Economic Burden of Patients in the United States with Moderate-to-Severe Chronic Obstructive Pulmonary Disease: A Focused Literature Review

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INTRODUCTION

- Chronic obstructive pulmonary disease (COPD) affects more than 15 million Americans, significantly impacting health outcomes and imposing considerable economic burden on both individuals and healthcare systems.[1,2]
- The overall cost related to COPD in the United States (US) was reportedly $49 billion in 2020, and an estimated annual medical cost of severe COPD was $18,070.[2]

OBJECTIVE

- This focused literature review (FLR) aimed to assess the direct and indirect costs, healthcare resource utilisation (HCRU) and cost drivers among patients with COPD in the US.

METHODS

Data source

- This FLR included all relevant articles from Embase, MEDLINE and the Cochrane Library, published between July 28, 2012 to July 28, 2022. Additionally, respiratory conference summaries and the websites of the American College of Chest Physicians and the Global Initiative for Chronic Obstructive Lung Disease were reviewed.

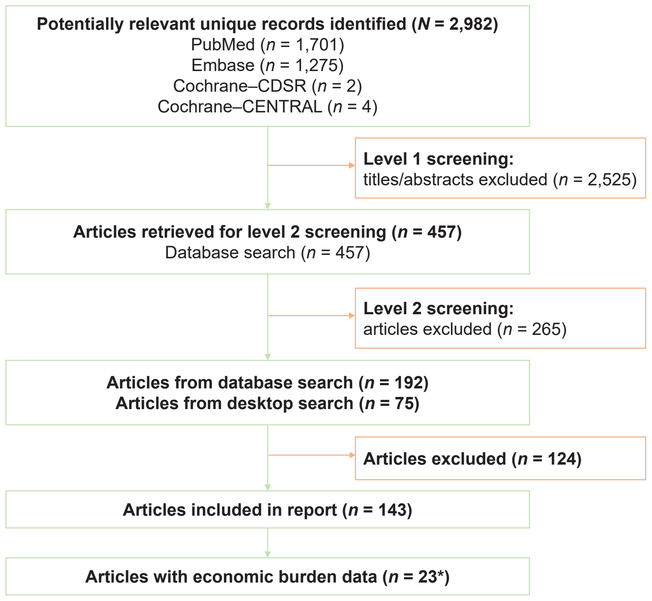
Study criteria and study selection

- All review articles (including targeted reviews and scoping reviews), systematic literature reviews (including reviews of observational studies) and meta-analyses describing economic burden of moderate-to-severe COPD in patients aged > 40 years were included. Economic modelling studies including cost-effectiveness and budget impact analysis were excluded.
- Studies were selected after a two-level screening process. Study selection is further described in **Figure 1**.

Data extraction

- Study design, sample size, study population, HCRU, total costs, direct costs including hospitalisation costs and costs by disease severity, indirect costs and cost drivers in the US.
- Quality check: Data from included studies were extracted by one researcher and quality-checked by a second researcher.

Figure 1. Study selection process flow chart



*Out of 143 articles, 22 reviews (8 SLRs and 14 non-SLRs) and one retrospective study reported data on economic burden of COPD.

CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane Central Register of Controlled Trials; SLR; systematic literature review.

RESULTS

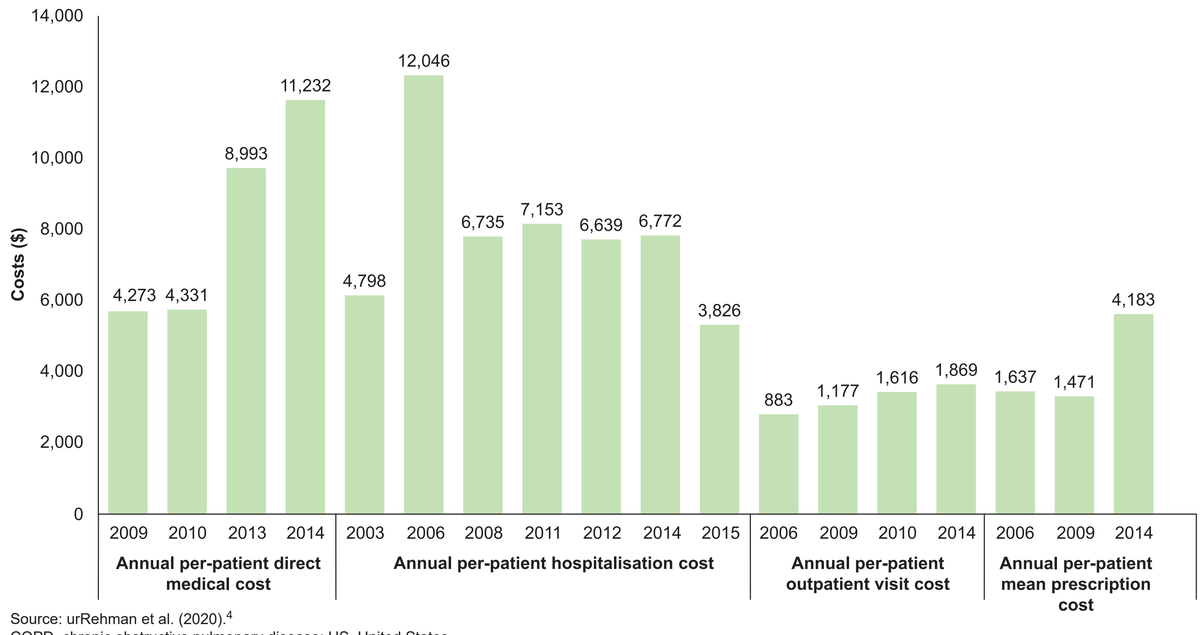
- A total of 143 articles were included in the report. Of which, 23 articles were identified with the economic burden outcome.
- Around 9%–31% of COPD patients with exacerbation required an emergency department (ED) visit and approximately 14%–35% required hospitalisation.[3]
- The annual per-patient direct cost increased from $1,425 in patients with no exacerbation to $12,765 in patients with ≥ 2 exacerbations. The highest reported mean cost for a hospitalised exacerbation was $18,120 (**Table 1**).[4] Furthermore, per-patient annual direct costs (in different years) are depicted in **Figure 2**.
- Indirect costs accounted for 27%–61% of total costs, and total annual mean indirect costs ranged from $893 to $2,234 per patient with COPD in 1994–2004 or from $1,521 to $3,348 in 2010 (**Table 2**).[5] The indirect cost due to morbidity and mortality in 1999 was estimated to be $1.26 and $0.88 billion, respectively, and the projected morbidity and mortality cost in 2010 was $8.0 and $15.0 billion, respectively.[5]
- COPD patients, particularly those suffering from nocturnal and early morning symptoms, reported higher absenteeism and productivity losses compared to healthy individuals.
- The average COPD-related HCRU was significantly higher for the ≥ 220 cells/μL, ≥ 300 cells/μL and ≥ 400 cells/μL subgroups than that for the < 220 cells/μL subgroups (All $P < 0.001$), except for ED visits, which was significantly higher in ≥ 400 cells/μL subgroup ($P < 0.05$) (**Table 3**).[6]
- After adjusting for baseline clinical characteristics, every 100-unit rise in eosinophil count was linked with a significant 4.54% increase in total COPD-related costs and a 2.24% rise in total all-cause costs ($P < 0.001$ for both). Hospital and prescription costs were significant contributors for COPD-related costs, whereas hospital and outpatient visits/procedures were the significant contributors for all-cause costs (**Table 4**).[6]
- Management of exacerbations is the major cost driver of COPD with annual healthcare costs being 10-fold higher for patients with COPD without exacerbations than for patients with COPD without exacerbations.

Table 1. US studies reporting costs estimates of treating exacerbations

Reference	Number of patients and year	Cost-related outcomes	
AbuDagga et al. (2013)[7]	*N* = 17,382; 2004–2012	Cost per exacerbation, mean (SD):	Moderate: $269 ($748) Severe: $18,120 ($31,592)
		Annual exacerbation costs, mean (SD):	≥ 1 moderate: $405 ($1,169) ≥ 1 severe: $25,364 ($43,493)
Dalal et al. (2011a)[8]	*N* = 71,493; 2005–2009	Cost per visit for exacerbation, mean (SD) ED visit:	$647 ($445)
		Simple admissions (no ICU/intubation):	$7,242 ($7,987)
		Complex admissions (general/surgical/medical ICU and/or intubation):	$20,757 ($41,370) (5.8% of all admissions)
Dalal et al. (2011b)[9]	*N* = 51,210 (commercial plan), and *N* = 42,166 (Medicare plans); 2006–2009	Per visit COPD-related healthcare costs (2009), mean ED visit (commercial):	$345
		ED visit (Medicare):	$429
		Standard hospitalisation (commercial):	$10,170
		Standard hospitalisation (Medicare):	$7,430
		Intensive care hospitalisation (commercial):	$39,229
		Intensive care hospitalisation (Medicare):	$14,112
Dhamane et al. (2015)[10]	*N* = 52,459; 2007–2012	Mean COPD-related total costs over 24 months No exacerbations:	$1,605
		≥ 1 exacerbation:	$3,707
		≥ 2 exacerbations:	$6,712
		≥ 3 exacerbations:	$12,257
Ke et al. (2016)[11]	*N* = 754; 2011–2014	Annual COPD-related healthcare costs for all patients,[a] mean (SD; median) ED visits:	$257 ($1,039; $0)
		Hospitalisations:	$7,625 ($21,785; $0)
Pasquale et al. (2012)[12]	*N* = 8,554; 2007–2011	COPD-related annual total costs, mean (95% CI) No exacerbations:	$1,425 ($1,404-$1,447)
		≥ 1 moderate or severe exacerbation:	$7,022 ($6,926-$7,119)
Perera et al. (2012)[13]	*N* = 1,254,703; 2006	Cost per hospitalisation for acute exacerbation, mean (SD) Overall (COPD or chronic bronchitis ICD-9 code with pneumonia or procedure code for mechanical ventilation):	$9,545 ($12,700)
		Principal diagnosis of COPD:	$7,015 ($8,289)
		With mechanical ventilation:	$24,374 ($26,608)
		Without mechanical ventilation:	$7,569 ($7,434)
Yu et al. (2011)[14]	*N* = 228,978; 2004–2009	Total healthcare cost per patient quarter (90 days), mean (SD) No exacerbations:	$4,762 ($13,082)
		Mild-to-moderate exacerbation:	$6,628 ($18,188)
		Severe exacerbation:	$17,016 ($24,675)
		COPD-related total cost per patient quarter (90 days), mean (SD) No exacerbation:	$658 ($3,336
		Mild-to-moderate exacerbation:	$1,522 ($11,505)
		Severe exacerbation:	$7,014 ($13,278)
Wallace et al. (2019)[15]	*N* = 1,505; 2011–2015	Annual COPD-related healthcare costs for all patients,[a] mean (SD) ED visits:	GOLD 1: $186 ($1,100) GOLD 2: $144 ($588) GOLD 3: $193 ($651) GOLD 4: $534 ($1,059)
		Hospitalisations:	GOLD 1: $3,853 ($12,462) GOLD 2: $4,449 ($12,728) GOLD 3: $6,277 ($12,970) GOLD 4: $12,139 ($15,599)

Source: Bollmeier et al. (2020)3, Wallace et al. (2019)[15].
[a]Costs calculated from whole population including patients who did not use the service. 2011 GOLD airflow limitation severity classification: GOLD 1 (mild), FEV_1 ≥ 80% predicted; GOLD 2 (moderate), FEV_1 50%-79% predicted; GOLD 3 (severe), FEV_1 30%-49% predicted; GOLD 4 (very severe), FEV_1 < 30% predicted.
All studies listed above had a retrospective claims design.
CI, confidence interval; COPD, chronic obstructive pulmonary disease; ED, emergency department; FEV_1, forced expiratory volume in 1 second; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICD-9, International Classification of Diseases Ninth Revision; ICU, intensive care unit; SD, standard deviation; US, United States.

Figure 2. Annual per-patient direct costs of COPD in US dollars



Source: urRehman et al. (2020).[4]
COPD, chronic obstructive pulmonary disease; US, United States.

Table 2. US studies reporting costs associated with the indirect burden of COPD

Study	Base year	Outcome measure	Reported cost	Cost inflated to 2010 US dollars[a]
		Mean cost per person affected by COPD		
Nair et al. (2012)[16]	2000–2007	Mean annual indirect expenditures	$909 higher for COPD vs. non-COPD employees	$1,016 higher for COPD vs. non-COPD employees
Darkow et al. (2007)[17]	2001–2004	Mean annual all-cause disability cost per case (COPD) or control with disability claim	$9,815 (case) vs. $6,335 (control)	$14,130 (case) vs. $9,121 (control)
		Mean cost per person for total COPD population		
Leigh et al. (2002)[18]	1996	Mean annual mortality (lost productivity) costs for occupational COPD	$526[b]	$896
		Mean annual morbidity costs for occupational COPD	$376[b]	$640
		Total mean indirect costs for occupational COPD	$893[b]	$1,521
Halpern et al. (2003)[19]	2000	Mean annual indirect costs	$1,527	$2,289
Darkow et al. (2007)[17]	2001–2004	Mean annual disability costs	$2,234[b]	$3,348

[a]Inflated using medical care component of the Consumer Price Index. [b]Calculated by authors using data provided in publication.
COPD, chronic obstructive pulmonary disease; US, United States.
Source: Patel et al. (2014).[5]

Table 3. COPD-related HCRU in the US

COPD-related outcome	Index eosinophil group			
	< 220 cells/μL (*n* = 22,542)	≥ 220 cells/μL (*n* = 17,397)	≥ 300 cells/μL (*n* = 13,913)	≥ 400 cells/μL (*n* = 7,440)
Inpatient hospitalisations				
Patients, *n* (%)	671 (3.0)	658 (3.8)[a]	531 (3.8)[a]	298 (4.0)[a]
Events[b] (per patient[c])	0.049 (0.3)	0.065 (0.4)[a]	0.066 (0.5)[a]	0.069 (0.5)[a]
ED visits				
Patients, *n* (%)	827 (3.7)	693 (4.0)	557 (4.0)	318 (4.3)[d]
Events (per patient)	0.066 (0.5)	0.072 (0.6)	0.073 (0.6)	0.085 (0.7)[d]
Outpatient office visits/procedures				
Patients, *n* (%)	6,435 (28.5)	5,429 (31.2)[a]	4,372 (31.4)[a]	2,410 (32.4)[a]
Events (per patient)	4.9 (16.3)	5.6 (21.3)[a]	5.7 (22.1)[a]	6.1 (25.2)[a]
Pharmacy use				
Patients, *n* (%)	17,287 (76.7)	13,697 (78.7)[a]	11,003 (79.1)[a]	5,917 (79.5)[a]
Events (per patient)	6.1 (8.9)	6.7 (9.1)[a]	6.9 (9.3)[a]	7.2 (9.7)[a]

[a]$P < 0.001$ (< 220 vs. ≥ 220, ≥ 300, ≥ 400 cells/μL). [b]Values are mean (SD) unless otherwise specified. [c]Events per patient for all patients in the category.
[d]$P < 0.05$ (< 220 vs. ≥ 220, ≥ 300, ≥ 400 cells/μL).
COPD, chronic obstructive pulmonary disease; ED, emergency department; HCRU, healthcare resource utilisation; SD, standard deviation; US, United States.
Source: Trudo et al. (2019)[6].

Table 4. Healthcare cost in the US: all-cause and COPD-related cost (per patient)

COPD-related outcome	Index eosinophil group			
	< 220 cells/μL *n* = 22,542)	≥ 220 cells/μL (*n* = 17,397)	≥ 300 cells/μL (*n* = 13,913)	≥ 400 cells/μL (*n* = 7,440)
All-cause cost				
Overall[a]	$21,049 (59,014)	$24,670 (72,026)[b]	$24,935 (72,169)[b]	$26,199 (80,476)[b]
Hospitalisation/inpatient	$4,837 (31,999)	$6,524 (44,676)[b]	$6,457 (42,300)[b]	$7,126 (46,786)[b]
ED visits	$427 (1,649)	$445 (1,918)	$446 (1,841)	$466 (1,929)
Outpatient visits/procedures	$10,282 (37,190)	$11,908 (47,094)[b]	$12,141 (50,096)[b]	$12,876 (56,685)[b]
Pharmacy	$5,503 (20,760)	$5,793 (12,365)	$5,891 (12,430)[c]	$5,731 (10,010)
COPD-related cost				
Overall	$4,357 (22,884)	$5,407 (28,402)[b]	$5,491 (28,974)[b]	$5,774 (31,376)[b]
Hospitalisation/inpatient	$2,065 (19,462)	$2,764 (24,630)[c]	$2,791 (25,206)[c]	$3,011 (27,516)[c]
ED visits	$80 (624)	$95 (906)	$94 (817)	$112 (1,001)[c]
Outpatient visits/procedures	$1,316 (7,125)	$1,532 (8,367)[b]	$1,555 (8,547)[b]	$1,548 (7,785)[b]
Pharmacy	$896 (2,554)	$1,016 (2,487)[b]	$1,051 (2,457)[b]	$1,102 (2,524)[b]

[a]Values are mean (SD) unless otherwise specified. [b]$P < 0.001$ (< 220 vs. ≥ 220, ≥ 300, ≥ 400 cells/ μL). [c]$P < 0.05$ (< 220 vs. ≥ 220, ≥ 300, ≥ 400 cells/ μL).
COPD, chronic obstructive pulmonary disease; ED, emergency department; SD, standard deviation; US, United States.
Source: Trudo et al. (2019)[6].

CONCLUSIONS

- **This literature review emphasises the substantial economic burden of COPD in the US. The impact escalates with disease severity, leading to increased direct medical, indirect and treatment costs.**
- **Disease severity, exacerbations and productivity loss are notable contributors to the escalating costs of COPD management.**

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CONFLICTS OF INTEREST

RHS is a paid consultant for Sanofi.

AN, **ML**, WN and **VD** are full-time employees of RTI Health Solutions, which received research funding from Sanofi to perform this study. RTI Health Solutions is a unit of Research Triangle Institute, an independent, non-profit, research organisation that does work for government.

EMH and **HD** are employees of Sanofi and may hold stocks and/or stock options in the company.

SM was an employee of Sanofi during the conduct of this study.

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