

The Impact of Aging and Smoking on the Future Burden of Chronic Obstructive Pulmonary Disease

A Model Analysis in the Netherlands

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Chronic obstructive pulmonary disease (COPD) causes extensive disability, primarily among the elderly. On the World Health Organization ranking list of disability-adjusted life years (DALYs), COPD rises from the twelfth to the fifth place from 1990 to 2020. The purpose of this study is to single out the impact of changes in demography and in smoking behavior on COPD morbidity, mortality, and health care costs. A dynamic multistate life table model was used to compute projections for the Netherlands. Changes in the size and composition of the population cause COPD prevalence to increase from 21/1,000 in 1994 to 33/1,000 in 2015 for men, and from 10/1,000 to 23/1,000 for women. Changes in smoking behavior reduce the projected prevalence to 29/1,000 for men, but increase it to 25/1,000 for women. Total life years lost increase more than 60%, and DALYs lost increase 75%. Costs rise 90%; smokers cause approximately 90% of these costs. The model demonstrates the unavoidable increase in the burden of COPD, an increase that is larger for women than for men. The major causes of this increase are past smoking behavior and the aging of the population; changes in smoking behavior will have only a small effect in the nearby future.

Keywords: COPD; epidemiology; smoking; costs; model

Chronic obstructive pulmonary disease (COPD) is a serious public health problem in many countries throughout the world. It is presently irreversible and causes high levels of disability, primarily among the elderly, but it also affects many patients before they reach retirement age. COPD morbidity and mortality are increasing, especially in countries with an aging population. On the worldwide ranking list of disability-adjusted life years (DALYs), COPD is predicted to rise from the twelfth place in 1990 to the fifth place in 2020, which makes it a major cause of disability and premature death. Part of this increase will take place in developing countries, but also for the developed world, a substantial rise in prevalence and a rise of the disease burden of COPD to ninth place in the ranking of DALYs is foreseen (1, 2). A concomitant increase in COPD-related health care costs may be expected. Country-specific studies on the current and future impact of COPD are scarce. A Swedish study reported an increase in inflation-corrected health care costs of COPD of 55% between 1980 and 1990 (3). We recently reported that the increase in health care costs in the Netherlands between 1993 and 2010 might be as high as 60%, at constant prices (4).

Smoking is the most important cause of COPD (5–7). Estimates of relative risks for COPD mortality among smokers compared with never-smokers vary from 2 to 32, depending on age, sex, and smoking history (8). It has been estimated that 80 to 90% of all patients with COPD have a history of smoking (8). Furthermore, approximately 90% of all health care costs of COPD in men and 80% of all costs of COPD in women are attributable to smoking (9) as is 75% of COPD deaths (10). Cessation of smoking is to date the only intervention that has proven to be successful in reducing the rate of decline in lung function (11, 12).

Therefore, a study investigating the burden of disease of COPD should pay attention to the role of smoking. We have previously modeled the impact of antismoking measures in the general population (4). Our model showed that, in the medium term, the health care costs of COPD are not very sensitive to changes in smoking behavior, because of the large time lag between intervention and effect. A longer time horizon is needed for the effects to become fully apparent. The current study considers the contribution of expected changes in smoking behavior to the future burden of disease related to COPD. These changes are found to explain only a small part of the expected medium-term increase in COPD prevalence. Because of a long disease duration and delayed effects, a large part of the projected increase is the result of past developments in smoking and the aging of the population; these are two factors that cannot be influenced further. Because the impact of even the most successful smoking intervention will be limited in the near future, at unchanged treatment patterns, we are facing a significant increase in the morbidity and mortality of COPD.

It is the purpose of this study to analyze this increase and its causes in more detail. The study reports projections for the future burden of COPD in the Netherlands, in terms of prevalence, mortality, life years lost, DALYs lost, and health care costs. The increases in morbidity, mortality, and costs of COPD that were found are related to the two main causes of the rise in the burden of COPD, that is, demographic changes and changes in smoking behavior.

METHODS

Model

To project the number of COPD patients over the period 1995 to 2015 in the Netherlands, we used a dynamic multistate life table model (13–15). In the model, successive birth cohorts are followed over time. Age, sex, and smoking behavior determine the incidence of COPD. Figure 1 presents the model structure, the arrows representing important transitions, viz. changes in health or smoking behavior and transitions from alive to dead. The model is described in APPENDIX E1 (see online data supplement). Because smoking is an important risk factor for COPD, the number of (former) smokers, and therefore, the incidence of other smoking-related diseases among patients with COPD will be relatively high. Consequently, patients with COPD also run a larger risk of dying from these diseases. The model takes these com-

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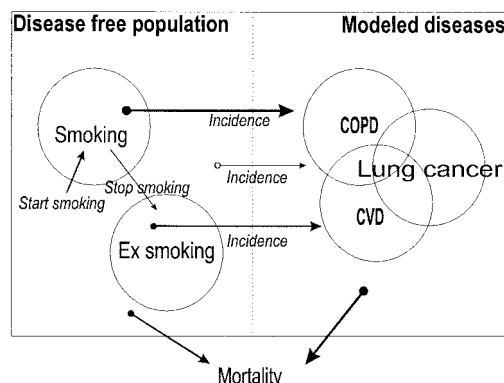


Figure 1. Basic structure of the dynamic life table model used to project future COPD prevalence, (disability adjusted) life years lost and costs of care.

peting risks into account in the estimation of mortality, because otherwise prevalence would be overestimated. The most important competing risks are due to cardiovascular diseases and lung cancer, and these diseases are separately modeled. Sensitivity analyses for some important model parameters were undertaken.

Projections

Two prevalence projections for 2015 were calculated for men and women separately and for the total population. The first assumes that age- and sex-specific incidence rates of COPD remain constant at their 1994 levels. This projection shows the impact of changes in the size and composition of the population. The second includes the effect of changes in smoking behavior. The difference between the two projections can be regarded as the effect of expected changes in smoking behavior.

We calculated the total number of life years lost as the sum of the remaining life expectancies of COPD victims. The total amount of DALYs lost in a certain year was computed as the prevalence of COPD multiplied by a factor 0.314 for quality-of-life loss (16), plus total life years lost. To estimate the projected costs of care related to the burden of COPD, prevalence projections were combined with age-specific information on the use of health care in physical units and the unit costs of care. These cost projections assumed constant prices and constant treatment patterns. Hence, they show the effect of prevalence increases only. Additionally, costs were projected including the effect of trends on the amount of care per patient and on the unit costs of the components of care.

Input Data

Input data for the model were as follows: demographic data, disease-specific data—incidence, prevalence, and excess-mortality rates (all presented in Table 1); smoking data—start and stop rates, relative

risks for smokers and former smokers (8, 17), and smoking prevalence rates (Table 2); quality-of-life data, and data on health care resource use and costs (Table 3). Details on these data can be found in APPENDIX 2 (see online data supplement). Figure 2 presents the growth in smoking prevalence as computed by the model for the period 1994 to 2015 based on observed trends over the period 1987–1994.

RESULTS

Prevalence of COPD

Figure 3 shows the 1994 prevalence and two prevalence projections for 2015 for men, women, and the total population, expressed as the number of patients per 1,000 persons. The first bar in each sex category shows that in 1994, COPD prevalence was 21, 10, and 15 per 1,000 for men, women, and the whole population. Each second bar shows model projections for the year 2015 at constant incidence rates. Changes in the size and composition of the population lead to an expected rise in prevalence to 33, 23, and 28 per 1,000, respectively. Each last bar includes the effect of changes in smoking behavior, with prevalence figures of 29, 25, and 27 per 1,000. Note that if the projections include changes in smoking behavior, they show a lower prevalence in men versus a higher prevalence in women.

Hence, for the period 1994 to 2015, including changes in smoking behavior, the model predicts an increase in prevalence of 43% for men and 142% for women. If changes in smoking behavior were left out, the projected increase in prevalence for men and women is 59% and 123%, respectively. In the population, the rise in COPD prevalence is 81% without changes in smoking behavior and 76% with these changes taken into account. It was computed that approximately 90% of the projected 2015 COPD prevalence is related to patients who smoke or used to smoke. The average length of disease was approximately 25 and 27 yr for 45-yr-old men and women in 1995. For all ages, disease duration was on average 10.5 yr for men and 12 yr for women.

DALYs Lost

Based on our input data, in 1994 almost 95 thousand life years were lost owing to premature death among patients with COPD. The projection that includes changes in smoking behavior leads to an increase of approximately 60% to more than 150 thousand life years lost in 2015. A similar increase was found for life years lost projected at constant incidence rates. Compared with a male without COPD, a male COPD patient lost on average 8 yr of life expectancy, whereas a female patient lost on average 10.5 yr.

For each year of disease, 0.314 of a healthy year equivalent was lost due to disability. With a mean disease duration of 10.5 and 12 yr, this implied that the average male patient lost 3 yr of healthy life, whereas the average female patient lost 4 yr of healthy life. Lost life expectancy and the loss due to disability add to the figures for DALYs lost. DALYs lost were 170 thousand in 1994 and 295 thousand (300 thousand at constant incidence rates) in 2015, representing an increase of approximately 75% (80%). This percentage is larger than the percentage increase in life years lost, because of a delay in increases in mortality compared with increases in prevalence. The difference in growth rates between men and women that was seen in prevalence projections was reflected in the years of life lost and in DALYs lost, with percentage increases for men of 40% and 50% respectively and for women of 100% and 120%. Figures 4A and 4B show 1994 levels and the two projections for 2015 at constant incidence rates and including the effects of changes in smoking behavior, for life years lost, and DALYs lost.

TABLE 1. EPIDEMIOLOGY OF COPD, BASED ON GP REGISTRATIONS IN 1994 (CASES PER 1,000)

Age	Incidence		Prevalence		COPD Mortality Patients
	Men	Women	Men	Women	
45–49	2	2	16	12	10
50–54	4	3	25	15	10
55–59	6	4	40	19	10
60–64	7	4	63	27	10
65–69	11	4	93	36	30
70–74	12	5	123	41	40
75–79	14	5	157	42	60
80–84	12	4	169	45	100
85+	12	5	127	49	130
45+	7	4	62	27	50

TABLE 2. SMOKING DATA USED AS INPUT IN THE MODEL

Age	Relative Risks for COPD				Proportions in 1994					
	Men		Women		Men			Women		
	smoker	f smoker	smoker	f smoker	n smoker	smoker	f smoker	n smoker	smoker	f smoker
20–24	1	1	1	1	0.59	0.34	0.07	0.60	0.32	0.08
25–29	1	1	1	1	0.49	0.40	0.12	0.49	0.37	0.14
30–34	1	1	1	1	0.42	0.43	0.16	0.41	0.39	0.20
35–39	9.6	8.7	10.2	7	0.37	0.44	0.19	0.40	0.39	0.21
40–44	9.6	8.7	10.2	7	0.33	0.44	0.23	0.43	0.37	0.20
45–49	9.6	8.7	10.2	7	0.31	0.43	0.26	0.46	0.34	0.19
50–54	9.6	8.7	10.2	7	0.30	0.42	0.28	0.50	0.31	0.18
55–59	13.6	11.2	12.3	8.3	0.30	0.40	0.31	0.55	0.28	0.17
60–64	13.6	11.2	12.3	8.3	0.30	0.38	0.33	0.60	0.24	0.17
65–69	13.6	11.2	12.3	8.3	0.30	0.35	0.35	0.65	0.19	0.16
70–74	9.8	7.4	8.9	5.9	0.31	0.33	0.36	0.70	0.15	0.15
75–79	9.8	7.4	8.9	5.9	0.32	0.30	0.38	0.76	0.10	0.14
80–84	9.8	7.4	8.9	5.9	0.34	0.27	0.39	0.82	0.05	0.13
85+	9.8	7.4	8.9	5.9	0.35	0.25	0.40	0.85	0.02	0.12
Total					0.52	0.31	0.17	0.63	0.24	0.13

Definition of abbreviations: f smoker = former smoker; n smoker = never-smoker.

Health Care Costs

Figure 5 shows the total costs of COPD care in 2015 compared with 1994. Two projections of future costs are given for men, women, and the total population. Both assume constant costs per patient; the first uses constant incidence rates, and the second includes changes in smoking behavior. For the projection that includes changes in smoking behavior, it was found that the total costs increase approximately 90% over the period 1994 to 2015. Costs increase more for women than for men, which is in line with the projected prevalence increases. To consider the effect of trends in costs, two further cost projections were made, both including changes in smoking behavior. First, changes in the use of health care resources per patient added 25% to the total cost increase. Second, changes in the costs per unit of health care again added about 25%. As a result, the maximum rise in total costs projected would be around 140%. Over the years, changes in the age and sex division of

the group of patients with COPD affect the contribution of various cost categories. However, these changes are small.

Sensitivity Analysis

Prevalence projections, including smoking, for four possible combinations of high and low incidence and excess mortality rates showed that the model is rather robust for changes in these rates. From the four prevalence projections, the single effect of a 20% change in incidence rates was a 17% change in prevalence, whereas the single effect of a 20% change in mortality rates was a 4% change in prevalence. Therefore, prevalence rates change relatively less than input rates and they are more sensitive to changes in incidence rates than to changes in mortality rates.

If all smokers would quit and become former smokers in 1995 and nobody would start smoking, the prevalence projected for 2015 would decrease by 2.4%, 13%, and 7% for

TABLE 3. UNIT COSTS AND TRENDS PER CATEGORY OF CARE

Category of Care	Unit	Unit Costs (1997 dollars)	Trend in Volume Per Patient Per Year (% increase)	Trend in Unit Costs Per Year*† (% increase)	Overall Trend
General practitioner	Contacts	16	0	1.7	1.7
Specialist	Outpatient contacts	58	0	1.7	1.7
Hospital					
University‡	Days	950	−1.4	8.5	6.9
General‡	Days	459	−1.4	4.8	3.3
Daycare	Treatments	159	0	1.7	1.7
Categoric	Days	387	0	1.7	1.7
Nursing home					
Inpatient	Days	132	0	3.3	3.3
Daycare	Days	90	0	1.7	1.7
Medication§	Prescriptions	79	1.6	0.6	2.2

* For all cost categories except hospital care, medication, and nursing homes, the Dutch rate of inflation for the health care sector over the years 1994 to 1996 was applied to unit costs. (Source: Statistics Netherlands.)

† For the computations, results using these price increases were deflated with the general rate of inflation in the economy, for which we used the consumer price index. (Source: CPB Netherlands Bureau for Economic Policy Analysis, appendices of the CEP, 1999.)

‡ For hospital days, volume trends were estimated for each age and sex class separately. For reasons of space, the table only presents overall averages. Hospital trends were based on data over the period 1993 to 1997.

§ For medication, trends were estimated for each age and sex class separately. For reasons of space, the table only presents overall averages. Overall trends were estimated from data on total per patient spending on medication over the period 1994 to 1998. From costs and number of prescriptions, average costs of a prescription were estimated for each age class and year, which gave price trends and unit costs.

For COPD, 23 ATC codes with specific medication were selected. The following categories of medication are included: β_2 -agonists, inhaled corticosteroids, anticholinergics, chromoglycic acid, xanthines, and antihistamines.

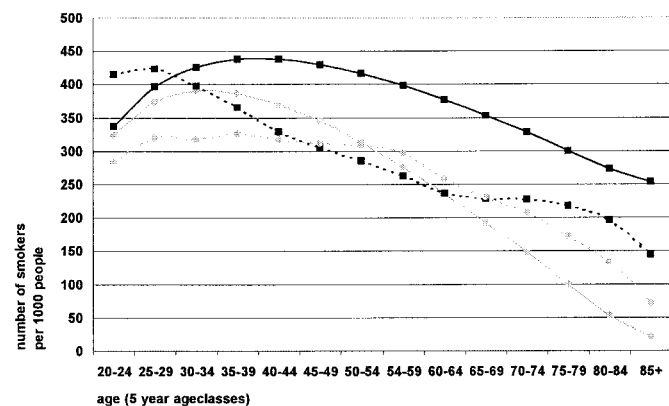


Figure 2. Smoke prevalence in 1994 and projections of smoke prevalence in 2015 for male and female population. Squares on solid lines = men, 1994; circles on solid lines = women, 1994; squares on dotted lines = men 2015; circles on dotted lines = women 2015.

men, women and the whole population, respectively. An increase in prevalence at an equal percentage for all age and sex classes implies a rise in total costs with that same percentage. An increase of 1% in the unit costs for general hospital care meant a 0.4% increase in total costs, if these were computed without trends in volumes or prices. Furthermore, a 1% increase in volume trends for general hospital care implied a 0.1% increase in total costs if these were computed with trends in volumes and prices, and a 1% increase in general hospital price trends implied a 0.4% increase in these costs.

DISCUSSION

To predict the future burden of COPD, we have developed a dynamic life table model that takes account of disease duration, aging and population growth, smoking behavior, and comorbidity. This model shows that changes in the size and composition of the population cause COPD prevalence to increase from 21/1,000 in 1994 to 33/1,000 in 2015 for men and from 10/1,000 to 23/1,000 for women. This corresponds to a 59% increase in COPD prevalence for men and a 123% increase for women. When expected changes in smoking behavior are taken into account too, projected prevalence decreases to 29/1,000 for men and increases to 25/1,000 for women. Note that

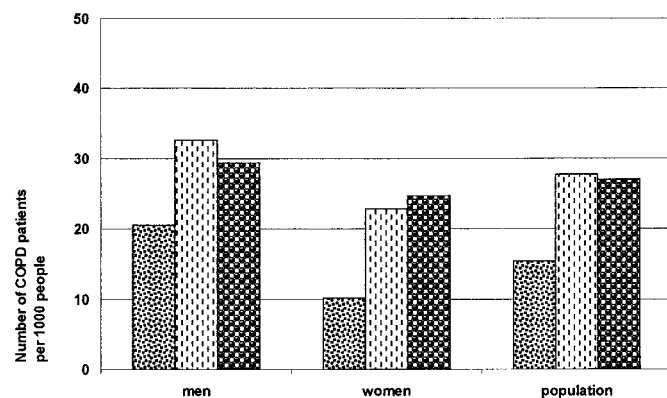


Figure 3. COPD prevalence in 1994 and projections for 2015 for male, female and total population. First bar from left in each group of three = 1994 level; middle bar in each group of three = 2015, projection at constant incidence rates; third bar from left in each group of three = 2015, projection including changes in smoking behavior.

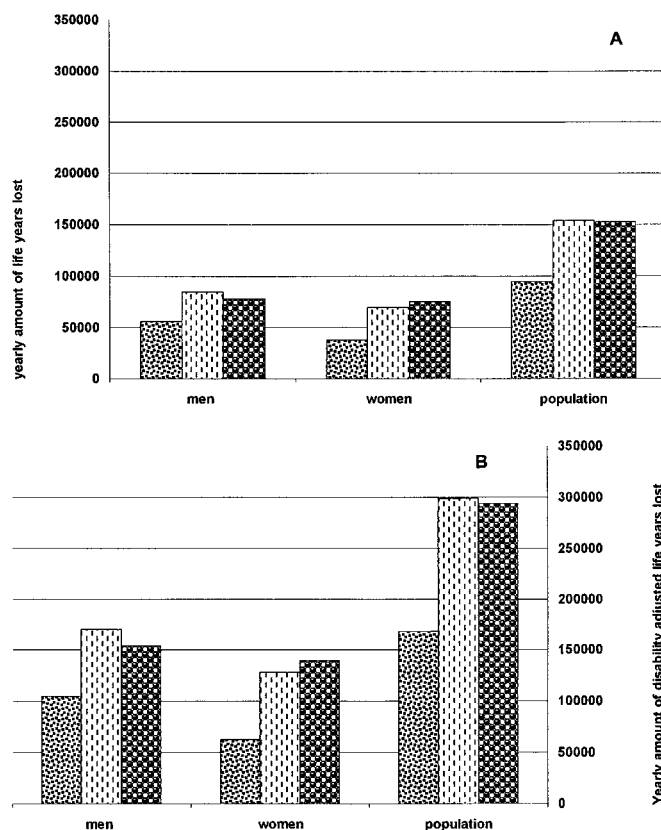


Figure 4. Life years (A) and disability adjusted life years (B) lost from COPD in 1994 and projections for 2015 for male, female and total population. First bar from left in each group of three = 1994 level; middle bar in each group of three = 2015, projection at constant incidence rates; third bar from left in each group of three = 2015, projection including changes in smoking behavior.

changes in smoking behavior have an opposite impact on the prevalence in men and in women.

Current high COPD prevalence rates among men are the result of past trends in smoking behavior. The increase in smoking prevalence among women came later, and its effect on COPD prevalence is now emerging (18). Our model pro-

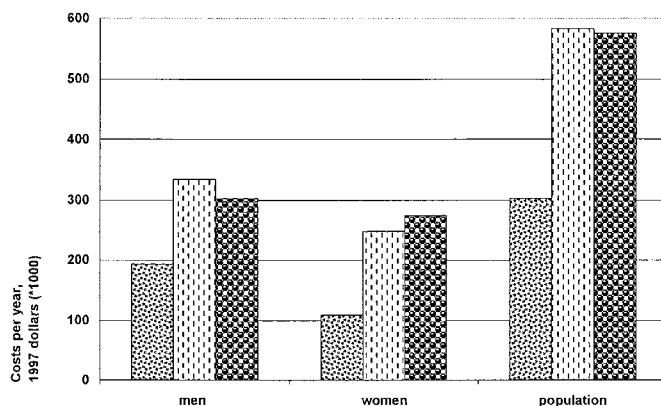


Figure 5. COPD costs of care at constant treatment patterns in 1994 and projections for 2015 for male, female and total population. First bar from left in each group of three = 1994 level, middle bar in each group of three = 2015, projection at constant incidence rates; third bar from left in each group of three = 2015, projection including changes in smoking behavior.

jection that takes account of changes in smoking behavior predicts a considerable increase in COPD prevalence among men. However, this increase is smaller than the increase that could be expected on the basis of demographic changes only, because our model assumes a 14% decrease in smoking prevalence among men between 1994 and 2015. This assumption is based on observed trends in past smoking behavior. In women, overall smoking prevalence is assumed to decrease with 6% between 1994 and 2015, but smoking prevalence in the age groups above 55 is assumed to increase. This increase in the higher age groups causes the increase in COPD prevalence among women to be higher than could be expected on the basis of demographic changes only. The comparison of the two prevalence projections that include and exclude the effect of changes in smoking behavior shows that changes in smoking behavior account for a small proportion of the changes in COPD prevalence only. This is partly due to the modest size of the changes in smoking behavior, the large time lag between changes in smoking behavior and their impact on COPD, and the long disease duration of COPD. For a 45-yr-old, the average duration of COPD is approximately 25 yr. The relatively modest impact of changes in smoking behavior in the medium term is clearly demonstrated under the very extreme scenario in which all smokers become former smokers and nobody starts smoking. Even then, the decrease in projected COPD prevalence rates is a modest 7% for the total population.

Small medium-term effects of changes in smoking behavior should not lead to the conclusion that smoking is unimportant for COPD. Approximately 90% of all projected COPD prevalence in 2015 and about 90% of 2015 COPD costs are caused by patients who smoke or used to smoke. (Due to age-dependent differences in costs and smoking behavior, it is not necessarily true that these two percentages are equal.) A better conclusion is that efforts to decrease the number of smokers hardly reduce the burden of disease of COPD in the medium term.

Our model projections also show that the increase in prevalence is associated with an increase in life years lost of more than 60% between 1994 and 2015. The predicted overall increase in DALYs lost is 75%; 50% for men and 120% for women. For the estimates of DALYs lost, a weight of 0.684 was used for the quality of life of a patient with COPD, computed as the average of the severity stages mild/moderate, with a weight of 0.83, and severe with a weight of 0.47. To average these, an estimated division of patients between the two stages of 3:2 was used, based on expert opinion (19). Two recent (non-Dutch) trials measured quality of life in specific groups of outpatients with COPD (20, 21). The studies report weights of 0.5 to 0.6 for a group of relatively severe patients and 0.78 for a group of patients whose disease severity was judged by clinicians to be mild in 16%, moderate in 71%, and severe in 13% of the patients.

Furthermore, our model projections indicate a 90% increase in costs between 1994 and 2015. This is a conservative estimate, because both the volume of care per patient and the unit costs of care are kept constant. When trends in volume and unit costs are added, the model shows a maximum cost increase of 140%. Especially, the increasing trend in costs per hospital day and the decreasing trend in the volume of hospital care per patient influence the total projected costs. The trend estimates are relatively uncertain, because we applied a linear extrapolation of trends based on a limited number of years. Hospital and medication costs are the two most important cost categories for all ages (4). We therefore updated these costs.

Our model was designed to give results on an aggregated, national level. Accordingly, we used as much as possible input

data from large registrations, that were considered representative for the Netherlands. However, data on incidence and prevalence are only available from regional general practitioner (GP) registrations. Therefore, we combined data from three GP registrations (22–24), which selected the participating GPs very carefully to produce representative data. In the Netherlands, GPs act as the gatekeepers of the health care system. Almost every citizen is registered in the practice of a GP, because the healthcare insurers require this registration. Although citizens are free to change this registration and enroll into another GP practice, many remain with the same GP practice for most of their lives. Thus, data from GP registrations represent the entire Dutch population.

The prevalence projections are rather robust for changes in incidence and mortality rates, but prevalence in the basic year is relatively important for the quantitative results. However, because incidence is higher than mortality over the period considered, any model projection would show a large growth in prevalence, regardless of the 1994 prevalence used.

In order to validate the model, we have compared our model projection of COPD prevalence to prevalence figures obtained from other sources. For 1997 the model computed approximately 262 thousand COPD patients 45 yr of age and over. This compares well with an estimate based on medication data from Dutch sickness funds, which find the number of patients in 1997 between 250 and 300 thousand (25). In addition, model projections of COPD prevalence for the years 1995 to 1998 based on continuous morbidity registration (CMR)-Nijmegen data compare well with the observed prevalence figures for the same years in this GP registration. The model predicts somewhat lower prevalence rates, but the differences in prevalence rates (number of patients with COPD per 1,000) between the model and the CMR varied from 0.66 for men in 1996 to 3.52 for women in 1995. This should be seen as an indication that there are no large biases in the model for short-term projections.

Necessarily, a model is a simplification of reality. One simplification in our model is that it assumes that smoking has an impact on the incidence of COPD, but not on the course of COPD once it is present. In reality, a patient's prognosis depends on his or her past and current smoking behavior (11, 26). However, this simplification has only limited effects on the predictions of the total prevalence and costs as long as there are no large changes in the smoking behavior among patients with COPD over time, for the model applies average excess mortality rates across smoking, nonsmoking, and formerly smoking patients with COPD. Another simplification is that our model distinguishes only three different categories of smoking behavior, with each category having a different risk of developing COPD: smokers, nonsmokers, and former smokers. In reality, the relative risk of developing COPD depends, among other things, on the number of pack-years smoked (27). Given the lack of more detailed data on smoking behavior, a refinement of this part of the model is not yet possible. A weakness of our analysis is that we can only present point estimates without confidence intervals. Most of our input data are counts without confidence intervals around them. Furthermore, like most model-based predictions of the future, the computations assume that currently observed behavior will be continued. Hence, the model allows us to consider what would happen if current trends in smoking behavior, demography, and COPD treatment are continued. It does not show what would happen if these would change dramatically. The results should therefore be interpreted with care and with due attention to the uncertainty surrounding them. This explains why we prefer to present our results as "projections," instead of "forecasts."

Do our projections apply to other countries? COPD morbidity and mortality vary substantially among countries. This variation may be caused by many interacting factors such as smoking behavior, type and processing of tobacco, air pollution, climate, medical practice, and genetic constitution of the population. Despite these differences, the projected increase in smoking rates throughout the world has led to the recognition that there will be a worldwide increase in the burden of COPD (10, 28). The smoking prevalence in the Netherlands is among the highest in the European Union, especially for women (14), and it is considerably higher than in the United States. Nevertheless, the increase in the burden of COPD as projected in this report is likely to be observed in many Western countries, because many of these countries are confronted with an aging population. Even in the United States, where millions of people have given up smoking, the effects of past cigarette smoking likely will be manifest for a long time. The hospital discharge rates for COPD in the U.S. population over 65 yr of age increased by 250% between 1988 and 1995 (29). The mortality attributable to COPD has more than tripled in the United States since 1970 (30). Moreover, data from young cohorts in economically developed countries show an increasing tendency to smoke among women (31). Thus, our observation that cigarette smoking is claiming an increasing health toll among women is likely to be observed in many other countries. Indeed, in the United States, sex-specific trends have begun to diverge too (32). For men, the mortality rate is showing a slight decrease, whereas for women, the mortality rate increases.

The increase in smoking prevalence in the low-income areas of the world can only lead us to expect future increases in the prevalence of COPD in these parts of the world too (10). However, because hospital-based care is less widely available in low-income countries than in high-income countries and long-term supportive care for severely disabled patients is usually absent, the predicted increase in health care costs does not apply to low-income countries. In low-income countries, the burden of COPD may be particularly large in terms of productivity lost, because labor is often the production factor that drives their economies.

In conclusion, our dynamic multistate life table model clearly demonstrates the unavoidable increase in the burden of COPD between 1994 and 2015; an increase that is larger for women (142% increase in prevalence) than for men (43% increase in prevalence). Past smoking behavior and aging of the population cause most of this increase. For the medium term (from 1994 to 2015), only a small part of the projected increases in prevalence, DALYs lost, and health care costs can be explained by expected changes in smoking behavior. This is not to say that smoking is not important, but successful efforts to reduce smoking in society as a whole can only reduce COPD prevalence substantially in the long run. For the medium term, reduction of the burden of disease should also focus on reduction of COPD exacerbations, improvement of patient's quality of life, and slowing down the progressive course of the disease.

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