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The global economic burden of asthma and chronic obstructive pulmonary disease

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SUMMARY

Non-communicable diseases are now the number one cause of disabilities and loss of life expectancy. Among them, chronic respiratory conditions constitute a major class. The burden of chronic respiratory diseases is generally increasing across the globe, and asthma and chronic obstructive pulmonary disease (COPD) are among the main causes of mortality and morbidity. However, the direct and indirect costs of these conditions vary across jurisdictions. This article reports on recent estimates of the costs of asthma and COPD, with

a focus on comparing disease burden across different regions. Overall, there is tremendous variation in per capita annual costs of asthma and COPD. However, the methodology of the cost-of-illness studies is also vastly different, making it difficult to associate differences in reported costs to differences in the true burden of asthma and COPD. Suggestions are provided towards improving the validity and comparability of future studies.

KEY WORDS: asthma; COPD; economic burden

THE MANAGEMENT of chronic diseases is a challenge, both in countries with established economies and in emerging economies.¹ The burden of non-communicable diseases (NCDs) is increasing worldwide, and chronic respiratory diseases play a major role in this growth.² Chronic respiratory diseases, especially asthma and chronic obstructive pulmonary disease (COPD), are among the main drivers of medical costs as well as productivity loss.³ COPD is

one of the most common chronic and disabling diseases and a growing cause of morbidity and mortality. It is currently the fourth leading cause of death worldwide, and the World Health Organization (WHO) predicts that it will become the third leading cause by 2030.³ Asthma is also a major global burden and, because it is more prevalent among younger working age groups, it has a major economic impact due to loss of productivity.⁴

The prevalence of asthma varies significantly throughout the world; according to WHO estimates, the number of asthma patients will increase by 100 million by 2025.⁵ Not only is the prevalence increasing, evidence also suggests that per-patient costs are increasing,⁶ resulting in a significant upward trend in the overall burden of asthma.

Several reviews have been published regarding the costs of asthma and COPD.^{7–9} However, very few studies are recent or have highlighted variations across geographical regions and health care jurisdictions. The evolution of risk factors and disease incidence, the emergence of new health technologies and disease management strategies, and updates in

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guidelines all create a dynamic landscape demanding constant monitoring of the changing burden so that policy, practice and research priorities are kept up to date. The purpose of this narrative review is to summarise the recent evidence on the economic burden of asthma and COPD and to highlight some of the noticeable variations and geographical and temporal trends in the economic burden of asthma and COPD. We focused on the more recent studies published between January 2008 and January 2015, as we and others have previously systematically reviewed the older literature.^{9,10} The detailed characteristics of all included studies are shown in Appendix Table A and the keywords used in the search are given in the Appendix.*

We have summarised the findings in terms of direct costs and their major components, as well as indirect costs, for asthma and COPD. Only studies that were based on well-defined study samples (with or without a comparison/control group) were included. Studies that estimated costs from secondary sources, from model-based predictions, or purely from expert opinion were excluded from this report. Our focus was on the costs per person-year (py). National-level costs were not reported in this study, as they are a direct function of the size of the country's population, and are thus not informative in cross-jurisdiction comparisons. We also compared costs across groups defined by accepted disease classification algorithms. To facilitate comparisons of reported figures, we converted all costs to United State (US) dollars for the year 2014 (\$US). This was performed in two steps: first, local currencies were converted into \$US for the same year based on historical purchasing power parities;¹¹ next, this value was converted to year 2014 values using the historical US consumer price index.¹²

ECONOMIC BURDEN

In general, the quantifiable economic burden of a disease is classified in terms of its direct and indirect costs.¹³ Direct costs are the costs associated with the utilisation of health care resources for diagnosis and treatment of disease such as out-patient clinic visits, emergency department (ED) visits, in-patient care, medications and diagnostic tests. Indirect costs refer to the costs incurred from the cessation or reduction of work productivity due to illness.¹⁴ They can be quantified as school days lost and productivity loss for patients and their care givers. This can be further classified as absenteeism (the withdrawal of labour, i.e., the individual does not attend work due to illness, resulting in a loss of productivity for the individual and potentially for co-workers in the context of

teamwork) or presenteeism (inefficiency of labour due to the impairment, i.e., the individual continues to work despite illness, but underperforms, with an associated significant loss of productivity).¹⁵

Issues in comparative assessment of reports on economic burden of diseases

Attributable vs. excess costs

Cost-of-illness studies reporting on direct costs typically measure either excess or attributable costs.¹⁶ Excess costs are the differences between the costs of the disease and the costs of a comparison population who do not have the disease. Attributable costs are costs that can be attributed directly to the disease (e.g., hospitalisation costs, if the main reason for hospital admission has been the disease of interest). Excess costs properly take into account the burden of comorbid conditions, but need careful analysis that controls for the confounding differences between the diseased and control population (e.g., sex, comorbidity before disease onset). The calculation of attributable costs is less affected by such confounding factors, but requires an inevitably subjective process of designating a particular costs component as being due to the disease or not.¹⁶

Miscellaneous medical and non-medical costs

There are some medical or non-medical expenses that cannot be classified into any of the major components of costs (in-patient, out-patient, medication), which are sometimes referred to as 'other direct costs'. Examples include expenditure on transportation and accommodation for medical care use, or costs associated with home care. As there is no comprehensive definition of this group, we feel they cannot be compared across different studies and they are hence excluded from consideration in this review. However, we acknowledge that the magnitude of these expenses can be large and difficult to ignore. For example, one asthma study reported home health care as the second largest proportion of medical expenditure.¹⁷ Similarly, in a COPD study in Canada, 'other' medical costs such as ambulance services, rehabilitation programmes, medical devices and procedures were the fourth largest component.¹⁸

ASTHMA

We included 18 studies published since 2008: four from Europe,^{19–22} five from the United States,^{17,23–26} three from Canada,^{27–29} one from the Middle-East,^{30,31} four from South-East Asia,^{32–35} and one from Latin America.³⁶ Eleven studies reported on costs of asthma,^{17,19,23,24,27,28,30,32–35} while six studies reported costs across control levels^{19,20,25,29,32,36} and three provided information on costs of asthma exacerbations^{21,22,26}

Table 1 presents the studies on included asthma

* The appendix is available in the online version of this article, at <http://www.ingentaconnect.com/content/ijuatld/ijtltd/2016/00000020/00000001/art00006>

costs. Estimated costs and their components varied between different regions of the world. This variation represents the combined variation in the burden of asthma and the vastly different methodologies used to estimate this burden. An obvious source of difference can be the demographic characteristics of the study population, as some studies included patients from all age groups,^{23,24,27,30,33,34} while others applied age cut-offs.^{17,19,28,32,35} Other aspects of study design are, however, more likely to have generated the differences in estimates. For example, some studies were survey-based,^{17,19,23,24} while others used administrative health data.^{27,28,30–33,35} In general, well-designed survey-based studies, such as those based on the US Medical Expenditure Panel Survey,^{17,23,24} are likely to have a high degree of representativeness and external validity. However, survey-based methods can also suffer from recall bias, which can distort the estimates of the burden, specifically if this bias is preferential (e.g., if individuals who self-report a disease also have a higher rate of recall of resource utilisation), although it has been previously demonstrated that there is good agreement between self-report and administrative data regarding direct costs.³⁷ On the other hand, administrative health data routinely record patient encounters and resource use as they occur, but are limited in scope in terms of cost items. For example, over-the-counter medications are largely absent in such databases. If the data are created to serve the administrative needs of a third-party insurer, out of pocket costs are often not captured (Table 1).

Direct costs

Annual costs varied from less than US\$150/py (Abu Dhabi, United Arab Emirates) to more than US\$3000/py (United States), a 20-fold difference in costs. In general, studies that measured attributable costs^{19,27,28,30–35} estimated lower values than those estimating the excess costs;^{17,23,24} this potentially indicates the role of comorbid conditions that are not fully captured in the former method.³⁸ Another source of difference between the two types of cost estimates could be the inclusion criteria: survey-based studies often relied on self-report of asthma diagnosis, but studies based on administrative health data applied case definitions based on asthma resource use. A potential source of confounding is that a recent record of asthma resource use, often used in studies based on administrative health data, can indicate less well controlled asthma that is consuming higher amounts of health care resources.

In terms of cost components, in North America and Europe, medication was the largest component of direct medical costs in the majority of studies, varying from 68% of total direct costs in Canada to 51% in the United States.^{23,27} During 1999–2002, in 11 European countries the costs of medications ranged

from 45% (Spain) to 84% (Germany) of total direct costs.¹⁹ Some of the recent findings suggest that the costs of medications in the United States and Canada are increasing over time. In British Columbia, Canada, there was a 1.5% increase in medication costs per py between 1996 and 2000,²⁸ with a 2.4% annual growth in costs between 2002 and 2007.²⁷ Likewise, in the United States there was a 49% increase in the costs of medications from 2000 to 2009.²⁴ On the other hand, in the Middle-East and South-East Asia, out-patient costs were responsible for a greater proportion of the total costs.^{30,33,35} This could be due to differences in the unit price of medication and health services across jurisdictions. However, another potential mechanism is the lack of access to asthma medications, particularly the more expensive combination inhalers, which can result in higher rates of poorly controlled asthma, causing frequent visits to care providers.

Another emerging pattern is a trend towards decreasing rates and costs of in-patient care for asthma in North America.^{24,27,28} In British Columbia, Canada, the number of hospitalisations decreased from 1.7 to 1.2 per 100 patients from 1996 to 2000,²⁸ a pattern that remains largely the same in an updated analysis that included data up to 2007.²⁷ The costs of physician visits also decreased by 9.7% per py between 2002 and 2007.²⁷ Between 2000 and 2009 in the United States, in-patient visits decreased by 2.3% per py, but still accounted for 27% of total direct costs.²⁴ In contrast, in the same study, the costs of out-patient visits and ED visits increased by 3% and 8%, respectively, but there were no specific patterns regarding the changes in the costs of ED visits in other studies.

Indirect costs

A previous review demonstrated that, in general, the loss of work/school days accounted for a greater proportion of the costs of asthma than direct costs.⁹ Since the publication of this review, very few additional studies have reported indirect costs of asthma (Table 1). Among those studies, the results varied widely across jurisdictions, with both the lowest and highest estimates coming from the same country (Republic of Korea).^{32,33} This might partly be due to different definitions and methods of measurement across the studies. In the study with the highest estimated indirect costs (US\$1274/py), work/school days lost, early retirement and work absenteeism were all included in the calculation of productivity loss. However, this study only included patients from tertiary hospitals, which creates further potential for an upwardly biased estimate caused by asthma severity.³² Furthermore, only one study mentioned the costs of school days lost separately,²³ and in other studies loss of school/work days made up one component. In that study, school days lost

Table 1 Average direct and indirect costs of asthma (per person-year) and its components (\$US)

Region	Study, country (study period)	Type of costs	Source of data	Target population	Total direct costs	Medication	Out-patient	In-patient	ED visits	Other direct medical/non-medical costs	Indirect costs
North America	Kamble, USA (2004) ¹⁷	Excess costs (adjusted*)	National population-based survey	≥18 years with asthma-related medical events or self-reported asthma	2309 [†]	715	510	364	61	672	
	Barnett, USA (2002–2007) ²³	Excess costs (adjusted ¹)	National population-based survey	All ages with asthma-related medical events or self-reported	3210	1817	792	482	119		426
	Jang, USA (2005–2009) ^{24,†}	Excess costs (adjusted*)	National population-based survey	All ages with asthma-related medical events or self-reported	2164	952	411	584	65	152	
	Bedouch, BC, Canada (2002–2007) ²⁷	Attributable costs	Administrative health data	All ages with asthma-related medical events	140	96	22	22			
Europe	Sadatsafavi, BC, Canada (1996–2000) ²⁸	Attributable costs	Administrative health data	5–55 years with asthma-related medical events	312	198	57	57			
	Accordini, Europe (1999–2002) ^{19,§}	Attributable costs	European Community Respiratory Health Survey	30–54 years with physician diagnosed asthma	693	368	113	141	31		1154
Middle East	Alzaabi, Abu Dhabi, United Arab Emirates (2011) ³⁰	Attributable costs	Administrative health data	All ages with asthma-related medical events	149	46	68	18	6		
South-East Asia	Kim, Republic of Korea (2009–2010) ³²	Attributable costs	Cohort study in tertiary hospitals	>14 years with physician diagnosis and asthma-related medical events	1432						1274
	Kim, Republic of Korea (2004) ³⁴	Attributable costs	National administrative health data	All ages with physician diagnosis	547						
	Lee, Republic of Korea (2008) ³³	Attributable costs	National administrative health data	All ages with asthma-related medical events	247	69	149	29			142
	Sun, Taiwan (2002) ³⁵	Excess costs	National administrative health data	18–55 years with asthma-related medical events	592		291	278	23		

* Adjusted for age, sex, race, ethnicity, education, marital status, insurance, region and Charlson Comorbidity Index

† Adjusted for age group, marital status, minority race, region, level of education, female sex, poverty, uninsured status and Charlson comorbidity index.

‡ This study reported costs separately within each year; only the last year of data was used. Share of cost components, however, was reported across the entire study period.

§ Belgium, Estonia, France, Germany, Iceland, Italy, Norway, Spain, Sweden, Switzerland, UK.

ED = emergency department; BC = British Columbia.

translated to an equivalent loss of productivity for parents, assuming they missed work during the same period.²³

An important, and often overlooked, component of indirect costs is presenteeism.³⁹ Studies that have calculated indirect costs based on reported time off work due to asthma fail to include the impact of presenteeism.^{19,23,33} Measuring presenteeism is challenging, but there are validated instruments for this purpose.^{40,41} Likewise, only a few studies calculated the effect of premature death on the indirect costs of asthma. In a US study, this component was higher than the measurable loss of productivity (12% vs. 8% total annual costs for loss of work/school days and mortality, respectively).²³

Costs associated with asthma control status

While asthma is not a curable disease, it is considered a largely controllable condition.⁴² The conventional wisdom is that with proper management, asthma can be symptomatically and clinically controlled in the majority of patients.⁴² The potential reduction in the costs of asthma when an individual moves from the uncontrolled to the controlled state can be considered a preventable source of burden. Studies that report on this value can therefore be more informative for policy making regarding asthma management than the asthma costing studies. Nevertheless, care should be taken in reporting and interpreting such results. A simple difference in the costs of asthma across control levels does not imply causality due to the effect of potential confounding variables, such as asthma severity and socio-economic status. Studies that rigorously adjust for such variables can produce results that approximate the causal association between asthma control and costs. Unfortunately, such studies are rare. Six studies reported costs across different levels of asthma control (Table 2),^{19,20,25,29,32,36} in only three of which regression-based methods were used to derive an adjusted estimate of the impact of control on costs.^{20,25,29} For the most part, asthma control was based on the Global Initiatives for Asthma (GINA) control criteria.^{19,20,25,29,36} One study used the asthma control categories defined in the asthma control test (ACT).³²

One Canadian study evaluated only indirect costs and demonstrated that a patient with uncontrolled asthma would avoid US\$7768/py in productivity loss, of which 90.6% was due to presenteeism, if the disease becomes controlled.²⁹ The other study that reported adjusted values assessed direct costs in Spain and France, which reported differences of US\$122/py and US\$129/py, respectively, in the uncontrolled group in comparison to the controlled group.²⁰ The indirect costs also had a reverse association with the level of control in other studies.^{19,20,29,32,36} In several studies, indirect costs were greater than direct costs in

partially controlled and uncontrolled asthma (Table 2).^{19,20,32}

Costs of asthma exacerbations

Asthma exacerbations are associated with increased consumption of resources.^{21,22,26} Interestingly, the level of asthma control prior to an exacerbation seems to have a role in health care resource utilisation and expenditure during the exacerbation, as the exacerbation costs were higher in patients with uncontrolled asthma.²¹ Exacerbations also differ in severity, varying from those occurring in the community to those being associated with an ED visit or hospitalisation.²¹ In a study in Turkey, total direct costs per exacerbation were higher in severe than in mild and moderate exacerbations, ranging from US\$152 for a mild exacerbation to US\$1939 for life-threatening episodes.²¹ However, the factors driving such increased costs are different across jurisdictions. In the United States, for example, outpatient and in-patient costs were the major component of the total costs of exacerbations,²⁶ whereas in Turkey medications were responsible for the highest share of costs.²¹

In a Spanish study, the costs of hospitalisation per exacerbation increased from US\$3033 in 2002 to US\$3562 in 2010. In the same period, the length of hospital stay decreased from 5.4 days to 5.2 days.²² This may represent a shift towards more aggressive but shorter episodes of in-patient care. The authors of the previous study attributed the observation to the concurrent increase in the usage of non-invasive ventilation.²² Studies also compared costs among patients with and those without a history of asthma exacerbations. In a US study, individuals with a history of moderate/severe exacerbations had US\$4681 and US\$992 higher total health care and asthma-related costs, respectively, than those without a history of exacerbations.²⁶

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Since 2008, 16 articles meeting our inclusion criteria have been published: 7 from North America,^{18,43–48} 8 from Europe^{49–56} and 1 from South-East Asia.⁵⁷ Nine studies reported on costs of COPD,^{18,43–46,49–51,57} while four studies reported costs across severity stages^{18,51–53} and six provided information on costs of COPD exacerbations.^{18,47,48,54–56} Table 3 summarises the studies on costs of COPD, in total and by cost components. As in the case of asthma, the costs of COPD varied across different regions of the world, a factor that can be attributable to both variations in the true costs of COPD and the significant differences in costing methods. A critical factor in the context of COPD seems to be the way comorbid conditions have been considered. COPD is known to be associated with a significant number of comorbid conditions.⁵⁸

Table 2 Average costs of asthma across asthma control levels per patient-year (\$US)

Study	Country	Definition of asthma control	Target population	Type of costs	Mean annual costs per patient		
					Controlled	Partially controlled	Uncontrolled
Accordini ¹⁹	11 European countries	GINA definition 2002	30–54 years with physician diagnosed asthma	Direct + indirect (unadjusted)	594	819	2663
Doz ²⁰	Spain	GINA definition 2009	≥ 18 years with asthma-related medical events	Direct (unadjusted)	594	328	959
				Indirect (unadjusted)	-	491	1704
				Direct + indirect (unadjusted)	178	281	650
				Direct (unadjusted)	173	268	507
				Direct (adjusted*)	Reference	2	122
	France			Indirect (unadjusted)	4	64	680
				Direct + indirect (unadjusted)	100	366	628
				Direct (unadjusted)	95	136	263
				Direct (adjusted*)	Reference	17	129
				Indirect (unadjusted)	5	230	365
Gold ³⁶	Argentina	GINA definition 2010	≥ 12 years with asthma	Direct + indirect (unadjusted)	193	2439	5488
				Direct (unadjusted)	181	1219	2846
				Indirect (unadjusted)	12	1220	2642
	Brazil			Direct + indirect (unadjusted)	71	386	935
				Direct (unadjusted)	54	338	772
				Indirect (unadjusted)	17	48	163
	Mexico			Direct + indirect (unadjusted)	112	315	681
				Direct (unadjusted)	85	262	549
				Indirect (unadjusted)	27	53	132
	Puerto-Ricco			Direct + indirect (unadjusted)	630	2205	4878
				Direct (unadjusted)	346	1087	3049
				Indirect (unadjusted)	284	1118	1829
	Venezuela			Direct + indirect (unadjusted)	620	681	1321
				Direct (unadjusted)	617	663	1270
				Indirect (unadjusted)	3	18	51
Gold ²⁵	USA	GINA definition 2010	≥ 12 years self-reported asthma or with asthma-related medical	Direct (unadjusted)	855	1633	5669
				Direct (adjusted†)	Reference	660	3667 [‡]
Kim ³²	Republic of Korea	Korean version of the Asthma Control Test	>14 years with physician diagnosis and asthma-related medical events	Direct + indirect (unadjusted)	1641	2948	7583
				Direct (unadjusted)	1211	1331	2639
				Indirect (unadjusted)	430	1617	4944
Sadatsafavi ²⁹	British Columbia, Canada	GINA definition 2013	1–85 years with self-reported asthma	Indirect (adjusted [§])	Ref	1438	7768

* Adjusted for sex, age, episodes of exacerbation of asthma, prescription of a controller treatment and follow-up by a lung specialist.

† Adjusted for age, sex, whether someone in the household smoked, race, education and insurance.

‡ Adjusted values are calculated by subtracting the costs of uncontrolled and partially controlled from controlled group.

§ Adjusted for sex, age at baseline visit, socio-economic status, education, the type of residence (urban or rural) and the possession of drug insurance (no coverage, partial coverage, and full coverage for medications).

GINA = Global Initiative for Asthma.

Estimating costs that are directly attributable to COPD fails to consider the burden of such comorbidities. The calculation of excess costs with an appropriate comparison group provides a better opportunity. However, adjusting for comorbidities in this context results in an underestimation of the costs of the comorbidities.^{43–45}

The impact of statistical adjustment for comorbidity is apparent in a US study.⁴⁵ Direct excess costs were reduced from US\$6213/py in the unadjusted analysis to US\$536/py after adjustment for demographic variables and up to 19 comorbid conditions. In one study, patients with more than one reimburse-

ment per year due to comorbidities such as cancer, renal failure and cerebrovascular disease were excluded due to difficulties in discriminating COPD attributable costs from the costs due to such comorbidities.⁵⁷ While this is justifiable from a statistical perspective, as very costly chronic conditions can generate outlying observations, these conditions could also be the consequence of the pathophysiological mechanisms underlying COPD, and thus be part of its burden.

The other issue to consider is the age disparity in the studies. Some of the studies limited their population to working age groups,^{44,49} while others

Table 3 Average direct and indirect costs of COPD (per person-year) and its components (\$US)

Region	Study	Type of costs	Source of data	Target population	Total direct costs	Medication	Out-patient	In-patient	ED visit	Other direct medical/non-medical costs	Indirect costs
North America	Akazawa, USA (2003–2004) ⁴³	Excess costs (adjusted*)	National administrative health data	≥40 years with COPD-related medical events	3179	487	289	667		1736	
	Nair, USA (2000–2007) ⁴⁴	Excess costs (adjusted [†])	National administrative health data	18–65 years with COPD-related medical events	2831	1032	461	425	182	731	972
	Ford, USA (2006–2010) ⁴⁵	Excess costs (adjusted [†])	National administrative health data	≥18 years with COPD-related medical events or self-reported	4162						985
		Excess costs (adjusted [‡])			3214						779
		Excess costs (adjusted [§])			536						648
		Excess costs (adjusted [¶])			6213						
Europe	Pasquale, USA (2007–2009) ⁴⁶	Attributable costs	National administrative health data	40–89 years with Medicare and COPD-related medical events to chronic bronchitis	4528	1516	1213	1705	94		
	Maleki-Yazdi, Canada (2009–2010) ¹⁸	Attributable costs	National population-based survey and chart review	≥50 years with at least one year diagnosis of COPD proven by post-bronchodilator spirometry test	3503	1596	275	1346	48	238	227
	Van Boven, Netherlands (2009) ⁴⁹	Attributable costs	National Population based surveys and cost calculator	45–64 years with COPD	1192						3754
	Dal Negro, Italy (2001–2003) ⁵⁰	Attributable costs	National population-based survey	≥18 years with COPD-related medical events	2865	1290	230	1154	5	186	124
	Jensen, Denmark (2004–2006) ⁵¹	Excess costs (Adjusted [#])	National administrative data	>65 years with COPD diagnosis based on spirometry	679	280	–15**	413			2486
South-East Asia	Kim, Republic of Korea (2009) ⁵⁷	Attributable costs	National administrative health data	≥40 years with COPD-related medical events	2888	229	1601	1286			

* Adjusted for age, sex, region and comorbid conditions.

† Adjusted for age, CDPS risk score; type of health plan; number of enrolment months following the index diagnosis claim, US geographic region; type of employment industry, and presence of comorbidities

‡ Adjusted for demographics.

§ Adjusted for demographics and 11 medical conditions.

¶ Adjusted for demographics and 19 medical conditions.

Adjusted for age, educational level, and comorbidity.

** Not significant.

COPD = chronic obstructive pulmonary disease; ED = emergency department; CPDS = Chronic Illness & Disability Payment System.

only included younger adults.^{45,50} Similar to asthma, the source of data varied among studies, with some studies being based on administrative health data,^{43–46,51,57} while others were based on population-based surveys.^{18,49,50} Finally, the severity and duration of the disease varied across the studies. There were studies that recruited patients with newly diagnosed COPD^{43,44} as well as studies in which the majority of patients had moderate to severe COPD (Table 3).¹⁸

Direct costs

Given the aforementioned issues, it is difficult to compare direct costs across different studies. More informative observations can be made by comparing the contribution of cost components to the overall costs of COPD. The component with the biggest share in the costs varied between studies. In one study from Canada¹⁸ and one from the United States,⁴⁴ medication costs were the largest component, while a more recent US study reported that in-patient costs were the largest component.⁴⁶ In some studies, direct non-medical costs or 'other' direct medical costs (not attributable to in- or out-patient care or medication) contributed to a significant fraction of total direct costs.⁴³

An important aspect of the economic burden of COPD is that COPD remains under-diagnosed in many jurisdictions.⁵⁹ Studies included in this review are all based on diagnosed COPD, and a simple multiplication of these values by the number of COPD patients to calculate the overall economic burden of COPD will underestimate the contribution of undiagnosed COPD. Some insight can be gleaned from the burden of undiagnosed COPD, as a few studies reported costs prior to a COPD diagnosis. Hospitalisation and out-patient visits 12 months before a COPD diagnosis were almost 1.5 times higher in one study than in the control group.⁴⁴ In the 12-month period before a COPD diagnosis, respiratory and non-respiratory drugs accounted for respectively 12.7% and 6.9% of the total costs, which increased to 31.1% and 12% in the 12 months after diagnosis.⁵⁰

Indirect costs

Several studies reported on the indirect costs of COPD.^{18,44,45,49–51} Estimates, however, varied widely, from as low as US\$227/py (Canada) to as high as US\$3754/py (The Netherlands). Again, the methodology of cost calculations, sample selection and statistical analysis techniques all likely contributed significantly to the variation in the estimates. Estimates of excess indirect costs are also subject to the same consideration regarding statistical adjustment as direct costs of COPD, as controlling for comorbid conditions will likely result in an underestimation of the excess burden. A study in the United

States demonstrated that as the number of variables controlled for in the regression analysis increased, the adjusted excess indirect costs (due to absenteeism) became smaller.⁴⁵

Only one study included presenteeism in the calculation of indirect costs, although separate cost estimates for presenteeism were not reported.⁴⁹ This was also the study with the highest ratio of indirect to total (indirect and direct) costs (76%), i.e., the indirect costs of COPD in this study were roughly three times the direct costs. In two other studies, indirect costs were around 20% of total costs.^{44,45} This ratio fell to low as 4% in a study from Italy.⁵⁰ In a Canadian study, only 6% of the total costs were due to indirect costs; however, work days lost for patients and their care givers were the only aspect considered in this study, and 71% of the recruited population were already retired.¹⁸

Costs across severity stages

Five studies (four from Europe, one from Canada) satisfied the inclusion criteria (Table 4), all reporting costs across Global Initiative for Chronic Obstructive Lung Disease (GOLD) severity stages.^{18,51–53} Two studies also calculated indirect costs,^{18,52} but only one reported direct and indirect costs separately. In all studies, there was a monotonical relationship between COPD severity and costs. In general, costs among GOLD III/IV subjects were two to six times higher than costs across GOLD I/II stages. The most dramatic difference in costs across severity grades was reported from a Swedish study in which total (direct and indirect) costs increased from US\$696/py to US\$20 260/py from GOLD stage I to GOLD stage IV, mainly because of a sharp increase in indirect costs. Unfortunately, variation in costs calculations resulted in a large variation in costs even within GOLD stages, with GOLD stage I costs varying from US\$205/py to US\$2462/py, and GOLD stage III/IV from US\$1936/py to US\$20 260/py in different studies. As all the study settings were from high-income countries, and variations in severity stages had been removed by applying the same severity classification, the variation across studies in cost estimates within severity stages most likely highlights the variation in costing methodologies (Table 4).

Some of the studies attempted to tease out the contribution of cost components to overall costs within levels of severity. A Swedish study concluded that in-patient costs were the largest component only in very severe disease, whereas medication costs were the largest component in other severity stages.⁵² However, and interestingly, according to a Danish study, in-patient costs were the largest component in all severity stages.⁵¹ In Canada, the share of exacerbation costs increased from GOLD stage I to GOLD stage III, from 25% to 45%, but was similar between GOLD stage III and GOLD stage IV.¹⁸

Table 4 Average annual costs of COPD per patient -year across severity grading (\$US)

Study	Country	Type of costs	Source of data	Target population	Type of costs	Mean annual costs per patient			
						GOLD I	GOLD II	GOLD III	GOLD IV
Maleki-Yazdi ¹⁸	Canada, 2009–2010	Attributable costs	National population-based survey and chart review	≥ 50 years with at least one year diagnosis of COPD proven by post-bronchodilator spirometry	Direct + indirect	2 462	3 169	4 852	5 520
Jansson ⁵²	Sweden, 2002–2004	Attributable costs	Population based survey	39–84 years with COPD diagnosis based on spirometry	Direct + indirect	696	3 788	6 638	20 260
Jensen ⁵¹	Denmark, 2004–2006	Excess costs (Adjusted*)	National administrative data	<65 years with COPD diagnosis based on spirometry	Direct	314	1 201	2 570	6 247
					Indirect	382	2 587	4 068	14 013
Nielssen ⁵³	Iceland, 2004 Norway, 2003	Attributable costs	Population based survey	≥ 40 years with COPD diagnosis based on lung function test	Direct	205	445	2 109	
						2 588	2 828		
						420	713	1 997	
						224	444	1 936	

* Adjusted for age, education level and comorbidity.

COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease.

Costs of COPD exacerbations

Globally, COPD is an important cause of ED visits and hospitalisations.⁶⁰ Even when managed in an out-patient setting, exacerbations remain a major source of economic and human burden.⁶⁰ The significant role of exacerbation to the economic burden of COPD is generally recognised;⁶⁰ however, quantitative estimates are needed for precise and efficient decision making. Table 5 provides estimates on costs of COPD exacerbations from eligible studies. Exacerbations can generally be defined in two ways: a symptom-based definition based on the presence of symptoms (and perhaps requirement for

medications),⁶¹ and an event-based definition based on the interaction between the individual and the health care system. The latter definition also further classifies exacerbations into moderate (requiring out-patient or ED visits) and severe (requiring hospital admission). From the data provided in Table 5, it is obvious that studies that defined exacerbations using event-based definitions resulted in generally higher cost estimates, an expected finding given that this definition is based on, and therefore guarantees, health care resource utilisation. The highest estimates of exacerbation costs were from hospital-based studies in Canada¹⁸ and

Table 5 Costs per COPD exacerbation per patient (\$US)

Study	Country	Type of costs	Definition of exacerbation	Target population	Type of costs	Total
Maleki-Yazdi ¹⁸	Canada, 2009–2010	Attributable costs	Symptom based	≥ 50 years moderate to severe COPD	Direct + indirect*	2 729
					Direct	2 504
Mittman ⁴⁷	Canada, 2001–2002	Attributable costs	Event based	≥ 40 years moderate COPD exacerbation (requiring out-patient care) ≥ 40 years severe COPD exacerbation (requiring in-patient care)	Indirect*	224
					Direct (medical and non-medical)	605
Miravittles ⁵⁴	Spain, 2009–2012	Attributable costs	Symptom based	≥ 40 years moderate to severe COPD	Direct (in-patient, out-patient, laboratory test, medication)	9 017
Varol ⁵⁵	Turkey, 2005–2006	Attributable costs	Symptom based	40–88 years hospitalised patients with severe to very severe COPD with severe exacerbation	Direct (hospitalisation and medication)	479
Ozkaya ⁵⁶	Turkey, 2005–2009	Attributable costs	Event based	Hospitalised patients with exacerbation	In-patient costs	1 561
Perera ⁴⁸	USA, 2006	Attributed costs	Event based	≥ 40 years hospitalised patients with acute exacerbation	In-patient costs	777
						11 966

* Indirect costs consist of absenteeism costs for patients and their care givers.

COPD = chronic obstructive pulmonary disease.

the United States,⁴⁸ reporting exacerbation costs of respectively US\$2729 (US\$9017 for severe exacerbations) and US\$11 966 per episode. The lowest estimate, US\$479, was reported in a Spanish study that used a symptom-based definition.⁵⁴ A Canadian study separately reported the costs of moderate and severe exacerbations, with the latter being US\$8412 higher than the former (Table 5).⁴⁷

Putting these costs in the broader context of the COPD burden, a retrospective study in Canada demonstrated that 40% of the total costs of COPD patients were attributable to treatment of acute exacerbations and the main driver of exacerbation costs was hospitalisation.¹⁸ In Spain, 72.9% of the costs attributable to exacerbations were due to hospitalisation and 9.6% due to medications, with costs being due to investigations and physician visits.⁵⁴ On the other hand, in a study from Turkey, among patients hospitalised with COPD exacerbation, 53.5% of the costs were due to medication and only 19.6% due to hospital costs.⁵⁶

CONCLUSIONS

This review of recent studies on the burden of asthma and COPD has demonstrated that these two conditions continue to impose a major economic burden across many countries. However, this study has also demonstrated large discrepancies and variations in the reported estimates that cannot plausibly be attributed to differences across jurisdictions or sampling variations. This, unfortunately, undermines the utility of such studies in providing a clear and consistent picture of the burden of asthma and COPD. In addition, there is a clear lack of studies from many regions of the world (e.g., South America, Africa) to complete the picture of the global burden of asthma and COPD.

Despite such discrepancies and insufficient data, some consistent patterns can still be observed. One is the finding that in industrialised countries, medication costs are generally the largest driver of direct costs of asthma,^{17,19,23,24,27,28} while out-patient and in-patient care seem to be the largest component in developing regions.^{30,33,35} This can reflect better access to asthma control medications in richer countries, with consequent improvements in asthma control and reductions in encounters with the health care system. Evidence also suggests that asthma medication costs are generally increasing, a trend that seems to parallel a reduction in the costs and numbers of hospitalisations and physician visits.^{24,27,28} While this association is ecological, it can be seen as a hypothesis-generating observation on the role of increased use of evidence-based asthma therapies in the declining rate of adverse asthma outcomes. However, alternative factors might be responsible for this trend, such as changes in exposure

to risk factors in early life due to improved environmental settings.⁶² Furthermore, there has been significantly less exposure to secondhand smoke in many settings during recent years. Studies have shown low levels of asthma control as well as disappointingly low adherence rates to controller medications in jurisdictions in which such trends have been observed. In all studies, total costs increased as the control status worsened, although there were discrepancies regarding the changes in cost components.^{19,20,25,26,29,36} These findings cast doubt on whether the observed reduction in adverse asthma outcomes can be entirely explained by higher rates of evidence-based treatment.

Few studies attempted to evaluate the indirect costs of asthma, and results varied widely. Presenteeism is a significant component of the indirect costs of asthma, and most studies fail to consider its contribution to the overall indirect costs of asthma. Given that asthma also affects many younger individuals, the contribution of loss of productivity can also be significant. A recent systematic review demonstrated that this is the largest component of the indirect costs of asthma.⁹ Unfortunately, the majority of the studies did not address the non-medical direct costs such as transportation, hotel costs and time spent in physicians' offices, mostly due to the difficulties in recognising and calculating them in cross-sectional or retrospective analyses.

Similar patterns also emerge in juxtaposing the figures on the burden of COPD. In these studies, the greatest proportion of direct costs was related to hospitalisation, most likely attributable to the impact of severe exacerbations.^{43,46,57} Costs across severity levels increase sharply, with the ratio of costs in severe stages (GOLD stage III or IV) to milder stages (GOLD stage I or II) reaching 29.⁵² There have been some encouraging efforts in measuring the indirect costs of COPD,^{18,44,45,49–51} and the results indicate the high impact of COPD on productivity loss, overcoming the myth that COPD is the 'disease of the retired'. Another important aspect of the burden of COPD is delayed diagnosis. The observation that health care costs before a formal COPD diagnosis is made are high^{44,50} can inform the debates about the utility of early diagnosis and its economic implications.

The significant variability in the methodology used in the reported studies is clearly a result of the actual variations that exist in costs of asthma and COPD across jurisdictions, disease severity levels or over time. Our suggestions to remedy these methodological inconsistencies are two-fold: first, we suggest that the methodology used in disease-costing studies be harmonised. Consistent methodology has been rigorously pursued in other disciplines such as clinical trials⁶³ and meta-analyses.⁶⁴ Development, validation and promotion of best practice guidelines and reporting checklists for burden of disease studies can

elevate the standards of this field. In the absence of such widespread methodological standards, harmonising research efforts in multi-jurisdiction studies can be pursued. A successful example of such an attempt is the ‘confronting COPD survey’, estimating the costs of COPD using a set of standardised methodology across several jurisdictions.⁶⁵

Second, we suggest that burden of disease studies adopt a ‘comparative’ approach by estimating the incremental (or relative) costs of the condition of interest against an appropriate comparison group. An example is the comparative costs of uncontrolled vs. controlled asthma as opposed to estimating the burden of asthma itself. The former is of more relevance for decision makers, as asthma cannot be eradicated or cured, but can be controlled with proper treatment. Such comparative studies can also be conducted more rigorously. For example, in such a comparative study, the issue of attributable vs. excess costs becomes obsolete. Instead, such studies need to capture, as comprehensively as possible, all-cause medical, non-medical, direct and indirect costs, as the presence of a comparison group enables the background cost to be removed without the need for the arbitrary process of cost attribution.

The landscape of health care systems across the globe is a dynamic one, influenced by the emergence of new treatments, shifts in disease management practices (e.g., updating disease guidelines), evolving environmental and behavioural risk factors (e.g., change in smoking rates) and changes in demographics (e.g., aging population). On the other hand, decision makers need to be able to make sound decisions on how to spend constrained resources to maximise population health. In this challenging context, up-to-date estimates of the burden of diseases can be of great value in informing resource allocations across and within the realm of specific health conditions. There are, however, major steps to be taken to improve the methodological validity and consistency of burden of disease studies.

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APPENDIX

SEARCH STRATEGY

Asthma searches were run in MEDLINE (Ovid), Embase (Ovid), National Health Service Economic Evaluation Database (NHSEED), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and EconLit

Asthma MEDLINE (Ovid) Search

Database: Ovid MEDLINE(R) In-Process and other non-indexed citations and Ovid MEDLINE(R) <1946 to present>

Search strategy

- 1 asthma/ (107912)
- 2 asthma, aspirin-induced/ or asthma, exercise-induced/ or asthma, occupational/ or status asthmaticus/ (3570)
- 3 asthma\$.mp. (146803)
- 4 wheez\$.mp. (10638)
- 5 reactive airway disease.mp. (282)
- 6 (allergic adj5 respirator\$).mp. (2120)
- 7 (chronic adj5 respirator\$).mp. (10879)
- 8 allergens/ (33092)
- 9 (airway\$ adj3 inflam\$).mp. (14837)
- 10 (whistl\$ adj10 chest).mp. (45)
- 11 (short\$ adj10 breath).mp. (5710)
- 12 (tight\$ adj10 chest).mp. (1133)
- 13 Dyspnoea/ (15931)
- 14 Respiratory sounds/ (7197)
- 15 Bronchial diseases/ (7219)
- 16 Bronchial hyperreactivity/ (7051)
- 17 bronchial hyperactivity.mp. (52)
- 18 Respiratory tract diseases/ (19072)
- 19 Bronchitis/ (19784)
- 20 bronchitis.mp. (29469)
- 21 hypersensitivity/ (38373)
- 22 respiratory hypersensitivity/ (8837)
- 23 hypersensitivity, immediate/ (11886)
- 24 hypersensitivity, delayed/ (18605)
- 25 hypersensitivity.mp. (138643)
- 26 (respiratory adj3 (hypersen\$ or inflam\$ or obstruct\$)).mp. (12622)
- 27 Bronchoconstriction/ (3777)
- 28 Bronchoconstrict\$.mp. (10672)
- 29 (bronch\$ adj3 constrict\$).mp. (627)
- 30 excessive airway narrowing.mp. (47)
- 31 (antiasthma\$ or anti-asthma\$).mp. (10599)
- 32 ((Bronchial\$ or respiratory or airway? or lung?) adj4 (Hypersensitiv\$ or hyperreactiv\$ or allerg\$ or insufficiency)).mp. (52378)
- 33 Bronchial spasm/ (4146)
- 34 bronchospas\$.mp. (4936)
- 35 (bronch\$ adj3 spasm\$).mp. (4356)
- 36 or/1–35 [Asthma] (394204)

- 37 economics/ (27435)
- 38 exp 'costs and cost analysis'/ (190833)
- 39 exp 'economics, hospital'/ (20284)
- 40 economics, medical/ (8895)
- 41 economics, nursing/ (4026)
- 42 economics, pharmaceutical/ (2645)
- 43 (economic\$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic\$).ti,ab. (501294)
- 44 (expenditure\$ not energy).ti,ab. (20137)
- 45 value for money.ti,ab. (1048)
- 46 budget\$.ti,ab. (20096)
- 47 or/37–46 [NHS EED Filter] (631703)
- 48 36 and 47 (8546)
- 49 asthma/ and ec.fs. [Economics] (1860)
- 50 or/48–49 (9007)
- 51 comment/ or letter/ or news/ (1317846)
- 52 50 not 51 (8735)
- 53 limit 52 to yr='2008–2014' (3298)
- 54 limit 53 to English language (3215)
- 55 Direct costs.kw. (20)
- 56 Direct cost.kw. (18)
- 57 Direct medical cost.kw. (4)
- 58 Economic cost.kw. (10)
- 59 Employer health costs/ (1069)
- 60 ((direct or indirect) adj5 cost?).tw. (11069)
- 61 (productivity adj3 (loss or cost?)).tw. (2424)
- 62 ((burden or cost?) adj3 societ\$).tw. (3993)
- 63 (Economic adj3 (impact or burden or cost?)).tw. (15404)
- 64 caregiver\$ burden.tw. (1977)
- 65 (caregiver adj3 cost?).tw. (130)
- 66 ((lost or work) adj7 productivity).tw. (2793)
- 67 ((work\$ or employ\$) adj5 disability).tw. (4591)
- 68 or/55–67 (37268)
- 69 36 and 68 (1184)
- 70 asthma, aspirin-induced/ or asthma, exercise-induced/ or asthma, occupational/ or status asthmaticus/ (3514)
- 71 ec.fs. [economics] (340387)
- 72 70 and 71 (27)
- 73 69 or 72 (1206)
- 74 comment/ or letter/ or news/ (1270738)
- 75 73 not 74 (1196)
- 76 limit 75 to yr='2008–2014' (512)
- 77 limit 76 to English language (477)

Search results

- 54 limit 53 to English language (3215)
 - 77 limit 76 to English language (477)
- COPD searches were run in MEDLINE (Ovid) and Embase (Ovid)

COPD Embase (Ovid) Search

Database: Embase <1974 to 2015 January 07>

SEARCH STRATEGY:

- 1 lung disease/ (64144)
- 2 obstructive airway disease/ (1554)
- 3 chronic lung disease/ (7231)
- 4 chronic obstructive lung disease/ (75177)
- 5 bronchiolitis/ or bronchiolitis obliterans/ or bronchiolitis obliterans organizing pneumonia/ (13689)
- 6 emphysema/ (11694)
- 7 lung emphysema/ or hypertranslucent lung/ or lung bulla/ or lung cyst/ (20195)
- 8 lung alveolitis/ or fibrosing alveolitis/ (12634)
- 9 bronchitis/ or chronic bronchitis/ or laryngotracheobronchitis/ or tracheobronchitis/ (37086)
- 10 subcutaneous emphysema/ (3765)
- 11 pneumomediastinum/ [mediastinal emphysema] (4478)
- 12 bronchitis.tw. (23564)
- 13 (bronchiolitis or bronchitides or bronchitis).tw. (33939)
- 14 chronic obstructive pulmonary disease?.tw. (37750)
- 15 airflow obstruction?.tw. (4323)
- 16 COPD.tw. (40702)
- 17 emphysema.tw. (22729)
- 18 obstructive lung disease?.tw. (6950)
- 19 COAD.tw. [chronic obstructive airway disease] (266)
- 20 chronic lung disease?.tw. (7126)
- 21 obstructive airway disease?.tw. (1526)
- 22 obstructive respiratory disease?.tw. (341)
- 23 obstructive respiratory tract disease?.tw. (106)
- 24 obstructive bronchopulmonary disease?.tw. (108)
- 25 or/1–24 (247285)
- 26 cost/ (52697)
- 27 ‘hospital cost’/ or ‘health care cost’/ or ‘hospitalisation cost’/ (147096)
- 28 economic evaluation/ or ‘cost benefit analysis’/ or ‘cost control’/ or ‘cost effectiveness analysis’/ or ‘cost minimization analysis’/ or ‘cost of illness’/ or ‘cost utility analysis’/ (219906)
- 29 pharmacoeconomics/ or ‘drug cost’/ (65348)
- 30 (expenditure\$ not energy).ti,ab. (25191)
- 31 (economic\$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic\$).ti,ab. (623354)
- 32 value for money.ti,ab. (1446)
- 33 fee/ or hospital charge/ or medical fee/ (28910)
- 34 health economics/ (34103)
- 35 indirect costs/ (1)
- 36 healthcare costs/ (3)
- 37 out of pocket cost/ (15)
- 38 reimbursement/ (39375)
- 39 economic aspect/ (104233)
- 40 or/26–39 (921853)
- 41 25 and 40 (10664)
- 42 productivity/ (26433)
- 43 absenteeism/ (13412)
- 44 health care utilization/ (42515)
- 45 hospitalization/ (217512)
- 46 emergency ward/ (68176)
- 47 work capacity/ (10209)
- 48 medical leave/ (3624)
- 49 disability/ (72744)
- 50 medical leave/ (3624)
- 51 permanent disability/ (4)
- 52 workman compensation/ (8016)
- 53 disability/ (72744)
- 54 presenteeism/ (78)
- 55 work disability/ (3745)
- 56 disease management/ (11562)
- 57 ((lost or work) adj7 productivity).tw. (4326)
- 58 caregiver/ (42603)
- 59 caregiver burden/ (3625)
- 60 caregiver support/ (1523)
- 61 informal care/ (19)
- 62 home care/ (48627)
- 63 or/42–62 (527732)
- 64 25 and 40 and 63 (2791)
- 65 note/ or editorial/ or letter/ (1911338)
- 66 64 not 65 (2612)
- 67 limit 66 to yr=‘2008–Current’ (1622)
- 68 limit 67 to English language (1565)

Table A Characteristics of included studies

Author	Year published	Year enrolled	Study design	Participants N	Age of participants years	Inclusion criteria regarding disease status	Country	Adjusted value	Type of costs
Accordini ¹⁹	2013	1999–2002	Prospective survey based	462	30–54	Persistent asthma	11 European countries USA	2010 euro	Direct and indirect
Akazawa ⁴³	2008	2000–2004	Retrospective administrative health based	8 551	≥40	COPD		USD*	Direct
Alzaabi ³⁰	2014	2011	Retrospective administrative health based	139 092	All ages	Asthma	Abu Dhabi, United Arab Emirates	2011 dirhams	Direct
Barnett ²³	2010	2002–2007	Retrospective administrative health based	8 719	All ages	Asthma	USA	2009 USD	Direct and indirect
Bavbek ²¹	2010	2008	Retrospective survey based	294	≥18	Asthma exacerbation	Turkey	2008–2009 euro	Direct
Bedouch ²⁷	2012	2002–2007	Retrospective administrative health based	398 235	All ages	Narrow definition of asthma	BC, Canada	2008 CAD	Direct
Dal Negro ⁵⁰	2008	2001–2003	Prospective survey based	561	>18	COPD	Italy	Euro*	Direct and indirect
Doz ²⁰	2013	2010	Prospective survey based	2 671	≥18	Asthma for at least 12 month COPD	Spain and France	2010 euro	Direct and indirect
Ford ⁴⁵	2015	2006–2010	Retrospective administrative health based	5 143	≥18		US	2012 USD	Direct
Gold ²⁵	2013	2009	Retrospective survey based	2 493	≥12	Persistent asthma	US	USD*	Direct
Gold ³⁶	2014	2011	Retrospective survey based	Argentina, <i>n</i> = 436 Brazil, <i>n</i> = 399 Mexico, <i>n</i> = 532 Puerto Rico, <i>n</i> = 401 Venezuela, <i>n</i> = 400 61 118	≥12	Asthma	Latin America	2013 USD	Direct and indirect
Ivanova ²⁶	2012	1999–2007	Retrospective survey based		12–64 years	Exacerbation of moderate to severe asthma	US	2007 USD	Direct
Jang ²⁴	2013	2005–2009	Retrospective survey based	31.4 M	All age groups 39–84	Asthma	US	2009 USD	Direct
Jansson ⁵²	2013	2009–2010	Prospective survey based	244		COPD	Sweden	2010 euro	Direct and indirect
Jensen ⁵¹	2013	2004–2006	Retrospective administrative health based	546	>65 years	COPD	Denmark	2004 Danish kroner	Total costs Direct and indirect
Kambel ¹⁷	2009	2004	Retrospective administrative health based	1 616	>18 years	Asthma	US	2007 USD	Direct
Kim ³⁴	2011	2003	Prospective administrative health based	NA	All ages	Asthma	Republic of Korea	2005 USD	Direct

Table A (continued)

Author	Year published	Year enrolled	Study design	Participants N	Age of participants years	Inclusion criteria regarding disease status	Country	Adjusted value	Type of costs
Kim ³²	2012	2009–2010	Retrospective survey based	314	>14 years	Persistent asthma	Republic of Korea	2009 USD	Direct and indirect
Kim ⁵⁷	2014	2009	Retrospective administrative health based	192 496	>40	COPD	Republic of Korea	2012 USD	Direct
Lee ³³	2011	2008	Retrospective administrative health based	2 273 290	All ages	Asthma	Republic of Korea	2008 USD	Direct + indirect
Maleki-Yazdi ¹⁸	2012	2009–2010	Retrospective survey based	285	≥50	Exacerbation of moderate to severe COPD	Canada	2009 CAD	Direct and indirect
Miguel Diez ⁶⁴	2014	2002–2010	Retrospective survey based	2 792	16–45	Asthma exacerbation	Spain	Euro*	Direct
Miravittles ⁵⁴	2013	2009–2012	Prospective survey based	1 365	≥40	COPD exacerbation	Spain	Euro*	Direct
Mittman ⁴⁷	2008	2001–2002	Prospective survey based	609	>40	COPD exacerbation	Canada	2006 CAD	Direct
Nail ⁴⁴	2012	2000–2007	Retrospective administrative health based	27 612	18–65	COPD	USA	2010 USD	Direct
Nielsen ⁵³	2009	2003 (Norway), 2004 (Iceland)	Retrospective survey based	757 (Iceland) 658 (Norway)	≥40	COPD	Norway and Iceland	2005 euro	Direct and indirect
Ozkaya ⁵⁶	2011	2005–2009	Retrospective survey based	7 832	NA	COPD exacerbation	Turkey	USD*	Hospitalisation
Pasquale ⁴⁶	2012	2007–2009	Retrospective administrative health based	8 554 Medicare population	40–89	COPD and exacerbation	US	USD*	Direct
Perera ⁴⁸	2012	2006	Retrospective administrative health based	53 748	≥40	Acute COPD exacerbation	US	2010 USD	Hospitalisation
Sadatsafavi ²⁸	2010	1996–2000	Retrospective administrative health based	158 516	5–55	Asthma	BC Canada	2006 CAD	Direct
Sadatsafavi ²⁹	2014	2011–2012	Prospective survey based	300	Employed adults ≥18	Asthma	BC, Canada	2010 CAD	Indirect
Sun ³⁵	2008	2002	Retrospective administrative health based	1 726	18–55	Asthma	Taiwan	New Taiwan dollar*	Direct
Van Boven ⁴⁹	2013	2009	Retrospective survey based	94 158	45–64	COPD	Netherlands	2009 euro	Direct and indirect
Varol ⁵⁵	2013	2005–2006	Retrospective survey based	376	40–88	COPD exacerbation	Turkey	2006 USD	Direct

* Costs were assumed adjusted by the last year of the study period

COPD = chronic obstructive pulmonary disease; USD = United States dollar; BC = British Columbia; CAD = Canadian dollar.

R E S U M E

Les maladies non transmissibles sont maintenant la première cause de handicaps et de réduction de l'espérance de vie. Parmi eux, les problèmes respiratoires chroniques en constituent une grande partie. Le fardeau des maladies respiratoires chroniques est en augmentation générale dans le monde et l'asthme et les broncho-pneumopathies chroniques obstructives (BPCO) font partie des causes majeures de mortalité et de morbidité. Cependant, les coûts directs et indirects de ces maladies varient en fonction des juridictions. Cet article rapporte les

estimations les plus récentes des coûts de l'asthme et des BPCO en mettant l'accent sur la comparaison du fardeau de ces maladies dans différentes régions. Dans l'ensemble, il y a des variations considérables dans les coûts per capita annuels de l'asthme et des BPCO. Cependant, la méthode d'étude des coûts des maladies est également très différente, ce qui ne permet pas vraiment d'associer les différences des coûts rapportés aux différences du fardeau réel de l'asthme et des BPCO. Des suggestions sont fournies afin d'améliorer la validité et la comparabilité des études futures.

R E S U M E N

En la actualidad las enfermedades no transmisibles representan la primera causa de discapacidad y de disminución de la esperanza de vida y los trastornos pulmonares crónicos conforman una de las principales categorías. La carga de morbilidad por enfermedades pulmonares crónicas está aumentando en todo el mundo y el asma y la enfermedad pulmonar obstructiva crónica (EPOC) ocupan un lugar predominante como causas de morbilidad y mortalidad. Ahora bien, los costos directos e indirectos de estas enfermedades varían en las diferentes jurisdicciones. En el presente artículo se

comunican las estimaciones recientes de los costos del asma y la EPOC, con especial interés en la comparación de la carga de morbilidad en las diversas regiones. En general, existe una enorme variabilidad del costo anual por habitante de estas dos enfermedades. Es de anotar, no obstante, que los métodos de los estudios sobre los costos difieren también de manera considerable, con lo cual es difícil asociar las diferencias publicadas con la carga económica real generada por el asma y la EPOC. Se proponen recomendaciones encaminadas a mejorar la validez y la comparabilidad de los estudios en el futuro.
