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COPD is characterized by a progressive deterioration of lung function and mental and physical comorbidities such as depression, dystrophy, and heart failure.1 The data suggest that COPD imposes an enormous burden on patients, health-care professionals, and society. COPD contributes to morbidity and mortality and to a significant use of health-care resources and expense on a global scale; this is especially true in developing countries.2-4 The burden of COPD in China is currently greater than that found in developed countries. This is probably due to greater exposure to epidemic risk factors, an imbalance in economic development, and health-care disparities between urban and rural areas. The reported prevalence of COPD morbidities and genetic susceptibility varies widely among geographic regions in China, and there is still a great need to learn more about the disease burden of COPD. In this review, we analyzed available studies on COPD in China, including data on prevalence, mortality, disease burden, risk factors, diagnosis, and patient management, to improve awareness of COPD and highlight its importance to facilitate the implementation of public health policies.
Epidemiology

Prevalence

There is still a need for well-designed nationwide epidemiologic studies of COPD in China. A population-based, cross-sectional survey of COPD conducted between 2002 and 2004 showed that the overall prevalence of the disease in people aged >40 years was 8.2%, which would result in a COPD patient population of >43 million in that time period. It was reported that the prevalence of COPD varied widely among locations across the country, from 5% to 13% (Table 1). Most locations had a higher prevalence of COPD than the World Health Organization model-estimated prevalence for China (6.7%) and the reported prevalence rates in Western countries (4%-10%). But the cross-sectional survey of COPD results were consistent with the pooled prevalence (meta-analysis) of the Western Pacific Region (9.0%). The crude prevalence of COPD was significantly higher in men than in women (8.3%-18.9% vs 3.8%-7.1%), in rural areas than in urban areas (4.4%-16.7% vs 6.7%-8.3%), in the elderly, and in nonsmoking rural women. These differences were associated with gender, smoking status, biomass fuel use, occupational dust exposure, socioeconomic status, and availability of health-care resources. It was reported that approximately two-thirds of the patients were underdiagnosed, and the prevalence of diagnosed COPD in rural areas was apparently lower than that in urban areas, suggesting an inferior diagnostic rate in rural areas.

Mortality and Hospitalization

The Global Burden of Disease study conducted in 2004 showed that about 3 million people die of COPD each year, of which 1.8 million deaths occur in middle-income countries. COPD is expected to become the third leading cause of death globally by 2030, trailing only ischemic heart disease and cerebrovascular disease. According to data published by the Chinese Ministry of Health, COPD ranks as the fourth leading cause of death in urban areas and third leading in rural areas. Both crude and age-adjusted COPD mortality rates have fluctuated but have displayed a decreasing trend from 1990 (Fig 1A), which is probably because of improved management of COPD, upgraded technologies, and awareness of the disease.

Another nationwide, large-scale, long-term prospective cohort study between 1990 and 2000 demonstrated that COPD-related mortality was 27.3 for men and 21.3 for women per 100,000 persons >40 years of age, making COPD the seventh leading cause of death in men and eighth leading in women. When cor pulmonale deaths with documented COPD history were included, COPD-related mortality increased to 179.9 for men and to 141.3 for women per 100,000 persons. Both rates were much higher than the corresponding estimated rates in the Asia-Pacific region (64-92 per 100,000 population in men and 21-35 per 100,000 population in women). It was reported that COPD-related mortality was higher in rural areas than in urban areas, mainly because of the unavailability of health-care resources and more exposure to indoor air pollution. Another finding showed that COPD-related mortality in northern China was higher than in other locations; the higher mortality rate in the north might be associated with a colder climate, more use of biomass fuel, heavier outdoor air pollution, and lower socioeconomic status. Although mortality rates fell, hospitalization rates continued to rise in the last decade. Hospitalization rates for COPD jumped from 1.0% in 1998 (urban vs rural was 1.4% vs 0.8%) to 1.6% in 2008 (urban vs rural was 1.5% vs 1.6%). Correspondingly, the gap between rural and urban areas narrowed (Fig 1B). This is partially a result of the increase in incidence but it also indicates that patients in rural areas are more aware of COPD, and that resources for rural residents have been increasing. The hospitalization rate trend is consistent with that of other Asian countries.

Burden of COPD

COPD treatments are extremely costly in China and impose an enormous economic burden on both families and society. Health-care expenses were investigated with person-to-person interviews in a cross-sectional survey conducted among 723 COPD outpatients in six large cities in China. It was found that the annual direct medical expense for urban patients in 2006 was $1732.24 per patient, whereas the estimated indirect expense spent on nutraceuticals, transportation, and end-of-life care was $231.6 per patient. Total expense for one COPD patient ($1963.8) accounted for 40% of the average family’s total income ($4849.8). Evidence showed that the cost of COPD was strongly correlated with the severity of disease and that hospitalization acted as a major contributor to total cost. It was suggested that reducing hospitalization frequency through better management could result in a crucial decrease in health-care expenses. Moreover, the burden of COPD has been underestimated consistently because of premature mortality and impaired productivity of patients and their family members. The overall disease burden, measured by disability-adjusted life years (DALYs), was predicted to double over the next 2.5 decades worldwide, at which point COPD would move from the 13th-highest cause of DALYs...
In 2002, about 30% of the world’s cigarettes were manufactured and consumed in China, which had worldwide to the seventh-highest by 2030. The burden of COPD in China was greater than that in developed Western countries, and it ranked second among chronic diseases as a leading cause of DALYs lost in 2001 (Fig 2).  

**Table 1 — COPD Prevalence in Various Provinces in China**

| Study/Year | City/Province | Age, y | N    | Diagnostic Criteria | Prevalence, % | Risk Factors |
|------------|---------------|--------|------|---------------------|---------------|--------------|
|            |               |        |      |                     |               |              |
| Tang et al/2001 | Anhui      | ≥ 35   | 29,319 | Physician diagnosis | 7.2/4.7, 4.4/6.7 | Gender; smoking; age of starting smoking; sites of inhaling smoke; time of heating; dust exposure; marital status; pepper consumption |
| Xu et al/2005   | Nanjing/Jiangsu    | ≥ 35   | 29,319 | Post-BD spirometry | 15.9/4.8, 12.0/7.4 | Gender; age; living condition; smoking; TACS |
| Liu et al/2005  | Guangdong        | ≥ 40   | 3,286  | Post-BD spirometry |               | Gender; age; smoking; biomass fuel use; ventilation in the kitchen; family history; respiratory infection during childhood |
| Shan and Chen/2007 | Tianjin    | ≥ 40   | 3,008  | Post-BD spirometry | 18.9/6.5, 16.7/8.0 | Gender; living condition; educational level; ventilation in the kitchen and living room; smoking; TACS; occupational exposure |
| Ma et al/2005   | Shanghai        | ≥ 65   | 1,214  | Post-BD spirometry |               | Gender; age; smoking; family history; living condition; educational level; smoking; TACS; occupational exposure |
| Cai et al/2009  | Shihlin/Yunnan  | ≥ 45   | 6,006  | Physician diagnosis | 8.3/5.1, 6.7/... | Gender; age; biomass fuel exposure |
| Wang et al/2005 | Shaoguan/Guangdong | ≥ 40   | 1,468  | Post-BD spirometry | 18.3/7.1, 12.0/... | Smoking; age; frequent cough during childhood; biomass fuel exposure |
| Yao et al/2005  | Yanqing/Beijing  | ≥ 40   | 1,624  | Post-BD spirometry | 15.1/3.8, 9.1/... | Gender; age; smoking; family history; frequent cough before age 14 y; BMI |
| Jiang et al/2007 | Hubei        | ≥ 40   | 1,883  | Post-BD spirometry | 13.7/6.6, 9.9/... | Gender; age; smoking; cooking time; family history; frequent cough before age 14 y; BMI |
| Chen et al/2008 | Lianjiang/Guangdong | ≥ 40   | 1,368  | Post-BD spirometry | 11.1/4.3, 7.0/... | Gender; age; smoking; BMI; biomass fuel exposure; ventilation in the kitchen; occupational exposure; respiratory infection during childhood; family history |
| Li et al/2009   | Chongqing      | ≥ 40   | 1,518  | Post-BD spirometry | 23.0/7.5, 12.8/... | Smoking; biomass fuel exposure |
| Hong et al/2009 | Changsha/Hunan | ≥ 15   | 8,243  | Spirometry        | 7.6/2.6, 5.3/4.8 | Smoking; biomass fuel exposure; gender; family history; educational level |
| Zhang et al/2006 | Qingdao/Shandong| ≥ 40   | 410    | Spirometry        | 7.9/5.9, 6.9/... | Age; smoking; biomass fuel exposure; living area; family history; BMI |
| Hou et al/2007  | Shenyang/Jinzhou/Liaoning | ≥ 40   | 1,100  | Post-BD spirometry |               | Age; family history; low BMI |

Data collected from literature covered by SCI or Chinese Core Journals. Postbronchodilator FEV1/FVC of 70% was defined as COPD according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) diagnostic criteria. BD = bronchodilator; F = female; M = male; Ph = physician diagnosis; R = rural; T = total; TACS = total amount of cigarettes smoked; U = urban. *Rural areas or urban areas.

**Tobacco Smoking**

In 2002, about 30% of the world’s cigarettes were manufactured and consumed in China, which had
an estimated(275,499),(318,506) million smokers; furthermore, the prevalence of smoking in women has been increasing (Fig 3). In addition, there has been a steady increase in the rate of household second-hand smoke exposure, and the rate of passive smoking among nonsmoking females has increased to 82.5%. Taking all smokers and passive smokers into consideration, 72% of Chinese aged > 15 years were tobacco exposed. Individuals who were less educated, poorer, and employed in stressful jobs were more likely to be heavy smokers and less likely to quit than were wealthier, better-educated individuals. Smoking the Chinese pipe was once prevalent in rural areas, but only a minority of people do it today. Smokers consumed cheaper cigarettes but spent a larger proportion of their personal income on smoking. The cost of cigarettes per pack varied from $0.294 to $33.971 in China. Smoking has been recognized as the most important causative factor in the pathogenesis of COPD. In 2005, a total of 673,000 deaths were attributed to smoking in China, whereas 268,000, 146,200, and 66,500 deaths were attributed to cancer, cardiovascular disease, and respiratory disease, respectively. In another case-control study, conducted from 2000 to 2001 in Nanjing, a significant dose-response relationship between COPD and total amount of cigarettes smoked was detected after adjusting for other risk factors. The study further showed that women smokers were more susceptible to COPD.

Because of a diversity of methodologies and exposure assessment criteria, there are conflicting results regarding an association between passive smoking and the risk of COPD. The aim of the Biobank Cohort Study was to demonstrate that the high prevalence of COPD among Chinese nonsmokers is the result of a positive dose-response relationship between passive smoking exposure and any respiratory symptom. It was estimated that 1.9 million excessive deaths from COPD without smoking could be attributed to passive smoking. In contrast to these findings, no significant association between COPD and passive smoking was revealed in other localized surveys.

In the survey conducted by Yang et al, about 74% of the smokers indicated that they did not want to quit, which may be partly because of ignorance about the harmful effects of smoking. About 20% of the smokers had intended to quit smoking at least once, of which about one-half reverted to smoking. Smoking cessation has been the most cost-effective intervention in COPD management, and the importance of effective tobacco-control programs cannot be emphasized too strongly. Men and women who stopped smoking in 2003 were expected to lower their absolute risks of COPD by 56% and 63% after 5 years relative to those who continued smoking. Antismoking education should focus the public’s attention on the risk of active and passive smoking, as well as the expense of smoking, especially among the poor.

### Use of Biomass Fuels

The use of biomass fuels has been considered one of the most important risk factors for COPD. Men and women who are exposed to biomass smoke have an odds ratio of 4.30 and 2.73, respectively, for developing COPD, relative to those not exposed to biomass smoke. It was reported that solid fuels, such as wood, crop residues, and coal, were used in > 70% of Chinese households, whereas in rural areas, the rate increased to 90%. In a cluster disproportional random sampling survey performed in populations aged > 40 years in urban and rural areas in Guangdong, COPD prevalence among rural nonsmoking women was found to be significantly higher than that among urban nonsmoking women (7.2% vs 2.5%). Univariate analysis showed a significant association between COPD and exposure to biomass fuel for cooking.

### Table 2—Laws Related to Smoking Control in China

| Laws Related to Smoking Control | Year | Content |
|---------------------------------|------|---------|
| Regulations on management of public places | 1987 | Prohibit smoking in public places |
| Law of the People’s Republic of China on the Prevention of Minors to Commit Crime | 1999 | Parents and teachers should educate minors not to smoke; Business units should not sell cigarettes to minors |
| Law of the People’s Republic of China on Tobacco Sales | 1991 | Forbid or restrict cigarette smoking on public conveyances or in public places; dissuade adolescents from smoking and forbid primary and middle school students from smoking |
| Law of the People’s Republic of China on Advertisement | 1994 | Smoking-related advertisements are prohibited through media or in any public places; all smoking-related advertisements should include the following label: “smoking is harmful to health” |
| Law of the People’s Republic of China on the Protection of Minors, article 11 | 2006 | The sale of cigarettes to minors is banned; no smoking in schools, kindergartens or any other places where minors are present |
| Framework Convention on Tobacco Control | 2006 | Raise taxes on cigarettes; prohibit smoking in public places; warning notices or pictures of fearful consequences of smoking are printed on the cigarette packets |

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"Minors" as used in this law refers to citizens under the age of 18 y.
uted to the combined effect of smoking and solid-fuel use, whereas 26 million deaths from COPD will be avoided by reducing smoking and solid-fuel use with intermediate magnitude. Halving solid-fuel use would lower the annual number of COPD cases by 2.2 million in men and by 4.3 million in women. Along with rapid development of the economy and urbanization in most rural areas, indoor air pollution and ventilation in the kitchen would be gradually improved and the negative influence of biomass fuel use on health would be expected to decrease.

Genetic Susceptibility

COPD is a complex condition resulting from the interaction of environmental and genetic factors. Familial clustering was reported in the studies of COPD in China. Several gene polymorphisms have been investigated in the Chinese population, but there is a need for further clarification and confirmation. Individuals with α1-antiprotease deficiency had a markedly increased risk of developing COPD in Europe, whereas few patients with α1-antiprotease deficiency developed COPD in China. Another case-control study among the Han population in southwest China failed to obtain evidence of the contribution of SERPINE2 polymorphism to COPD susceptibility, although it has been accepted as a candidate gene in other populations. It was suggested that there might be other genetic factors involved in the development of COPD in the Chinese population.

Microsomal epoxide hydrolase is an enzyme that potentially reduces oxidative stress by detoxifying epoxide compounds such as those found in cigarette smoke. An updated meta-analysis of 16 studies on such hydrolase polymorphisms in COPD in the Asian population suggested that the slow activity phenotype of the enzyme is associated with an increased risk of COPD, and the fast activity phenotype is a protective factor in the development of COPD. Genetic polymorphism in Heme oxygenase-1, one of the antioxidant enzymes, was found to be associated with the severity of COPD in southwest China. γ-Glutamylcysteine synthetase and 8-hydroxy-guanine glycosylase both play roles in the antioxidant defenses, and both were reported to be not associated with susceptibility to COPD in a southern Chinese population. Polymorphisms of IL-27 gene, matrix metalloproteinase-9 gene, tumor necrosis factor-α, and aquaporin were demonstrated to play roles in susceptibility to COPD. Clara cell 16 kDa secretory protein, which plays a potential role in the control of inflammatory response, was not found to be associated with the development of COPD. The study of gene polymorphisms might be helpful in defining patient...
subgroups, leading to the development of different approaches to the prevention and treatment of COPD.

Others

Studies have shown that smoking and the individual’s socioeconomic status are correlated to the influence of occupational exposure on COPD prevalence. 79-73 Studies have investigated green tea as an antioxidant in the treatment of COPD and have found that its use might prevent the occurrence of the disease. 74 There is a need to evaluate how tea drinking or other dietary habits may influence the development or treatment of COPD in China. Malnutrition may aggravate dyspnea and exercise intolerance in COPD patients by weakening respiratory muscle strength. Low BMI was reported to be closely connected with a high incidence of COPD, 75,76 as well as an increased hospitalization rate and poor prognosis. 77,78 Outdoor air pollution is also considered an important risk factor for COPD, evidenced by the fact that ambient concentrations of air pollutants have an adverse effect on hospital admissions for COPD. 79 Another case-control analysis of air pollution and daily mortality in Shanghai showed an association between air pollution and mortality with COPD and cardiovascular causes. 80 The results confirmed the deleterious role played by the current air pollution level in COPD, especially in large cities like Shanghai. In addition, low educational level, chronic cough or respiratory infection in childhood, low socioeconomic status, and reduced physical activities have all been reported to contribute to the increased incidence of COPD independently or jointly.

MANAGEMENT OF COPD IN CHINA

A national strategy for the management of COPD, drafted by the Chinese Medical Association, was first published in 2002 and then updated annually. 81 Doctors are also encouraged to adopt the GOLD (Global Initiative for Chronic Obstructive Lung Disease) guideline for the care of patients with COPD. 1 Despite widely disseminated evidence-based clinical practice guidelines, current knowledge of primary care physicians and management of patients with COPD remain suboptimal. 82-84 Barriers to the implementation of guidelines are multifarious, whether physician related or patient related.

Delayed Diagnosis and Intervention

A lack of awareness about biomarkers and risk factors for COPD among physicians had led to delayed diagnosis and interventions for patients. Early diagnosis may help patients quit smoking and lead to the adoption of effective therapies to prevent progression of COPD. However, more than one-third (35.3%) of COPD patients were asymptomatic, whereas only one-third of subjects with GOLD stage I COPD were diagnosed with respiratory disease. 85 In a recent study, the diagnosis of COPD was made in 148 of the 1,624 subjects aged 40 years in five villages of northern China according to the standards set in the GOLD guideline, whereas none of the patients had ever been diagnosed previously. 86 Another retrospective study demonstrated that only 15.9% of the patients in southern China were diagnosed with mild-degree COPD, whereas most of the patients were at a severe or extremely severe stage when first diagnosed. 86 This could be attributed to the fact that most Chinese patients, especially those in rural areas with major health-care disparities, are used to bottling up their discomfort until the development of significant symptoms and/or exacerbations.

Diagnosis Without Spirometry

Physicians continue to diagnose and manage patients with COPD without verifying the diagnosis and assessing the severity with spirometry. According to GOLD guidelines, spirometry is the gold standard in the measurement of airflow limitation because of its reliable, simple, safe and inexpensive grading, monitoring, and assessing of the disease. However, less than one-third of COPD diagnoses were made with the aid of spirometry 87 and in some rural areas none of the...
patients diagnosed with COPD received a spirometry test. In 185 previously diagnosed COPD patients, 67 were confirmed by spirometry based on diagnostic criteria, 47 had normal lung function, and 63 had mixed ventilation disorder. Profound underuse of spirometry was considered to be a barrier to decent care of Chinese COPD patients. Barriers hindering use of spirometry in clinical practice include ignorance of the crucial role of spirometry, facility inaccessibility, and limited budgets, especially in most of the primary care settings.

**Patient Self-Management of COPD**

Patients are not knowledgeable about how to manage their COPD. Health education on self-management for patients should be taken into account to reduce the frequency and severity of exacerbations and to improve quality of life. However, COPD patients were found to lack general knowledge about the disease. For example, the term “COPD” was recognized by <30% of the patients who regularly visited hospitals, whereas an even lower number of rural patients recognized the term. Patients also lacked awareness of COPD risk factors, the importance of lung function tests, inhalation therapy, and oxygen therapy. About 20% of patients were current smokers, of which 23% did not know the harmful effect of smoking on the disease. Unfortunately, no health education program was available in rural areas, although all patients were willing to read information about COPD. Patients took the initial advice for smoking cessation from primary care physicians, so there is a great need to implement evidence-based guidelines and demand that physicians take immediate action. Studies in some urban hospitals demonstrated that 64.5% of the COPD patients quit smoking after application of general interventions, whereas the cessation rate of the control group was only 28%. Underuse of home oxygen therapy, lung function training, and nutrition support among patients also suggested the necessity of patient education to facilitate comprehensive rehabilitation.

**Physician Recommendations**

The recommendations made by physicians often do not meet the standard of the GOLD guidelines. According to the GOLD guidelines, bronchodilators, including β₂-agonists, anticholinergics, and methylxanthines, should be the basic agents for all patients, whereas inhaled corticosteroids are recommended only for patients with moderate/severe airflow obstruction and/or frequent exacerbations. An investigation of the application of pharmacologic therapy conducted in six cities, using face-to-face interviews among 723 patients with stable COPD and 258 pulmonary physicians, showed that expectorants were the most often prescribed medications, followed by β₂-agonists and anticholinergics. Instead of long-acting bronchodilators, more than one-half of the patients were prescribed short- or medium-acting bronchodilators, which was inconsistent with the guidelines. Most of the physicians underused oxygen therapy, noninvasive intermittent positive pressure ventilation, and antiinflammation therapy. Only 20% of the primary care physicians were fully knowledgeable about pharmacologic therapies for COPD.

**Prospects**

COPD represents a challenging issue because of its impact on both personal and public health and its economic consequences. There is an urgent need to understand the present and future burden of COPD in China from well-designed epidemiologic studies on its prevalence and morbidity. Because of ethnic differences, studies on genetic susceptibility to COPD among the Chinese population should be carried out to improve prevention and lead to early diagnosis. Because China is the world’s largest cigarette manufacturer and because it is the world’s largest consumer of cigarettes, there is a great challenge to restrict and regulate smoking in China with an intent to reduce the burden of COPD. During the last decade, smoking prevention and cessation programs have been implemented widely and preliminary results have been observed (Tables 2, 3). However, there are many factors affecting the execution of smoking laws and regulations by the government. Rural workers, teenagers, and women with high or rising rates of smoking need to be targeted specifically for tobacco-control measures. The existing public health policies should be strengthened and new strategies, including raising taxes and the price of cigarettes, should be put into effect. On the other hand, physicians should take the leading role in the fight against smoking. It has been found that about 40% of male physicians are current smokers, which adds to the difficulty of smoking control.

**Table 3—Smoking Control Mechanisms in China**

| Smoking control is required for the criterion of “national clean city” |
| Smoking is prohibited in public places |
| Knowledge that “smoking is harmful to health” is spread through media |
| Attend international smoking cessation contest, encourage the building of a no smoking community and no smoking unit |
| Smoking by teenagers is reduced through laws or local regulations and school-based prevention programs |
| Doctors are encouraged to give up smoking to raise society’s awareness of its harmful effects |
| Smoking cessation clinic has been set up |
Another challenge is delayed diagnosis and under-estimation of frequent exacerbations in the management of COPD. Screening by spirometry is impractical in most primary care settings and rural areas, indicating the urgent need for disease-specific biomarkers to facilitate early diagnosis and identify high-risk populations. Management techniques of COPD should take into consideration cultural variations and mental and physical comorbidities, such as psychologic depression. Comorbidities could influence patients’ quality of life, increase hospitalization, and reduce survival. The role played by finances should also be taken into account to improve the poor management of COPD. For example, the cost for drug therapy ($443-$738 per year) in the maintenance phase is a huge economic burden for families and individuals, especially for rural residents. Less than 40% of patients with chronic hypoxemia use oxygen therapy because the cost ($517 per year) is too high. It is necessary to implement a community-based comprehensive intervention, which requires support from national polices, to ensure the availability of medical resources, such as essential drugs, equipment, and human resources, and to improve the affordability of COPD therapy for patients. Continuous educational programs on quality-improving skills and management strategies should be more effective and comprehensive in China to improve health-care quality and physicians’ clinical practice skills and to reduce health-care disparities among regions and economic groups.

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