

Poor Control Increases the Economic Cost of Asthma

A Multicentre Population-Based Study

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Key Words

Asthma epidemiology · Asthma cost · Asthma control · Cost variation, determinants of

Abstract

Background/Aims: Up to now, few cost-of-illness (COI) studies have estimated the cost of adult asthma at an individual level on general population samples. We sought to evaluate the cost of current asthma from the societal perspective in young Italian adults and the determinants of cost variation.

Methods: In 2000, a COI study was carried out in the frame of the Italian Study on Asthma in Young Adults on 527 current asthmatics (20–44 years) screened out of 15,591 subjects from the general population in seven centres. Detailed

information about direct medical expenditures (DMEs) and indirect costs due to asthma was collected at an individual level over the past 12 months. **Results:** The mean annual cost per patient was EUR 741 (95% CI: 599–884). DMEs represented 42.8% of the total cost, whereas the remaining 57.2% was indirect costs. The largest component of DMEs was medication costs (47.3%; 23.0% was due to hospitalization). The mean annual cost per patient ranged from EUR 379 (95% CI: 216–541) for well-controlled asthmatics to EUR 1,341 (95% CI: 978–1,706) for poorly controlled cases that accounted for 46.2% of the total cost. Poor control, coexisting chronic cough and phlegm, and low socio-economic status were significantly associated with high DMEs and indirect costs. **Conclusions:** In Italy, asthma-related costs were substantial even in unselected patients and were largely driven by indirect costs. Since about half of the total cost was due to a limited proportion of poorly controlled asthmatics, interventions aimed at these high-cost patients could reduce the economic burden of the disease.

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Introduction

Bronchial asthma, a common chronic disease [1, 2], is an important social problem in industrialized countries. Moreover, the economic cost of the disease is high [3], both because bronchial asthma affects a considerable number of patients and because it causes productivity losses concerning young subjects, premature deaths, disability and hospital admissions, as well as requiring daily drug treatment to control its exacerbation.

The economic cost of asthma is estimated through cost-of-illness (COI) analyses, which allow an evaluation of the impact of the disease ranging from clinical to socio-economic aspects, by assessing health care expenditures, productivity losses and leisure time forgone because of the illness. Over the past 20 years, there have been several COI studies on the economic impact of asthma in different industrialized countries [4–17]. However, many of these studies derived their cost estimates from official statistics or from clinically selected samples. Consequently, there is a need for COI analyses of bronchial asthma at an individual level in general population samples to get a more realistic estimate of the economic cost of the disease.

The aim of this study was (1) to estimate the total cost of current asthma from the societal perspective [18] in young Italian adults (20–44 years), (2) to assess the relative contribution of different cost components to the total cost, and (3) to evaluate the determinants of cost variation, by valuing all the cost components at an individual level on nationwide general population samples.

Materials and Methods

Study Design

This analysis is a cost identification study [18] on the economic impact of current asthma in Italy, which was performed in the frame of the Italian Study on Asthma in Young Adults (ISAYA) [19, 20].

The ISAYA was a multicentre cross-sectional survey on respiratory health in the young adult general population, carried out between 1998 and 2000 in nine centres located throughout Italy. Each centre selected an up-to-date sampling frame of the residents living in the target area, from which a random sample of approximately 3,000 people aged 20–44 years (men/women ratio = 1) was chosen, using the same design as the European Community Respiratory Health Survey (ECRHS) – stage I [21, 22]. The protocol of the study was approved by the locally appointed Ethics Committees, and the individual information was collected in compliance with the Italian law (No. 675/1996) concerning the protection of privacy regarding individual health data.

A two-page screening questionnaire, which had been previously tested in a pilot study [23], was mailed to each subject up to 3 times in the case of non-response, and eventually given over the phone to the remaining non-responders. The first page contained validated questions (mainly taken from the ECRHS questionnaires) on the presence of asthma and asthma-like symptoms, frequency of asthma attacks, age at onset and remission of asthma, doctor's diagnosis of asthma, chronic cough and phlegm, and smoking habits. The second page collected information about direct medical expenditures [DMEs; type and frequency of doctor visits and laboratory tests, pharmacological treatment, frequency of emergency department (ED) visits and hospital admissions per type of ward] and indirect costs (number of lost working days and number of days with limited daily life activities, such as looking after the children, housework, studying) due to the disease over the past 12 months.

The COI analysis involved the 527 physician-diagnosed current asthmatics screened out of the 15,591 responders to the ISAYA questionnaire in seven centres (Ferrara, Pavia, Pisa, Sassari, Sassuolo, Turin and Verona; overall response rate: 75.8%) [19], who gave a positive answer to the question on ever having had asthma confirmed by a doctor and a positive answer to either the question on currently taking medicines for asthma or having had an asthma attack over the past 12 months.

In the year 2000, all these asthmatics gave further information over the phone on pharmacological treatment through a questionnaire specifically designed to measure drug use (overall response rate: 75.9%) (available at <http://biometria.univr.it/isaya/medication.doc>). Each subject was asked to list all the inhaled and oral medicines taken over the past 3 months for respiratory problems and to specify for each medication: if used continuously – the number of doses per day; if used in short courses – the number of doses per day, the number of days per course and the number of courses; if used when needed – the number of doses per month.

All costs were estimated from the societal perspective [18] and were calculated in euros on the basis of rates, wages and prices in 2000 obtained from Italian official publications. The evaluation of costs was done using a bottom-up approach, that is, by multiplying the number of times a patient resorted to health care services, the number of doses of each drug consumed, the number of lost working days and the number of days with limited (not work related) activities reported by each subject, by a proper monetary unit value (table 1).

Statistical Analysis

The monetary value of each cost component was expressed as the mean annual cost per patient with 95% confidence interval (CI). Confidence limits were computed by the bias-corrected bootstrap method when approximated formulas were not applicable [25].

The economic cost of the disease was also evaluated according to the level of disease control. For each patient a current symptom score was devised as a linear combination of five asthma-like symptoms (wheezing, wheezing with breathlessness, wheezing without having a cold, waking with tightness in the chest and waking with shortness of breath) and the number of asthma attacks (0; 1–3; 4–10; >10) reported over the past 12 months through a multiple correspondence analysis [20, 26]. The individual scores were computed by assigning the weights obtained through the multiple correspondence analysis to the symptoms reported by each patient

Table 1. Monetary unit value of each cost component considered in the COI analysis

Cost component	Source	Monetary unit value, EUR
Doctor visits	INHS rates	12.91 (general practitioner) 20.66 (chest physician, allergy/internal medicine specialist or ENT doctor)
Laboratory tests	INHS rates	37.18 (baseline spirometry and bronchodilator challenge) 23.24 (skin prick test for allergy) 5.78 (blood sampling and haemochrome) 107.47 (blood sampling, haemochrome and specific IgE measurement) 15.49 (X-rays)
Pharmacological treatment ^a	Market price of a single dose of each drug (Italian Directory of Medicines and Manufacturers)	
ED visits	INHS rates for treatment received during an emergency ^b	100.19
Hospital admissions	Italian DRG rates	1,863.89 (general and internal medicine wards) ^c 2,374.15 (intensive care unit) ^d
Productivity losses	Market daily wages ^e (Bank of Italy)	203.72 (manager) 184.14 (entrepreneur and businessman) 120.35 (clerk) 91.60 (blue-collar worker) 29.45 (housewife) ^f
Leisure time forgone	Market hourly wage of part-time help (Italian collective labour agreement of domestic employment)	17.67 (per day) ^g

INHS = Italian National Health Service; DRG = diagnosis-related group.

^a Cost over the past 12 months = (cost over the past 3 months)•4, on the assumption that drug consumption in the 3-month reference period was representative of the entire year.

^b Doctor visit, non-invasive monitoring of oxygen saturation, X-rays, pharmacological treatment (4–8 puffs of inhaled short-acting β_2 -agonist; 2 vials of i.v. cortisone; theophylline), administration of oxygen, arterial blood gas analysis, haemochrome, electrocardiogram and measurement of peak flow.

^c Diagnosis-related group for bronchitis and asthma without complications in adults.

^d Diagnosis-related group for bronchitis and asthma with complications in adults.

^e Earnings assumed to reflect productivity, according to the human capital approach [24].

^f Market hourly wage of part-time help (EUR 5.89), 5 working hours per day assumed.

^g Market hourly wage of part-time help (EUR 5.89) as replacement value, 3 h of limited activities per day assumed.

and were then transformed in order to be non-negative (range: from 0 for subjects with neither asthma-like symptoms nor asthma attacks to 5.175 for subjects with all the symptoms and >10 asthma attacks over the past year). Based on the distribution of the individual scores, current asthmatics were divided into four groups of a decreasing level of disease control, according to the quartiles (first quartile: 'good control'; fourth quartile: 'poor control').

Current asthmatics were defined as having high DMEs or indirect costs if the individual cost was higher than the third quartile of the distribution of direct (EUR 350) and indirect (EUR 0) costs, respectively. Two-level logistic regression models [27] with level 1 units (subjects) nested into level 2 units (ISAYA centres) were used to evaluate the relationship between the risk of having

high DMEs or indirect costs and the following potential predictors: gender, age, socio-economic status (divided into four classes on the basis of current occupation: manager, entrepreneur, businessman, clerk; blue-collar worker; unemployed person; retired person, student, housewife), smoking habits (non-smoker; past smoker; current smoker), level of disease control (quartiles of the current symptom score) and coexisting chronic cough and phlegm (having had cough and phlegm on most days for as much as 3 months per year and for at least 2 successive years). Both models had a random intercept term at level 2 and all the predictor variables as fixed effects.

The statistical analysis was performed using STATA software, release 8.0 (StataCorp, College Station, Tex., USA).

Table 2. Main characteristics of the 527 physician-diagnosed current asthmatics who participated in the COI study, according to gender

	Men (n = 255)	Women (n = 272)	Total (n = 527)	p value ^a
Mean age (SD), years	31.3 (7.1)	33.0 (7.1)	32.2 (7.2)	0.006
Socio-economic status, %				<0.001
Managers, entrepreneurs, businessmen, clerks	51.8	55.9	53.9	
Blue-collar workers	24.7	10.6	17.5	
Unemployed persons	5.1	4.8	4.9	
Retired persons, students, housewives	18.4	28.7	23.7	
Smoking habits, %				0.43
Non-smokers	45.5	51.1	48.4	
Past smokers	18.8	17.4	18.1	
Current smokers	35.7	31.5	33.5	
Age at onset, %				0.006
<10 years	42.5	30.6	36.3	
10–19 years	29.2	29.0	29.1	
≥ 20 years	28.3	40.4	34.6	
Mean asthma duration (SD), years	17.8 (10.4)	15.9 (10.7)	16.8 (10.6)	0.17 ^b
Number of asthma attacks over the past 12 months, %				0.51
0	16.3	12.6	14.4	
1–3	55.4	61.1	58.3	
4–10	20.8	18.2	19.5	
>10	7.5	8.1	7.8	
Asthma-like symptoms over the past 12 months, %				
No symptoms	14.6	14.4	14.5	0.97
Diurnal symptoms ^c	79.1	79.3	79.2	0.95
Nocturnal symptoms ^d	51.2	64.4	58.0	0.002
Chronic cough and phlegm, %	28.4	38.3	33.5	0.016

^a p values obtained through two-sample t test and χ^2 test.

^b p value obtained adjusting for the effect of age at onset.

^c Diurnal: wheezing and/or wheezing with breathlessness and/or wheezing without having a cold.

^d Nocturnal: waking with tightness in the chest and/or waking with shortness of breath.

Results

Of the 527 physician-diagnosed current asthmatics who participated in the COI study, 36.3% had developed asthma early in childhood (<10 years) while 34.6% in adulthood (≥20 years) (table 2); the average duration of the disease was 16.8 years. Only 3.8% of our patients were symptom-free and did not report asthma attacks over the past 12 months. Women had a statistically significant later onset, a higher prevalence of nocturnal symptoms, a higher prevalence of chronic cough and phlegm, and a different socio-economic status than men.

In 2000, the estimated mean annual cost per young adult patient (20–44 years) was EUR 741 (95% CI: EUR

599–884). DMEs represented 42.8% of the mean annual cost per patient in Italy (EUR 317, 95% CI: EUR 258–376), whereas the remaining 57.2% (EUR 424, 95% CI: EUR 307–542) was due to productivity losses and leisure time forgone.

Ninety percent of the asthmatics participating in the study had various costs due to the disease over the past 12 months: 64.4% of patients had only direct costs, 1.0% only indirect costs and 24.6% had both direct and indirect costs.

DMEs mainly depended on pharmacological treatment, which amounted to 47.3% of the mean annual direct costs per subject (EUR 150, 95% CI: EUR 113–187) and, to a lesser extent, on doctor visits/laboratory tests

Table 3. Components of the total cost of current asthma in the year 2000

Direct costs	Number of users ^a	Total number of interventions	Mean number of interventions per user	Mean number of interventions per patient ^c	Estimated mean annual cost per patient (95% CI) EUR
Doctor visits:	275 (54.7%)	1,145	4.2	2.3	37 (29–45)
General practitioner	210 (41.9%)	681	3.2	1.4	
Specialist	164 (33.4%)	464	2.8	0.9	
Laboratory tests:	207 (40.6%)	857	4.1	1.7	57 (48–67)
Spirometry	141 (27.6%)	222	1.6	0.4	
Tests for allergy	139 (27.3%)	239	1.7	0.5	
Blood tests	112 (22.0%)	219	2.0	0.4	
X-rays	89 (17.5%)	177	2.0	0.3	
Pharmacological treatment	446 (86.4%)	–	–	–	150 (113–187)
ED visits	48 (9.2%)	76	1.6	0.1	15 (9–20)
Hospital admissions	15 (2.9%)	16	1.1	0.03	58 (28–88)
Indirect costs	Number of patients who lost days ^b	Total number of days	Mean number of days per patient who lost days	Mean number of days per patient ^c	Estimated mean annual cost per patient (95% CI) EUR
Lost working days	81 (15.8%)	2,082	25.7	4.1	266 (167–366)
Days with limited activities	79 (15.5%)	4,559	57.7	9.0	158 (107–210)

^a User: physician-diagnosed current asthmatic with at least one intervention (doctor visit, laboratory test, pharmacological treatment, ED visit, hospital admission) due to asthma.

^b Patient who lost days: physician-diagnosed current asthmatic who lost at least one working day or had at least one day with limited (not work-related) activities due to asthma.

^c Patient: physician-diagnosed current asthmatic.

(29.7%; EUR 94, 95% CI: EUR 80–109) and ED visits/hospital admissions (23.0%; EUR 73, 95% CI: EUR 39–107) (table 3). In fact, 86.4% of our asthmatics reported currently using medication for their asthma, whereas 54.7% reported at least one doctor visit, 40.6% at least one laboratory test (spirometry, skin and blood tests for allergy, X-rays) and 9.6% at least one hospital admission and/or one ED visit over the past 12 months. About half (48.6%) of the total cost due to pharmacological treatment derived from the use of inhaled corticosteroids (alone or in combination), whereas 23.5 and 2.2% from the use of long-acting and short-acting β_2 -agonists, respectively (table 4).

Productivity losses, whose mean annual cost per patient was equal to EUR 266 (95% CI: EUR 167–366), represented 62.7% of the indirect costs generated by the disease (table 3); the remaining 37.3% depended on the limited (not work related) daily activities caused by the disease (EUR 158; 95% CI: EUR 107–210). Approximately 1 current asthmatic out of 4 (24.7%) reported losing at

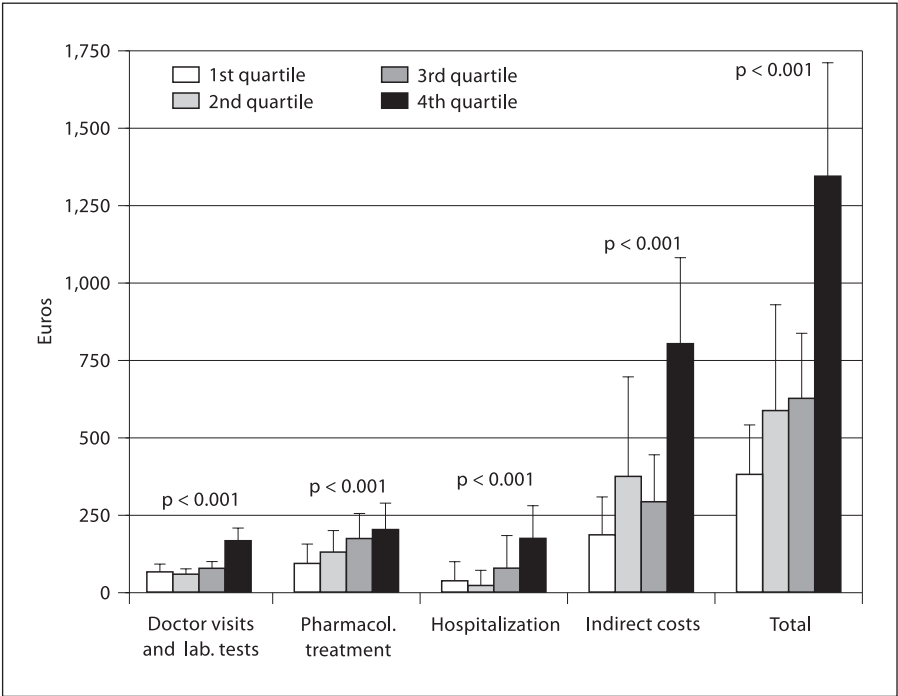
least one working day and/or having at least one impaired day a year due to the disease.

The mean annual cost per patient increased as the level of disease control decreased (non-parametric test for trend: $p < 0.001$), ranging from EUR 379 (95% CI: EUR 216–541) for patients with a good control of symptoms (first quartile of the current symptom score) to EUR 1,341 (95% CI: EUR 978–1,706) for patients with a poor control of the disease (fourth quartile) (fig. 1). The percentage contribution of the various components of direct costs differed according to the level of disease control: current asthmatics with a poor control were characterized by the lowest percentage of direct costs due to pharmacological treatment (37.5%) and by the highest percentage of direct costs due to hospitalization (both ordinary admissions and emergency visits; 31.4%), whereas pharmacological treatment and hospitalization accounted for 48.7 and 18.0% of the direct costs in subjects with a good control of symptoms, respectively.

Table 4. Distribution of the total medication costs over the past 3 months according to the type of drugs

Type of drugs		% of total medication costs
Inhaled corticosteroids	Inhaled corticosteroids	36.2
	β ₂ -agonists + corticosteroids	12.4
Long-acting β ₂ -agonists		23.5
Short-acting β ₂ -agonists	Inhaled β ₂ -agonists	1.9
	Inhaled β ₂ -agonists + anticholinergic agents	0.3
	Oral β ₂ -agonists	0.03
Other drugs	Antileukotrienes	9.1
	Cromones	6.4
	Oral corticosteroids	3.3
	Antihistamines	3.2
	Anticholinergic agents	2.3
	Ketotifen	1.1
	Theophylline	0.3
Total		100.0

Fig. 1. Components of the estimated mean annual cost per patient of current asthma (with 95% confidence limits) in the year 2000 according to the level of disease control, as indicated by the quartiles of the current symptom score (first quartile: ‘good control’; fourth quartile: ‘poor control’). p values refer to non-parametric tests for trend among the quartiles.



Patients with a poorly controlled asthma (25.0% of the subjects in the sample) accounted for 46.2% of the total cost of the disease in Italy. They generated 55.0% of the total cost due to hospitalization, 48.1% of the total indirect costs, 45.1% of the total cost due to doctor visits and laboratory tests, and 33.2% of the total cost due to phar-

macological treatment. In contrast, subjects with a good control of symptoms (25.0% of the subjects in the sample) accounted for 12.4% of the total cost of the disease.

The risk of having high DMEs (EUR >350 per patient in a year) and the risk of incurring indirect costs because of current asthma increased as the level of disease control

Table 5. Mutually adjusted odds ratios (OR)^a for the risk of having high DMEs (EUR >350 vs. ≤350 per patient in a year) and for the risk of having indirect costs (present vs. absent)

	High DMEs		Indirect costs	
	OR	95% CI	OR	95% CI
Gender, female vs. male	1.66*	1.00–2.75	1.40	0.87–2.27
Socio-economic status (vs. manager, entrepreneur, businessman, clerk)				
Blue-collar worker	1.99*	1.01–3.90	2.15*	1.13–4.11
Unemployed person	2.12	0.80–5.59	2.93*	1.15–7.45
Retired person, student, housewife	1.29	0.69–2.42	2.03*	1.12–3.69
Smoking habits (vs. non-smoker)				
Past smoker	1.77	0.92–3.43	0.85	0.45–1.62
Current smoker	0.87	0.50–1.52	0.67	0.39–1.14
Current symptom score (vs. 1st quartile)				
2nd quartile	1.36	0.65–2.87	1.48	0.69–3.17
3rd quartile	1.49	0.71–3.12	2.57*	1.25–5.27
4th quartile	3.61**	1.77–7.36	4.82**	2.36–9.83
Chronic cough and phlegm (vs. absent)				
Present	2.67**	1.63–4.37	1.92*	1.18–3.13

^a The ORs were also adjusted for age and were obtained through two-level logistic regression models.

* $p < 0.05$; ** $p < 0.001$.

decreased, and resulted significantly higher for poorly controlled subjects as compared to those who were well-controlled (table 5). Asthmatic subjects with coexisting chronic cough and phlegm had a significantly higher risk of having both high DMEs and indirect costs compared to subjects without this symptom. Moreover, the risk of having high DMEs was significantly higher for women as compared to men and for blue-collar workers as compared to managers, entrepreneurs, businessmen and clerks. The latter group of subjects was characterized by the lowest risk of incurring indirect costs because of the disease.

Discussion

To our knowledge, the present study is the first COI analysis that has attempted to estimate the cost of current asthma in Italy in nationwide general population samples of young adult asthmatic subjects encompassing a wide spectrum of disease severity (rather than in clinically selected groups), by assessing all the cost components at an individual level and evaluating the potential determinants of cost variation. Despite the fact that the centres participating in the ISAYA were selected on a voluntary basis, their different geographical locations and the relatively high response rates obtained (75.8%

on average in the seven centres) should guarantee that the patients studied represent current asthmatics in Italy.

The main findings of our study are that (1) asthma-related costs were substantial even in unselected patients and were largely driven by indirect costs, (2) pharmacological treatment was the main cost driver of DMEs, and (3) failure to control symptoms was a major determinant of the economic cost of current asthma in Italy.

We found that the mean annual cost per patient was EUR 741. Our estimate is consistent with the findings of previous COI studies [28], even if the comparability of results from different countries could be limited because of differences in health care systems, definition of costs, data sources, time periods or reference populations. Moreover, our estimate must be interpreted as the annual cost for the 'average patient', independently from the duration of his/her disease. In fact, new cases are expected to be more expensive in the first few months of their illness than those with an earlier onset.

When extrapolated to the whole young Italian adult population, the total cost of the disease would have been about EUR 797 million (the prevalence of current asthma being equal to 5.01%) [22], which represents 0.068% of the Italian gross domestic product in 2000. If the cost of premature mortality due to asthma (not considered in our analysis) had also been included, the total cost of the

disease would have increased by a non-negligible amount [6, 9, 11, 12].

Indirect costs accounted for the largest part of the total cost (57.2%) and were mainly due to productivity losses, pointing out that asthma is a substantial burden for society. Moreover, high indirect costs highlight the great impact of asthma on individuals and families, because these costs also reflect the functioning and quality of life of patients in the presence of the disease [24]. Therefore, our results confirm that asthma is to a large extent uncontrolled in Italy [20, 29], since indirect costs only occur when the disease has become sufficiently intrusive to interfere with a patient's lifestyle [3].

As shown in recent economic evaluations [30], pharmacological treatment was the main cost driver of DMEs (47.3%) and was largely due to the use of inhaled corticosteroids, which are considered the first-line therapy for asthma by the Global Initiative for Asthma (GINA) guidelines [31]. However, our estimate of drug costs was lower than those obtained in other European countries (France and Spain) [13, 17], probably because of the underusage of inhaled anti-inflammatory medication in Italy [17, 29, 32]. Instead, hospitalization accounted for only 23.0% of direct costs. An inverse relationship has been reported between costs due to hospitalization and costs due to medication [24], suggesting that good control achieved by adequate therapy could prevent hospitalization [33]. Accordingly, we found that patients with poorly controlled asthma were characterized by a relatively lower expenditure for medication and a relatively higher expenditure for hospital services than better controlled patients.

Failure to control symptoms increased the mean annual cost per patient by more than 3-fold (from EUR 379 for well-controlled cases to EUR 1,341 for poorly controlled cases), which suggests that poor control is a major determinant of the economic burden of the disease [3, 7, 8]. The negative association between the level of control and the economic cost of the disease was confirmed by a multivariate analysis, after adjusting for potential confounders. Moreover, poorly controlled asthmatics, who represent a minority of patients, accounted for about half of the total cost, in accordance with the results of other studies [8, 10]. This points out that the economic burden of asthma could be reduced by proper management of a restricted group of high-cost patients.

The presence of chronic cough and phlegm was significantly associated with both high DMEs and indirect costs. This symptom is often a sign that asthma is not properly controlled, as found in a previous analysis of the

ISAYA data [20]. Alternatively, the presence of chronic cough and phlegm, which is now considered the 'stage 0' of chronic obstructive pulmonary disease when lung function is normal [34], could indicate the most difficult patients to treat, in whom asthma and chronic obstructive pulmonary disease coexist [35].

An increased risk of having high DMEs and of incurring indirect costs was found in patients with a low socioeconomic status, as indicated by their current occupation. This association could be due to factors that affect respiratory health and are more frequent in lower social classes, such as residential and workplace pollutant exposures (environmental inequity) [36]. Moreover, it could also reflect a cumulative life course disadvantage [37].

Finally, our analysis supports the evidence that women have higher DMEs compared to men. In fact, females affected by a chronic disease are probably more concerned about their health than males, and they are therefore more likely to seek medical care more often and have more medicines prescribed [10].

A few caveats should be taken into account when interpreting our results. The cost of the disease has been partially underestimated since some cost components were not assessed due to a lack of data. In particular, we did not consider early mortality due to asthma because of the cross-sectional nature of our study. No information was collected on non-medical direct costs, such as costs for transportation to and from health providers [24], on health-related quality of life and on the adverse impact of the disease on daily work performance (i.e. productivity losses that did not result in lost working days) and on work history (i.e. premature retirement, change of job, change of work duties and reduction of working hours) [38]. In addition, we could not estimate the influence of comorbidities on asthma costs [39]. Moreover, the confidence intervals could be too narrow, since the uncertainty pertaining to the monetary unit values used was not taken into account in the analysis.

It was also impossible to assess the level of asthma control through objective measures [40], such as lung function tests. Instead, we used a subjective measure based on perceived symptoms [20], which may not reflect the actual degree of control [41].

Furthermore, self-reporting could have influenced the accuracy of our estimates, since all the information was collected through a self-administered postal questionnaire and a telephone interview. In fact, it has been reported that patient recall of resource utilization declines over time, that demographic variables and social characteristics may influence recall, and that not all elements of

healthcare consumption are recalled to the same degree [42]. However, the potential of measurement error could have been mainly related to indirect costs and it could have influenced our estimates only to a minor extent, because our study did not involve elderly patients and because the recall period considered in our questionnaires was quite short for drug consumption (3 months) and relatively short for crucial events, such as ED visits and hospitalization (12 months), which tend to be recalled with a greater accuracy.

In conclusion, our results suggest that considerable cost savings could be achieved by improving the level of disease control. Since about half of the total cost was due to a limited proportion of poorly controlled asthmatics, interventions aimed at these high-cost patients could reduce the economic burden of the disease, as well as its morbidity.

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