evidence-based management guidelines. Barriers to the implementation of disease management guidelines are related to issues of resource conflict and lack of organizational support rather than cultural differences in medical practice. To reduce this burden of COPD in Asian countries, there is a need for a multifaceted approach in improving awareness of prevalence and disease burden, in facilitating accurate diagnosis of COPD among chronic respiratory diseases, in championing health policies that reduce the burden of the main risk factors for COPD and in the wider use of evidence-based management for COPD.

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Key words: bronchodilators; COPD; pulmonary epidemiology; pulmonary rehabilitation; smoking

Abbreviations: α_1-AT = α_1-antitrypsin; GOLD = Global Initiative for Chronic Obstructive Lung Disease; ICD = *International Classification of Diseases*; WHO = World Health Organization

COPD is a global health concern. It is a major cause of morbidity and mortality worldwide, and is among the top 10 global contributors to the global burden of disease as measured by disability-adjusted life years.[1] In 2002, COPD was the fifth leading cause of death. According to the World Health Organization (WHO),[2] the total number of deaths in the world from COPD are projected to increase by > 30% in the next 10 years; by 2030, COPD would become the fourth leading cause of death worldwide. Among all major chronic diseases, COPD is the only disease that shows a rising mortality. This trend is predicted to rise further in the next decades with the escalating increase in the associated risk factors for COPD and an aging population in many parts of the world.

The burden of COPD in Asia is currently greater than that in developed Western countries, both in terms of the total number of deaths and the burden of disease, as measured in years of life lost and the number of years spent living with disability, and is mainly linked to the epidemic of tobacco exposure and indoor and outdoor air pollution in Asian coun-

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tries.[1] The objective of this article was to review the current literature on COPD in Asia and to highlight how COPD in Asia is different from or similar to that seen in the West.

Epidemiology: Increasing Trends in Burden of disease

Most of the available information on the burden of disease of COPD comes from the established economies of the world.[3] Comparison of the mortality, morbidity, and prevalence data among these countries is problematic due to a lack of standardization of death certification, changes in the *International Classification of Diseases* (ICD), and differences in the diagnostic standards of COPD among the countries. Despite these limitations, mortality rates from national statistics are the only epidemiologic data that are readily available for comparison.

These methodological problems are often magnified in Asian countries by an absence of medical and death documentation in remote rural areas.[4] According to the updated Global Burden of Disease report,[1] uncertainty in all-cause mortality estimates ranged from around 1% in high-income countries to 15 to 20% in low-income countries. Uncertainty was larger for mortality from specific diseases, and for incidence and prevalence of nonfatal outcomes. Death registration data, containing useable information on cause-of-death distributions, may be patchy or not available. The proportion of deaths coded to ill-defined causes such as COPD, has been found to vary from 4% in New Zealand to > 40% in Sri Lanka and Thailand.[1]

Mortality

COPD was the sixth-leading cause of death worldwide in 1990, but by 2002 the ranking had risen to fifth and is projected to double within the next 2 decades.[1] COPD was ranked as the fourth-leading cause of death in the United States in 2002, accounting for 4 to 5% of total deaths.[5] Rising trends in COPD mortality dating from 1990 have been reported in the United States, the United Kingdom, France, Australia, and Canada.[6–10] Gender difference was observed in these trends with changes in previous male-dominated mortality rates rising more steeply among women than among men, as seen in North America.[6]

Mortality rates in Asia are similar to or higher than those in the West.[11–13] COPD was listed as the seventh most common cause of death in China based on a national cohort study conducted in 2000.[13] However, COPD deaths were deduced from the deaths categorized as "cardiopulmonary deaths/cor pulmonale," as there were no separate categories for COPD such as those based on the ICD codes. This diagnostic transfer coupled with a lack of death certification in rural areas are likely to result in an underestimation or overestimation of the total COPD deaths in China.

There are a few Asian mortality reports using ICD codes for COPD. In higher income Asian countries, mortality rates are similar to that reported in the West. For example, in multiethnic Singapore, COPD is ranked as the sixth-leading cause of death, accounting for 4.6% of total deaths and 5.8% of those persons ≥ 55 years of age. Trend analysis of the Singapore national health statistics from 1991 to 1998 showed that while COPD morbidity is relatively stable, COPD mortality is decreasing, which is a reflection of the decline in smoking prevalence over the preceding decades. Gender and ethnic differences in mortality rates are linked to tobacco exposure, with the rate in men being five times that in women, and there being an almost twofold difference among the main ethnic groups[11] (Table 1).

In Taiwan, COPD mortality based on ICD codes ranked sixth as a cause of death in 2002, with a rising trend due to increased mortality in men.[12] In sharp contrast to the industrialized countries of the West, COPD mortality remains male predominant in Asian countries. These differences in rates and trends for men and women most likely reflect the different trends in the prevalent risk factor profiles for COPD in the different countries.

Table 1—*Gender and Ethnic Differences in COPD Hospitalization and Mortality in Population Aged ≥ 55 Years, Singapore 1991—1998

	Hospitalization		Mortality	
Characteristics	Rate†	Rate Ratio (95% CI)‡	Rate†	Rate Ratio (95% CI)‡
Overall	52.4		16.3	
Gender				
Female	18.2	1.00	6.9	1.00
Male	94.1	5.15 (1.07–1.68)	28.2	4.05 (3.40–4.84)
Age group				
55–64	17.5	1.00	4.5	1.00
65–74	68.0	3.90 (3.44–4.41)	15.4	4.40 (3.35–5.78)
75+	129.5	7.41 (6.56–8.38)	55.9	16.0 (12.4–20.5)
Ethnicity				
Chinese	53.9	1.25 (1.04–1.50)	16.4	1.48 (1.03–2.14)
Malay	45.1	1.07 (0.86–1.34)	19.3	1.76 (1.15–2.68)
Indian	43.9	1.00	10.7	1.00

*CI = confidence interval. Data are from the study by Ng et al.[11]
†Per 10,000 population and directly adjusted for age, sex, and ethnicity according to the 1991 general population.
‡Calculated using Poisson regression models (SAS; SAS Institute; Cary, NC) including age, gender, and ethnicity.

Morbidity: Hospitalizations

Morbidity includes physician visits, emergency department visits, and hospitalizations. COPD databases for these outcome parameters are not readily available and usually are less reliable where they are affected by a pattern of health-care utilization such as excess utilization or lack of access.

Hospitalization is an important health economic outcome as it accounts for more than half of all the health-care cost for COPD in most countries. The limited available Asian data indicate that morbidity due to COPD increases with age and is considerably greater in men than women,[11,14,15] in contrast to the narrower gender gap in most Western countries,[7,10] and the reversal of the gender ratio in the United States where female rates have exceeded male rates.[6] Acute triggers associated with hospitalization for COPD in Asian countries include environmental factors such as acute rise in air pollution[14] and influenza infection.[16]

In Asia, hospitalization is the single largest item in the direct health-care cost for COPD (Table 2).[15] The associated risk factors for frequent hospital admissions for acute exacerbations of COPD are disease severity and psychosocial distress.[17]In particular, comorbid depressive symptoms in COPD patients are associated with poorer survival, longer hospital stay, persistent smoking, increased symptom burden, and poorer physical and social functioning.[18] Comprehensive hospitalization records are not widely available. Hospitalizations for COPD are increasing in most Asian countries.[11,14,15] In some Asian countries such as Singapore, even as the trend for mortality rates fell, hospitalization rates continued to rise. This dichotomy in trends is most likely the result of a sustained decline in the cigarette-smoking epidemic due to well-established antismoking measures, but it also indicates that the disease burden would continue for some time beyond the peak and the decline of the associated risk factors.[11,15]

Table 2—*Direct Medical Costs for COPD in Japan in 1999**

Variables	Total Care, %	Outpatient Care, %	Inpatient Care, %
Physician services	16.3	25.8	
Laboratory	8.1	8.7	7.2
Chest radiography	4	4.6	3.2
Medication	18.1	22.8	10.7
Home oxygen therapy	22.9	35.8	
Rehabilitation	0.7	0.1	1.7
Hospital admission†	24.2		63.5

*Source of data is from the Ministry of Health, Labour, and Welfare "Report on the Survey of Medical Care Activities in Public Health Insurance." Table modified from the study by Izumi.[15]

†Hospital admission fees include the physician services fee.

Prevalence

The WHO estimates that the world prevalence of COPD is 340 million,[1] with world prevalence rate in 2001 of 1.01% in all age groups, thus underestimating the prevalence in adults and elderly. Accurate estimates of prevalence in most countries are unknown, as there have been few published population-based studies on the prevalence of COPD worldwide, especially in developing countries, including most of Asia. Even in countries where data are available, published prevalence rates vary appreciably across countries, due to different methods and criteria for detecting COPD in the community, such as symptoms of chronic bronchitis, physician-diagnosed COPD, or spirometric airflow limitation[19] (Table 3[6,10,20–23,25,26,28–30,32,33]).

In the United States, the prevalence of physician-diagnosed emphysema or chronic bronchitis in 2000 was 4.6% in men and 7.3% in women,[6] and the rates for Canada were 2.8% for men and 3.6% for women.[10] In the United Kingdom, a retrospective analysis of the General Practice Database,[21] covering 3.4 million patients, showed that in 1990 the prevalence of physician-diagnosed COPD was 1.4% in men and 0.8% in women; but, between 1990 and 1997, the rates rose more sharply for women (69%) compared with men (25%). However, using self-reported physician diagnoses of COPD results in a serious underestimation of prevalence, as those with the disease tend not to seek medical advice until the disease is severe. One European report[22] has suggested that only 25% of COPD cases are diagnosed (Table 3).

Using spirometric airflow limitation as a more objective diagnostic criteria for COPD, the prevalence of COPD is about 6% among men and women of all ages in Norway[23] and northern Italy.[24] When COPD was defined in terms of a postbronchodilator airflow limitation as an FEV_1/FVC ratio of < 0.7,[3] the prevalence in populations ≥ 40 years of age in five major Latin American cities ranged from 7.8% in Mexico City to 19.7% in Montevideo.[25] Using a similar protocol, a recent study[26] from Salzburg, Austria, reported an overall prevalence of COPD of 26.1%, equal in men and women, and a prevalence for moderate-to-severe COPD of 10.7%. A symptom-based doctor diagnosis of COPD was reported by only 5.6% of participants, indicating that most cases of COPD were undiagnosed and that spirometry is essential for the accurate detection of COPD in the community[26] (Table 3).

In Asian countries, epidemiologic studies are scant, patchy, or localized. Population-based studies are rare, because of limitations in resources, the complexity of organization, and the unavailability of lung function equipment. Yet, there is a need for

Table 3—*Prevalence Data From Key Field Studies in the West and in Asia

Study/Year	Country	Age Distribution, yr	Diagnostic Label	Prevalence, %		
				Male	Female	All
West						
Mannino et al[6]/2002	United States	≥ 25	Physician diagnosis CE/CB	4.6	7.3	6.0
Locasse et al[10]/1999	Canada	≥ 55	Physician diagnosis CE/CB	6.3	5.2	5.7
Soriano et al[21]/2000	United Kingdom	≥ 20	Physician diagnosis COPD	1.4	0.8	
Bakke et al[23]/1991	Norway	> 18	Spirometry			4.5
Menezes et al[25]/2005	South America	> 40	Post-BD spirometry	11.4–24.2†	6.5–14.5†	7.8–19.7†
Schirnhofer et al[26]/2007	Salzburg, Austria	> 40	Post-BD spirometry	26.6	25.7	26.1
Halbert et al[20]/2006	Global systemic review	≥ 40	Chronic bronchitis			6.4
			Emphysema			1.8
			COPD (spirometry)			8.9
			COPD all‡			7.6
East						
Pandey[28]/1984	Nepal	≥ 20	Chronic bronchitis			18.0
Jindal[30]/2006	India	≥ 35	Chronic bronchitis	5.0	3.2	4.1
Woo and Pang[29]/1988	Hong Kong	≥ 60	Spirometry (pre-BD)			6.8
Fukuchi et al[32]/2004	Japan	≥ 40	Spirometry (pre-BD)	16.4	5.0	10.9
Kim et al[33]/2005	South Korea	> 45	Spirometry (pre-BD)	25.8	9.6	17.2

*Pre-BD = prebronchodilator; Post-BD = postbronchodilator; CE = chronic emphysema; CB = chronic bronchitis.
†Range for five cities.
‡Spirometry, patient reported, physician diagnosed, and physical/radiology.

local data on prevalence to provide some insight into the extent of the burden of COPD to facilitate disease awareness and health-care planning. According to the WHO estimates,[27] the number of COPD cases in Asia exceeds by three times the total number of COPD cases for the rest of the world. In a symptom-based study[28] in Nepal, the crude prevalence in a rural community was 18% based on symptoms of chronic bronchitis. A study[29] of elderly Chinese living in Hong Kong found a prevalence of 6.8% for all severity based on spirometry findings. In a large population-based, multicentric study[30] in India, the prevalence of chronic bronchitis was found to be 4.1% in adults ≥ 35 years of age, with a male/female ratio of 1.56 and a smoker/nonsmoker prevalence ratio of 2.65 (Table 3).

The Asia Pacific Round Table group,[31] consisting of a panel of regional respiratory experts, used a statistical model with a standardized protocol to project and compare the prevalence of moderate-to-severe COPD in 12 Asian countries or cities. The projected prevalence rates range from 3.5% for Hong Kong and Singapore to 6.7% in Vietnam, with an overall prevalence rate of 6.3% for the region, which is considerably higher than that estimated by the WHO for the region (3.8%) [Table 4].

Two recent large, well-conducted, community-based studies from Japan[32] and Korea[33] used a standardized questionnaire and measured baseline lung function. In a population-based study[32] conducted in Japan in 2001, the prevalence of airflow limitation was 10.9% for adults ≥ 40 years of age, rising with age to 24% in those persons > 70 years of age, which are rates that are several times larger than the previously accepted COPD prevalence rate of 1.7%.[15] Airflow limitation was significantly more prevalent in men than women (16.4% vs 5.0%, respectively). The prevalence in smokers was 17.1% in men and 7.5% in women, while that in nonsmokers was 5.8%. The authors also found a high degree of underrecognition of COPD, as 90% of patients with airflow limitation did not have a previous diagnosis of COPD.

Table 4—*Model Projections of the Prevalence of Moderate-to-Severe COPD in Those Persons ≥ 30 Years of Age for 12 Countries/Cities in the Asia-Pacific Region

Model	Country	Moderate-to-Severe COPD Cases	Prevalence, %
1	Australia	558,000	4.70
2	China	38,160,000	6.50
3	Hong Kong	139,000	3.50
4	Indonesia	4,806,000	5.60
5	Japan	5,014,000	6.10
6	South Korea	1,467,000	5.90
7	Malaysia	448,000	4.70
8	Philippines	1,691,000	6.30
9	Singapore	64,000	3.50
10	Taiwan	636,000	5.40
11	Thailand	1,502,000	5.00
12	Vietnam	2,068,000	6.70
	Total	56,553,000	6.30

*Data are from the Study by the Regional COPD Working Group.[31]

In Korea, the prevalence of COPD based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD)[3] criteria (*ie*, FEV_1/FVC ratio of < 0.7) was 17.2% among subjects > 45 years of age. Airflow limitation was more prevalent in men (25.8%) than in women (9.6%). Among adults of all ages (*ie*, those ≥ 18 years of age), the prevalence of airflow obstruction was 7.8% (men, 10.9%; women, 4.9%). The majority of these cases were found to be mild in degree, and only a minority of these subjects had received physician diagnosis or treatment. These conclusions reflect those found in Japan[32] and in the West.[26]

As more epidemiologic studies in the world become available using a standardized methodology, such as that in the multisite Burden of Obstructive Lung Disease initiative,[19] standardized comparison of COPD burden between cities and regions may be feasible in the near future.[25]

Overall, the existing data support the concept that COPD is a common worldwide disease in countries of Asia and the West. The similarities between East and West are that COPD is a disease of older individuals, is linked to the local smoking prevalence, and the trend is of rising mortality and morbidity. The differences are in the size of the disease burden between genders and in the trend rate, which is largely related to the "maturity" of the cigarette-smoking epidemic and the population demographics, compounded by other risk factors such as indoor air pollution from biomass fuel combustion and poorer socioeconomic circumstances.

Associated Risk Factors

The pathogenesis of COPD is due to an interaction between host factors (*ie*, genes, airway hyperresponsiveness, and lung growth) and exposure to environmental pollutants (*ie*, tobacco smoke, occupational dust and fumes, respiratory infection, outdoor air pollution, and indoor air pollution caused by biomass or traditional fuels and coal) and socioeconomic status.

Genetic Factors

It is believed that many genetic factors may influence an individual likelihood of COPD developing. Studies have demonstrated an increased risk of COPD within families with COPD probands. Some of this risk may be due to shared environmental factors, but several studies[34,35] in diverse populations have also suggested a shared genetic risk. To date, α_1-antitrypsin (α_1-AT) deficiency, a major circulating serine protease inhibitor, is the only genetic factor that is definitely linked to the development of emphysema or COPD, independent of tobacco exposure. Affected individuals have a 40-fold increase in the risk of the development of COPD compared to unaffected people. This rare hereditary deficiency is a recessive trait most commonly seen in individuals of Northern European origin and is extremely rare among Asians. Limited data have failed to link COPD with α_1-AT deficiency in Chinese either by determining the levels in the serum[36] or by genotyping and electrophoretic phenotyping for cases of PiZ and PiS.[37,38] Although variants of α_1-AT deficiency have been reported such as variant Siiyama in Japan,[39] and METokyo an Mpirare among Chinese, they have not been linked to COPD.[38]

A number of candidate genes in whites have been implicated in an increased risk for COPD, including ABH nonsecretor status,[40] microsomal epoxide hydrolase level,[41] glutathione S-transferase level,[42] α_1-antichymotrypsin level,[43] the complement component GcG level,[44] cytokine tumor necrosis factor-α level,[45] and microsatellite instability.[46] The results are often inconsistent but could be related to the potential pathogenic mechanisms of COPD. In Asians, studies on putative candidate genes found in whites have not yielded consistent results in Chinese,[47,48] Thais,[49] Koreans,[50] or Japanese.[51]

Environmental Exposures

Tobacco Smoking: Cigarette smoking is the main risk factor and the main method by which tobacco exposure is involved in the development of COPD, a fact that has been well established by pivotal cross-sectional and longitudinal studies.[52–54] Cigarette smokers have a higher prevalence of respiratory symptoms and lung function abnormalities, a greater annual rate of decline in FEV_1, and a greater COPD mortality rate than nonsmokers.[55] In susceptible smokers, the decline in lung function is twice that in nonsmokers, though what determines this susceptibility remains unknown. The respiratory abnormalities increase in proportion to the number of cigarettes smoked.[56,57] Pipe and cigar smokers also have greater COPD morbidity and mortality rates than nonsmokers, but their rates are lower than those for cigarette smokers.[55] Passive exposure to cigarette smoke (also known as *environmental tobacco smoke*) may also contribute to chronic respiratory symptoms and COPD by increasing the burden of inhaled particles and gases.[3] Environmental tobacco smoke exposure is increasingly recognized in Asia as an important risk factor for COPD in nonsmokers.[30]

Additional types of tobacco smoking such as bidi and hookah (*ie*, water pipes), which are popular in various Asian countries, are also risk factors for COPD. Bidi are small brown cigarettes, often flavored, consisting of tobacco hand-rolled in tendu or temburni leaf and

secured with a string at one end; they are the preferred means of smoking in subcontinent India, especially in the rural areas. Although the risk of smoking bidis relative to smoking cigarettes has not been fully studied, existing data suggest that bidis are at least as harmful as cigarettes. The population prevalences of chronic bronchitis were 8.2% in bidi users compared with 5.9% in cigarette users in adults > 35 years of age.[58] In one cohort study[59] of tobacco users in Mumbai, India, the relative risks of all-cause mortality were 1.8 for bidi smokers compared with 1.4 for cigarette smokers. Much less is known of the extent of harmful outcomes from the hookah or water pipe, which is used to smoke tobacco in several Asian countries such as China, India, and Pakistan, and is causing global concern as it has become a fashionable or exotic form of tobacco smoking among the young in both the East and West.[60,61]

According to the WHO, there are 1.1 billion smokers worldwide, of whom 800 million are in developing countries.[1] Globally, 4.9 million deaths each year are attributed to tobacco use, and this annual toll is projected to increase to 10 million within the next 20 years.[61]

The highest prevalence of smoking is found in Asia, which is experiencing a smoking epidemic at the same time as the prevalence for smoking is falling in the Western world (Fig 1). China has the largest production and consumption of tobacco worldwide. Approximately 67% of men and 4% of women > 15 years of age in China are smokers, and the total of > 320 million Chinese smokers represents about one third of all smokers worldwide. The incidence of smoking-related diseases has yet to peak, while it is estimated that currently 1 million Chinese die annually from these diseases.[62] Smoking among teenagers is a cause for major concern, as the prevalence for many countries in Asia is among the highest in the world, with sharp increases in smoking among young women.[62,63] It would seem inevitable that the social and economic burden of deaths and morbidity will increase exponentially in the future unless effective antismoking measures are in place to reduce the burden of smoking.

Occupational Dust and Fumes Inhalation: Occupational exposures to dust, vapors, and fumes can cause specific occupational respiratory diseases, collectively termed *pneumoconiosis*,[64] or can add to the risk of COPD developing due to cigarette smoking.[65] Although incompletely defined, the role of occupational dust and fumes in the development of chronic airflow limitation is well recognized in Asia.[66,67] High levels of cotton dust exposure in India and China have been associated with accelerated declines in FEV_1 in longitudinal studies.[68,69] The relationship between smoking and various dust exposures to coal dust, silica, and asbestos, and a decline in lung function have been reported in Asia.[67]

Indoor Air Pollution: The combustion of biomass fuel in the form of wood, coke, charcoal, coal, or

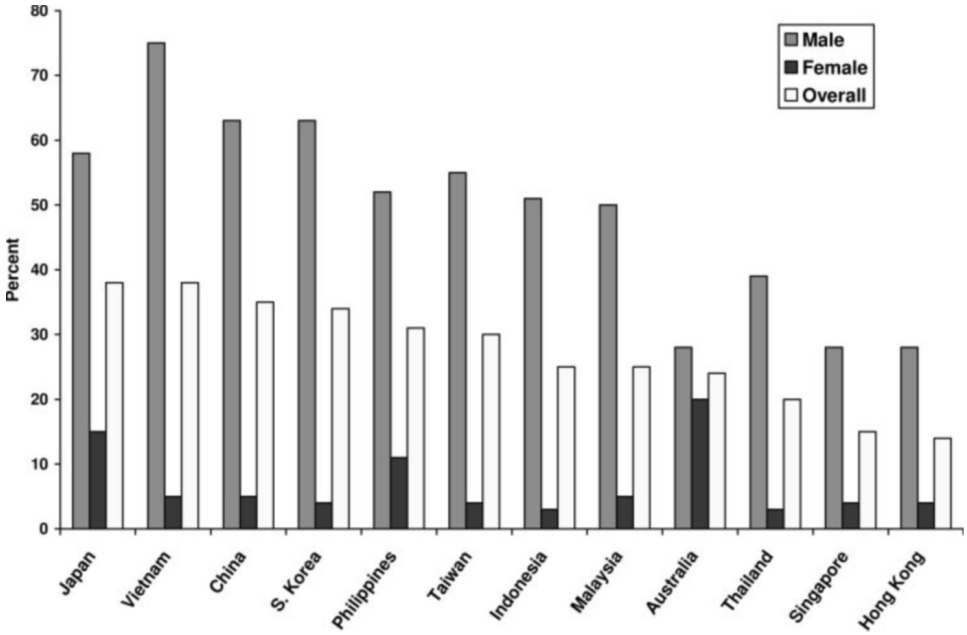

FIGURE 1. Smoking prevalence by country and gender in Asia-Pacific countries/regions. Redrawn from data from the study of the Regional COPD Working Group.[31]

animal dung for cooking and for heating in poorly ventilated homes, is an important risk factor for COPD in nonsmokers in many developing countries including Asia.[70] Depending on the type of fuel used, the ventilation and combustion duration, biomass fuel combustion generates respiratory particulates at concentrations of 1,000 to 2,000 $\mu g/m^3$, which is equivalent to 10 to 50 times the pollution in heavy urban traffic.[71] The association between biomass fuel combustion as a risk factor in the development of COPD in nonsmoking women has been well documented in India,[70] China,[72] and Mexico,[73] but rarely occurs in the West, according to a report from Barcelona, Spain.[74]

Outdoor Air Pollution: Ambient air pollution is a long-term problem in many Asian countries, which are undergoing rapid industrialization and urbanization. Over the past 2 decades, air pollution in most cities in developed countries has decreased appreciably, but air pollution has increased markedly in many cities in developing countries. Although it is not clear which specific elements of ambient air pollution are harmful, an acute increase in air pollution has been associated with increased numbers of deaths and hospitalizations from cardiopulmonary illnesses.[75,76] The cumulative effect of chronic air pollution and its potential multiplicative effect with cigarette smoking in the development of COPD is unclear, but heavy air pollution could add to the individual burden of inhaled particles. This is especially pertinent in Asian countries that have persistent heavy urban air pollution due to traffic and industries, with recurrent acute exacerbations of air pollution due to climatic changes[77] and forest fires.[78] In the 1990s, nitrogen oxide emissions from Asia surpassed those from North America and Europe, and are projected to continue to exceed them for the coming decades.[79]

Infection: The prevalence of respiratory illnesses in early childhood, pulmonary tuberculosis, and HIV-positive status are common in developing Asian countries. Early childhood respiratory illnesses and low birth weight have been associated with the development of airflow limitation. A sequela of pulmonary tuberculosis is chronic airflow limitation, but the relationship is complex as smoking itself reduces host defense and may predispose the patient to the development of tuberculosis.[3] The prevalence of pulmonary tuberculosis remains high in many Asian countries and is an important additive risk factor to smoking in the development of chronic airflow limitation. The presence of HIV infection has been shown to accelerate the development of emphysema,[3] but the impact on the development of COPD in Asians is unknown.

Clinical Diagnosis

In Asian countries, patients with COPD are mostly under the care of primary care physicians. Synonyms for COPD, which include chronic bronchitis and chronic emphysema, complicate the diagnostic labeling. Doctors who practice alternative/traditional medicine do not differentiate asthma from COPD, resulting in the underdiagnosis of COPD. The diagnosis is usually based on a clinical history of persistent respiratory symptoms in a cigarette smoker, as spirometric documentation of fixed airflow limitation is not routine.[14] In tertiary care practice, a spirometric determination is often included.[80] In Japan, COPD is underdiagnosed in the population, where a large epidemiologic study[32] found that 90% of people with COPD, based on spirometry findings, did not have a prior diagnosis of the condition, which is comparable to a corresponding 63% reported in the National Health and Nutrition Examination Study[6] in the United States. In Japan, in a primary care setting of smokers followed up for nonrespiratory conditions, 31% were found to have COPD based on screening spirometry findings,[81] which is within the range of 14 to 46% reported in the United States.[82]

Pulmonary tuberculosis is a major confounder in the diagnosis of COPD as the sequelae from healed tuberculosis include restrictive, obstructive, or mixed restrictive-obstructive pulmonary dysfunction, which could modify the interpretation of the spirometric evaluation.[3] In addition, pulmonary tuberculosis often coexists with COPD, as regions with high prevalence rates of pulmonary tuberculosis, such as Indonesia, China, and Vietnam, also experience high cigarette smoking rates.[31]

Management

A comprehensive description of the management of COPD in Asia is beyond the scope of this review. The focus is therefore on the management of stable patients with COPD and regional COPD guidelines. Most Asian countries either have national guidelines for the management of COPD,[83,84] or adapt the GOLD[3] guidelines for the care of patients with COPD.[80] The Asia-Pacific COPD Roundtable group, a taskforce of representative opinion leaders in respirology in the region, has formulated a consensus statement[80] on implementation of the GOLD strategy for COPD[3] in the Asia-Pacific region. In this consensus statement, universally applicable aspects of the recommendations were emphasized, while possible difficulties in the implementation of the global guidelines were highlighted; amendments were made to ensure their relevance, applicability, and usefulness in developing countries, in different health-care settings, and in different

cultures. The implementation of the WHO symptom-based approach for the management of chronic respiratory diseases, called the *practical approach in lung health*, has also been adopted with success in developing countries in Asia.[85]

Smoking Cessation and Tobacco Control

Smoking cessation is the single most effective way to prevent the development of COPD and to stop its progression in the individual, and is the central recommendation in international and national guidelines for the management of COPD.[3,83,84] Many countries in Asia have increasingly adopted comprehensive tobacco control policies with multiprong approaches, including the following: information-dissemination programs to the public through the media; national and local campaigns to reduce smoke exposure in public and work places; through a concerted effort by academia, health-care organizations, government and legislation, and through a global network (www.jhsph.edu/global_tobacco/policy_development/).

Oral and Noninhaled Bronchodilators

Although the inhaled route is widely recognized as being the best mode of delivery for bronchodilator therapy in Asia, the use of oral bronchodilators (*ie*, β-agonists and theophyllines) remains common and is thought to be appropriate where the cost of the inhaled bronchodilator or patient preference may be barriers to treatment.[80] The transdermal route has been found to be an effective route of delivery for bronchodilators,[86] and the long-acting tulobuterol patch has been shown to improve adherence in patients in Korea and Japan.[87]

Inhaled Bronchodilators

Although the targeted delivery of respiratory drugs is recognized as the ideal, elderly patients in Asia have traditionally preferred oral medications, which are culturally familiar. With persistence and training, inhaler therapy is now increasingly accepted by many patients with COPD in Asian countries. In the treatment of acute bronchospasm during an acute exacerbation of COPD, the use of a metered-dose inhaler together with a spacer is recommended in preference to nebulization. This practice originated during the period of an epidemic of severe acute respiratory syndrome in the spring of 2003, during which consensual efforts were made to control droplet spread of the disease, which could occur with the nebulization of solutions of bronchodilators.[88]

Oxygen Therapy

Oxygen therapy is administered in long-term continuous therapy for chronic respiratory failure in COPD patients, during exercise, and to relieve acute dyspnea. There is little published literature on home oxygen use from Asian countries, with the exception of Japan.[89] The Japanese experience suggests that the challenges in the delivery of home oxygen are awareness in the public and health-care giver coordination and cost considerations, which are similar to those in the West.

Influenza Vaccination

Influenza vaccination is underutilized in most Asian countries. It is not routinely offered to COPD patients in Asia but is given by some pulmonologists or in response to requests from patients.[80] Even in patients who require frequent hospitalizations, the prevalence of influenza vaccination is $< 12\%$.[17] Possible reasons for this include concern about allergenicity, low surveillance data from tropical countries, apparent lack of or a bimodal seasonality in tropical countries and hence uncertainty about the number of vaccinations, and a lack of reimbursement. However, in a world altered by the severe acute respiratory syndrome epidemic in 2003, the specter of bird flu, and clinical trial data[16,90] on the efficacy of flu vaccination in Asian patients with COPD, there is now wider acceptance of the role of influenza vaccination in COPD patients.

Pulmonary Rehabilitation

Pulmonary rehabilitation is also underutilized, with $< 17\%$ of patients having ever received some form of pulmonary rehabilitation in one study.[17] In Asian countries, there is wide recognition that a comprehensive pulmonary rehabilitation, consisting of key components of exercise training, smoking cessation, nutritional counseling, and education, is one of the most effective management strategies for patients with COPD, and that its use and benefits should be promoted to COPD patients, health-care professionals, funding agencies, and governments in the region.

Unfortunately, in reality, comprehensive pulmonary rehabilitation programs as detailed in the global guidelines (*ie*, the GOLD) are beyond the means of many Asian health-care systems and, therefore, are unavailable to most patients in the region. Most Asian countries have limited resources for patient care and lack the infrastructure to organize complex, multidisciplinary types of programs for pulmonary rehabilitation that are recommended in the key guidelines.[3] The difficulties of providing pulmonary rehabilitation programs are similar but magnified compared to those experienced in resource-rich countries, where reality surveys have shown that a minority of COPD patients actually have access to

pulmonary rehabilitation.[91] There is a need for validated simplified programs containing the most important components of pulmonary rehabilitation[92] or home-based programs.[3]

In Summary, there is global concern for the burden of COPD, which is ubiquitous with similar trends in the East and the West. The overall burden of COPD is several-fold greater in Asia than in the West, and is mainly determined by the size of the risk factors and the phase of the tobacco epidemic in the region. Treatment aims in Asian countries are based on evidence-based management guidelines. Barriers to the implementation of disease management guidelines are related to issues of resource conflict and lack of organizational support rather than cultural differences in medical practice. There is a need for a multifaceted approach in improving the awareness of prevalence and disease burden, in facilitating the accurate diagnosis of COPD among chronic respiratory diseases, and in championing health policies that reduce the burden of the main risk factors for COPD and the wider use of evidence-based management for COPD.

References

1 Lopez AD, Mathers CD, Ezzati M, et al. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. Lancet 2006; 367:1747–1757

2 World Health Organization. World health report 2002: reducing risks, promoting healthy life. Available at: www.who.int/whr/2002. Accessed December 21, 2007

3 Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: NHLBI/WHO workshop report, 2000. Available at: http://www.goldcopd.com/. Accessed December 21, 2007

4 Yang G, Rao C, Ma J, et al. Validation of verbal autopsy procedures for adult deaths in China. Int J Epidemiol 2006; 35:741–748

5 Jemal A, Ward E, Hao Y, et al. Trends in the leading causes of death in the United States, 1970–2002. JAMA 2005; 294:1255–1259

6 Mannino DM, Homa DM, Akinbami LJ, et al. Chronic obstructive pulmonary disease surveillance: United States, 1971–2000. MMWR Surveill Summ 2002; 51:1–16

7 Pride NB, Soriano JB. Chronic obstructive pulmonary disease in the United Kingdom: trends in mortality, morbidity, and smoking. Curr Opin Pulm Med 2002; 8:95–101

8 Cooreman J, Henry C, Neukirch C. Mortality by respiratory disease in ten European and North American countries (1979–1990). Rev Mal Respir 1996; 13:47–53

9 Crockett AJ. Trends in chronic obstructive pulmonary disease mortality in Australia. Med J Aust 1994; 161:600–603

10 Lacasse Y, Brooks D, Goldstein RS. Trends in the epidemiology of COPD in Canada, 1980 to 1995: COPD and Rehabilitation Committee of the Canadian Thoracic Society. Chest 1999; 116:306–313

11 Ng TP, Niti M, Tan WC. Trends and ethnic differences in COPD hospitalization and mortality in Singapore. COPD 2004; 1:5–11

12 Kuo L, Yang P, Kuo S. Trends in the Mortality of Chronic Obstructive Pulmonary Disease in Taiwan 1981–2002. J Formos Med Assoc 2005; 104:89–93

13 He J, Gu D, Wu X, et al. Major causes of death among men and women in China. N Engl J Med 2005; 353:1124–1134

14 Ip MS. Chronic obstructive pulmonary disease in Hong Kong. Respirology 2001; 6:S3–S7

15 Izumi T. Chronic obstructive pulmonary disease in Japan. Curr Opin Pulm Med 2002; 8:102–105

16 Wongsurakiat P, Maranetra KN, Wasi C, et al. Acute respiratory illness in patients with COPD and the effectiveness of influenza vaccination: a randomized controlled study. Chest 2004; 125:2011–2020

17 Cao Z, Ong KC, Eng P, et al. Frequent hospital readmissions for acute exacerbation of COPD and their associated factors. Respirology 2006 Mar; 11:188–195

18 Ng TP, Niti M, Tan WC, et al. Depressive symptoms and chronic obstructive pulmonary disease: effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. Arch Intern Med 2007; 167:60–67

19 Buist AS, Vollmer WM, Sullivan SD, et al. The Burden of Obstructive Lung Disease Initiative (BOLD): rationale and design. COPD 2005; 2:277–283

20 Halbert RJ, Natoli JL, Gano A, et al. Global burden of COPD: a systematic review and meta-analysis. Eur Respir J 2006; 28:523–532

21 Soriano JB, Maier WC, Egger P, et al. Recent trends in physician diagnosed COPD in men and women in the UK. Thorax 2000; 55:789–794

22 Siafakas NM, Vermeire P, Pride NB, et al. Optimal assessment and management of chronic obstructive pulmonary disease: the European Respiratory Task Force. Eur Respir J 1995; 8:1398–1420

23 Bakke PS, Baste V, Hanoa R, et al. Prevalence of obstructive lung disease in a general population: relation to occupational title and exposure to some airborne agents. Thorax 1991; 46:863–870

24 Viegi G. Epidemiology of COPD: a European perspective. Eur Respir J 2003; 22(suppl):1S–44S

25 Menezes AMB, Perez-Padilla R, Jardim JRB, et al. Chronic obstructive pulmonary disease in five Latin American cities (the PLATINO study): a prevalence study. Lancet 2005; 366:1875–1881

26 Schirnhofer L, Lamprecht B, Vollmer WM, et al. COPD prevalence in Salzburg, Austria: results from the Burden of Obstructive Lung Disease (BOLD) Study. Chest 2007; 131:29–36

27 Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: global burden of disease study. Lancet 1997; 349:1269–1276

28 Pandey MR. Prevalence of chronic bronchitis in a rural community of the hill region of Nepal. Thorax 1984; 39:331–336

29 Woo J, Pang J. Spirometry in healthy elderly Chinese. Thorax 1988; 43:617–620

30 Jindal SK. Emergence of chronic obstructive pulmonary disease as an epidemic in India. Indian J Med Res 2006; 124:619–630

31 Regional COPD Working Group. COPD prevalence in 12 Asia-Pacific countries and regions: projections based on the COPD prevalence estimation model. Respirology 2003; 8:192–198

32 Fukuchi Y, Nishimura M, Ichinose M, et al. COPD in Japan: the Nippon COPD Epidemiology study. Respirology 2004; 9:458–465

33 Kim DS, Kim YS, Jung K, et al. Prevalence of chronic obstructive pulmonary disease in Korea: a population- based

spirometry survey. Am J Respir Crit Care Med 2005; 172: 842–847
34 Silverman EK, Speizer FE. Risk factors for the development of chronic obstructive pulmonary disease. Med Clin North Am 1996; 80:501–522
35 Chen Y. Genetics and pulmonary medicine: 10. Genetic epidemiology of pulmonary function. Thorax 1999; 54:818–824
36 Chen XY, Cheng XS, Li JZ, et al. Changes of serum elastase, α_1-antitrypsin, procollagen III, and malonaldehyde in smokers with and without chronic obstructive pulmonary disease. Zhonghua Nei Ke Za Zhi 1999; 38:178–180
37 Yin QL, Liang ZQ. The frequency distribution of alleic gene of α_1-antitrypsin deficiency in Chinese. Chin Sci 1980; 10: 897–903
38 Huo JM, Shi YZ, Liu XH, et al. The phenotype and content of α_1-antitrypsin in patients with COPD. J Harbin Med Univ 1990; 24:246–248
39 Seyama K. State of α_1-antitrypsin deficiency in Japan. Respirology 2001; 6(suppl):S35–S38
40 Cohen BH, Bias WB, Chase GA, et al. Is ABH nonsecretor status a risk factor for obstructive lung disease? Am J Epidemiol 1980; 111:285–291
41 Smith CA, Harrison DJ. Association between polymorphism in gene for microsomal epoxide hydrolase and susceptibility to emphysema. Lancet 1997; 350:630–633
42 Harrison DJ, Cantlay AM, Rae F, et al. Frequency of glutathione S-transferase M1 deletion in smokers with emphysema and lung cancer. Hum Exp Toxicol 1997; 16:356–360
43 Faber JP, Poller W, Olek K, et al. The molecular basis of α_1-antichymotrypsin deficiency in a heterozygote with liver and lung disease. J Hepatol 1993; 18:313–321
44 Schellenberg D, Pare PD, Weir TD, et al. Vitamin D binding protein variants and the risk of COPD. Am J Respir Crit Care Med 1998; 157:957–961
45 Huang SL, Su CH, Chang SC. Tumor necrosis factor-alpha gene polymorphism in chronic bronchitis. Am J Respir Crit Care Med 1997; 156:1436–1439
46 Siafakas NM, Tzortzaki EG, Sourvinos G, et al. Microsatellite DNA instability in COPD. Chest 1999; 116:47–51
47 Liu S, Li B, Zhou Y, et al. Genetic analysis of CC16, OGG1 and GCLC polymorphisms and susceptibility to COPD. Respirology 2007; 12:29–33
48 Lee YL, Chen W, Tsai WK, et al. Polymorphisms of p53 and p21 genes in chronic obstructive pulmonary disease. Lab Clin Med 2006; 147:228–233
49 Chierakul N, Wongwisutikul P, Vejbaesya S, et al. Tumor necrosis factor-alpha gene promoter polymorphism is not associated with smoking-related COPD in Thailand. Respirology 2005; 10:36–39
50 Yim JJ, Park GY, Lee CT, et al. Genetic susceptibility to chronic obstructive pulmonary disease in Koreans: combined analysis of polymorphic genotypes for microsomal epoxide hydrolase and glutathione S-transferase M1 and T1. Thorax 2000; 55:121–125
51 Homma S, Sakamoto T, Hegab AE, et al. Association of phosphodiesterase 4D gene polymorphisms with chronic obstructive pulmonary disease: relationship to interleukin 13 gene polymorphism. Int J Mol Med 2006; 18:933–939
52 US Department of Health, Education and Welfare. Smoking and health: a report of the Advisory Committee to the Surgeon General of the Public Health Service. Washington, DC: US Department of Health, Education and Welfare, 1964; Public Health Service publication No. 113
53 Fletcher C, Peto R. The natural history of chronic airflow obstruction. BMJ 1977; 1:1645–1648
54 Bates DV. The fate of chronic bronchitis: a report of the ten year follow-up in the Canadian Department Veterans Affairs Coordinated study of chronic bronchitis. Am Rev Respir Dis 1973; 108:1043–1065
55 US Surgeon General. The health consequences of smoking: chronic obstructive pulmonary disease. Washington, DC: US Department of Health and Human Services, 1984; Publication No. 84–50205
56 Burrows B, Knudson RJ, Cline MG, et al. Quantitative relationships between cigarette smoking and ventilatory function. Am Rev Respir Dis 1977; 115:195–205
57 Lebowitz MD, Burrows B. Quantitative relationships between cigarette smoking and chronic productive cough. Int J Epidemiol 1977; 6:107–113
58 Jindal SK, Aggrawal AN, Chaudhury K, et al. Tobacco smoking in India: prevalence, quit-rates and respiratory morbidity. Indian J Chest Dis Allied Sci 2006; 48:37–42
59 Gupta PC, Mehta JC. Cohort study of all-cause mortality among tabcco users in Mumbai, India. Bull World Health Organ 2000; 78:877–883
60 Maziak W, Ward KD, Soweid RAA, et al. Tobacco smoking using a waterpipe: a re-emerging strain in a global epidemic. Tob Control 2004; 13:327–333
61 Global Youth Tobacco Survey Collaborating Group. Differences in worldwide tobacco use by gender: findings from the global youth tobacco survey. J Sch Health 2003; 73:207–215
62 Zhang H, Cai B. The impact of tobacco on lung health in China. Respirology 2003; 8:17–21
63 Chan-Yeung M, Ait-Khaled N, White N, et al. The burden and impact of COPD in Asia and Africa. Int J Tuberc Lung Dis 2004; 8:1–13
64 US Centers for Disease Control and Prevention. Criteria for a recommended standard: occupational exposure to respirable coal mine dust. Morgantown, WV: National Institute of Occupational Safety and Health, 1995; Publication No. 95–106
65 Oxman AD, Muir DC, Shannon HS, et al. Occupational dust exposure and chronic obstructive lung disease: a systematic review of the evidence. Am Rev Respir Dis 1993; 148:38–48
66 LeVan TD, Koh WP, Lee HP, et al. Vapor, dust, and smoke exposure in relation to adult-onset asthma and chronic respiratory symptoms: the Singapore Chinese Health Study. Am J Epidemiol 2006; 163:1118–1128
67 Wang X, Yano E, Nonaka K, et al. Respiratory impairments due to dust exposure: a comparative study among workers exposed to silica, asbestos, and coalmine dust. Am J Ind Med 1997; 31:495–502
68 Kamat SR, Kamat GR, Salpekar VY, et al. Distinguishing byssinosis from chronic obstructive pulmonary disease: results of a prospective five year study of cotton mill workers in India. Am Rev Respir Dis 1981; 124:31–40
69 Lam TH, Ong SG, Baratawidjaja KG. A study of byssinosis in Hong Kong and Jakarta: research methods and objectives. Am J Ind Med 1987; 12:767–771
70 Smith KR. National burden of disease in India from indoor air pollution. Proc Natl Acad Sci U S A 2000; 97:13 286–93
71 de Koning HW, Smith KR, Last JM. Biomass fuel combustion and health. Bull World Health Organ 1985; 63:11–26
72 Peabody JW, Riddell TJ, Smith KR, et al. Indoor air pollution in rural China: cooking fuels, stoves, and health status. Arch Environ Occup Health 2005; 60:86–95
73 Perez-Padilla R, Regalado J, Vedal S, et al. Exposure to biomass smoke and chronic airway disease in Mexican women: a case-control study. Am J Respir Crit Care Med 1996; 154:701–706
74 Orozco-Levi M, Garcia-Aymerich J, Villar J, et al. Wood smoke exposure and risk of chronic obstructive pulmonary disease. Eur Respir J 2006; 27:542–546

75 Arden Pope C, Bates D, Raizenne ME. Health effects of particulate air pollution: time for reassessment? Environ Health Perspect 1995; 103:472–480
76 Wong TW, Tam WS, Yu TS, et al. Associations between daily mortalities from respiratory and cardiovascular diseases and air pollution in Hong Kong, China. Occup Environ Med 2002; 59:30–35
77 Chen B, Hong C, Kan H. Exposures and health outcomes from outdoor air pollutants in China. Toxicology 2004; 198: 291–300
78 Tan WC, Qiu DW, Liam BL, et al. The human bone marrow response to acute air pollution caused by forest fires. Am J Respir Crit Care Med 2000; 161:1213–1217
79 Akimoto H. Global air quality and pollution. Science 2003; 302:1716–1719
80 Tan WC, Seale P, Ip M, et al. GOLD strategy for the diagnosis, management and prevention of COPD: an Asia-Pacific perspective. Respirology 2005; 10:9–17
81 Takahashi T, Ichinose M, Inoue H, et al. Underdiagnosis and undertreatment of COPD in primary care settings. Respirology 2003; 8:504–508
82 Stang P, Lydick E, Silberman C, et al. The prevalence of COPD: using smoking rates to estimate disease frequency in the general population. Chest 2000; 117:354s–359s
83 Jindal SK, Gupta D, Aggarwal AN et al. Guidelines for management of chronic obstructive pulmonary disease (COPD) in India: a guide for physicians (2003). Indian J Chest Dis Allied Sci 2004; 46:137–153
84 Kitamura S. COPD guideline of Japanese Respiratory Society. Nippon Rinsho 2003; 61:2077–2081
85 Shrestha N, Samir KC, Baltussen R, et al. Practical approach to lung health in Nepal: better prescribing and reduction of cost. Trop Med Int Health 2006; 11:765–772
86 Nishiyama O, Taniguchi H, Kondoh Y, et al. Comparison of the effects of tulobuterol patch and salmeterol in moderate to severe asthma. Clin Exp Pharmacol Physiol 2006; 33:1016–1121
87 Tamura G, Ohta K. Adherence to treatment by patients with asthma or COPD: comparison between inhaled drugs and transdermal patch. Respir Med 2007; 101:1895–1902
88 Ho Pl, Tang XP, Seto WH. SRAS: hospital infection control and admission strategies. Respirology 2003; 8(suppl):S41–S45
89 Takahashi Y, Fukuda T. The indication and practice of home oxygen therapy. Nippon Rinsho 2003; 61:2193–2199
90 World Health Organization. Influenza vaccination for the 2003–2004 season: recommendations in the context of concern about SARS. Available at: www.who.int/csr/disease/influenza/sars. Accessed December 21, 2007
91 Brooks D, Lacasse Y, Goldstein RS. Pulmonary rehabilitation programs in Canada: national survey. Can Respir J 1999; 6:55–63
92 Hui KP, Hewitt AB. A simple pulmonary rehabilitation program improves health outcomes and reduces hospital utilization in patients with COPD. Chest 2003; 124:94–97