

The economic burden of lung disease in Europe. Online supplement.

1. Introduction

A bottom-up prevalence-based costing approach was used to estimate the economic burden of lung disease, using a methodology loosely based on a study by Sobocki *et al.* [1]. Our analysis covers the 28 countries of the European Union.

A literature search was carried out to identify suitable published cost estimates (see below). We included direct costs of outpatient care, inpatient care and drugs, and indirect costs of lost production due to absence from work and early retirement, in so far as such data were available in the literature. Indirect costs were estimated using the Human Capital Approach [2]. These cost categories were chosen to include a societal cost perspective.

The year and local currency (*e.g.* year 2001 Swedish Crowns) of estimates in each publication was determined. The identified cost estimates in the literature were converted to year 2011 euro, and adjusted for differences in purchasing power, in order to be comparable. All cost data in the Economic Burden chapter are presented as at year 2011 in euros according to Belgian purchasing power. This was a methodological choice made by the European Respiratory Society.

Typically, cost estimates such that they could be used together in our analysis were found for only a few of the 28 countries of our scope. Originally, Norway and Switzerland were included in our scope (hence their inclusion in the literature search), but these were later excluded from our estimates of the total burden for the sake of consistency in the White Book, although literature findings from these two countries were still retained and used as input data in the analysis. It was necessary to take different approaches for different diseases in order to predict the total costs in the 28 countries. This governed which type of cost estimates were extracted from the literature (see below).

2. Systematic literature search

A structured literature search of PubMed was performed on 23 January 2012 to identify studies estimating the cost of lung diseases in European countries (table 1). The literature search identified 2204 articles.

Titles and abstracts of all identified articles were screened for possible full-text retrieval based on the following inclusion criteria: a) studies of the cost of 10 pulmonary diseases, including asthma, bronchiectasis, chronic obstructive pulmonary disease (COPD), cystic fibrosis, lung cancer, obstructive sleep apnoea (OSA), pneumonia, pulmonary fibrosis, pulmonary vascular disease, and tuberculosis; b) studies performed in a European setting defined according to the World Health Organization [3]; c) original research articles

(reviews, comments, and letters were excluded). The following exclusion criteria were applied: a) cost studies based on clinical trials; b) studies of the cost of specific types of treatment; c) economic evaluations; and d) studies without an abstract in English.

This left 169 articles in which the costs of lung diseases in European countries were presented. A brief review of full-text articles led to the exclusion of 50 articles because they did not fulfil the inclusion criteria, or because there were other and better articles included that provided the same information. In total, 119 articles were included in the study, which were eligible for obtaining cost-per-patient estimates suitable for our analytic approach. In addition, we included a number of articles published after the literature review was carried out, or which were encountered and found to be potentially relevant.

Initially, the geographical scope of our study was the whole of Europe, but findings were scarce in many countries. A decision was therefore taken to use a more narrow scope of the 27 EU countries (at the time) plus Croatia, Norway, and Switzerland. Furthermore, the analysis was limited to include asthma, COPD, cystic fibrosis, lung cancer, OSA, pneumonia, and tuberculosis, because insufficient literature findings were made for the remaining medical conditions.

3. Economic models

Estimates of annual costs per patient were combined with prevalence data in asthma, COPD, OSA and cystic fibrosis. In asthma and COPD, the estimates of annual costs per patient by cost category were subjected to regression analysis, in order to predict the annual cost per patient by degree of disease severity. Asthma severity was graded according to GINA levels (intermittent, mild persistent, moderate persistent and severe persistent), and COPD severity was graded according to GOLD stages (mild, moderate, severe and very severe). The regression analysis further controlled for patient enrolment in primary care, and for patient enrolment with a specialist. The fitted regression models are presented in the Appendix below. The regression analyses were used to predict the annual cost per patient by severity.

In the case of lung cancer, the cost per patient from diagnosis to death was combined with annual incidence data, and in the case of tuberculosis, the cost per treated patient was combined with annual incidence data. The identified estimates were used separately to obtain a range of the predicted total costs.

For pneumonia, the cost of a 24-hour inpatient stays in Spain and Germany were used to predict inpatient costs, using total annual number of bed-days related to pneumonia for each country.

The sources from which the cost estimates were taken are presented in the White Book.

Literature findings were not made regarding all cost categories in all countries. Extracted costs, or predicted costs in the case of asthma and COPD, were used to impute missing cost categories where it was possible.

3.1 Adjustment for average income level.

The estimated costs in each country were adjusted according to the relative income level of that country. We used $Average\ income_c$ = gross net income per capita [4], in country c , and M = the Maximum of $Average\ income_c$ among the 28 countries considered, to derive the relative income in country c as $R_c = Average\ income_c / M$.

3.2 Aggregated costs per country.

The aggregation of costs into a grand total for the 28 countries was undertaken, for one medical condition at a time, by adding up its contributions in each country as illustrated in table 2. Depending on medical condition, four different approaches were used, described as follows. When using approach (a), some countries did not provide detailed enough data, and their contributions were derived using approach (b) instead.

(a) Prevalence approach with regards to disease severity (Asthma, COPD):

The cost in a country for a specific disease was estimated as the annual cost per patient, by disease severity, multiplied by the number of patients in the country with that disease severity, and finally adjusted for the average income level.

*Cost in country_c = R_c * (Annual cost per mild disease patient * Number of mild disease patients + Annual cost per moderate disease patient * Number of moderate disease patients + Annual cost per severe disease patient * Number of severe disease patients + Annual cost per very severe disease patient * Number of very severe disease patients)*

(b) Prevalence approach without regards to disease severity (Cystic Fibrosis and OSA):

Performed as above, but not subdivided by disease stage or degree of severity.

*Cost in country_c = R_c * (Annual cost per patient * Number of patients)*

(c) Incidence approach (Lung cancer, Tuberculosis)

The cost per patient in lung cancer was defined as the cost from diagnosis till death (or end of follow-up in the studies). In tuberculosis it was defined as the cost per patient from when treatment is initialised until it is completed (unless the patient is lost to follow-up).

*Cost in country_c = R_c * (Cost per patient * Number of new patients per year)*

(d) Number of bed-days approach (Pneumonia)

This approach only estimates inpatient costs. Furthermore, the same cost per 24-hour stay was used for all countries.

*Cost in country_c = R_c * (Total annual number of bed-days related to pneumonia * ...)*

Cost per 24 hour stay)

3.3 Final notes on aggregated costs

Not all cost categories were estimated for all medical conditions (table 3), as this depended on literature findings. Furthermore the analytic approach for pneumonia resulted in inpatient costs only.

Table 1: PubMed search criteria.

<p>(("cost"[Title/Abstract] OR "economic burden"[Title/Abstract]) NOT ("cost-effectiveness"[Title/Abstract] OR "cost-benefit"[Title/Abstract] OR "cost-utility"[Title/Abstract])) AND ("Asthma"[Mesh] OR "Bronchiectasis"[Mesh] OR "Pulmonary Disease, Chronic Obstructive"[Mesh] OR "Cystic Fibrosis"[Mesh] OR "Lung Neoplasms"[Mesh] OR "Sleep Apnea, Obstructive"[Mesh] OR "Pneumonia"[Mesh] OR "Pulmonary Fibrosis"[Mesh] OR "Tuberculosis"[Mesh] OR "Pulmonary Embolism"[Mesh] OR "Hypertension, Pulmonary"[Mesh]) NOT "Americas"[Mesh] AND ("2002/01/26"[PDat] : "2012/01/23"[PDat])</p>
<p>Comments: [Title/Abstract] means that the search term should be included in the title or article to be included. [Mesh] refers to Medical Subject Headings which arranges medical terms in a hierarchy so that subgroups and medical terms with a similarity of meaning are automatically searched for.</p>

Table 2: Model for aggregation of the contributions from the countries.

Country	Cost in country	Relative income	Contribution
1	Cost ₁	R ₁	Cost ₁ * R ₁
2	Cost ₂	R ₂	Cost ₂ * R ₂
...
n	Cost _n	R _n	Cost _n * R _n
Total	---	---	Total of above

Table 3: Cost categories included (X) in the estimates of economic burden in 28 European countries.

Medical condition	Direct costs			Indirect costs		
	Inpatient	Outpatient	Drugs	Absence from work	Early retirement	Premature death
Asthma	X	X	X	X	X	-
COPD	X	X	X	X	X	-
Cystic Fibrosis	X	X	X	-	-	-
Lung cancer	X	X	X	-	-	X
OSA	X	X	X	X	-	-
Pneumonia	X	-	-	-	-	-
Tuberculosis	X	X	X	X	-	-

COPD: chronic obstructive pulmonary disease; OSA: obstructive sleep apnoea.

4. Disability adjusted life year (DALY) estimates

DALY estimates are published for the WHO European region rather than for the European Union, so it was necessary to adjust these figures to make estimates for the EU. As disease levels vary considerably for some diseases between EU and non-EU countries in the WHO European region, it was necessary to adjust more precisely than is possible simply by relative population size. The WHO gives DALY values for each disease for three different sub-groups of the WHO European region for 2004, with most of the EU falling into subgroup A. We have weighted the DALYs in each subgroup by the EU population in that group and summed to obtain the best estimate of DALYs for each disease separately for 2004. We then estimated this as a proportion of the DALYs given for each disease for WHO Europe, and assuming that this proportion is reasonably constant between 2004 and 2008, have applied each ratio to the 2008 DALY figure for each disease.

This made little difference from the results of a simple population adjustment for lung cancer and COPD, or for asthma or otitis media, but gave a greatly lower estimate for TB and upper and lower respiratory disease, as these diseases were much more prevalent in non-EU WHO European region countries.

Set out below is the estimate for TB.

		subgroup A	subgroup B	subgroup C	Total
1. Population million	2004	422.026	223.210	238.074	878.085
2. Population in EU	2004	398.444	70.387	16.068	
3. EU/WHO pop 2/1	2004	.944	.315	.067	
4. WHO DALYS million	2004	.070	.622	2.167	2.859
5. Est of EU DALYs 3x4	2004	.066	.195	.1452	.4062

EU DALYs are therefore 14.2% ($0.4062 / 2.859$) of WHO DALYs for 2004

WHO DALYs for 2008 are given as 1.7 million

Therefore by proportion EU DALYs for 2008 should be about 0.241 million or 241 000.

Appendix: Summary of regression models for annual cost per patient

A1. COPD.

Variable	Explanation
c_med	Annual cost per patient for medicine.
c_hosp	Annual cost per patient for inpatient stays.
c_outp	Annual cost per patient for outpatient visits (includes all other direct costs).
G1	Proportion of patients in GOLD stage I.
G2	Proportion of patients in GOLD stage II.
G3	Proportion of patients in GOLD stage III.
G4	Proportion of patients in GOLD stage IV.
primary	Indicator of patient enrolment in primary care.
special	Indicator of patient enrolment in specialist care / lung clinic.

Call:

```
lm(formula = c_med ~ G1 + G2 + G3 + G4 + special + primary - 1, data = cpytab.COPD)
```

Residuals:

Min	1Q	Median	3Q	Max
-686.01	-316.06	-83.15	164.40	964.93

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)	
G1	806.3	584.0	1.380	0.19484	
G2	1169.5	502.6	2.327	0.04009	*
G3	1597.6	502.6	3.179	0.00878	**
G4	2113.0	502.6	4.204	0.00148	**
special	294.3	365.6	0.805	0.43789	
primary	-1001.1	332.6	-3.010	0.01187	*

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 551.6 on 11 degrees of freedom

Multiple R-squared: 0.8745, Adjusted R-squared: 0.806

F-statistic: 12.77 on 6 and 11 DF, p-value: 0.000215

Call:

```
lm(formula = c_hosp ~ G1 + G2 + G3 + G4 + special + primary - 1, data = cpytab.COPD)
```

Residuals:

Min	1Q	Median	3Q	Max
-1114.1	-198.7	-138.7	140.9	1813.0

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)	
G1	261.6	746.6	0.350	0.732641	
G2	818.0	642.4	1.273	0.229173	
G3	1524.7	642.4	2.373	0.036935	*
G4	3474.1	642.4	5.408	0.000214	***
special	199.2	467.4	0.426	0.678131	
primary	-577.5	425.2	-1.358	0.201580	

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 705.1 on 11 degrees of freedom

Multiple R-squared: 0.9169, Adjusted R-squared: 0.8716

F-statistic: 20.23 on 6 and 11 DF, p-value: 2.404e-05

Call:

```
lm(formula = c_outp ~ G1 + G2 + G3 + G4 + special + primary -  
1, data = cpytab.COPD)
```

Residuals:

Min	1Q	Median	3Q	Max
-934.4	-470.9	109.6	315.5	1367.9

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)	
G1	579.4	719.4	0.805	0.43767	
G2	817.4	619.1	1.320	0.21352	
G3	1222.5	619.1	1.975	0.07394	.
G4	2040.1	619.1	3.295	0.00714	**
special	461.5	450.3	1.025	0.32749	
primary	-602.1	409.7	-1.470	0.16968	

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 679.4 on 11 degrees of freedom

Multiple R-squared: 0.8561, Adjusted R-squared: 0.7777

F-statistic: 10.91 on 6 and 11 DF, p-value: 0.0004398

A2. Asthma.

Variable	Explanation
c_med	Annual cost per patient for medicine.
c_inp	Annual cost per patient for inpatient stays.
c_outp	Annual cost per patient for outpatient visits (includes all other direct costs).
imi	Proportion of patients with intermittent Asthma.
mip	Proportion of patients with mild persistent Asthma.
mos	Proportion of patients with moderate persistent Asthma.
sep	Proportion of patients with severe persistent Asthma.
primary	Indicator of patient enrolment in primary care.
special	Indicator of patient enrolment in specialist care / lung clinic.

Call:

```
lm(formula = c_med ~ imi + mip + mop + sep + primary + special
- 1, data = cpytab.Asthma)
```

Residuals:

Min	1Q	Median	3Q	Max
-423.22	-110.21	46.55	103.37	441.92

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)	
imi	186.4	222.6	0.837	0.418682	
mip	467.3	220.2	2.123	0.055277	.
mop	665.3	219.9	.026	0.010543	*
sep	1214.5	218.8	5.551	0.000126	***
primary	-281.4	140.6	-2.001	0.068573	.
special	254.6	167.9	1.516	0.155393	

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 259.5 on 12 degrees of freedom

Multiple R-squared: 0.9319, Adjusted R-squared: 0.8979

F-statistic: 27.38 on 6 and 12 DF, p-value: 2.469e-06

Call:

```
lm(formula = c_inp ~ imi + mip + mop + sep + primary + special
- 1, data = cpytab.Asthma)
```

Residuals:

Min	1Q	Median	3Q	Max
-327.7	-105.6	32.4	133.8	204.5

Coefficients:

Estimate	Std. Error	t value	Pr(> t)
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imi	-191.32	201.35	-0.950	0.3698	
mip	-52.69	200.39	-0.263	0.7992	
mop	30.44	200.11	0.152	0.8829	
sep	388.17	199.09	1.950	0.0870	.
primary	304.60	136.51	2.231	0.0562	.
special	115.60	136.51	0.847	0.4217	

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 210.8 on 8 degrees of freedom
(4 observations deleted due to missingness)

Multiple R-squared: 0.8667, Adjusted R-squared: 0.7668

F-statistic: 8.672 on 6 and 8 DF, p-value: 0.003777

Call:

```
lm(formula = c_outp ~ imi + mip + mop + sep + primary +
special - 1, data = cpytab.Asthma)
```

Residuals:

Min	1Q	median	3Q	Max
-310.12	-107.40	12.97	92.51	376.73

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)	
imi	-236.83	172.85	-1.370	0.1957	
mip	-84.38	170.97	-0.494	0.6305	
mop	-38.77	170.73	-0.227	0.8242	
sep	343.68	169.90	2.023	0.0659	.
primary	108.95	109.21	0.998	0.3382	
special	361.83	130.40	2.775	0.0168	*

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 201.5 on 12 degrees of freedom

Multiple R-squared: 0.8599, Adjusted R-squared: 0.7898

F-statistic: 12.27 on 6 and 12 DF, p-value: 0.0001642

References

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