ERJ Express. Published on April 8, 2009 as doi: 10.1183/09031936.00166108

Title: Present and future costs of COPD in Iceland and Norway: Results from the BOLD Study.

Short title: Costs of COPD in Norway and Iceland

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Abstract:

Background: The Burden of Obstructive Lung Disease (BOLD) initiative provides standardized estimates of the burden of COPD worldwide. We estimate the current and future economic burden of COPD in Reykjavik, Iceland and Bergen, Norway using data from the BOLD initiative.

Methods: Data on utilization of healthcare resources were gathered from the BOLD survey, existing literature and unit costs from national sources. Economic data were applied to a Markov model using transition probabilities derived from Framingham data. Sensitivity analyses were conducted varying unit costs, utilization and prevalence of disease.

Results: Current cost of COPD was €478 per patient/year in Iceland and €284 in Norway. The estimated cumulative costs of COPD for the population 40 years and older, were €130 million and €1539 million for the following 10 years in Iceland and Norway respectively. Costs of COPD accounted for 1.2% and 0.7% of healthcare budgets in Iceland and Norway, respectively. Sensitivity analyses showed estimates were most sensitive to changes in exacerbation frequency.

Conclusion: COPD has a significant economic burden in both Iceland and Norway and will grow in the future. Interventions aimed at avoiding exacerbations will have the most impact on costs of COPD over the next twenty years.

Keywords: cost of illness, Markov chains, computer simulation, disease progression, chronic obstructive pulmonary disease, Norway, Iceland

Word count excluding abstract, references and tables: 3453

Abstract word count: 198

Introduction:

The burden of chronic obstructive pulmonary disease (COPD) is considerable (1). To fully understand the implications of this chronic condition, the burden of illness also needs to be described in terms of societal economic consequences.

The Obstructive Lung Disease in Northern Sweden (OLIN) studies (2) estimated that in 1999 annual costs of COPD were € 1 448 per patient aged 28-80 years. COPD was defined as $FEV_1/FVC < 0.7$ without bronchodilator. Other cost-of-illness studies have been register-based studies that ignore un-diagnosed patients (3, 4).

There are several difficulties related to cost-of illness studies. Firstly, estimates get outdated quickly, as unit costs, treatment patterns and prevalence of diseases change. Secondly, the methods to survey complex chronic diseases are both time-consuming and expensive. Finally, results in different studies are subject to considerable variation (e.g. (5) vs (6)). Thus the comparison between surveys and countries is questionable (7).

A supplement to cost-of-illness-studies is disease modeling with predicted economic estimates as an outcome. Cost-evaluations can be carried out as simulations entering prevalence and progression rates from existing literature and combining them with utilization rates and costs of services (unit costs). However, previous health economic COPD models (8-11) have mainly been using incomplete transition probabilities from the Lung Health Study (12), or unpublished probabilities from the OLIN studies in Northern Sweden (8).

The Burden of Obstructive Lung diseases (BOLD) initiative is a multicentre international study aiming to estimate the burden of COPD worldwide (13). COPD prevalence is estimated using current guidelines from The Global Initiative for Chronic Obstructive Lung Disease (GOLD) (14), and data have already been published for the first 12 sites (1). As a part of the BOLD initiative an economic model (15) has been developed using data from the Framingham Heart Study (16) as basis for modeling disease progression.

Using prevalence and cost data from the Icelandic (Reykjavik) and Norwegian (Bergen) BOLD sites our aim was to estimate and compare the economic burden of COPD in these two Nordic countries. We have used the BOLD health economic model to estimate current and future costs of COPD in Iceland and Norway. Limiting the study to these two countries enables a more comprehensive presentation of the simulations and a more thorough discussion of the results. The viewpoint of our analyses has been at the society level.

Methods

Population

The BOLD study has been comprehensively described elsewhere (13). All participating sites provided population based random samples from non-institutionalized individuals aged 40 years and above. The fixed ratio $FEV_1/FVC<0.7$ after bronchodilation was applied as the primary disease criterion for COPD, and GOLD stages were used for severity classification (14). Data were collected by interviews covering the last 12 months. Certified technicians performed pre- and post-bronchodilator spirometry by using quality criteria complying to, or even stricter than the ATS standards (17). All predicted values are based on the NHANES III equations (18).

The Norwegian BOLD sample was a stratified random sample, of which the target population was defined as the city of Bergen with 105 000 residents aged 40 years and older in 2005 (19). The BOLD sample consisted of participants and non-participants from the year 2003 follow-up of a simple randomized cohort study first examined in 1985 (20). The Icelandic BOLD sample was a simple random sample from all Icelandic citizens aged 40 years and older living in the city of Reykjavik and surrounding suburbs with a target

population of 73 391 subjects as of November 2004. In total 658 (response rate 63.0%) and 757 subjects (response rate 80.6%) were considered full responders in Norway and Iceland, respectively (E-Table 1). Further details of the samples are given in the online supplement.

The economic model

The structure of the economic model has been described previously (13, 15). The model is based on Markovian transition probabilities (21). That is, using published literature and data from the Framingham Heart Study (16) we have derived probabilities of transition between 9 states of health (Table 1). In addition death is included as a separate state. Annual transition probabilities are age, gender and smoking status specific for each health state. Risk of mortality was gathered from NHANES (22). Mortality estimates are country specific in the model. Overall mortality rates and respiratory-specific mortality rates are based on national statistics from both Norway and Iceland (23). The online supplement provides further detail on the calculation of transition probabilities and e-table 2 shows annual progression rates by age, gender, smoking status and baseline COPD severity.

Subjects can transition from non-COPD health states to COPD health states. Within COPD health states subjects can only transition to more severe COPD. Events (e.g. exacerbations) do not impact transition rates. For each (annual) time cycle costs are added for each of the modeled subjects. The simulations were run as a cohort. For future costs we have used an annual discount rate of 3%.

The model cohort

The model begins with an estimate of the population of Iceland and Norway 40 years of age and older. Subjects are placed into one of the model health states based on population statistics and results of the BOLD prevalence survey from each site (1), in which the

prevalence of post-bronchodilator COPD (stage I or higher) was estimated to be 18.0% in Iceland and 18.8% in Norway. The incidence of COPD, according to gender and age, for both Iceland and Norway is based on data from the Hordaland County Respiratory Health Survey, which showed that 7 per 1000 of a general adult population developed post-bronchodilator COPD each year (24). This is combined with relative risks for development of COPD according to smoking status from the Framingham Heart Study (unpublished), to account for the effect of smoking status on COPD incidence. All incident COPD cases are placed in GOLD stage I. Smoking rates are based on BOLD survey results and population statistics for both countries (25, 26). Smoking relapse rate is estimated using the 1990 US Surgeon General's Report on Smoking Cessation (27), while smoking cessation rates are based on results from the National Health Interview Survey in the United States (28).

Costs and costs methodology

The model includes annual costs related to scheduled visits to physicians (general practitioners (GPs), specialists), exacerbations (hospital admissions, unscheduled healthcare provider contacts, antibiotics, oral steroids), prescription medication, pulmonary rehabilitation and home oxygen treatment. Table 2 shows unit costs for Iceland and Norway. E-table 3 shows unit costs specific for exacerbations. The cost estimated is the sum of costs for patients and the respective national health insurance systems. The online supplement provides details on the sources for unit costs.

Frequency of utilization

Estimates for scheduled annual contacts with health providers were based on data from the OLIN studies (2, 29). Annual exacerbation rates were gathered by pooling data from the Icelandic and Norwegian BOLD sites. An exacerbation was defined based on responses in the

BOLD survey, as an episode of "breathing problems that got so bad that they interfered with your usual daily activities or caused you to miss work." We differentiated between mild exacerbations (self-managed), moderate exacerbations (healthcare provider contacted) and severe exacerbations (admitted to hospital). Frequency of exacerbations was counted for the preceding 12 months in subjects with post-bronchodilator COPD (E-table 4). Health resource use during exacerbation was estimated using local expert opinion.

Estimates of prescription medication utilization for each of the health states of COPD were gathered from the BOLD survey for Iceland and Norway, respectively. Frequency of home oxygen use and pulmonary rehabilitation was based on expert opinion, using information from local healthcare authorities in Iceland (Reykjavik) and Norway (Bergen). All the data on frequency of utilization are available as online supplementary material (E-table 5).

Analyses

Both cost and disease prevalences were compared using chi-square tests and tests of equality of proportions. Means were compared using t-tests after assessing normality. Estimates for the Norwegian sample were weighted to the target population using population statistics (19).

Economic modeling was carried out using Microsoft Excel 2003 (Microsoft Corp, Redmond, WA). For remaining analyses we used Stata 10 SE for Macintosh OS X (Stata Corp, College Station, TX). All p-values were two-sided, and values below 0.05 were considered statistically significant. All results are given in 2005 euros (€) based on exchange rates from the Central Bank of Norway (30) and The Central Bank of Iceland (31).

To estimate the current and future burden of COPD, we simulate the current population of adults aged 40 years and older from each country over a 20-year period. With the model, we estimate the future prevalence of COPD in each of the severity strata during

each year of the 20-year simulation. The COPD-related healthcare costs are estimated for each of the years of the simulation to determine the future economic burden associated with COPD. For costs, we estimated the current direct healthcare costs, the per capita costs and the costs per patient with COPD overall and by severity of disease. When estimating the future costs of COPD, we estimated the cumulative amount spent on COPD over a 10-year and 20-year period. Furthermore we estimated the average annual costs over that time period. Finally, we estimated the proportion of costs attributable to exacerbations, physician visits, prescription medication and other healthcare utilization for each of the severity groups.

Sensitivity analyses

We conducted several sensitivity analyses to determine the influence of model assumptions on the overall results. The sensitivity analyses focused on the key components of COPD-related costs, exacerbations and medication use, and the development and progression of the disease. Further details of the sensitivity analyses are given in the online supplement.

Results

Response rates in the Norwegian site were slightly lower than in Iceland (E-table 1). Using chi-square statistics, there seemed to be a proportionately larger number of women declining to participate in Norway ($p < 0.05$). In Iceland elderly females (≥70 years) had a lower participation rate than younger females ($p < 0.05$). No other discrepancies between responders and non-responders were observed with regards to gender, age or smoking status.

There were 53% men among the participants in Iceland, and 48% men in Norway. The mean age (SEM) in the Icelandic sample was 56.4 (0.4) years and 57.8 (0.5) years in the Norwegian sample. The rates of current smokers were 15.7% and 27.2%, among men, and 21.2% and 28.4 % among women, in Iceland and Norway respectively (Table 3).

In the Icelandic sample the annual prevalence of mild, moderate and severe exacerbations in COPD patients was 0.0%, 4.6% and 1.5% respectively while in Norway it was estimated to 0.6%, 2.5% and 0.7%, respectively.

Current burden of COPD

The annual direct COPD-related medical costs in Iceland in 2005 were estimated to be € 12 million for the population 40 years and older, and € 478 per COPD patient (GOLD stage I and above). In Norway the respective estimates were € 141 million and € 284. Patients with the most severe COPD (GOLD stage III and IV) accounted for 29% of annual costs in Iceland and 32% of annual costs in Norway. Cost estimates are given in Table 4.

The main cost driver in year 2005 was medication costs, which accounted for 51% of total costs in Iceland, and 48% of total costs in Norway. Costs for healthcare provider visits accounted for 26% and 23% and costs for exacerbations accounted for 17% and 19% in Iceland and Norway respectively. Other costs, which included home oxygen treatment and rehabilitation programs, accounted for 7% of total COPD costs in Iceland, and 11% of total costs in Norway (Figure1).

Future burden of COPD

The modeled future COPD prevalence in Iceland and Norway for the population aged 40 years and older is shown in Figures 2 and 3. After 10 years the prevalence of COPD stage I+ will have reached 22% and 24% in Iceland and Norway, respectively. The accumulated 10 years discounted COPD-related direct medical costs were estimated to € 130 million in Iceland and € 1 539 million in Norway. The discounted annual total costs were largely unchanged from the 2005 estimates in both countries, but the burden of costs from COPD stage III+ increased to 37% in Iceland and 43% in Norway. These numbers increased from 29% to 39% and from 32% to 47%, respectively, in the 20 years scenario.

Sensitivity analyses

All sensitivity analyses are given in table 5. When changing exacerbation rates to those reported by the OLIN survey (29), the cost estimates increased by 236% in Iceland and 226% in Norway. The change was largest within stage III+ (online supplement, E-table 6). When excluding costs from GOLD stage I COPD, the estimates for Iceland and Norway decreased with 31% and 30%, respectively. Excluding hospitalization costs for stage I decreased total 10 years costs with 5% in both countries. For the remaining sensitivity analyses the largest impact was seen when changing utilization of prescription medication.

Discussion

By using prevalences from the Icelandic and Norwegian sites of the BOLD survey, we have estimated the current burden of COPD for year 2005 in Iceland to be € 12 million and in Norway to be € 141 million, for the population 40 years of age and older. The cost per patient with COPD was € 478 in Iceland and € 284 in Norway. We used a Markov chain model based on progression rates from the Framingham Heart study to model future costs, which at a 3% annual discount rate estimated the 20-years cumulative burden to reach € 256 million for Iceland and € 3 222 million for Norway. The robustness of the model was investigated by several sensitivity analyses. Variation of exacerbation rates revealed large changes in the cost estimates.

These are the first published estimates of costs of COPD, both for Iceland and for Norway. The model is based on COPD prevalence estimates that have been obtained using identical state-of-the-art methods in both sites, adding further strength to the results, and facilitating cross-country comparison. We have also modeled the future COPD-related costs,

which showed the considerable burden imposed on these two healthcare systems. The relatively constant annual costs after 10 years are partly a result of holding the unit costs and treatment patterns at the 2005 level. The sensitivity analyses on exacerbation rates could also be interpreted as simulations of the effect of implementing new treatment. Thus, an intervention reducing the observed exacerbation rates by 25%, implicates a cost reduction of 4% of the treatment-related costs (not including costs of the new intervention).

The healthcare systems in Iceland and Norway are very similar – both countries provide universal healthcare through a national, government-funded health insurance. In 2005 the Icelandic government spent € 1.1 billion on healthcare (32), that is € 3 782 per inhabitant or 8% of the Gross Domestic Product (GDP). The Norwegian government spent € 22 billion on healthcare in 2005 (33). That amounts to € 4 588 per inhabitant or 9% of the GDP. Thus our estimates for COPD-related direct medical costs accounts for 1.2% of healthcare costs in Iceland and 0.7% of healthcare costs in Norway.

Some methodological considerations are needed. Firstly, the Norwegian sample is not a simple random sample, but a follow up of a cohort from 1985 with two strata according to response status at a previous follow-up. We believe that this is the main reason for the different response rates between the two sites. Another effect of the different sampling techniques might be a "healthy survivor effect." However, the cohort has had high response-rates at all follow-ups (20, 34). The distribution of gender and smoking habits has previously been comparable to those of the Norwegian population (19), and the present results have been weighted to the general Norwegian population using census data.

Secondly, we have used transition probabilities from the Framingham Heart Study (16).

The current model does not take into account the changing smoking patterns. However, Feenstra and colleagues (35) have shown that if all smokers were to quit as of today, the

prevalence 20 years in the future would only decrease by 7% from almost doubling in their base case scenario. Due to cohort effects, the impact of changing smoking patterns will probably be minor in view of the effect of the ageing population (35). The high prevalence of smoking among women in both Iceland and Norway combined with higher utilization of healthcare among women might lead to increased COPD-related resource. Results might also have differed if local transition rates were available – accounting for geographic and exposure variation.

Thirdly, this is among the first publications that use post-bronchodilator spirometry when defining COPD in a health economic setting. Other authors have either used spirometry without bronchodilation (2) or have defined COPD according to self-reports (36) or diagnosis in medical records (3). Also, we have used the fixed FEV1/FVC<0.7 as disease criterion for COPD. It has been shown that this methodology has a tendency of overestimating COPD prevalence, especially among the elderly (37). However, this debate is not yet resolved, and there are even contradictory findings (38). In line with the BOLD study protocol (13), we have thus chosen to use the FEV1/FVC<0.7 as disease criterion, although we acknowledge the growing support for the lower limit of normal when diagnosing COPD.

Finally, in the present study, we have not gathered detailed information concerning resource use during exacerbation. To some degree we have based estimates on local expert opinion. However, the exacerbation rates were based on participant information in the Norwegian and Icelandic BOLD site. Our definition of exacerbations was based on resource use and we have thus partly based our exacerbation cost estimates on own empirical data.

The most striking difference between the Icelandic and Norwegian estimates is that in spite of more money spent on healthcare in Norway, the Icelandic COPD patient consumes more resources for direct COPD-related care. To investigate these differences, several possible contributing factors call for attention. Firstly almost all unit costs are more expensive

in Iceland than in Norway. A smaller healthcare system, in terms of scale, may contribute to this. Secondly, treatment patterns and traditions may differ between the two countries. Hospital costs for COPD are higher in Iceland (table 2) possibly indicating fewer possibilities in care for endstage COPD as previously shown by Janson et al, the length of stay in COPD hospitalizations is almost twice as long in Iceland (Reykjavik) compared to Norway (Bergen) (39). The input used for the model from the BOLD survey indicated that in Iceland more individuals in stage I and II COPD were treated with inhaled corticosteroids than in Norway (E-table 5), and they received more expensive drug alternatives (table 2). Finally, the rapidly changing value of Icelandic currency might influence the perceived differences between Iceland and Norway (31). When using purchasing power parities (PPP), a tool developed to standardize currency to US dollars while taking GDP into account (40), the difference between the Icelandic and Norwegian annual costs per COPD patient decrease from a 168% difference to a 144% difference.

The OLIN studies have given estimates for both total COPD-related costs (2), and costs related to exacerbations (29). Their estimates are based on a prospective one-year cost-of-illness study in COPD patients from a general population 28 years and older. Compared to the findings in the current study, costs in Sweden for direct medical care are higher than for both Iceland and Norway (€ 644 per patient with COPD per year). This difference is mostly attributable to more hospitalizations in the Swedish data, where subjects with FEV_1 less than 40% of predicted on average stays 8.9 days in hospital each year. The rate of hospitalization in our study was 4 hospitalizations per 100 patients per year for COPD stage III+. The low hospitalization and exacerbation rates in our study were responsible for the finding that only 16% and 17% of COPD-related costs was accounted for by exacerbations, whereas drug costs accounted for 48% and 51% of COPD-related costs. In the OLIN studies 37% of annual costs per patient were attributable to hospitalizations. However, results of comprehensive

sensitivity analyses were not provided in the OLIN studies, and the impact of varying assumptions regarding unit costs and frequencies of utilizations remain unknown. Nevertheless, we suspect that differences between the OLIN studies and the current study partly can be explained by low exacerbation rates in the current study. This might be due to enhanced recollection in the prospective design of the OLIN studies, although hospitalizations generally are well remembered (41). The strict population based samples in the BOLD study might also have contributed to the low exacerbation rates found. More documentation of exacerbation rates in Iceland and Norway is needed. It remains to be seen what the use of a symptom-based definition of exacerbations will lead to in terms of variation of exacerbation rates between countries.

In conclusion, we have estimated that the costs of COPD in Iceland and Norway in 2005 amounted to €12 million and €141 million, respectively for the population 40 years and older. Besides giving the first estimates for costs of COPD in Iceland and Norway, we have also elucidated some of the differences between the two healthcare systems. Both estimates give useful information for local decision makers seeking to optimize the care for COPD patients. Restricting the analyses to these two Nordic countries have enabled a comprehensive description of the modeling and presentation of the results. We have demonstrated the feasibility of the BOLD economic model, both in conducting sensitivity analyses and estimating future costs of COPD. In the future the BOLD economic model will be available for investigators from other BOLD sites, enabling similar analyses for other countries. Our estimates were particularly sensitive to changes in exacerbation frequency, which emphasizes this as an important cost driver and the critical point of intervention when aiming to reduce costs of COPD.

Acknowledgements:

The authors wish to acknowledge the support of the BOLD Operations Center in Portland, Oregon, USA for their assistance in carrying out the study. Funding for the Operations Center was provided by unrestricted educational grants from ALTANA, Aventis, AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, Merck, Novartis, Pfizer, Schering-Plough, Sepracor and University of Kentucky.

The Reykjavik BOLD site was funded by the Landspitali University Science Fund, Astra Zeneca in Iceland and GlaxoSmithKline in Iceland. The Norwegian BOLD site was funded by the Research Fund for Respiratory Medicine, Haukeland University Hospital and The Norwegian Association of Heart and Lung Patients and EXTRA funds from the Norwegian Foundation for Health and Rehabilitation.

The authors thanks participants in the BOLD study and field workers Lovisa Gudmundsdottir (Reykjavik), Kristin Bara Jorundsdottir (Reykjavik), Sigrun Gudmundsdottir (Reykjavik), Lene Svendsen (Bergen) and Tina Endresen (Bergen).

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Table 1: The Nine Health States of the BOLD Economic Model and their prevalence in the Icelandic (Ice) and Norwegian (Nor) BOLD sites.

	Smoker	**Never-smoker**	**Former smoker**
Non-COPD	Smoker, non-COPD (Ice: 14.3% Nor: 21.7%)	Never-smoker, non-COPD (Ice: 33.8% Nor: 31.8%)	Former smoker, non-COPD (Ice: 34.7% Nor: 27.6%)
COPD stage I	Smoker, COPD stage I (Ice: 2.3% Nor: 3.3%)	Non-smoker (never and former), COPD stage I (Ice: 6.3% Nor: 7.2%)	
COPD stage II	Smoker, COPD stage II (Ice: 1.3% Nor: 2.5%)	Non-smoker (never and former), COPD stage II (Ice: 5.4% Nor: 4.7%)	
COPD stage III+	Smoker, COPD stage III+ (Ice: 0.5% Nor: 0.3%)	Non-smoker (never and former), COPD stage III+ (Ice: 1.3% Nor: 0.9%)	

COPD stage I: FEV1/FVC<0.7, FEV1 % predicted ≥ 80%
COPD stage II: FEV1/FVC<0.7, FEV1 % predicted 50-79%
COPD stage III+: FEV1/FVC<0.7, FEV1 % predicted < 50%

Table 2: Unit Costs associated with COPD in Iceland and Norway in 2005 euros

	Iceland	Norway
Healthcare Provider Visit Cost Estimates		
Telephone contact	4.0	4.4
General Practitioner/Primary Care Provider visit, euros	46.6	52.5
Specialist provider visit, euros	77.5	166.6
Daily Medication Cost Estimates		
Inhaled-beta agonists, euros per day	1.2	0.8
Inhaled corticosteroids, euros per day	2.0	2.0
Anticholinergics, euros per day*	2.4	0.6
Systemic corticosteroids, euros per day	0.9	0.4
Antibiotics,euros	2.5	1.6
Other Treatment Cost Estimates		
Home Oxygen, yearly costs in euros	2706	3 184
Pulmonary Rehabilitation, euros per stay†	10232	2 329
Hospitalization		
Cost for average COPD hospitalization in euros	5966	3 920

† Rehabilitation in Iceland (Reykjavik) takes place over 6 weeks as an in-patient. In Norway (Bergen) the rehabilitation programme last for 16 days and the participants are out-patients, thus the cost difference.

***** Cost difference due to dominance of tiotropium on Iceland, while in Norway ipratropium dominates.

Table 3: Estimated population characteristics of the Icelandic and Norwegian study samples:

	Iceland	Norway
N (response rates)	757 (81 %)	658 (63 %)
Male sex, %	53.2	48.0
Age (years)		
40-49, %	35.9	32.2
50-59, %	29.0	28.5
60-69, %	18.0	18.7
70 +, %	17.1	20.6
Smoking status (males)		
Current smokers, %	15.7	27.2
Former smokers, %	45.7	40.2
Never smokers, %	38.6	32.6
Smoking status (females)		
Current smokers, %	21.2	28.4
Former smokers, %	39.4	31.0
Never smokers, %	39.4	40.6
Dyspnoea at level ground, % *	6.9	4.8
3 months of coughing per year, %	11.3	7.6
Doctors diagnosis of COPD, %	1.1	2.4
Post-bronchodilator spirometry		
FEV1/FVC < 0.7, %	18.0	18.8
FEV1 % predicted, mean (SEM)	93.0 (0.59)	95.1 (0.60)
FVC % predicted, mean (SEM)	94.2 (0.48)	97.2 (0.53)
COPD, GOLD stage II+, %	9.0	8.3

* excluded individuals with physical disabilities

Table 4: Estimated current and future direct medical costs of COPD in Iceland and Norway. Estimates in 2005 euros, discounted at 3% annual rate

	Iceland				Norway			
	Overall cost estimate	Stage I	Stage II	Stage III+	Overall cost estimate	Stage I	Stage II	Stage III+
Current burden								
Annual costs, million euros	12	4	5	4	141	41	55	45
Costs per COPD patient, euros	478	329	559	1566	284	176	348	1 518
Burden in 10 years								
Annual costs, million euros	13	5	4	5	154	47	41	66
Cumulative burden, million euros	130	45	37	48	1 539	468	413	657
Burden in 20 years								
Annual costs	13	5	3	5	153	47	34	72
Cumulative burden, million euros	256	96	61	99	3 066	941	684	1 440

Table 5: Sensitivity analyses for the 10 years accumulated direct COPD-related costs. Discounted at a 3% annual rate. All in million euros (2005). Change from base case in parenthesis. All estimates are for the population 40 years and older.

Model variable	Iceland	Norway
Base case	130	1 539
Variation of Stage 1		
Excluding costs of stage 1	85 (-34%)	1 070 (-30%)
Only medication costs and costs of physician visits included in stage I costs	124 (-5%)	1 455 (-5%)
Transition rates		
Excluding fatalities	122 (-6%)	1 376 (-11%)
Expert panel on transition rates	124 (-5%)	1 414 (-8%)
25% decrease / increase from base case	125 / 136 (-/+ 4%)	1 438/ 1 654 (-/+7%)
Exacerbation rates		
Using BOLD-exacerbation proportions, rather than rates	127 (-2%)	1 495 (-3%)
Exacerbation rates from the OLIN studies	438 (+236%)	5 015 (+226%)
Exacerbation resource use from OLIN studies	129 (-1%)	1 526 (-1%)
25% decrease/increase from base case	124 / 136 (-/+ 4%)	1 473 / 1 604 (-/+ 4%)
Utilization of prescription medication		
Medication use from pooled data set (Iceland and Norway)	128 (-2%)	1 638 (+6%)
50% decrease/increase from base case	98 / 163 (-/+ 25%)	1 183 / 1 894 (-/+ 23%)
COPD development		
Incidence rates from Feenstra (35)*	118 (-10%)	1 423 (-8%)
Relative risk of COPD incidence by gender, age and smoking from (35)*	131 (0%)	1 544 (0%)

* see online supplement for a more comprehensive explanation (section heading ”Sensitivity analyses”)

Figure Legends

Figure 1: Distribution of COPD-related costs in Iceland and Norway, year 2005.

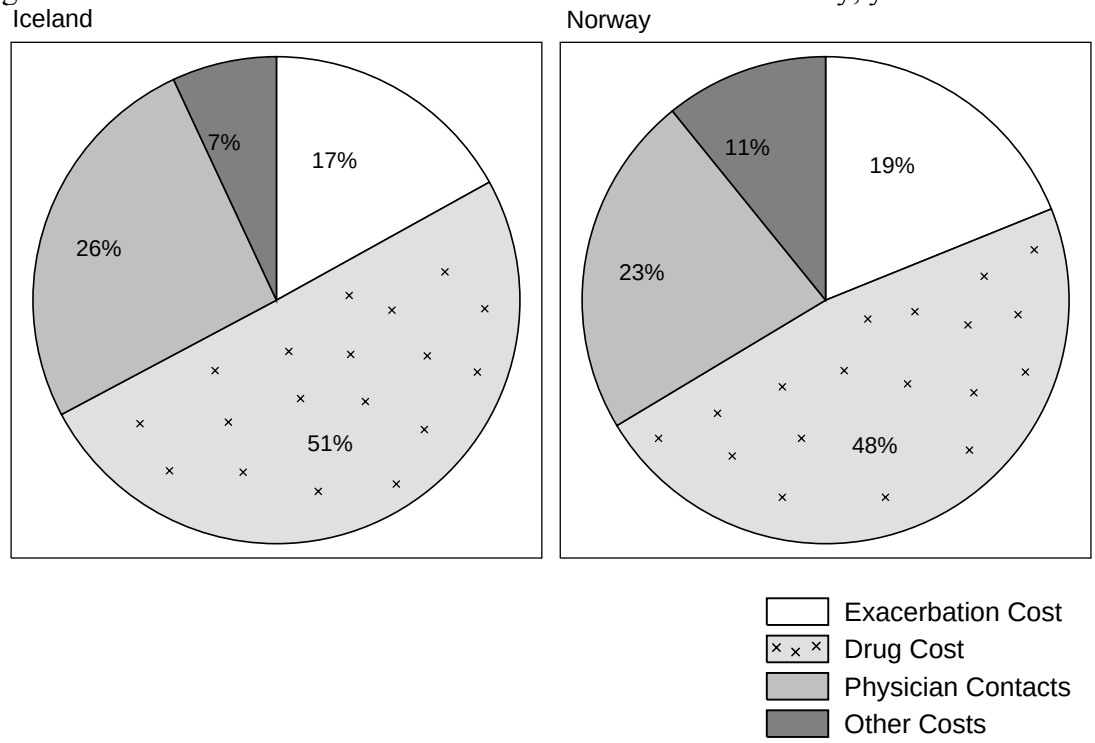

Figure 2: Modeled COPD prevalence in Iceland from year 2005 to year 2025, subjects 40 years and older

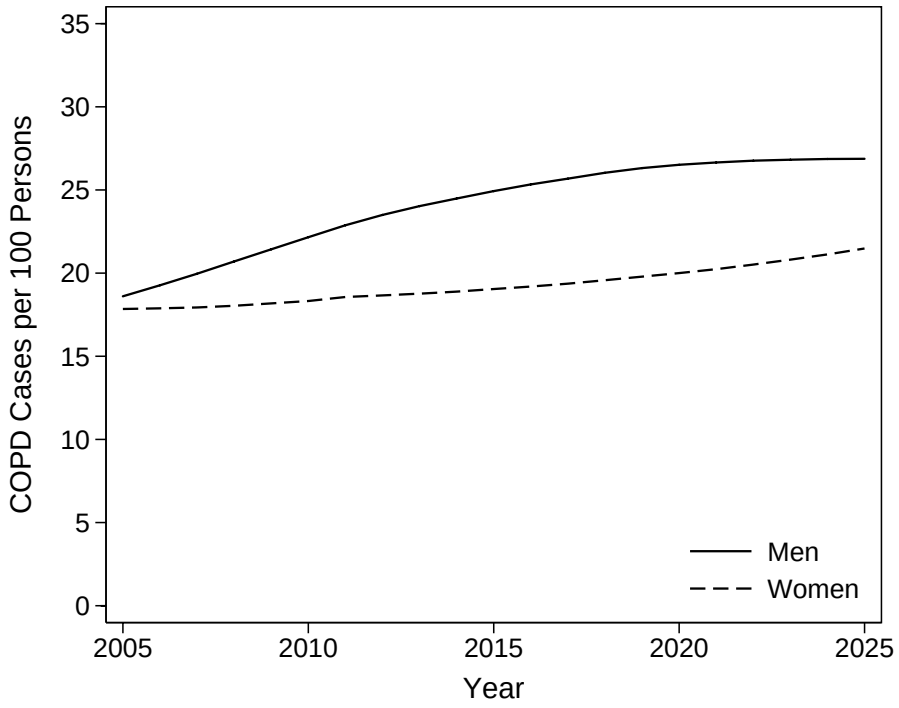

Figure 3: Modeled COPD prevalence in Norway from year 2005 to year 2025, subjects 40 years and older