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The cost of moderate and severe COPD exacerbations to the Canadian healthcare system

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Received 14 May 2007; accepted 12 October 2007

Available online 20 December 2007

KEYWORDS

Chronic obstructive pulmonary disease;
Cost;
Exacerbations;
Health care utilization

Summary

Background: The cost of exacerbations in chronic obstructive pulmonary disease (COPD) has not been well studied. The aim of this study was to identify and quantify the (average) cost of moderate and severe exacerbations (ME and SE, respectively) from a Canadian perspective.

Methods: Resources used during ME and SE were identified in a year long prospective, observational study (Resource Utilization Study In COPD (RUSIC)). The units of analysis were ME and SE. Unit costs (2006\$CAN), based on provincial, hospital and published sources, were applied to resources. The overall cost per ME and SE were calculated. The population burden of exacerbations was also calculated.

Results: Among study participants ($N = 609$, aged 68.6 ± 9.4 years, 58.3% male) there were 790 exacerbations: 639 (80.9%) MEs and 151 (19.1%) SEs. Of the 790 exacerbations, 618 (78.2%), 245 (31.0%) and 151 (19.1%) included a visit to an outpatient clinic, emergency department (ED) or hospital, respectively. For ME, 85.9% and 13.1% involved visits to GPs and respirologists, respectively. Pharmacologic treatment changes in the outpatient setting involved antibiotics (63.1%) and corticosteroids (34.7%). The overall mean costs for outpatient and ED services for MEs were \$126 ($N = 574$) and \$515 ($N = 105$), respectively. The average overall cost of a ME was \$641. For SEs, the average hospital stay was 10.0 days. The overall mean costs of outpatient, ED and hospitalization services for SE

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were \$114 ($N = 44$), \$774 ($N = 140$) and \$8669 ($N = 151$), respectively. The average overall cost of a SE was \$9557.

Conclusion: The economic burden associated with MEs and especially SEs, in Canada, is considerable and likely has a substantial impact on healthcare costs. The overall burden of exacerbations has been estimated in the range of \$646 million to \$736 million per annum. © 2007 Elsevier Ltd. All rights reserved.

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by progressive airway obstruction which is not completely reversible with bronchodilator medications.¹ Exacerbation symptoms include increased dyspnea, cough, and sputum, as well as changes in sputum colour. Exacerbations are associated with a significant worsening of pulmonary function² and are considered the key drivers, in terms of increased medical visits and hospitalizations, in the costs of COPD.³

COPD is a serious public health problem in many countries throughout the world.⁴ According to World Health Organization (WHO) estimates, 80 million people have moderate to severe COPD and three million people died of COPD in 2005. WHO predicts that COPD will become the fourth leading cause of death worldwide by 2030.⁵ Important risk factors include tobacco smoking, indoor air pollution (such as biomass fuel used for cooking and heating), outdoor air pollution and occupational dusts and chemicals (vapours, irritants, and fumes).⁵ The burden of COPD extends beyond the patient and to the health care system and society as a whole.

A number of studies have attempted to estimate the burden of COPD using various research techniques (e.g., retrospective telephone surveys, database analyses).^{6–14} The majority of studies have assessed the overall burden of COPD in general. However, two studies have specifically evaluated the cost associated with exacerbations. Andersson et al.¹³ examined the cost of COPD exacerbations by severity by surveying 202 individuals previously identified in an ongoing longitudinal survey in Sweden. Results showed that exacerbations accounted for 35–45% of the total health care cost of COPD. Moderate and severe exacerbation costs were SEK 2111 and SEK 21852, respectively. In the other study, Miravittles et al.¹⁴ identified 2414 Spanish COPD patients treated for an acute exacerbation in a primary care setting. The study prospectively collected 30 days of resource use data in order to assess the total costs associated with the management of acute exacerbations and relapses. A mean cost of \$159 US per exacerbation was reported, where an exacerbation was based on clinical criteria. Costs were not stratified by exacerbation severity.

Canada has a publicly funded health care system that provides universal, comprehensive coverage for medically necessary hospital and physician services. These services are administered and delivered by provincial and territorial governments.¹⁵ In Canada, 750,000 people have been diagnosed with COPD by a health professional.¹⁶ COPD is the fourth leading cause of death in Canada, after heart disease, cancer, and stroke.¹⁷ Prevalence rates for men and women over the age of 35 years are 2.8% and 3.6%,

respectively.¹⁶ The true prevalence is thought to be underestimated.⁶ The recent publication of the Burden of Obstructive Lung Disease (BOLD) appears to confirm that previous prevalence estimates are low.¹⁸

A recently published Canadian 52 week, prospective, multicentre, observational study, Resource Utilization Study In COPD (RUSIC), reported the health care resources associated with moderate and severe exacerbations in COPD patients who completed the year long study.¹⁹ 609 patients were recruited by 50 sites located in all 10 provinces in Canada. Sites ranged from urban and rural primary care settings. Physicians included community and academic respirologists (the ratio of community to academic physicians was representative of the Canadian physician population). Study physicians were instructed to enrol the next eight to 10 eligible patients during regular office/clinic visits. Inclusion criteria were willingness to provide informed consent, a diagnosis of stable COPD (airway obstruction with FEV₁ of 65% or less and a FEV₁/FVC of 71% or less) with a pulmonary function test within 6 months of visit 1 (a test within 10 days of visit 1 was deemed acceptable), >40 years old, current or ex-smokers with a 10 pack-year history. Patients were excluded if they had a history of other lung disease (asthma, cystic fibrosis, bronchiectasis, interstitial lung disease, pulmonary thromboembolic disease), other medical conditions deemed to prevent compliance and completion of study, receiving an investigational drug 30 days prior to screening visit, were participants in another clinical trial, living outside of Canada for >8 consecutive weeks.

An exacerbation was defined as a complex of COPD-related symptoms including one or more of the following: cough, wheeze, dyspnea, or sputum production lasting ≥ 3 days. Exacerbations were categorized as mild, moderate or severe based on definitions used in prospective clinical trials. Only health resource utilization (HRU) associated with moderate and severe exacerbations was collected. The definitions for exacerbation severity were:

- Moderate exacerbation—visit to an outpatient facility, including an emergency department (ED) (but not requiring admission to hospital) and an alteration in medication (for example, addition of antibiotics or oral corticosteroids).
- Severe exacerbation—hospitalization.

All resource information was collected prospectively. Data for HRU attributable to moderate and severe exacerbations were collected in a standardized fashion. Records of patients who experienced an exacerbation were reviewed and medications and outcomes were documented. All concomitant medications were recorded, including rescue

use of short-acting inhaled beta-agonists. Information on non-scheduled contacts with physicians and other health care providers that were due to an exacerbation of COPD, including date, reason for contact, medications prescribed, outcome (e.g., discharge, admission to hospital, follow-up visit), disability days and employment status was collected prospectively using a standardized questionnaire. To aid with the accuracy of information recorded in diaries, patients were contacted by study coordinators every 5–6 weeks in order to obtain information on exacerbations over the previous time horizon. Resource utilization information collected included number of exacerbation-related hospitalizations, hospital length of stay, number of unscheduled physician visits, number of ED visits, home care and community services, allied health professional visits, medications, diagnostics and laboratory values.

Among study participants ($N = 609$), the mean age of the patient population was 68.6 years (SD 9.4) and the majority of patients were male (58.3%). Mean FEV₁ was 1.01L (SD 0.4L), 43.9% predicted (SD 14.3%), with an average smoking history of 47.9 pack years (SD 23.5). Most patients were taking a bronchodilator (99.6%). Ninety-seven patients were admitted to hospital with an average length of stay of 10.0 days.

Patient characteristics are summarized elsewhere in detail and may be considered representative of the Canadian COPD population.^{19,20}

The objectives of this study were to quantify the resources collected in the RUSIC study and to calculate the average cost of a moderate and a severe exacerbation. The other objective was to use those exacerbation costs to estimate the national burden of moderate and severe COPD exacerbations in Canada.

Methods

Study design

The perspective of the analysis was that of the Canadian provincial health care system. The units of analysis/costing were a moderate and a severe exacerbation, (ME and SE, respectively). HRU data associated with ME and SE, namely ED visits, outpatient visits and hospitalizations, were collected. Outpatient resources included physician visits, laboratory and diagnostic testing, mode of transportation to visit and change in medication. ED resources included ED visit (physician cost+visit cost), mode of transportation and change in medication. Hospital resources consisted of physician visits, length of stay, type of bed (ward/ICU), mode of transportation, change in medication and laboratory/diagnostic testing. Concomitant medications including rescue drugs were considered. Information on scheduled and non-scheduled contacts with physicians and other health care providers due to an exacerbation included date, reason, medications prescribed, outcome (e.g., discharge, admission), transportation and tests.

Cost determination

2006 Canadian unit costs were applied to the resource utilization elements of ME and SE. Unit costs were applied to

resources utilized by the patient population (Table 1). Costs were obtained from provincial sources, hospital databases and published sources (Ontario Case Costing Initiative, Ontario Schedule of Benefits, Ontario Drug Benefit Formulary, published literature). All variables were reviewed by the clinical experts for appropriateness. Costs obtained in non-2006 dollars were inflated using the Canadian Consumer Price Index. Discounting was not applied to costs or outcomes given the 1 year time horizon. Costs were presented in a format similar to an intent to treat analysis (ITT) and a clinically evaluable (CE) analysis. For the ITT analysis, the denominator for the total number of ME and SE was used to determine the average cost per exacerbation. For the CE analysis, the denominator was based on the number of exacerbations that used a resource variable. The difference between the two analyses is illustrated below:

- *ITT analysis:* Forty-four exacerbations used outpatient resources but 19 of those exacerbations used laboratory/diagnostic test resources. The mean cost per laboratory/diagnostic tests was based on the total number of exacerbations ($N = 44$).
- *CE analysis:* Forty-four exacerbations used outpatient resources but 19 of those exacerbations used laboratory/diagnostic test resources. The mean cost per laboratory/diagnostic tests was based on the total number of exacerbations with laboratory/diagnostic tests ($N = 19$).

Assumptions

Several assumptions were made. Exacerbation episodes >7 days apart were considered to be separate events. All resource use that preceded a hospitalization was included in the SE category if it occurred within 7 days of hospitalization (e.g., patient visited an ED on day 1 but was hospitalized on day 2, the resources associated with the ED were considered severe exacerbation costs). Double counting was avoided with a hierarchy of rules. Costs were applied to the first point of contact for the patient during the exacerbation (e.g., ED, outpatient or inpatient). Medication utilization was applied to each area (ED, outpatient and inpatient). Medication costs were based on a 1 month drug treatment duration post ME/SE. For medications, salbutamol and salmeterol were used to represent all short-acting beta-agonists (SABAs) and long-acting beta-agonists (LABAs), respectively.²¹ Costs associated with pulmonary function testing were assumed to be simple spirometry rather detailed pulmonary function (unlikely to be conducted at time of exacerbation). Ciprofloxacin represented antibiotic utilization and prednisone represented corticosteroid use. Resources not utilized were costed at \$0.

Analyses

The primary analysis calculated the overall mean cost of a ME and a SE based on the ITT analysis. Mean value is used in preference to median, as mean value is a parametric estimate of interval data. A secondary analysis calculated the overall mean cost per exacerbation based on the CE

Table 1 Unit cost list.

Description	Cost (2006 \$ CAD)	Source
<i>Drugs (per month)</i>		
Inhaled corticosteroid	\$64.02	Ontario Drug Benefit Formulary (ODBF)
Oral corticosteroid	\$1.00	ODBF
Theophylline	\$15.16	ODBF
Anticholinergic (short acting) inhaled	\$68.12	ODBF
Beta agonist (long acting) inhaled	\$60.53	ODBF
Beta agonist (short acting) inhaled	\$6.26	ODBF
Leukotriene receptor antagonist	\$55.92	ODBF
Antibiotic	\$28.60	ODBF
<i>Physician</i>		
General practitioner	\$58.20*	Ontario Schedule of Benefits (OSB) version July 1, 2006
Respiratory specialist	\$58.25 [†]	OSB
Other specialist	\$58.25	OSB
Emergency physician	\$86.10	OSB
<i>Allied health professionals</i>		
COPD case manager (RN)	\$35.80	Ontario Nurses's Ass (ONA) http://www.ona.org/faq/index.html#ont_sal
<i>Laboratory/diagnostics</i>		
Spirometry	\$17.05	Ontario Schedule of Laboratory Fees (OSLF)
Blood gases	\$47.05	OSLF
Sputum	\$11.37	OSLF
Urine	\$2.59	OSLF
X-ray chest	\$32.05	OSLF
Bronchial endoscopy	\$184.61	OSLF
ECG	\$105.95	OSLF
<i>Outpatient/Inpatient tests</i>		
Arterial blood gases	\$17.89	OSB/OSLF
Auscultation	\$30.70	OSB/OSLF
CAP gases	NA	OSB/OSLF
Oximetry	\$4.30	OSB/OSLF
Peak flow	\$28.80	OSB/OSLF
Pulmonary function test	\$154.38	OSB/OSLF
<i>Transportation</i>		
Ambulance	\$845.61	http://www.health.gov.on.ca/english/public/program/ehs/land/service_qa.html
House call	\$41.75	OSB
Nurse home care	\$20.60	http://www.eldercarehomehealth.com/Rates.html
<i>Rehabilitation</i>		
Inpatient+outpatient	\$17,122	²⁹
Outpatient programme (6 weeks)	\$1600	³⁰
<i>Oxygen</i>		
Oxygen [‡]	\$0.00	http://www.health.gov.on.ca/english/public/pub/adp/pdf/oxygen.pdf Full reimbursement by OMOH ADP oxygen program

*Due to exacerbation billed as general assessment.

[†]Due to exacerbation billed as medical specific assessment.

[‡]No oxygen volume information was collected in the RUSIC study, therefore not possible to cost.

analysis. Descriptive statistics for both resource utilization and costs were calculated. Continuous clinical and cost data were reported as means \pm standard deviations (SD). Data were analysed using SAS Version 9.1.

The national cost of exacerbations was estimated in two ways: (1) based on the national COPD population hospitalization statistics and (2) based on the exacerbation rate observed in RUSIC.

Results

There were 790 episodes of exacerbations during the study period, of which 639 (80.9%) were classified as moderate and 151 (19.1%) were severe. Of the 790 exacerbations, 618 (78.2%) used outpatient resources, 245 (31.0%) used ED resources, and 151 (19.1%) were hospitalized (Table 2).

Moderate exacerbations

Outpatient visit resources

85.9% of ME involved a visit to a general practitioner, 13.1% to a respirologist, 3.3% to an emergency physician, and 1% to other. The most common outpatient laboratory and diagnostic tests conducted were chest X-rays (19.5%), followed by spirometry (9.8%). The mode of transportation to the outpatient visits was primarily private car (77.0%), with only 0.7% of ME involving an ambulance. Medication changes occurred with antibiotics (63.1%), corticosteroids (34.7%) and beta-agonists (12.4%).

Emergency department resources

In the ED, 47.6% and 47.6% of ME episodes had changes to corticosteroids and antibiotics, respectively. Transportation to the ED involved the use of a private car in 43.8% of ME, an ambulance in 25.7%, and the remaining cases arrived by public transportation or did not report transportation.

Costs

The average overall cost of a ME was \$641 (\$126 outpatient+\$515 ED). The cost drivers for MEs were ED visit and mode of transportation to the ED. When exacerbations were weighted by resources used, the average overall cost was \$756 (\$165 outpatient+\$591 ED) (Table 3).

Severe exacerbations

Hospitalization resources

Resources were stratified into inpatient hospital, ED and outpatient costs. The majority of patients (80.8%) were discharged from hospital to their home.

Table 2 Number of exacerbation events by severity and location.

Resource utilization variable	All exacerbations (N = 790)	Moderate exacerbation (N = 639)	Severe exacerbation* (N = 151)
Outpatient visits	618	574	44
Emergency department visits	245	105	140
Hospitalization	151	N/A	151

*By definition, a severe exacerbation must include a hospitalization.

Table 3 Cost of moderate exacerbations.

	Intent to treat analysis average cost (Mean ± SD)	Clinically evaluable analysis average cost (mean ± SD)
<i>Outpatient resources (N = 574)</i>		
Outpatient physician visits	\$61 ± \$14 (N = 574) Median: \$58 Range: \$0–\$180	\$61 ± \$13 (N = 570) Median: \$58 Range: \$58–\$180
Laboratory and diagnostic tests	\$16 ± \$37 (N = 574) Median: \$0 Range: \$0–\$370	\$49 ± \$50 (N = 185) Median: \$32 Range: \$3–\$370
Transportation	\$23 ± \$70 (N = 574) Median: \$23 Range: \$0–\$866	\$25 ± \$72 (N = 535) Median: \$20 Range: \$0–\$866
Medication changes	\$26 ± 24 (N = 574) Median: \$29 Range: \$0–\$182	\$30 ± \$23 (N = 494) Median: \$29 Range: \$0–\$182
Total outpatient resource cost	\$126	\$165
<i>Emergency resources (N = 105)</i>		
Emergency department visit	\$252 ± \$0 (N = 105) Median: \$252 Range: \$252–\$252	\$252 ± \$0 (N = 105) Median: \$252 Range: \$252–\$252
Transportation	\$241 ± 386 (N = 105) Median: \$20 Range: \$0–\$1500	\$313 ± \$413 (N = 81) Range: \$0–\$1500 Median: \$20
Medication changes	\$21 ± 24 (N = 105) Median: \$29 Range: \$0–\$104	\$26 ± \$24 (N = 84) Median: \$29 Range: \$0–\$104
Total emergency resource cost	\$515	\$591
Total ME cost	\$641	\$756

Hospital resources

The average length of hospital stay due to an exacerbation was 10.0 days (±14.5 days). Sixteen percent of patients were in an ICU for an average of 6.2 days (±6.5 days). 57.6% and 44.4% of exacerbations involved changes in antibiotic and corticosteroid medications while in hospital, respectively. The most common inpatient laboratory and diagnostic tests were blood tests (94.0%), chest X-rays (88.1%) and ECG (65.6%). 13.2% of SE episodes arrived to hospital via

Table 4 Cost of severe exacerbations.

	Intent to treat analysis average cost (mean \pm SD)	Clinically evaluable analysis average cost (mean \pm SD)
<i>Hospital resources (N = 151)</i>		
Hospital stay	\$7060 \pm \$10,826 (N = 150*) Median: \$4263 Range: \$609–\$100,426	\$7060 \pm \$10,826 (N = 150*) Median: \$4263 Range: \$609–\$100,426
Laboratory and diagnostic tests	\$1483 \pm \$1036 (N = 151) Median: \$1959 Range: \$17–\$4072	\$1483 \pm \$1036 (N = 151) Median: \$1959 Range: \$17–\$4072
Transportation	\$125 \pm \$312 (N = 151) Median: \$0 Range: \$0–\$1646	\$411 \pm \$453 (N = 46) Median: \$20 Range: \$0–\$1646
Total hospital resource cost	\$8669	\$8954
<i>Emergency resources (N = 140)</i>		
Emergency department visit	\$252 \pm 0 (N = 140) Median: \$252 Range: \$252–\$252	\$252 \pm 0 (N = 140) Median: \$252 Range: \$252–\$252
Transportation	\$496 \pm 418 (N = 140) Median: \$846 Range: \$0–\$1500	\$499 \pm \$417 (N = 139) Median: \$846 Range: \$6–\$1500
Medication changes	\$25 \pm \$30 (N = 140) Median: \$29 Range: \$0–\$104	\$33 \pm \$31 (N = 105) Median: \$30 Range: \$0–\$104
Total emergency resource cost	\$774	\$786
<i>Outpatient resources (N = 44)</i>		
Outpatient physician visits	\$72 \pm \$46 (N = 44) Median: \$58 Range: \$0–\$203	\$83 \pm \$39 (N = 38) Median: \$58 Range: \$36–\$203
Laboratory and diagnostic tests	\$24 \pm \$51 (N = 44) Median: \$0 Range: \$0–\$206	\$82 \pm \$65 (N = 13) Median: \$50 Range: \$11–\$206
Transportation	\$5 \pm \$9 (N = 44) Median: \$0 Range: \$0–\$20	\$19 \pm \$4 (N = 12) Median: \$20 Range: \$6–\$20
Medication changes	\$13 \pm \$24 (N = 44) Median: \$0 Range: \$0–\$104	\$29 \pm \$30 (N = 19) Median: \$29 Range: \$0–\$104

Table 4 (continued)

	Intent to treat analysis average cost (mean \pm SD)	Clinically evaluable analysis average cost (mean \pm SD)
Total outpatient resource cost	\$140	\$213
Total SE cost	\$9557	\$9953

*Although 151 exacerbations resulted in hospitalizations, one case did not have a discharge date. Consequently, the mean hospital stay cost was based on 150 exacerbations.

ambulance, private car (8.6%) and other transportation modes (13.2%) (which could include transfers from other institutions). There was no transportation information available for 45.0% of the SE episodes.

Outpatient resources

For outpatient physician visits, 38.6% of SE involved a visit to a general practitioner, 34.1% to an ED physician, 22.7% to a respirologist and 11.4% to another physician. The most common outpatient laboratory and diagnostic tests conducted were chest X-rays (20.5%), blood tests (13.6%), sputum analysis (9.1%) and spirometry (6.8%).

Emergency resources

92.7% of SE involved use of the ED prior to hospitalization. Transportation to the ED involved an ambulance in 56.4% of the SE episodes.

Costs

The average overall cost of a SE was \$9557 (\$774 ED+\$114 outpatient+\$8669 hospitalization). The cost drivers for SE's were hospital length of stay and inpatient laboratory and diagnostic testing. When exacerbations were weighted by resources used, the average overall cost for a SE was \$9953 (\$786 ED+\$213 outpatient+\$8954 hospitalization) (Table 4).

Deaths

Thirty-three (5.4%) deaths were reported in RUSIC. Eighteen deaths were reported among patients who were hospitalized. The cause of death was not always reported. Four patients with SE episodes died during hospitalization. Non-COPD-related deaths such as lung cancer, complications from COPD and a scooter accident were recorded, however, the majority of cases did not have a reason for death reported.

National burden of moderate and severe exacerbations

We used two different methods to estimate the National exacerbation rate per year. Both methods applied different

patient population estimates (one for hospitalizations and one for the COPD) in order to determine the national cost.

The first method used published estimates of COPD-related hospitalizations obtained from Canadian hospitalization data. There were approximately 60,000 hospital admissions due to COPD in Canada in 1997.²² If we assume that all of these COPD-related hospitalizations are as a result of SEs (per the definition used in this study) we are able to calculate an estimate of the annual burden of SEs in Canada. Based on our estimates of the cost of a SE (i.e., \$9557), the annual national burden of severe exacerbations alone is approximately \$573 million. Current estimates predict that COPD-related hospitalizations will double by the year 2015, thereby increasing the national cost of SE to over \$1 billion per annum. To estimate the number of MEs in Canada, we used the ratio of moderate to severe exacerbations as observed in the RUSIC study (639 moderate:151 severe). Applying this ratio to the 60,000 estimated SEs results in approximately 250,000 MEs nationally. At \$641 per ME, this would translate into a national annual cost of \$163 million. When combined, the burden of ME and SE in Canada exceeds \$736 billion dollars per annum.

The second method calculated the national burden of illness using RUSIC specific data. In RUSIC, during the year of observation, 278 (53.1%) of the COPD patients had an exacerbation. There were 691 exacerbations (2.5 exacerbations per patient), of which 615 (89.0%) were ME. Based on published estimates, there are approximately 750,000 patients diagnosed with COPD in Canada.¹⁶ If 53.1% of COPD patients have exacerbations ($N = 398,250$), then 354,443 have MEs and 43,807 have SEs in Canada. At \$641 per ME and \$9557 per SE, the national cost burden would be \$227 million and \$419 million, respectively. When combined, the burden of moderate and severe exacerbations in Canada exceeds \$646 million dollars per annum. These values do not take into account the cost associated with mild COPD (where patients may experience ME or SE) and the economic burden of mild exacerbations.

Discussion

Determination of the cost of an exacerbation is important for two main reasons, namely resource allocation and economics. From a resource allocation perspective, costing by exacerbation provides insight into direct medical expenditures borne by the health care system and aids in the resource allocation planning. From an economic perspective, this information helps to put into context the value of treatments or programs that prevent or reduce the number of exacerbations, or reduce the severity of exacerbations.

This study is unique in that it is the first study to prospectively examine the economic burden of moderate and severe COPD exacerbations from a Canadian perspective based on the resources collected in a 1 year long prospective study that examined a large cohort of COPD patients.

Our results show that the overall cost per moderate exacerbation was \$641 and \$9557 for a severe exacerbation. The ITT average cost of exacerbation is not substantially different from the CE estimate. The key cost driver in severe exacerbations was hospitalization, with an average length of

stay of 10 days, accounting for 73% of the total cost. Laboratory, diagnostic and medication costs were generally overshadowed by hospitalization, clinic and ED visits. Transportation costs were also considerable.

Based on this average cost, our calculation showed a national cost burden for moderate and severe exacerbations of \$646–736 million (CAN). This value may be an underestimate given that the prevalence of moderate exacerbations is not well documented, COPD is under-diagnosed and prevalence of hospitalization due to COPD is increasing.⁶ Because of the health care system perspective used, these estimates only include direct costs and do not take into account societal costs such as caregivers or lost wages.

Our study builds on the results of other economic analyses investigating the burden of COPD and COPD exacerbations.^{6–14} Miravittles et al.¹⁴ reported an average cost of exacerbation at \$159. Costs were based on a cohort of 2414 patients over a 1 month time horizon. This value was calculated as the weighted average cost per exacerbation where only a small proportion (3.4%) of the population investigated were hospitalized at a cost of \$2652. The mean cost was primarily based on medication costs, outpatient clinic visits and ED costs. Study patients were recruited through primary practices and thus represented a milder COPD population. Long-term time horizons and the cost of patients presenting directly to hospitals with severe exacerbations were not evaluated as in the present study.

Andersson and colleagues reported costs of moderate and severe exacerbation at SEK 2111 and SEK 21852, respectively. The small study cohort ($N = 61$) was based on a larger epidemiological cohort. Definitions of mild, mild/moderate, moderate and severe exacerbations were different than those used in the present study. The cost driver in the severe category was hospitalization cost, which accounted for more than 90% of the overall mean cost. However, the average length of stay (6.6 days) was approximately half of that found in the RUSIC study.¹⁹ Patients were required to recall events occurring over a previous 4–6 months time horizon which may introduce recall bias.¹³

The *Confronting COPD in North America and Europe* study was a large international retrospective survey that examined the burden of COPD in eight different countries.^{6–12} That study used telephone interviews with physicians and patients to collect information on symptom severity and frequency, management and treatment, quality of life, health care resource utilization and lost productivity. This retrospective survey relied on the 12-month recall of patients for COPD-related hospitalizations, ED visits, primary care consultations, treatment and laboratory tests.²³ Costs were derived by multiplying the unit cost of a resource by the frequency of the resource use in currency of the country studied. Recall bias was a major limitation of the international study. Chapman and colleagues examined the burden of illness of COPD, not exacerbation-related costs, from a Canadian perspective using telephone surveys to document direct and indirect costs. Here, the direct cost was \$2000 per COPD patient annually.⁶ This is a weighted cost for all severities. Limitations of that study included the telephone sampling method, patient recall bias and the study did not use exacerbation-specific severity information. The overall national burden was not reported in that study. However, if we extrapolate the \$2000 per COPD

patient by the number of COPD patients in Canada (750,000), the national burden of illness for Canada would be \$1.5 billion. This estimate is inline with our national calculations.

The results presented in this study are considered to be a conservative estimate of the real cost of an exacerbation. Only resource utilization data collected during the prospective study was available for costing. Indirect costs associated with moderate and severe exacerbations were not considered as part of this perspective but would increase the overall cost of an exacerbation. The study did not collect information on the volume of oxygen used per patient. Although most patients likely received oxygen therapy, the cost of this therapy is not likely to be significant.²⁴ In this study, medication use was based on the cost of a 1 month period, however longer utilization would lead to increased costs. Long-term medication use may occur as the recovery period after a COPD exacerbation is quite prolonged.^{2,25} This is unlike asthma, where a patient may have a severe life threatening asthma exacerbation and return to normal lung function relatively quickly.

The economic burden associated with moderate exacerbations and especially severe exacerbations is considerable from a health care system and national perspective. Based on the anticipated increase in health care utilization by patients with COPD, a multifaceted approach to improve COPD management would likely be successful in substantially reducing health care costs. Interventions should include optimization of the maintenance treatment of patients with COPD,²⁶ better use of chronic disease management strategies,²⁷ greater access to pulmonary rehabilitation¹⁶ and systemic corticosteroid utilization to treat acute exacerbations.²⁸

Conclusions

The economic burden associated with moderate and especially severe COPD exacerbations is considerable for the Canadian health care system and national perspective. Focus on the prevention of exacerbations through medical and non-medical interventions may reduce these overall costs.

Conflicts of interest

Dr. Mittmann is a Scientist at Sunnybrook Health Sciences Centre and received unrestricted funding from Boehringer Ingelheim Canada for this analysis. Professor FitzGerald holds a BC Lung/CIHR Investigator Award. He is also the recipient of a Michael Smith Foundation for Health Research Distinguished Scholar Award. The data were analyzed independently at the Centre for Clinical Epidemiology and Evaluation.

Drs. Mittmann and FitzGerald have been members of advisory boards for a number of pharmaceutical companies including the sponsors of this trial. Dr. FitzGerald is also a member of Speakers Bureaux for these companies. Both Ms. Haddon and Ms. Carole Bradley-Kennedy are employees of Boehringer Ingelheim. Ms. Kuramoto and Ms. Seung have no conflict of interest.

Acknowledgements

This study was funded by Boehringer Ingelheim Canada Limited and Pfizer Canada. The data were analysed independently at the HOPE Research Centre.

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