RESEARCH ARTICLE

Economic outcomes among chronic obstructive pulmonary disease Vietnamese patients: Approach considerations from a social perspective

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Abstract

Objective: Chronic obstructive pulmonary disease (COPD) is associated with major burden on economic effects. The objective of this study was to explore cost categories caused by COPD in Vietnam and the relationships between those costs and some demographic factors.

Methods: A cross-sectional study was carried out among 359 COPD patients who visited Dong Nai General Hospital in Vietnam in 2018. Patients were classified according to codes from the International Classification of Diseases, 10th revision (ICD-10) (J44: Chronic obstructive pulmonary disease). Demographic information and clinical status of the data were illustrated by descriptive statistics. With the bootstrapping method, cost data are represented as an arithmetic mean cost (Bootstrap 95% CI).

Results: The sample of this study consisted of 359 patients, of which 280 (78.0%) were outpatient department (OPD) patients compared to the 79 (22%) inpatient department (IPD) patients. Total costs per visit were estimated at $87.10 (95% CI $76.20-$99.50) and $372.10 (95% CI $320.10-$430.00) for OPD and IPD, respectively. The costs had an increasing trend with the number of comorbidities, the severity, and the duration of COPD. The annual costs were higher in men than in women, but there was a "low burden" group of OPD stage IV patients. Costs per visit of the "low burden" group were more correlated with demographic categories than those of the "high burden" group.

Conclusion: The results of this perspective study illustrate that Vietnamese COPD is associated with a significant economic burden. The cost of this disease per case is shown to be proportional to the severity and comorbidities of COPD; additionally, "high burden" groups have double the total costs of COPD.

Keywords: COPD, burden, social perspective, direct cost, indirect cost, Vietnam. (JPMA 69: S-64 (Suppl. 2); 2019)

Introduction

Chronic obstructive pulmonary disease (COPD), a common disease that can be prevented and treated, is identified by continuous, often progressive airflow obstruction leading to enhanced chronic inflammatory airways and lung response to harmful particles or gases.[1] COPD patients usually have poor quality of life, particularly exacerbations and comorbidities, which have been gradually attracting attention among COPD researchers and are contributing factors to the disease severity.[2-6] Moreover, COPD can also cause disability, loss of productivity, and premature mortality — a dead-weight on a country's socioeconomic situation and on its health care systems.[7]

Among adults, the prevalence of COPD remains between 8% and 10% across the world.[8] The World Health Organization (WHO) reported that COPD caused approximately 3 million deaths (5.3% of all deaths) globally in 2016.[9] According to WHO projections, COPD will be one of top leading causes of death globally in 2030.[10] In Europe, COPD prevalence ranges between 2.1% and 26.1%.[11] In 2011, the prevalence of COPD in England and Scotland was estimated to be 1.79% and 2.03%, respectively, which is estimated to increase to 2.19% and 2.20% by 2030.[12] The COPD prevalence in Greece varied across different groups: 3.5% in the general population, 8.4% of people who are 35 years of age with a smoking history, and up to 18.4% of the 30-year-old population.[13-15] Among WHO regions, COPD prevalence was found to be highest in the United States (13.3% in 1990 and 15.2% in 2010), while the lowest figure was for Southeast Asia (7.9% in 1990 and 9.7% in 2010).[16] In the Chinese population over 40 years, COPD prevalence was estimated to be 8.2% (12.4% for men and 5.1% for women) in 2008.[17] In South Korea, COPD morbidity reportedly stands at 8.8% in individuals who are over 19 years of age and 13.4% in people over 40 years of age; although this is a high percentage, it is similar to other countries.[18] In Vietnam, the prevalence of COPD diseases was 4.2% across the general population.[19] Because of the high smoking rate and other risk factors, more than 4% of people over 40 years of age suffered from COPD.[20] A previous study showed that the Vietnamese COPD

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prevalence defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages II-IV was 3.7% in 2014.[21]

COPD has an enormous effect on economic burdens across the world.[22,23] From a report of the European Lung White Book, direct costs of this disease equaled 23.3 billion euro (€23.3 billion), while indirect costs were €1.8 billion higher among the European Union countries in 2011.[24] COPD costs per case range from €1,212 to €3,492 in Germany.[25] In Greece, the total costs of COPD management were €4,730 per patient per year -62.5% from direct costs (medical and non-medical) and 37.5% from indirect costs.[26] In the Netherlands, the direct medical costs were €180 million in 2000, with a projected increase to €495 million by 2025.[27] In England and Scotland, direct health care costs of this disease per year were around 1.50 billion pounds (£1.50 billon) and £159 million in 2011, respectively, and are estimated to reach £2.32 billion and £207 million in 2030, respectively.[12] The annual cost of COPD was forecasted to increase to €166 million by 2030.[28] In 2010, the total cost burden of COPD in the United States was estimated at 36 billion US dollars (US$36 billion), with direct medical costs accounting for approximately nine tenths of the total cost.[29] In Vietnam, the annual direct medical costs of COPD were US$593 per hospitalization while the outpatient figures were US$58 per patient.[30]

Previous studies showed that direct medical costs are highly associated with the comorbidity and severity of COPD, while hospitalization is one of the key drivers of direct medical costs.[31-34] Due to the scarcity of comprehensive and representative evidence on the economic impact of COPD, there is a need for reliable cost estimates to increase COPD awareness and to provide a rational basis for decision makers.[7] However, the social impact of COPD costs has been limited in Vietnam. Therefore, the objective of this perspective study was to explore three main cost categories associated with COPD patients in Vietnam: direct medical costs, direct non-medical costs, and indirect costs from both patients and caregivers, as well as to explore the relationships between those costs and some demographic factors.

Patients and Methods

This cross-sectional study follows the sum-all cost and prevalence-based approach from a societal perspective to estimate cost-of-illness.[35,36] The sum-all medical cost method considered all the medical costs of providing care to a patient, irrespective of who incurred them.[37] Incorporation with a prevalence-based approach yields a general picture of the economic burden of COPD as well as component costs to provide a better point of reference for policymakers to manage the disease on a societal level.[38]

This study was conducted within a three-month period from January to March in 2018 at Dong Nai General Hospital, Vietnam. Construction of the Dong Nai General Hospital, which contains 1,400 beds, was started in 2008. The Dong Nai General Hospital is the first public-private hospital in Vietnam.[39] All patients with a primary diagnosis of COPD according to codes from the International Classification of Diseases, 10th revision (ICD-10) (J44: Chronic obstructive pulmonary disease), were invited to participate via consecutive sampling.[40] Patients diagnosed with stage III and stage IV COPD according to the GOLD classification[41] and with a baseline (post-bronchodilator) FEV1/ FVC ratio of $\leq$70% in the previous 6 months were included in the study. COPD severity was classified using FEV1 as a percentage of predicted normal values (FEV1% predicted) according to the GOLD guidelines, with an FEV1 of $\geq$ 80% indicating stage I COPD, and 50%-79% indicating stage II COPD, 30%-49% indicating stage III COPD, and < 30% indicating stage IV COPD. FEV1 values were obtained from the retrospective medical records of patients.[41] Patients diagnosed with unstable ischemic heart disease, aortic valve stenosis, musculoskeletal disease (which severely limited their exercise capacity), cognitive problems (eg, dementia and psychiatric disorders), or who were impaired in their ability to participate in the study and complete the questionnaires were excluded from the study. Moreover, patients who were lacking the ability to speak or read Vietnamese were also excluded from the study.

The relevant data were collected from an electronic database and interviews. The electronic database provided information related to direct medical costs, whereas face-to-face interviews with COPD patients were conducted through the questionnaire to collect demographic characteristics, direct non-medical costs, and indirect costs. The structured questionnaire consisted of two parts. The first form included information about socio-demographic and clinical characteristics, namely age, gender, weight, height, diagnosis, dialysis status, marital status, education level, monthly income and occupation, residential area, lifestyle, and presence of comorbidities. The second form was associated with transport expenses, supported accommodation costs, meals, working days lost, and caregivers.

The costs consisted of two parts: direct costs and indirect costs.[42] In the present study, the unit cost of health care services has been calculated using the standard costing method.

Direct costs include both the direct medical cost and the direct non-medical cost. The direct medical costs were calculated through the summation of medications, consulting doctor/hospitalization, laboratory tests and functional/imaging tests, and other medical service costs. The other medical services included costs of consulting doctors for other diseases, surgery, and medical supply costs. The cost was calculated through the summation of the products produced by multiplying the quantities of each resource by its acquisition unit cost. Direct non-medical costs were collected from the reports of COPD patients and their family members, including meals (special food or supplements), transportation, accommodation, and informal care costs.

Indirect costs are associated with the costs caused by productivity loss, including work loss of patients and their caregivers. To estimate lost productivity, this study uses an approach characterized by:

(Number of days out of work * GDP per capita in 2017) / number of working days per year.

The gross domestic product (GDP) per capita in 2017 was $2,343,[43] the number of working days per month and per year in 2017 were 22 and 251, respectively, the percentage to be applied to the theoretical labor force was 48.2%, and the national unemployment rate was 2.24%.[44] All costs were collected and calculated in terms of the Vietnamese currency (dong [₫]), then converted to USD by the exchange rate of US$1 = ₫22,594.[45]

Statistical Analysis: All analyses in this study were conducted with Microsoft Excel 365. Demographic information and clinical status of the data were illustrated by descriptive statistics (frequency, percentage, mean, standard deviation, median, 25th-75th interquartile, minimum, maximum). With the bootstrapping method, cost data are represented as an arithmetic mean (Bootstrap 95% CI) cost. The costs of demographic categories were divided by median split into low-burden and high-burden groups, and the Kruskal-Wallis or the Wilcoxon test was applied to test the differences of costs among groups. Statistical significance was considered to be $P < 0.05$.

Ethical Approval: The study protocols were approved by the Dong Nai General Hospital. All the patients provided informed consent after receiving an explanation of the study. The information in the study was used for research purposes only. Anonymity of each patient was maintained by assigning alphanumeric codes.

Results

The sample of this study consisted of 359 patients. According to the GOLD classification, 92 (32.5%) of the 280 OPD patients had GOLD stage III COPD, while 189 (67.5%) patients had GOLD stage IV COPD. All IPD patients had GOLD stage IV COPD.

Approximately four-fifths of them (n=280, 78.0%) were outpatient department (OPD) patients compared to the more than one-fifth (n=79, 22.0%) inpatient department (IPD) patients. A majority were male (OPD: n=253, 90.4%; IPD: n=71, 89.9%) and at the age of 60-69 years old OPD: n=117, (41.8%); IPD: n=51, (64.6%). Well over three-fifths of them had received > 9 years of education (OPD: n=190, 67.9%; IPD: n=51, 64.6%) and had a mean monthly income of around US$132.80 ($0.00-$188.10). The majority of COPD patients had at least one concomitant disease; those who had ≥ 2 comorbidities ranged from 18/79 in IPD patients (22.8%) to 29/91 in OPD stage III patients (31.9%). The most common were cardiovascular diseases, followed by diabetes mellitus, and

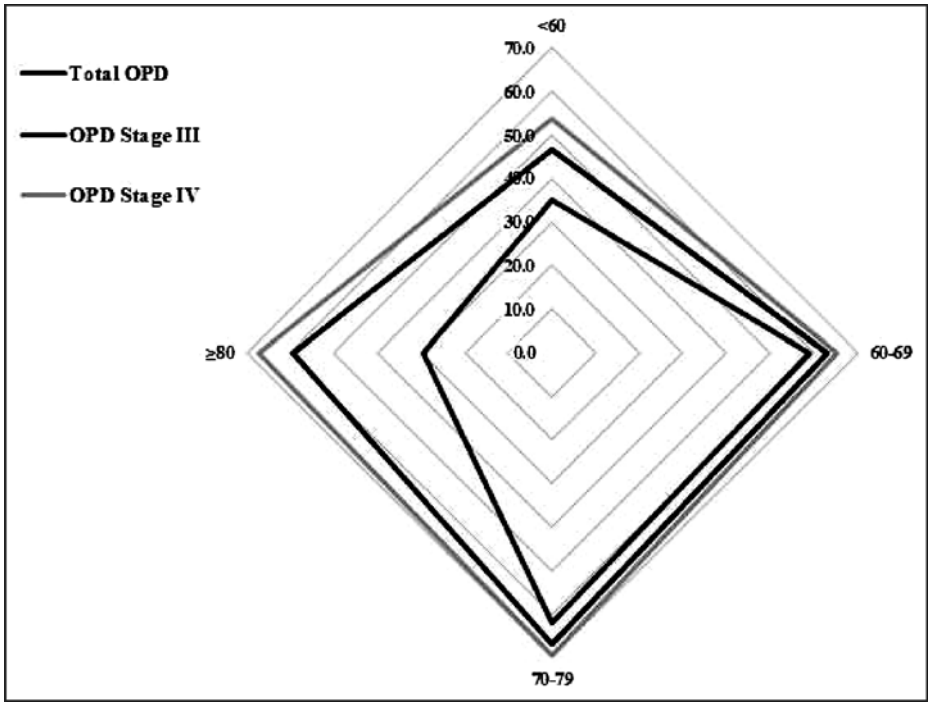

Figure-1: Average total cost of OPD patients with COPD by age groups.

Table-1: Demographic and clinical characteristics of study subjects.

Characteristics n (%)	OPD Stage III n=91	OPD Stage IV n=189	Total OPD n=280	IPD n=79	Characteristics n (%)	OPD Stage III n=91	OPD Stage IV n=189	Total OPD n=280	IPD n=79
Age (years)					Exercise				
<60	17 (18.7)	27 (14.3)	44 (15.7)	8 (10.1)	Yes	43 (47.3)	98 (51.9)	141 (50.4)	20 (25.3)
60-69	41 (45.1)	76 (40.2)	117 (41.8)	51 (64.6)	No	35 (38.5)	65 (34.4)	100 (35.7)	38 (48.1)
70-79	22 (24.2)	45 (23.8)	67 (23.9)	4 (5.0)	Past	13 (14.2)	26 (13.7)	39 (13.9)	21 (26.6)
≥80	11 (12.0)	41 (21.7)	52 (18.6)	16 (20.3)	Duration of COPD (year)				
Mean ± SD	67.9 (11.5)	69.6 (10.6)	69.1 (10.9)	69.2 (9.6)	<1	6 (6.5)	4 (2.1)	10 (3.7)	8 (10.2)
Median (Q1-Q3)	68 (63-72)	68 (62-78)	68 (62-77)	68 (63-72.5)	1-3	14 (15.4)	37 (19.6)	51 (18.2)	12 (15.2)
Range (Min-Max)	39-94	42-97	39-97	51-90	4-5	15 (16.5)	30 (15.9)	45 (16.1)	25 (31.6)
Gender		6-9	25 (27.5)	41 (21.7)	66 (23.6)	14 (17.7)			
Male	79 (86.8)	174 (92.1)	253 (90.4)	71 (89.9)	?10	31 (34.1)	77 (40.7)	108 (38.6)	20 (25.3)
Female	12 (13.2)	15 (7.9)	27 (9.6)	8 (10.1)	Mean ± SD	10.0 (10.4)	8.6 (8.5)	9.9 (15.8)	6.8 (4.9)
Health insurance status (%)					Median (Q1-Q3)	6.0 (3.0-10.0)	7.0 (3.0-10.0)	7.0 (3.0-10.0)	25.0 (14.0-20.0)
80	46 (50.5)	96 (50.8)	142 (50.7)	41 (51.9)	Range (Min-Max)	0.5-40.0	0.5-55.0	0.5-55.0	1.5-20.0
95	4 (4.4)	16 (8.5)	20 (7.2)	4 (5.1)	Smoking status				
100	41 (45.1)	77 (40.7)	118 (42.1)	34 (43.0)	Current smoker	15 (16.5)	28 (14.8)	43 (15.4)	8 (10.1)
Residence					Non-smoker	16 (17.6)	33 (17.5)	49 (17.5)	12 (15.2)
Urban	84 (92.3)	173 (91.5)	257 (91.8)	62 (78.5)	Ex-smoker	60 (65.9)	128 (67.7)	188 (67.1)	59 (74.7)
Rural	7 (7.7)	16 (8.5)	23 (8.2)	17 (21.5)	Years of smoking				
Marital status		Mean ± SD	31.2 (13.4)	33.6 (12.5)	32.8 (12.8)	34.0 (12.9)			
Married	88 (96.7)	185 (97.9)	273 (97.5)	66 (83.5)	Median (Q1-Q3)	30.0 (20.0-40.0)	34.0 (28.5-40.0)	30.0 (22.3-40.0)	30.0 (30.0-45.0)
Single	3 (3.3)	3 (1.6)	6 (2.1)	4 (5.1)	Range (Min-Max)	5.0-55.0	1.0-60.0	1.0-60.0	2.0-50.0
Separated/ Divorced	-	1 (0.5)	1 (0.4)	9 (11.4)	No. of packs of cigarette per day				
BMI[1]					Mean ± SD	1.1 (0.6)	1.1 (0.6)	1.1 (0.6)	1.4 (0.5)
<18.5	20 (22.0)	54 (28.6)	74 (26.4)	51 (64.6)	Median (Q1-Q3)	1.0 (0.8-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.5 (1.0-2.0)
18.5- <23	50 (54.9)	87 (46.0)	137 (48.9)	16 (20.3)	Range (Min-Max)	0.3-3.0	0.6-1.0	0.3-4.0	0.3-2.0
23- <25	13 (14.3)	21 (11.1)	34 (12.2)	4 (5.0)	Family history				
≥25	8 (8.8)	27 (14.3)	35 (12.5)	8 (10.1)	Yes	3 (3.3)	20 (10.6)	23 (8.2)	8 (10.1)
Mean ± SD	21.0 (2.9)	20.8 (3.6)	20.9 (3.4)	18.8 (4.2)	No	88 (96.7)	169 (89.4)	257 (91.8)	71 (89.9)
Median (Q1-Q3)	20.7 (18.7-22.9)	20.1 (18.0-23.1)	20.4 (18.4-22.9)	17.8 (15.6-20.3)	(ICD-10) Comorbidities				
Range (Min-Max)	15.6-28.5	10.1-31.1	10.1-31.1	15.1-30.5	None	21 (23.1)	44 (23.3)	65 (23.2)	11 (13.9)
Education level					N188, N189	-	4 (2.1)	4 (1.4)	13 (16.5)
No school/ Illiterate	2 (2.2)	4 (2.1)	6 (2.1)	4 (5.0)	E119	8 (8.8)	24 (12.7)	32 (11.4)	-
Primary school	24 (26.4)	60 (31.7)	84 (30.0)	24 (30.4)	D648, D649	-	4 (2.1)	4 (1.4)	-
Junior high school	36 (39.5)	56 (29.6)	92 (32.9)	30 (38.0)	I10, I110, I251	51 (56.0)	80 (42.3)	131 (46.9)	42 (53.2)
High school or over	29 (31.9)	69 (36.6)	98 (35.0)	21 (26.6)	K219	9 (9.9)	26 (13.8)	35 (12.5)	8 (10.1)
Employment					M814, M819	2 (2.2)	7 (3.7)	9 (3.2)	5 (6.3)
Employed	8 (8.8)	26 (13.8)	34 (12.2)	8 (10.1)	No. of comorbidities				
Unemployment	25 (27.5)	30 (15.9)	55 (19.6)	30 (38.0)	None	24 (26.4)	40 (21.2)	64 (22.9)	8 (10.1)
Retirement	46 (50.5)	70 (37.0)	116 (41.4)	24 (30.4)	1	38 (41.7)	96 (50.7)	134 (47.8)	53 (67.1)
Other	12 (13.2)	63 (33.3)	75 (26.8)	17 (21.5)	2	27 (29.7)	43 (22.8)	70 (25.0)	14 (17.7)
Monthly income (USD)					≥3	2 (2.2)	10 (5.3)	12 (4.3)	4 (5.1)
No income	52 (57.1)	107 (56.6)	159 (56.8)	51 (64.6)	Mean ± SD	1.1 (0.8)	1.1 (0.9)	1.1 (0.8)	1.2 (0.7)
<180.00	19 (20.9)	57 (30.2)	76 (27.1)	24 (30.4)	Median (Q1-Q3)	1.0 (0.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0)
180.00-<300.00	12 (13.2)	17 (9.0)	29 (10.4)	4 (5.0)	Range (Min-Max)	0.0-3.0	0.0-5.0	0.0-5.0	0.0-3.0
≥300.00	8 (8.8)	8 (4.2)	16 (5.7)	-	MMRC scale[2]				
Mean ± SD	196.3 (128.4)	75.9 (183.5)	181.9 (215.0)	123.3 (37.8)	1	20 (22.0)	27 (14.3)	47 (16.8)	0 (0.0)
Median (Q1-Q3)	177.0 (132.8-188.1)	0.0 (0.0-132.8)	132.8 (88.5-181.5)	132.8 (88.5-132.8)	2	17 (18.7)	31 (16.4)	48 (17.1)	13 (16.4)
Range (Min-Max)	66.4-486.9	0.0-2213.0	0.0-2213.0	88.5-199.2	3	10 (11.0)	16 (8.5)	26 (9.3)	0 (0.0)
					4	32 (35.1)	99 (52.3)	131 (46.8)	33 (41.8)
					5	12 (13.2)	16 (8.5)	28 (10.0)	33 (41.8)

Abbreviations: OPD, Outpatient Department; IPD, Inpatient Department; Total OPD, OPD Stage III and OPD Stage IV; Q1-Q3, 25th - 75th quartile; 1BMI, Body Mass Index; COPD, Chronic Obstructive Pulmonary Disease; 2MMRC scale, Modified Medical Research Council scale; ICD-10 International Classification of Diseases version 10; N188, Chronic kidney disease; N189, Chronic kidney disease, unspecified; I10, Essential (primary) hypertension; I110, Hypertensive heart disease with (congestive) heart failure; I251, Atherosclerotic heart disease; D648, Other specified anaemias; D649, Anemia, unspecified; E119, Non-insulin-dependent diabetes mellitus, Without complication; K219, Gastroesophageal reflux disease without oesophagitis; M814, Drug-induced osteoporosis; M819, Osteoporosis, unspecified; Health insurance status (100%), patients are 100% covered by insurance for costs; 2MMRC scale by level, 1=only breathless with strenuous exercise; 2=breathless when hurrying on level or up a slight hill; 3=walk slower than people of same age on the level due to breathlessness or stop for breath when walking on level at own pace; 4=stop for breath after walking 100 yards or a few minutes on the level; 5=too breathless to leave house or breathless when dressing.

Table-2: Annual direct and indirect costs per patient for COPD [Arithmetic mean (Bootstrap 95% CI)] (USD, 2018).

Characteristics	OPD III n=91		OPD IV n=189		Total OPD n= 280		IPD n=79	
	n	Arithmetic mean (bootstrap 95% CI)	n	Arithmetic mean (bootstrap 95% CI)	n	Arithmetic mean (bootstrap 95% CI)	n	Arithmetic mean (bootstrap 95% CI)
Direct medical cost (1)	91	33.5 (29.3-37.8)	189	44.8 (41.2-48.7)	280	41.2 (38.3-44.4)	79	179.7 (153.1-209.0)
Consulting Doctoc/Hospitalzation	91	2.2 (1.9-2.5)	189	2.6 (2.4-2.8)	280	2.4 (2.3-2.6)	79	56.3 (50.5-62.7)
Medications, intravenous fluids	91	29.7 (25.8-34.0)	189	40.2 (36.8-43.8)	280	36.7 (34.0-39.5)	79	94.0 (77.1-116.2)
Laboratory tests	59	0.9 (0.9-0.9)	21	3.9 (2.5-5.5)	26	3.3 (2.1-4.8)	38	13.3 (9.2-18.0)
Functional/ Imaging tests	9	5.8 (3.5-8.7)	33	4.8 (3.5-6.4)	31	5.2 (3.9-6.6)	13	14.1 (7.3-20.9)
Other	70	1.4 (1.2-1.6)	134	1.7 (1.4-1.9)	204	1.6 (1.4-1.7)	79	20.4 (18.3-22.7)
Direct non-medical cost (2)	91	13.0 (8.8-18.1)	189	14.3 (9.3-20.2)	280	13.9 (9.1-19.9)	79	52.9 (41.7-65.9)
Patients								
Travel costs	37	2.6 (0.9-4.6)	135	5.2 (3.0-8.0)	172	4.8 (2.9-7.2)	39	10.5 (7.2-14.2)
Food costs	40	5.1 (2.6-8.1)	109	2.6 (2.0-3.5)	149	3.2 (1.5-5.5)	67	21.9 (18.7-25.8)
Caregivers								
Food costs	25	0.9 (0.9-0.9)	65	1.0 (0.6-1.5)	90	0.9 (0.7-1.1)	41	20.4 (15.8-25.9)
Accomodation costs	16	4.4 (4.4-4.4)	52	5.5 (3.7-7.3)	68	5.0 (4.0-6.1)	-	-
Indirect cost (3)	91	33.5 (32.1-34.9)	189	31.3 (26.9-36.1)	280	31.9 (28.8-35.2)	79	139.5 (125.4-155.1)
Caregivers' productivity loss	91	14.9 (13.5-16.3)	189	16.1 (15.2-17.0)	280	15.8 (15.0-16.6)	79	69.7 (63.9-75.9)
Patients' productivity loss	91	18.6 (18.6-18.6)	189	15.2 (11.7-19.1)	280	16.2 (13.8-18.6)	79	69.9 (61.5-79.1)
Total cost [(1)+(2)+(3)]	91	80.0 (70.2-90.8)	189	90.4 (77.4-105.0)	280	87.1 (76.2-99.5)	79	372.1 (320.1-430.0)

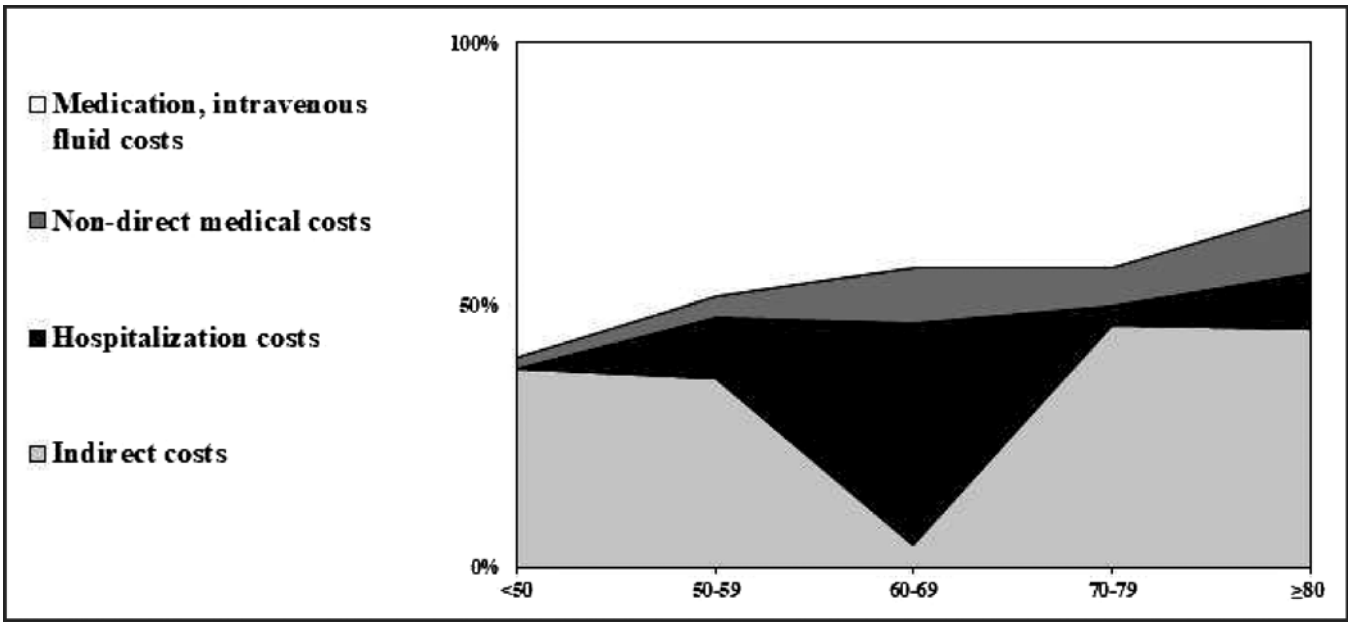

Figure-2: The proportion of the component of chronic obstructive pulmonary disease-related costs (the costs were the summary of 359 patients).

gastroesophageal reflux diseases. Less than one-fifth of the patients (OPD: n=43, 15.4%; IPD: n=8, 10.1%) were current smokers (Table-1).

This evaluation of the health care costs incurred by COPD patients suggested that the direct costs per case were $41.20 (95% CI $38.3-$44.43) for OPD and $179.70 (95% CI $153.1-$209.0) for IPD. In terms of these medical institutions, the costs due to medication and intravenous fluids were the largest contributor to direct medical costs in both OPD and IPD (Table-2). Laboratory tests included both complete blood counts and biochemical tests, while functional and imaging tests included spirometry, electrocardiography, chest radiography (X-ray), and computed tomography (CT).

The mean direct non-medical cost for medical visits of both OPD and IPD were $13.90 (95% CI $9.10-$19.90) and

Table-3: Costs of COPD by demographic category [Arithmetic mean (Bootstrap 95% CI)] (USD, 2018).

Characteristics	OPD Stage III n=91		OPD Stage IV n=189		Total OPD n=280		IPD n=79	
	Low burden	High burden	Low burden	High burden	Low burden	High burden	Low burden	High burden
Gender								
Male	31.0 (17.8-48.2)	95.6 (54.2-137.2)	41.3 (16.5-63.2)	89.9 (64.2-156.7)	36.4 (22.0-54.2)	85.8 (54.2-137.2)	197.9 (67.9-267.4)	439.6 (302.1-875.1)
Female	26.9 (23.8-35.1)	68.0 (50.7-89.0)	42.1 (22.0-64.7)	78.2 (67.0-100.6)	36.5 (17.8-58.4)	84.0 (61.3-140.1)	150.0 (150.0-150.0)	334.9 (334.9-334.9)
p- value	0.19	0.03 (*)	0.42	0.12	0.38	0.33	0.04 (*)	0.24
Health insurance status (%)								
80	29.8 (17.8-50.7)	30.8 (30.3-31.2)	38.0 (19.8-61.3)	81.3 (62.1-120.1)	34.9 (17.8-54.2)	80.5 (56.4-137.2)	188.4 (138.6-245.1)	378.1 (313.0-469.1)
95	23.5 (23.5-23.5)	72.7 (50.7-137.2)	41.3 (25.2-68.2)	89.1 (75.5-118.5)	31.4 (23.5-46.1)	83.8 (59.1-118.5)	267.4 (267.4-267.4)	267.4 (267.4-267.4)
100	34.6 (23.8-51.0)	73.7 (51.0-98.8)	44.5 (23.0-65.0)	98.3 (68.0-271.4)	41.1 (23.0-63.2)	89.8 (63.8-157.1)	225.7 (138.7-302.1)	503.6 (302.1-875.1)
p- value	0.03 (*)	0.03 (*)	0.14	0.04 (*)	0.01 (*)	0.05	<0.01 (*)	<0.01 (*)
Residence								
Urban	31.5 (21.0-48.2)	72.9 (50.7-137.2)	40.5 (19.8-62.2)	88.1 (64.2-140.1)	36.4 (19.8-56.4)	85.7 (61.0-140.1)	205.1 (138.6-258.2)	342.8 (267.4-469.1)
Rural	30.8 (17.8-57.1)	66.4 (63.2-75.7)	42.5 (25.7-61.4)	92.4 (72.6-157.1)	39.7 (17.8-61.4)	83.3 (63.2-157.1)	245.2 (169.2-321.7)	678.1 (451.0-875.1)
p- value	0.17	0.36	0.32	0.29	0.23	0.44	0.05	<0.01 (*)
Marital status								
Married	30.8 (17.8-48.2)	72.7 (50.7-137.2)	41.2 (19.8-62.2)	90.1 (64.2-156.7)	36.4 (17.8-56.6)	85.4 (61.0-156.7)	213.6 (138.6-302.1)	448.2 (302.1-875.1)
Single	63.2 (63.2-63.2)	63.2 (63.2-63.2)	27.9 (25.0-30.6)	94.5 (94.5-94.5)	40.0 (25.0-63.2)	73.8 (63.2-94.5)	451.0 (451.0-451.0)	451.0 (451.0-451.0)
Separated/ Divorced	-	-	-	-	-	-	171.1 (150.0-258.2)	258.2 (258.2-258.2)
p- value	<0.01 (*)	0.27	0.07	0.24	0.50	0.18	<0.01 (*)	<0.01 (*)
BMI								
<18.5	30.1 (23.8-37.3)	67.0 (53.5-100.0)	37.6 (19.8-61.5)	98.4 (62.1-271.4)	35.0 (19.8-54.4)	75.0 (55.0-103.1)	274.8 (238.6-321.7)	459.5 (267.4-875.1)
18.5- <23	30.6 (21.0-46.0)	70.6 (48.2-137.2)	40.6 (15.8-61.7)	84.8 (63.2-118.5)	35.4 (21.0-54.3)	79.7 (56.4-137.2)	215.1 (138.6-267.4)	533.4 (321.7-875.1)
23<25	68.8 (51.0-78.4)	54.2 (39.4-67.9)	39.6 (16.5-58.6)	80.3 (61.3-106.9)	42.5 (16.5-61.3)	85.3 (67.3-106.9)	138.7 (138.7-138.7)	138.7 (138.7-138.7)
≥25	22.5 (17.8-27.4)	54.1 (39.4-67.9)	51.0 (30.9-69.9)	88.9 (71.9-140.1)	41.2 (17.8-67.0)	84.6 (67.9-140.1)	169.2 (169.2-169.2)	302.1 (302.1-302.1)
p- value	<0.01 (*)	0.04 (*)	0.06	0.55	0.20	0.28	<0.01 (*)	<0.01 (*)
Education level								
No school/ Illiterate	17.8 (17.8-17.8)	17.8 (17.8-17.8)	30.9 (24.2-38.1)	61.0 (40.5-80.9)	19.9 (17.8-24.2)	53.9 (38.1-80.9)	334.9 (334.9-334.9)	334.9 (334.9-334.9)
Primary school	31.5 (23.8-53.0)	68.0 (53.0-100.0)	42.0 (22.0-63.2)	91.9 (63.8-157.1)	38.2 (22.5-54.4)	85.2 (56.4-140.1)	232.7 (150.0-302.1)	413.5 (321.7-469.1)
Junior high school	26.3 (21.0-36.9)	77.6 (61.6-98.8)	43.7 (19.8-66.2)	97.5 (67.6-271.4)	42.2 (23.0-61.6)	89.3 (63.2-156.7)	194.6 (138.6-258.2)	490.1 (258.2-875.1)
High school or over	26.3 (21.0-36.9)	66.9 (37.3-137.2)	39.7 (15.8-63.2)	81.0 (63.6-118.5)	33.7 (21.0-54.9)	78.9 (58.6-137.2)	202.4 (138.7-267.4)	413.6 (321.7-469.1)
p- value	<0.01 (*)	0.01 (*)	0.46	0.09	<0.01 (*)	0.04 (*)	0.02 (*)	0.33
Employment								
Employed	38.3 (34.7-48.2)	51.8 (48.2-53.0)	36.0 (19.8-59.1)	82.0 (63.2-109.7)	35.2 (19.8-53.0)	76.5 (53.0-109.7)	238.6 (238.6-238.6)	321.7 (321.7-321.7)
Unemployment	24.6 (17.8-28.1)	63.4 (35.1-82.3)	40.6 (16.5-61.3)	85.5 (62.2-140.1)	31.8 (16.5-53.1)	77.1 (58.4-140.1)	200.2 (138.7-313.0)	558.3 (313.0-875.1)
Retirement	32.9 (23.5-50.7)	75.3 (50.7-137.2)	41.2 (15.8-64.7)	95.6 (65.0-271.4)	36.3 (22.6-57.1)	88.8 (61.0-157.1)	272.5 (239.7-328.3)	397.8 (334.9-469.1)
Other	38.3 (27.5-54.2)	86.4 (67.9-100.0)	42.1 (22.0-62.1)	88.3 (64.2-156.7)	42.0 (24.3-62.1)	86.6 (64.2-156.7)	154.4 (138.6-169.2)	262.4 (258.2-267.4)
p- value	0.01 (*)	0.01 (*)	0.38	0.88	0.01 (*)	0.05	<0.01 (*)	<0.01 (*)
Monthly income (USD)								
No income	27.3 (17.8-39.4)	74.6 (39.9-100.0)	43.2 (22.0-61.4)	86.5 (62.2-140.1)	37.3 (17.8-61.3)	83.2 (61.5-140.1)	184.4 (138.6-258.2)	443.8 (267.4-875.1)
<180.00	38.3 (27.1-50.7)	60.2 (51.0-78.4)	35.2 (15.8-61.0)	96.4 (65.0-271.4)	35.3 (22.6-53.0)	90.1 (53.5-271.4)	269.3 (238.6-321.7)	400.7 (334.9-469.1)
180.00-<300.00	32.9 (23.5-46.0)	84.9 (46.0-137.2)	40.3 (19.8-63.2)	78.2 (65.0-100.6)	34.7 (19.8-56.4)	82.4 (57.1-137.2)	239.7 (239.7-239.7)	300.6 (272.9-328.3)
≥300.00	38.5 (35.2-48.2)	64.2 (48.2-69.9)	49.4 (29.2-64.7)	84.8 (72.4-106.3)	41.3 (29.2-63.2)	76.6 (64.7-106.3)	-	-
p- value	<0.01 (*)	0.07	0.02 (*)	0.34	0.36	0.74	<0.01 (*)	0.13
Exercise								
Yes	27.9 (17.8-35.1)	60.6 (35.1-88.2)	41.8 (22.5-65.0)	88.0 (67.0-128.6)	35.2 (17.8-55.0)	82.1 (58.4-128.6)	199.4 (138.6-245.1)	335.4 (245.1-396.1)
No	37.1 (21.0-57.1)	83.1 (61.6-137.2)	36.8 (16.5-61.3)	87.4 (61.4-157.1)	37.3 (19.8-61.3)	86.9 (61.6-156.7)	186.1 (138.7-258.2)	470.7 (258.2-875.1)
Past	31.7 (27.4-37.3)	69.6 (54.2-84.4)	46.8 (29.2-62.2)	96.0 (64.2-271.4)	40.4 (27.4-53.0)	60.7 (53.1-71.0)	301.2 (239.7-334.9)	388.9 (334.9-469.1)
p- value	0.04 (*)	0.01 (*)	0.10	0.49	0.19	<0.01 (*)	<0.01 (*)	0.24
Duration of COPD (year)								
<1	26.0 (25.2-27.1)	35.3 (27.1-39.9)	42.0 (40.4-43.7)	62.0 (52.2-72.4)	29.0 (25.2-39.4)	49.0 (39.9-72.4)	302.1 (302.1-302.1)	469.1 (469.1-469.1)
1-3	27.7 (27.4-28.1)	51.8 (29.3-63.2)	39.4 (15.8-62.1)	88.7 (63.6-157.1)	36.4 (19.8-58.4)	81.9 (58.6-157.1)	144.1 (138.6-169.2)	595.2 (169.2-875.1)
4-5	31.9 (17.8-51.0)	67.0 (51.0-84.4)	47.2 (16.5-68.2)	87.3 (69.9-122.2)	41.1 (16.5-61.6)	86.0 (61.7-137.2)	212.9 (169.2-245.1)	333.4 (245.1-396.1)
6-9	39.9 (23.5-61.6)	83.4 (67.9-137.2)	39.7 (28.8-54.3)	77.4 (61.0-100.2)	37.7 (23.5-61.0)	76.6 (62.2-100.2)	260.8 (258.2-267.4)	324.5 (267.4-347.4)
≥10	32.0 (21.0-46.0)	72.0 (50.7-100.0)	40.3 (22.5-63.2)	95.1 (64.2-271.4)	37.2 (21.0-55.0)	90.8 (60.5-140.1)	200.9 (150.0-239.7)	322.8 (272.9-334.9)
p- value	0.44	<0.01 (*)	0.45	0.11	0.32	<0.01 (*)	<0.01 (*)	<0.01 (*)

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Smoking status								
Current smoker	36.4 (25.2-53.0)	65.6 (53.0-78.4)	40.5 (22.5-63.2)	85.7 (63.2-122.2)	38.7 (22.5-61.3)	90.7 (60.5-140.1)	264.3 (239.7-302.1)	302.1 (302.1-328.3)
Non-smoker	47.4 (35.1-54.2)	80.8 (54.2-100.0)	36.0 (15.8-61.7)	79.5 (64.7-104.2)	39.9 (15.8-54.2)	79.7 (57.1-104.2)	142.4 (138.7-150.0)	312.7 (150.0-396.1)
Ex-smoker	27.6 (17.8-35.2)	69.7 (35.2-137.2)	41.9 (19.8-62.2)	92.5 (64.2-157.1)	35.5 (17.8-58.4)	85.9 (61.0-156.7)	224.4 (138.6-267.4)	454.7 (313.0-875.1)
p- value	<0.01 (*)	0.08	0.37	0.34	0.29	0.54	<0.01 (*)	0.02 (*)
Family history								
Yes	69.9 (69.9-69.9)	69.9 (69.9-69.9)	53.6 (16.5-67.3)	92.5 (73.8-120.1)	54.7 (16.5-69.9)	88.7 (69.9-120.1)	238.6 (238.6-238.6)	321.7 (321.7-321.7)
No	30.4 (17.8-46.0)	71.1 (50.7-137.2)	38.8 (19.8-61.3)	91.6 (62.2-157.1)	35.7 (19.8-54.6)	83.2 (57.1-140.1)	205.7 (138.6-267.4)	439.9 (272.9-875.1)
p- value	<0.01 (*)	0.45	<0.01 (*)	0.07	<0.01 (*)	0.06	0.32	0.05
No. of comorbidities								
None	26.9 (17.8-34.6)	63.4 (35.1-84.4)	33.2 (19.8-49.7)	76.4 (58.4-118.2)	30.2 (17.8-42.3)	72.8 (45.4-118.2)	138.6 (138.6-138.6)	321.7 (321.7-321.7)
1	29.8 (21.0-46.0)	70.7 (46.0-137.2)	39.5 (16.5-61.3)	90.4 (61.5-157.1)	36.4 (16.5-54.4)	85.4 (55.0-157.1)	200.0 (138.7-267.4)	465.4 (267.4-875.1)
2	37.7 (25.2-54.2)	77.2 (61.6-98.8)	50.8 (29.2-71.0)	96.0 (71.9-156.7)	45.9 (25.2-67.6)	90.1 (68.0-156.7)	253.0 (239.7-258.2)	333.6 (272.9-347.4)
≥3	67.9 (67.9-67.9)	67.9 (67.9-67.9)	46.6 (33.8-67.0)	82.8 (68.2-100.6)	50.1 (33.8-67.9)	80.1 (67.9-100.6)	334.9 (334.9-334.9)	334.9 (334.9-334.9)
p- value	0.01 (*)	0.18	<0.01 (*)	0.02 (*)	<0.01 (*)	0.01 (*)	<0.01 (*)	0.43
MMRC								
1	31.2 (21.0-46.0)	79.7 (48.2-137.2)	35.6 (15.8-61.4)	86.5 (61.7-156.7)	32.3 (15.8-47.8)	83.6 (48.2-156.7)	-	-
2	38.8 (25.9-61.6)	87.7 (78.4-100.0)	40.3 (16.5-63.2)	86.0 (63.2-120.1)	38.2 (16.5-61.6)	85.7 (63.2-120.1)	148.3 (138.6-169.2)	296.9 (169.2-347.4)
3	37.2 (27.1-50.7)	62.5 (50.7-69.9)	37.0 (22.0-55.7)	81.4 (58.6-94.8)	36.5 (22.0-50.7)	74.2 (50.7-94.8)	-	-
4	28.8 (17.8-37.3)	70.1 (53.0-88.2)	42.7 (22.6-64.7)	92.5 (66.2-157.1)	38.4 (17.8-61.4)	87.9 (63.6-157.1)	257.6 (238.6-302.1)	375.9 (302.1-469.1)
5	34.1 (28.1-51.0)	58.2 (51.0-63.2)	44.2 (31.4-54.3)	76.1 (56.6-100.6)	39.6 (28.1-53.9)	69.5 (54.2-100.6)	193.1 (138.7-267.4)	499.7 (267.4-875.1)
p- value	0.43	0.01 (*)	0.46	0.53	0.30	0.01 (*)	<0.01 (*)	0.50

Abbreviations: OPD, Outpatient Department; IPD, Outpatient Department; Total OPD included OPD Stage III and OPD Stage IV, BMI, Body Mass Index; COPD, Chronic Obstructive Pulmonary Disease; MMRC, Modified Medical Research Council; MMRC scale, 1= only breathless with strenuous exercise; 2=breathless when hurrying on level or up a slight hill; 3=walk slower than people of same age on the level due to breathlessness or stop for breath when walking on level at own pace; 4=stop for breath after walking 100 yards or a few minutes on the level; 5=too breathless to leave house or breathless when dressing. (*), p-value < 0.05

$52.90 (95% CI $41.70-$65.90) per patient per case, respectively; the costs for patients were slightly higher than those for caregivers. The mean indirect costs per visit for COPD in OPD and IPD patients were $31.90 (95% CI $28.80-$35.20) and $139.50 (95% CI $125.40-$155.10), respectively. The costs for IPD patients were significantly higher than those for OPD patients because IPD patients had to stay in hospitals much longer, which led to greater productivity loss for both patients and their caregivers (Table-2).

Total costs per visit were estimated at $87.10 (95% CI $76.20-$99.50) and $372.10 (95% CI $320.10-$430.00) for OPD and IPD, respectively (Table-2). Direct medical costs accounted for more than half of the total costs whereas indirect costs were second highest (Figure-1). The mean annual cost for OPD patients with GOLD stage III was $80.00 (95% CI $70.20-$90.80), while the cost for patients with GOLD stage IV it was $90.4 (95% CI $77.40-$105.00). The mean annual per-patient costs related to stages of disease severity are presented in Table-2. Furthermore, the annual total cost for patients in the GOLD stage IV group was slightly higher compared to the cost for patients in the GOLD stage III group. Average expenditures for OPD patients in the 70-79 age group were higher than those for other age groups (Figure-2).

Costs for outpatient visits of patients with GOLD stage IV were significantly correlated with health insurance status, BMI, education level, employment, and exercise. The costs had an increasing trend with the number of comorbidities, the severity, and the duration of COPD. The annual costs were higher in men than in women, but there was a "low burden" group of OPD stage IV patients. Costs per visit of the "low burden" group were more correlated with demographic categories than those of the "high burden" group (Table-3).

Discussion

This study uncovered the full economic impact of demographic, clinical, and economic characteristics of COPD patients in Vietnam. It was found that most Vietnamese patients with COPD were male (86.8%-92.1%) while 65.9%-74.7% were ex-smokers. Regarding economic impact, over 50% of direct medical costs came from medication, intravenous fluids, functional/imaging tests, and hospitalization. The results of this study showed that the indirect costs for COPD patients were considerable and nearly as high as the direct medical cost of COPD.

COPD is a disease related to high economic burden worldwide. One previous Vietnamese study focused only on direct health costs, which varied between $22.40 and $247.60 per patient per case. Due to the large sample of the study, the costs related to OPD expenses ranged from $22.40 to $23.50 while those for IPD costs were in the

range of $180.90-$247.60.[46] The results of this study indicate that the cost of direct medical care for OPD patients is slightly higher than these estimates ($33.50-$44.80), and those for IPD patients are significantly lower than previous findings ($179.70). The direct expenditure and total costs per patient were equivalent to 18.6%-99.7% and 44.4%-206%, respectively, of their personal income. Indirect costs accounted for 34.6%-41.9% of total costs; these results are quite similar to a report published in the US (27%-61%).[47] Indirect costs of COPD were found to have an upward trend in the past several years.[28]

On the international level, there are significant variations of COPD costs worldwide. Societal per-patient costs have been found to vary enormously, from $1,721 in Russia to $30,826 in the US.[48] In general, observed cost differences between studies are large because of the difference between national treatment patterns, labor markets, and price structures. However, there is a consistent pattern across countries, showing that increased costs are associated with more severe disease and a greater number of comorbidities.[48] Particularly, according to disease severity, the mean per-patient costs of OPD patients was slightly higher for those with stage IV COPD compared to those with stage III in this study. Similarly, the cost was doubled or tripled for patients in "high burden" groups compared to the "low burden" groups. Similar results were also reported in a previous study, which only looked at the pharmaceutical cost of the disease,[49] and in the study of Boland et al[50] which showed that GOLD stages and groups were strongly related with the total health care costs of COPD. Moreover, a Swedish study also showed that the costs of COPD were highly associated with disease severity, with the mean total costs for a subject with a very severe case being 29 times higher than for a subject with mild COPD.[51]

Gender did not illustrate any relationship with the cost categories, while total costs by age groups showed that elderly patients incur higher direct costs. Due to increased risks of comorbidities and poor health, elderly people generally have a high need for hospitalizations and caregivers. A long hospital duration may lead to the increase in daily costs due to treatment-resistant, severe cases of many accompanying comorbidities. The relationship between increased costs and a lengthy hospital stay has been demonstrated in many previous studies.[33,52,53]

Comorbidities are recognized as a critical factor associated with high mortality in COPD.[54,55] Diabetes, heart failure, renal failure, cancer, and neuropsychiatric diseases are common with aging and often occur together;[56,57] if any of these diseases exist in these individuals, the possibility that others exist is higher in these individuals compared to healthy adults.[58] In a previous study, 28.9% of patients had two comorbid diseases including hypertension (most common) and other cardiovascular diseases, such as coronary artery disease and congestive heart failure, as well as diabetes mellitus.[59] In this study, the existence of two comorbid diseases occurred in 22.2%-29.7% of patients, the most common being cardiovascular diseases (42.3%-56.0%), followed by diabetes mellitus (8.8%-12.7%), and gastroesophageal reflux diseases (9.9%-13.8%). Similarly, some previous studies showed that cerebrovascular disease, mainly hypertension, was the most common comorbidity related to COPD.[54,60,61]

The comorbidity existence is significantly associated with the total costs of COPD patients. The expenditure of this disease associated with cardiovascular diseases, diabetes, gastroesophageal reflux diseases, chronic kidney disease, anemia, and osteoporosis were estimated to be higher than those associated with COPD without comorbidities. Some previous studies have also demonstrated a strong relationship between the yearly costs of COPD and the number of comorbid diseases.[52,62,63] One study assessed the factors associated with the increase costs for patients hospitalized due to exacerbation and reported a significant relationship between increased costs and comorbidities.[52] COPD patients with comorbidities require hospitalization, which leads to increased costs. Moreover, approximately 50% of COPD patients use cardiovascular medications and, more frequently, analgesics, antibiotics, and psychotherapeutic drugs.[62] Another study discovered that the direct costs of COPD patients with comorbid diseases were 4.7 times higher than those without a comorbidity.[61] Dalal et al observed that yearly direct costs were 38% more in COPD patients with cardiovascular disease compared to patients with COPD only.[64] Pasquale et al also found that the yearly costs of COPD cases with the existence of cardiovascular disease and diabetes mellitus were found to be 1.69 times and 1.46 times higher, respectively, than those for COPD patients without a comorbidity.[65]

Limitations

This study is subject to certain limitations. First, COPD patients involved in this study were not randomly selected but were chosen from only one hospital of the country, which may affect its external validity. Therefore, future studies should focus on the prevalence in the general population. Second, this study was designed to estimate the total cost of COPD but not to evaluate the cost of exacerbations (which significantly contribute to the total cost in many studies) due to the absence of

related data.[26,48,51,59,66] Moreover, the retrospective data used to calculate direct medical costs are highly associated with COPD in the past three months, but it is possible that a proportion of these resources may not be strictly associated to COPD but to its related comorbidities. Thus, a clear distinction between costs strictly COPD-related and costs related to its comorbidities cannot be made from the database, and results show all costs associated with COPD and its comorbidities.

Third, there are some related-cost parameters not included in the study which might have led to an underestimation of true costs. Cost estimates do not include any disability pensions or other health care benefits COPD patients might receive. Another limitation is that it does not incorporate productivity losses related to premature death due to COPD. Premature death is a significant component of indirect costs, especially in the case of diseases causing significant mortality as COPD, because we only aimed to capture the costs associated with absence from work due to illness. Due to the difficulty in estimating the intangible costs associated with COPD-such as the loss of quality of life, and pain and suffering of both patients and their caregivers-intangible costs were not taken into consideration in calculations.

Conclusion

The results of this perspective study illustrate that Vietnamese COPD is associated with a significant economic burden. The cost of this disease per case is shown to be proportional to the severity and comorbidities of COPD; additionally, "high burden" groups have double the total costs of COPD. In brief, estimations of direct and indirect costs of COPD might provide valuable information for decision making based on empirical evidence that will benefit not only patients but also society in general.

Recommendations

This study provides up-to-date cost estimates of COPD in Vietnam that are needed to raise COPD awareness. The results of this study can contribute to discussions around cost rationalization policies in the field of health care to minimize costs. The economic impacts of COPD are mainly associated with the severity of the disease and its comorbidities, so there is a need for early detection of COPD as well as reasonable management of the most common comorbidities, such as diabetes mellitus, hypertension, and kidney failure, which might to reduce these costs. The implementation of these measures would decrease the cost load of COPD and increase the cost effectivity of managing the disease. Overall, COPD has an enormous economic impact on society and a joint effort of all stakeholders is required to develop cost-effective interventions, prevention, and disease management programs. It should be noted that further research is needed on this topic for results of this study to be comparative and representative, and to be able to conclude with more reliable estimates.

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