Chronic Obstructive Pulmonary Disease: Definition and Epidemiology

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Chronic obstructive pulmonary disease (COPD) continues to cause a heavy health and economic burden in the United States and around the world. Some of the risk factors for COPD are well known and include smoking, occupational exposures, air pollution, airway hyperresponsiveness, asthma, and certain genetic variations, although many questions remain, such as why < 20% of smokers develop substantial airway obstruction. There are several different definitions of COPD and the definitions depend on accurate diagnosis. Small differences in the definition can have large effects on the estimates of COPD in the population. In addition, newer measures, such as functional status or exercise capability, have emerged as important in determining the prognosis of COPD patients. Furthermore, evidence continues to emerge that COPD represents several different disease processes, with potentially different interventions required. In most of the world COPD prevalence and mortality are still increasing and will probably continue to rise in response to increases in smoking, particularly by women and adolescents. Resources aimed at smoking cessation and prevention, COPD education, early detection, and better treatment will be of the most benefit in our continuing efforts against this important cause of morbidity and mortality. *Key words: chronic obstructive pulmonary disease, COPD.* [Respir Care 2003;48(12):1185–1191.]

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by airflow obstruction with breathing-related symptoms such as chronic cough, exertional dyspnea, expectoration, and wheeze.[1] These symptoms may occur in conjunction with airway hyperresponsiveness and may be

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partially reversible. Even though COPD is a nonspecific term referring to a set of conditions that develop progressively as a result of various disease processes, COPD most commonly refers to chronic bronchitis and emphysema and a subset of patients with asthma, and these conditions can be present with or without substantial impairment. COPD has been defined in several different ways, and the definition used can have a large impact on the population estimates of the burden of disease.[2–5]

Definitions

Several different definitions exist for COPD, and I have italicized parts of the following definitions to emphasize the differences. The American Thoracic Society (ATS) defined COPD as "a disease state characterized by the *presence of airflow limitation due to chronic bronchitis or emphysema*; the airflow obstruction is generally progressive, may be accompanied by airway hyperreactivity, and may be partially reversible."[4] The European Respiratory Society (ERS) defined COPD as "*reduced maximum expiratory flow* and slow forced emptying of the lungs, which is slowly progressive and mostly irreversible to present medical treatment."[3] The Global Initiative for Chronic Obstructive Lung Disease (GOLD) report classified COPD as "*a disease state characterized by airflow limitation that is not fully reversible*. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases."[5] Figure 1 shows the subsets of disease that compose COPD. In the above COPD definitions the precise classification of airflow limitation, reversibility, and severity of disease differs. In addition, the definitions and diagnoses of chronic bronchitis, emphysema, and asthma can also differ.

Airflow Limitation

Airflow limitation is the slowing of expiratory airflow, as measured by spirometry, with a persistently low forced expiratory volume in the first second (FEV_1) and a low ratio of FEV_1 to forced vital capacity (FVC), not reversible with treatment. The 1995 ATS definition of COPD did not define a specific FEV_1/FVC as airflow limitation,[4] although a previous ATS document listed an FEV_1/FVC of less than the fifth percentile of the normal population as evidence of airflow limitation.[6] The 1995 ERS definition of airflow limitation was a ratio of FEV_1 to slow vital capacity of < 88% of the predicted value for men and < 89% of the predicted value for women.[3] The GOLD definition of airflow limitation is an FEV_1/FVC of < 70%.[5]

Airflow Limitation Reversibility

Airflow limitation reversibility can be acute, in response to an inhaled bronchodilator or oral or inhaled corticoste-roids.[5,7] The ATS definition of COPD does not specifically define reversibility, although a previous ATS statement classified reversibility as an FEV_1 increase of 200 mL and 12% above baseline FEV_1 after inhaled bronchodilators.[6] The ERS definition of COPD classified reversibility as a > 10% improvement in percent-of-predicted FEV_1 after a bronchodilator.[3,5] The GOLD definition of COPD classified reversibility as an FEV_1 increase of 200 mL and 12% improvement above baseline FEV_1 after either inhaled corticosteroids or bronchodilators.[8]

The term "partial reversibility" is frequently mentioned but not fully defined. In the context of the definitions, "partial reversibility" probably defines patients who have "reversibility" in response to either corticosteroids or bronchodilators (as defined above), but their best FEV_1 and FEV_1/FVC classify them as having airflow limitation.

Disease Severity

Disease severity has typically been determined using the degree of lung function impairment, although the wisdom of this approach has been questioned recently, with the suggestion that factors such as arterial blood gas values, timed walk distance, sensation of dyspnea, and body mass index be included in this determination.[9] The ATS criteria[4] classify COPD into 3 stages:
Stage 1: $FEV_1 \geq 50\%$ of predicted
Stage 2: FEV_1 35–49% of predicted
Stage 3: $FEV_1 < 35\%$ of predicted
The ERS criteria[3] also classify COPD into 3 stages:
Mild: $FEV_1 \geq 80\%$ of predicted
Moderate: FEV_1 50% to < 80% of predicted
Severe: $FEV_1 < 50\%$ of predicted)
The GOLD criteria[5] also classify COPD into 4 stages:
Stage 1: $FEV_1 \geq 80\%$ of predicted
Stage 2: FEV_1 50% to < 80% of predicted
Stage 3: FEV_1 30 to < 50% of predicted
Stage 4: $FEV_1 < 30\%$ of predicted

Chronic Bronchitis

Chronic bronchitis, which is defined in clinical terms, is the presence of a chronic productive cough for 3 months in each of 2 successive years, provided other causes of chronic cough have been ruled out.[4] Airway obstruction is caused by inflammation and nonspecific bronchial hyperreactivity associated with chronic bronchitis. Unfortunately, many surveillance systems that attempt to estimate the burden of chronic bronchitis do not use that specific definition and only estimate "physician-diagnosed" chronic bronchitis or recurrent episodes of bronchitis (typically 3 episodes) in the previous year.
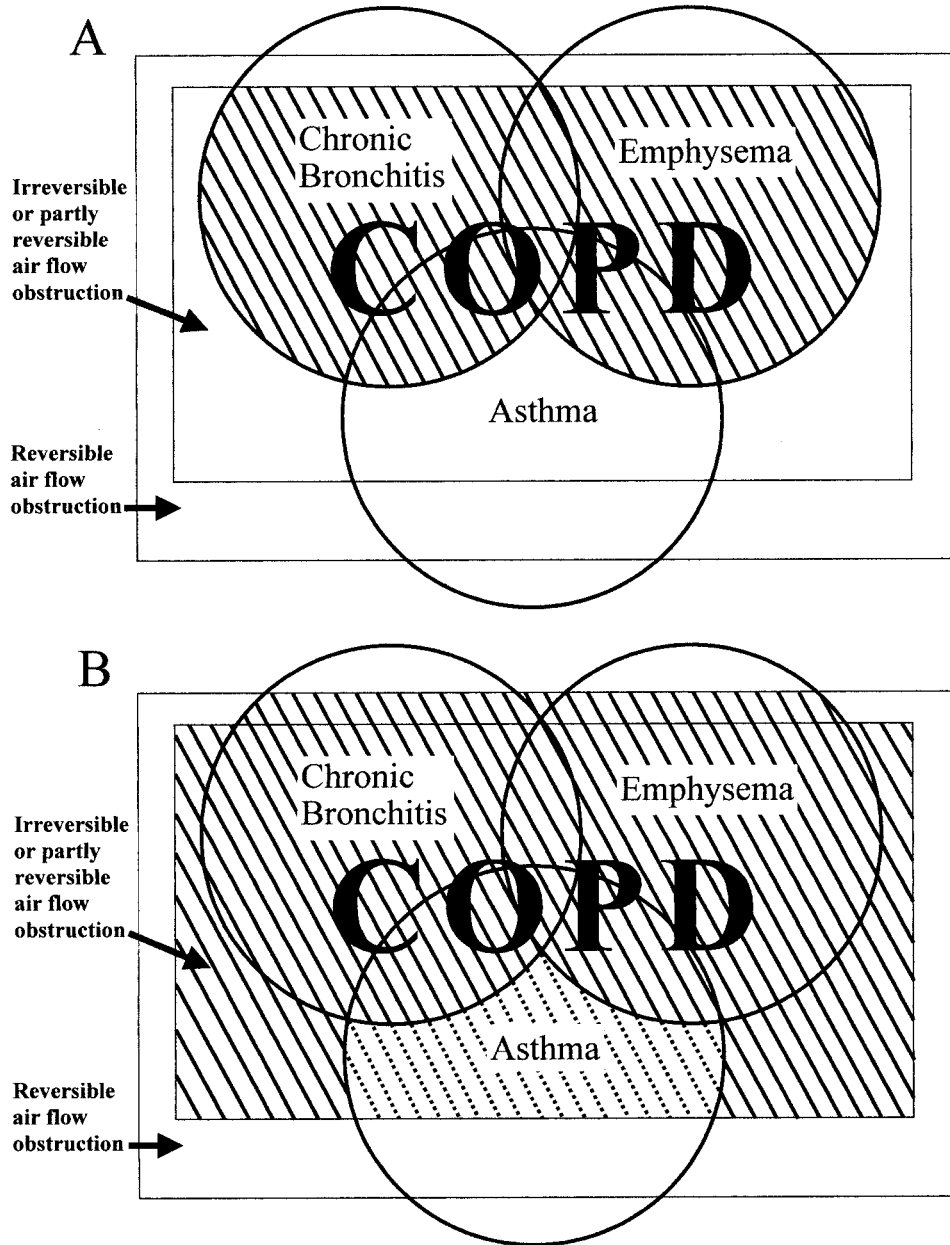
Fig. 1. Venn diagrams depicting the subsets of disease that compose chronic obstructive pulmonary disease (COPD) and the relationships between them. The subset areas shown are not proportional to the sizes of the subset populations. A: Modified version of the American Thoracic Society's COPD definition. B: COPD definition of the Global Initiative for Chronic Obstructive Lung Disease. The hatched areas represent COPD. In diagram B the zone representing the nonreversible component of asthma is hatched with dashed lines to indicate that it is controversial whether the disease represented by that area of the diagram is in fact COPD; some authorities do not consider that subset to be true COPD.

Emphysema

Emphysema, which is defined in anatomical terms, is the destruction of alveolar walls and permanent enlargement of the air spaces distal to the terminal bronchioles.[4] The ensuing loss of lung elastic recoil and intraluminal pressure in the terminal airways causes small airways to lose their patency, especially during forced expiratory ma-neuvers. The collapse of these airways causes airflow limitation independent of exertion. Clinically, the patient experiences progressive dyspnea and variable cough. It is not clear how most clinicians diagnose emphysema. Though the use of imaging, such as a computed tomography, would be optimal, it is likely that the majority of cases are diagnosed using different methods.

Asthma

Asthma, which is defined in physiologic terms, is reversible smooth muscle contraction that narrows the airway lumen, limiting expiratory airflow and resulting in symptoms, including wheeze, cough, and exertional dyspnea.[10] Asthma's distinguishing feature is the reversibility of symptoms in response to inhaled bronchodilators such as β agonists, anticholinergics, methylxanthines, and corticosteroids.

Newer Components of COPD Definition

Though the above-noted factors remain important for the diagnosis of COPD, other factors have emerged as being important predictors of both the quality of life and the survival of COPD patients. Some of these factors include fat-free body mass,[11,12] functional status,[13,14] exercise capability,[15] respiratory symptoms other than cough or sputum,[16] and the presence of comorbidities such as depression or heart failure.[17,18] Though those factors have not been formally included in the definition of COPD, they are clearly important both clinically and epidemiologically and need to be considered in the evaluation of patients.

Prevalence of COPD

As noted above, estimates of the prevalence of COPD depend on the COPD definition used. In national surveys in the United States the primary means of determining COPD prevalence has been to ask adults whether they have had any one of 17 respiratory diseases in the past 12 months. Three of the diseases asked about in that list are chronic bronchitis, emphysema, and asthma, with the estimate of COPD prevalence made by adding the cases of chronic bronchitis and emphysema. The National Health Interview Survey is an annual, nationally representative survey of about 40,000 United States households.[19] In the United States in 1996 the estimated number of adults ≥ 25 years old with COPD was 10.1 million or 6.0% of the population. In 1997 the National Health Interview Survey was redesigned to ask about physician-diagnosed disease, including chronic bronchitis and asthma, and whether the respondent had had a chronic bronchitis or asthma attack or episode in the previous 12 months. Although the survey redesign resulted in a 30% decrement in the estimate of asthma prevalence,[20] there was virtually no change in the prevalence of COPD, with an estimated 10.2 million or 5.9% of the adult population. During 2000 an estimated 10 million United States adults reported physician-diagnosed COPD (Figure 2).[21]

There are 2 main limitations to the National Health Interview Survey. First, it depends on the proper recognition and diagnosis of COPD by both the study participants and their health care providers, which would tend to bias
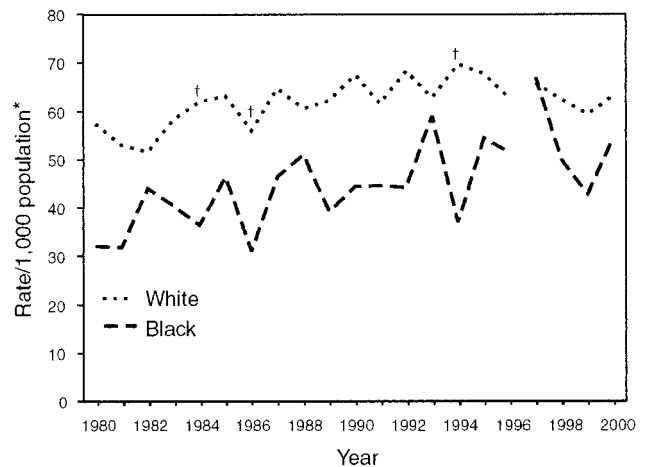

Fig. 2. Estimated annual prevalence of self-reported chronic obstructive pulmonary disease among whites and blacks, 1980–2000, in the United States. The data are from the United States National Health Interview Survey. * Age adjusted to 2000 United States population. † Denotes a statistically significant difference between whites and blacks. (Adapted from Reference 21)

the estimates towards there appearing to be fewer cases than actually exist. A bias in the opposite direction, however, is that in the survey the term "chronic bronchitis" is not precisely defined and could be interpreted as recurrent episodes of acute bronchitis. The finding that 3–4% of children have reported "chronic bronchitis" suggests the presence of the latter bias. Second, the survey is not able to validate through physiologic evaluation whether airway obstruction is present or absent. These limitations have been addressed in part by a separate nationally representative study. In the Third National Health and Nutrition Examination Survey (NHANES III) a stratified multistage clustered probability design was used to select a representative sample of the civilian, noninstitutionalized United States population from 1988–1994.[22] Survey participants completed extensive questionnaires in the household and received a comprehensive physical examination, including pulmonary function testing, at a specially equipped mobile examination center. Procedures for spirometric testing were based on the 1987 ATS recommendations.[23] With the NHANES III survey data it is possible to determine the presence of airway obstruction, the prevalence of diagnosed COPD, and the estimated prevalence of COPD in the population. The ATS definition of COPD (airway obstruction and chronic bronchitis or emphysema) resulted in an estimated national prevalence of 4.8 million adults or 2.9% of the adult population, whereas the ERS and GOLD definitions, which are based on the presence of airway obstruction only, resulted in much higher prevalence estimates of 24.2 million adults (14.3%) and 23.6 million adults (13.9%) with COPD, respectively. An estimated 2.4 million adults, or 1.4% of the population, have moderate to severe airways obstruction, with an FEV_1 of $< 50\%$ of predicted. Thus, the majority

of the subjects classified as having COPD by ERS and GOLD criteria have mild disease.

A limitation of the NHANES III survey and most similar surveys is that there was no determination of the reversibility of the airway obstruction. Many studies have looked at airways responsiveness (usually in response to methacholine or another nonspecific irritant), but that testing typically is done in a scenario of normal or near-normal lung function. The existing studies are often difficult to compare because of differences in definitions of "reversibility." For example, among participants in the Lung Health Study 10.9% had a $\geq 10\%$ improvement in FEV_1 over baseline in response to an inhaled bronchodilator.[24] That study, however, excluded subjects with FEV_1 values $< 50\%$ of predicted and subjects with FEV_1/FVC variability.[25]

A clinic-based study of subjects in Denmark included subjects with FEV_1 values $< 50\%$ of predicted and found that 60% of 1,095 COPD patients and 64% of asthma patients showed 15% improvement in baseline FEV_1 after a 7-day course of oral corticosteroid treatment and an inhaled bronchodilator (Ejvind Frausing Hansen, Hvidovre University Hospital, Hvidovre, Denmark, personal communication, 2003). If in that study one defined reversibility as a 10% improvement relative to the predicted FEV_1, only 33% of COPD patients and 49% of asthma patients demonstrated reversibility.

In another clinic-based study, of subjects ≥ 69 years old, 31% demonstrated reversibility, defined as a 15% improvement (from baseline) in FVC and FEV_1 following an inhaled bronchodilator.[26] In that study, as in the previously-discussed study, subjects with more severe obstruction were more likely to have reversibility but were also more likely to continue to have diminished lung function after maximum improvement was obtained, and were thus classified as having "partial reversibility."

The presence of substantial reversibility or partial reversibility in COPD patients[27] and nonreversible airflow obstruction in asthma patients[28] demonstrates that these diseases can coexist. Reduction in the pretreatment percent-of-predicted FEV_1 is an important means of classifying patients with asthma: patients with $FEV_1 < 60\%$ of predicted are classified as having severe persistent asthma, and those with values of 60–80% of predicted are classified as having moderate asthma.[10] The relationship between asthma, COPD, and markers of disease severity is discussed below.

Morbidity and Mortality

COPD is a leading cause of morbidity and mortality in the United States. The National Center for Health Statistics conducts ongoing surveillance of a number of United States health indicators and collects medical data. Data from physician office visits are collected with the National
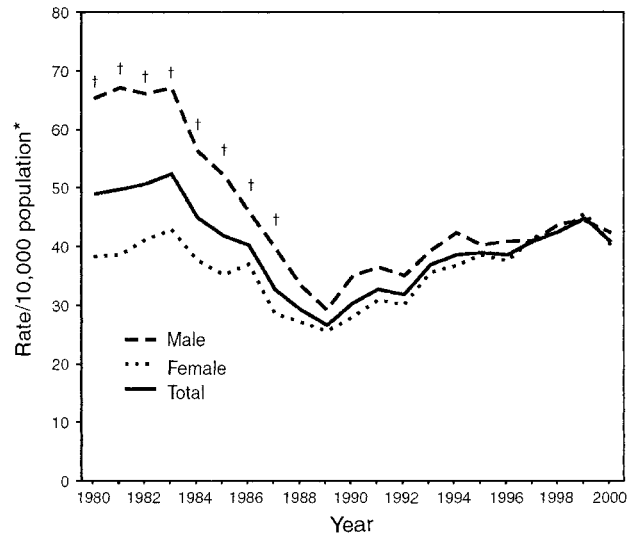

Fig. 3. Estimated annual rate of hospitalizations with chronic obstructive pulmonary disease as the first-listed diagnosis, by sex and year, in the United States. The data are from the United States National Hospital Discharge Survey. * Age adjusted to 2000 United States population. † Denotes a statistically significant difference between men and women. (Adapted from Reference 21)
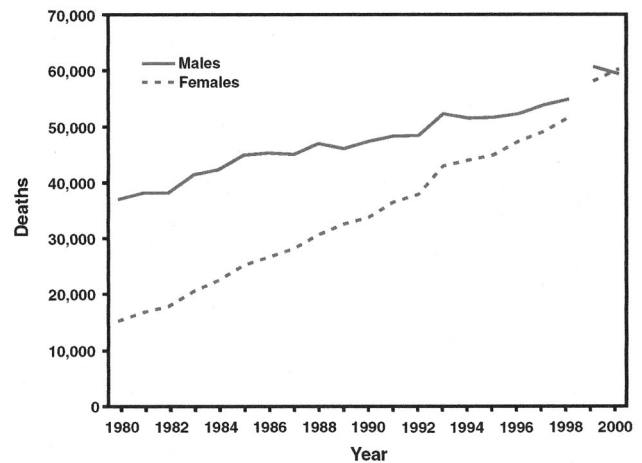

Fig. 4. Chronic obstructive pulmonary disease deaths, by sex, 1980–2000, in the United States. (Adapted from Reference 21)

Ambulatory Medical Care Survey.[29] Emergency-room-visit data and hospital out-patient data are collected with the National Hospital Ambulatory Medical Care Survey.[30] Hospitalization data are collected with the National Hospital Discharge Survey.[31,32] Death data are collected with the Mortality Component of the National Vital Statistics System.[33] In the present article I report the number and rate of COPD events in United States adults (using International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 490, 491, 492, and 496 or ICD-10 codes J40–J44) from the latter data sets, for the most recent years available.
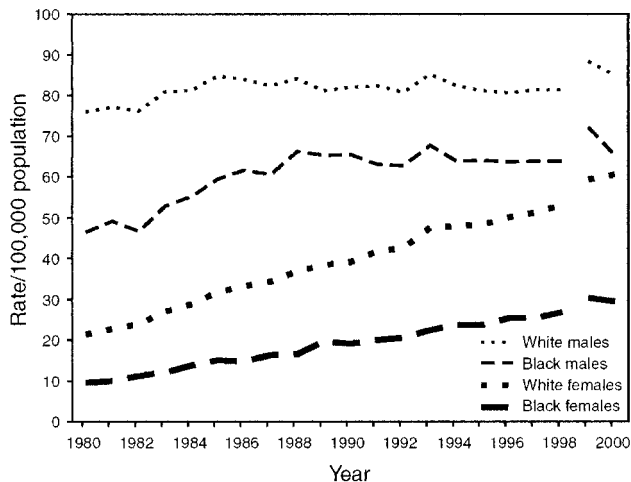
Fig. 5. Annual rate of death with chronic obstructive pulmonary disease as the underlying cause of death, by sex, race, and year, in the United States, 1980–2000. The data are from the Mortality Component of the National Vital Statistics System. (Adapted from Reference 21)

During 2000 COPD was responsible for 8 million physician office and hospital outpatient visits, 1.5 million emergency department visits, 726,000 hospitalizations, and 119,000 deaths (Figs. 3, 4, 5).[21] During the period analyzed the most substantial change was the increase in the COPD death rate among women, from 20.1/100,000 in 1980 to 56.7/100,000 in 2000, compared with the more modest increase in the COPD death rate among men, from 73.0/100,000 in 1980 to 82.6/100,000 in 2000. In 2000, for the first time, the number of women dying from COPD surpassed the number of men dying from COPD (59,936 vs 59,118). Another substantial change was that the proportion of the population < 55 years old with mild or moderate COPD (on the basis of pulmonary function testing) decreased between the period 1971–1975 and the period 1988–1994, possibly indicating that the upward trends in COPD hospitalizations and mortality might not continue.[21]

One of the limitations of the mortality database is that many decedents with COPD have their deaths attributed to other causes.[34] In 1998 only 45.4% of the 233,610 decedents with COPD mentioned on their death certificates had COPD listed as the underlying cause of death. This is despite prospective studies showing that people with COPD listed on their death certificate frequently have severe disease.[35]

COPD is a very costly disease, with estimated direct medical costs in 1993 of $14.7 billion.[36] The estimated indirect costs related to morbidity (loss of work time and productivity) and premature mortality is an additional $9.2 billion, for a total of $23.9 billion. When the indirect and direct medical costs attributable to asthma of $12.6 billion are added to this, the total cost of obstructive lung disease

in the United States is $36.1 billion. Because COPD is frequently not listed as the underlying cause of death or the primary reason for hospitalization, these cost estimates may underestimate the true cost of COPD.

Another manifestation of the importance of COPD is its effect on the burden of disease determined using disability-adjusted life-years (DALYs).[37] In 1996 COPD was estimated to be the 8th leading cause of DALYs among men and the 7th leading cause of DALYs among women.[37] Worldwide, COPD is expected to move up from the 12th leading cause of DALYs in 1990 to the 5th leading cause in 2020.[38]

Summary

COPD is a common disease that causes a great deal of morbidity and mortality in the United States and worldwide. Current symptom-based and clinically-based definitions of COPD underestimate the actual disease, and we may need to progress to a definition based on objective measurements. Furthermore, the importance of COPD in both deaths and hospitalizations is frequently underestimated. Finally, smoking cessation remains the cornerstone of COPD treatment, yet success rates in the best programs are < 30%,[39] demonstrating that better smoking-cessation interventions are needed.

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Discussion

Hansen-Flaschen: Conventional concepts of COPD add an etiologic component and often talk about exposure to tobacco smoke or other inhaled toxins. The growing recognition that a substantial fraction of patients with life-long asthma have substantial irreversible airways disease in later life suggests there is at least one other mechanism for irreversible airflow obstruction besides inhaled agents or toxins.[1,2] To the extent that is borne out by further research, I think it will make us go back and revise our thinking on COPD etiology when we're describing the disease.

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Mannino: I couldn't agree with you more. One of the ongoing struggles we fight is whether COPD is only from smoking. The assumption seems to be that if you take care of smoking, you take care of COPD, and "Let's move on to our next real problem," is sort of the perception that's out there. But there's so much more to COPD than quitting smoking.

We have a huge problem with regard to *former* smokers. People who have quit smoking have done the right thing, but I have many patients who stopped

smoking 15 years ago but who have COPD that continues to progress. I'm sure all of you have had that experience clinically. What do we have to offer these people? I think that's something we have to continue to struggle with. But of course smoking is clearly part of it.

The question is, why do only 15–20% of smokers develop COPD? There's always this conflict that you don't want to be perceived as saying that it's OK for some people to smoke, because they're not going to develop COPD. There's this concern out there that we have to address and dismiss. But certainly, by learning more about smokers who develop COPD, former smokers and never-smokers who develop COPD, and former smokers who have rapidly progressing COPD, we can make some inroads into understanding what the risk factors are.

Hill: Would you expand on what you said about gender differences? Did you indicate that there are nearly equivalent death rates for men and women with COPD but a lower COPD prevalence among women? Does that mean that women are more likely to die if they have COPD?

Mannino: Actually, it's the other way around. Currently women have a higher reported prevalence of COPD.[1] Hospitalization rate is fairly similar between men and women. The absolute *number* of deaths is higher among women than among men, but the death *rate* is lower. I think in about 15 years women will surpass men. It's still an open question whether women are more susceptible to COPD than men, and I personally don't believe that they are, based on the data I've seen,[2] although I'm sure Dr Silverman from Harvard would disagree with me. He has some compelling data to the contrary.[3]

I think a lot depends on how you look at the data. Just from a standpoint of basic epidemiology statistics, women on average smoke less than men. They need less tar and nicotine to satisfy the addiction, so they smoke

20% less than men. But if you do statistical analysis to control for intensity of smoking so that you look at women and men all smoking 30 cigarettes a day, it may well be that the women are getting a 30% higher dose than men at the equivalent number of cigarettes. So it may not be much of a surprise that in that sort of cohort analysis they would be more likely to get COPD or lung cancer. I think those are issues we need to work out.

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Wedzicha: Can you say more about the relationship between COPD and cardiac mortality? This is a subject that has interested us. In a small group of patients we found that fibrinogen levels were very high; in fact, the median fibrinogen levels were something like 3.74 g/L, which is equivalent to what you see in patients with peripheral vascular disease, I'm told. Did you look at fibrinogen in addition to C-reactive protein?

Mannino: Yes, fibrinogen's in there also, and it was also higher; it was similar to what you found.[1]

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Wedzicha: And the relationship was with severity? The more severe the dis-

ease, the more the cardiovascular mortality? How tight was that relationship?

Mannino: We haven't looked at that specifically yet, but we just gained access to the United States National Heart, Lung, and Blood Institute's database that includes lung function data, so we'll be able to do that soon. I had to jump through various hoops, but we just got the Atherosclerosis Risk in Communities data, and we'll be able to look at that. They have lung function data measured at 2 points in time, and they also have all the various validated cardiovascular outcomes. What they don't have in that database on everybody is things like fibrinogen, but they certainly have validated outcomes.

Heffner: You made the point that the choice of COPD definition has a major impact on our understanding of its epidemiology. I am bothered that we dichotomize smokers into having disease or no disease. If, as you state, a continuum of anatomical and functional changes occurs that progresses from health to disease, how do we establish a precise boundary for when a smoker transitions from good health to COPD?

Mannino: Clinically, we like cut points, but what is the appropriate cut point? There is no bright, clear line. For instance, in some of our studies of children, the cut point we're using for FEV_1/FVC is 80%. For people in their 70s, perhaps a lower cut point might be reasonable, but there is no clear line above which people are safe and below which you can guarantee they have a problem. It's something we struggle with, but at least when we're doing these analyses, we should look at data both continuously and then categorically. It's just a lot easier for me to make sense of things and explain things categorically, because frequently when you look at some of these data continuously, there are other factors that emerge.

Pierson: Do you think we'll get to a point where we will define people as

having disease by virtue of their smoking history? That is, once you meet a certain number of packs lifetime smoked, you should properly be characterized no longer as "healthy"?

Mannino: We do a little of that now, but I don't know. There are some smokers who don't develop lung disease. One of the hypotheses that we're looking at, called "cadmium theory," is that there are inducible proteins that protect against damage from metals. Perhaps some smokers have more of those proteins. That may predict what's going on. That may be one of the genetic components we're looking at.

There's so much variability, and some people who have 120 pack-years might have had 115 of those pack-years in the ashtray. The relationship between actual dose to the person and biologically effective dose is really difficult to disentangle epidemiologically. We'll always get a smoking history. It's my hope that ultimately we may have some better biologic markers of dose so that we could say that a person has a certain number of years of tobacco in their lungs, based on a certain radiographic assay.

Pierson: Once a person has alpha-1 antitrypsin deficiency, he has it regardless of whether he has any evidence of emphysema, and maybe smoking of a certain dose is going to turn out to be an analogous marker.

Mannino: Maybe. I haven't seen a threshold in anything I've looked at.

Gay: I've always been fascinated by the patients who have a tremendous number of pack-years behind them and absolutely minimal disease. In fact, I think we don't spend enough time seeing what's special about those people. I wondered if you've seen more data on that.

Mannino: It definitely happens. I'm not sure whether those people are eating more broccoli; as you know, COPD is a

systemic disease. There are components of nutrition and exercise, and, in general, smokers tend to have worse lifestyle: they tend to exercise less, to be more depressed, and a host of other things. This doesn't discount the reality that smoke is the reason for the disease, but there are definitely healthy smokers out there, and it's a conundrum.

Make: Can you give us an epidemiological perspective on nonsmokers who have COPD and who don't have asthma. Do you think second-hand smoke might be an etiology in that group? Or do these patients really have some other disease, and we just label it COPD in epidemiologic studies because we don't have any better clinical perspective on the individual patients?

Mannino: There's a small group of people—really small, based on the data we've seen—who are never-smokers, who do not have a history of asthma, and who meet the criteria for COPD. I think it's 70–80%, at least, with a lifetime history of asthma. We don't know whether those non-smoking, non-asthmatic people get COPD from passive smoke, occupational exposure, or air pollution, which in some parts of the world is a serious problem; some data from India, for instance, is dramatic.[1] There, women who are lifelong never-smokers suffer exposure to smoke from burning cow dung or whatever they're using to cook their food or heat their homes, and they have terrible COPD. So, clearly, environmental exposure to pollutants can be a factor.

REFERENCE

1. Smith KR. Inaugural article: national burden of disease in India from indoor air pollution. Proc Natl Acad Sci USA 2000; 97(24):13286–13293.

Hill: Have you observed any ethnic differences with regard to COPD susceptibility?

Mannino: We haven't looked at that a great deal. It does appear, for example, that Mexican-Americans or Mexi-

cans seem to have less COPD, but we haven't seen any major ethnicity differences in our population. If you take asthma out of the picture, clearly there's ethnicity differences in asthma susceptibility. Puerto Ricans have much more than Mexicans, for instance. Blacks are marginally higher in terms of problems but had much higher severity measures to hospitalization and mortality. But I think with COPD it's been a little less apparent and less studied.

Giordano:* To comment on those people who never seem to get COPD but smoke a lot, my wife and I coined a term for them: we call them "leather people." They're just made of leather and they will endure.

My question is two-fold. First, fast forwarding over the next 5 to 10 years, what do you think will be the impact of COPD's incidence on the health care system, just in terms of care delivery and access. Second to that, of course, is what about the cost implications?

Mannino: I, of course, think that COPD is important and is a growth area. We've gotten better at treating other diseases that kill people early, such as heart disease, and COPD is basically a disease of survivors. Based on the numbers we're seeing, things are going nowhere but up right now for COPD, particularly if you look at COPD as a co-morbid condition. I think it's going to be increasingly important.

The flip side is that as new therapies come onboard, it's my hope we'll be able to catch disease earlier and be able to apply appropriate interventions. Of course, the number one intervention is smoking cessation, but even in those who have stopped smoking we see disease progression, so I think that's a topic that's been ignored and that we need to do a better job of dealing with.

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