

Understanding emphysema burden and treatment patterns in the United States: A systematic literature review

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OBJECTIVES

- Chronic obstructive pulmonary disease (COPD) consists of the disease processes of emphysema and chronic bronchitis.¹ Despite the large body of literature on COPD, there is limited evidence on the specific burden of emphysema
- The aim of this systematic literature review (SLR) was to understand disease risk factors, current treatments, patterns of disease progression, and economic burden specific to emphysema in the United States

METHODS

- The literature search was conducted using Medline, EMBASE, EconLIT, and the Cochrane Database of Systematic Reviews
- The scope of this review and search strategies were pre-defined for each of the four specific areas of interest (risk factors, current treatments, disease progression, and economic burden) using the PICOS (Population, Intervention, Comparator, Outcomes, Study Design) framework (**Table 1**)

Table 1. Search scope				
PICOS	Area of interest			
	Risk factors for emphysema	Current treatments	Disease progression	Economic burden
Population	Emphysema adult patients			
Intervention/Comparator	Disease predisposition Occupational risk and exposures Health risk behavior	Pharmacotherapy Surgery Oxygen therapy	Not applicable	Not applicable
Outcomes	Emphysema diagnosis	Mortality Disease progression Patient-reported outcomes Quality of life Treatment-related HRU	Disease-progression Staging Severity Treatment failure	HRU Direct costs Indirect costs
Study design	Clinical studies Post-marketing, observational, retrospective, prospective, longitudinal, case-control, and cross-sectional studies Real world data, including registries Systematic reviews or meta-analyses of observational studies Excluded: Editorials, notes, commentaries, letters, case reports			Excluded: Editorials, notes, commentaries, letters, case reports
Restrictions	US data; Studies and abstracts published in English in January 2008-November 2018			

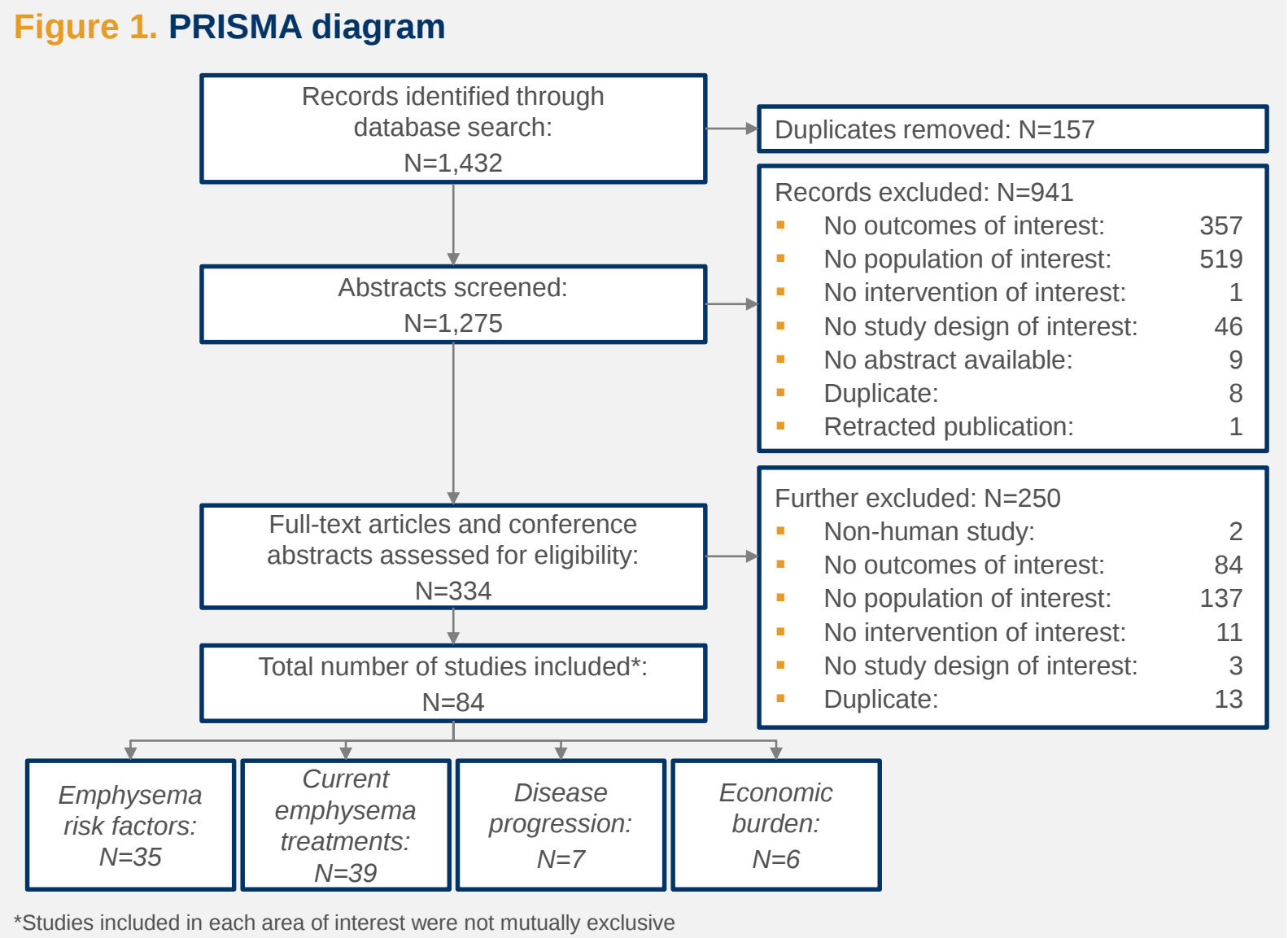
Abbreviations: HRU: Healthcare Resource Utilization; PICOS: Population, Intervention, Comparator, Outcomes, and Study Design; US: United States

- Data on study and patient characteristics, and relevant outcomes were extracted using standardized data extraction tables
- Extracted data were summarized by area of interest
 - Criteria used to assess emphysema or to define emphysema were also extracted from studies and summarized across all areas of interest
- The study methodology followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines²

RESULTS

Included studies and conference abstracts

- A total of 84 studies (22 conference abstracts and 62 journal articles) were identified (**Figure 1**)



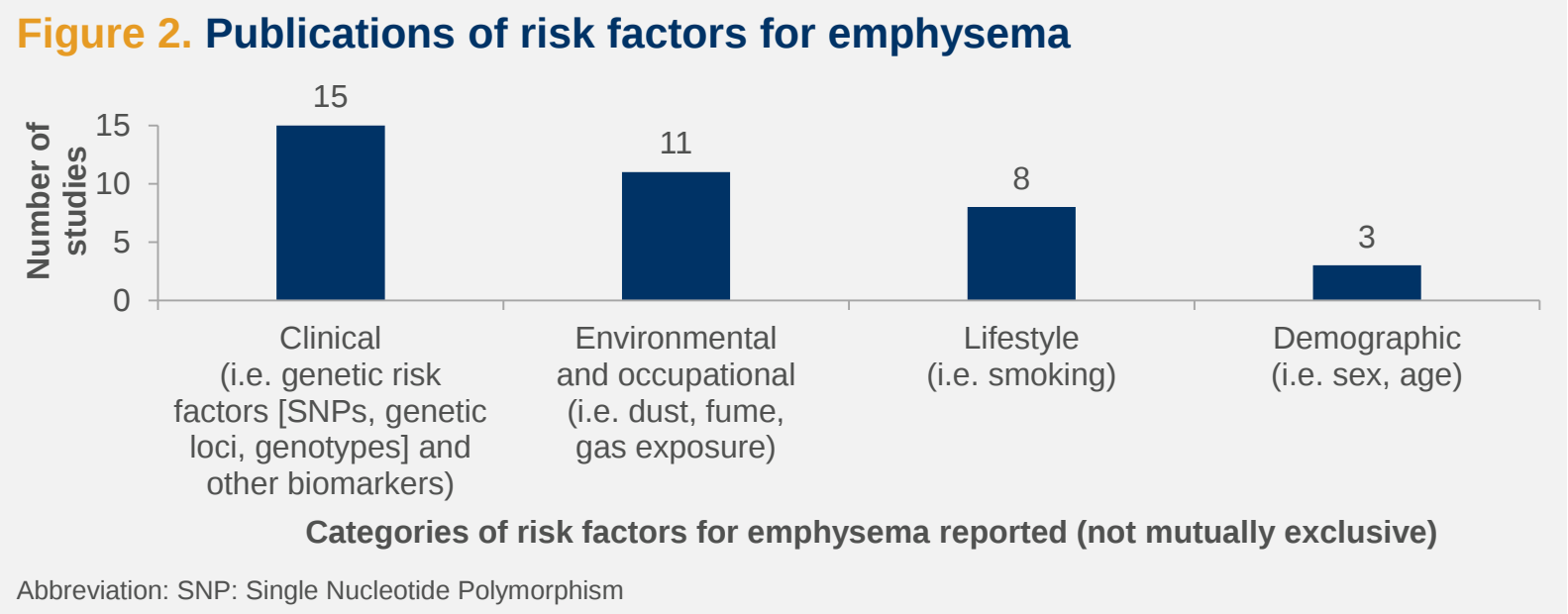
Studies reporting risk factors for emphysema

Characteristics of study design and population

- Of the 84 studies included, 35 studies (42%) reported risk factors for emphysema
- Nearly all studies (94%, n=33) assessed prevalent emphysema populations
- The mean/median age ranged from 46 to 70 years; the proportion of males ranged from 15% to 67% (To note: there were 2 other studies that were 100% male)
- The majority of these studies (69%, n=24) were prospective cohort studies
- Included studies used multiple approaches to assess risk factors, including logistic regression (46%, n=16) and linear regression (37%, n=13)
- Emphysema was identified via visual assessment of CT scan (54%, n=19) or autopsied lung (3%, n=1), or self-reported physician diagnosis (26%, n=9); the remaining studies (17%, n=6) did not specify how emphysema was identified

Outcomes of included studies

- The most frequently reported risk factor types for emphysema diagnosis and/or increased severity were clinical factors, followed by, environmental and occupational, lifestyle, and demographic factors (**Figure 2**)



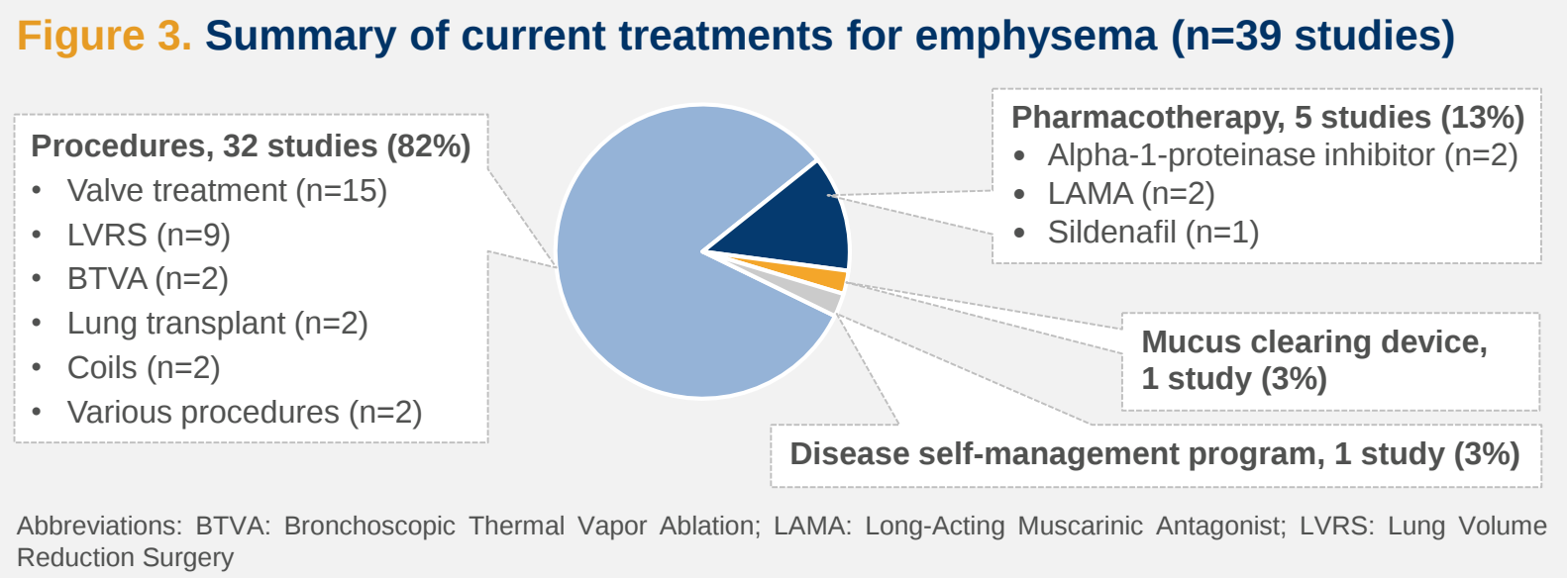
Studies reporting current treatments for emphysema

Characteristics of study design and population

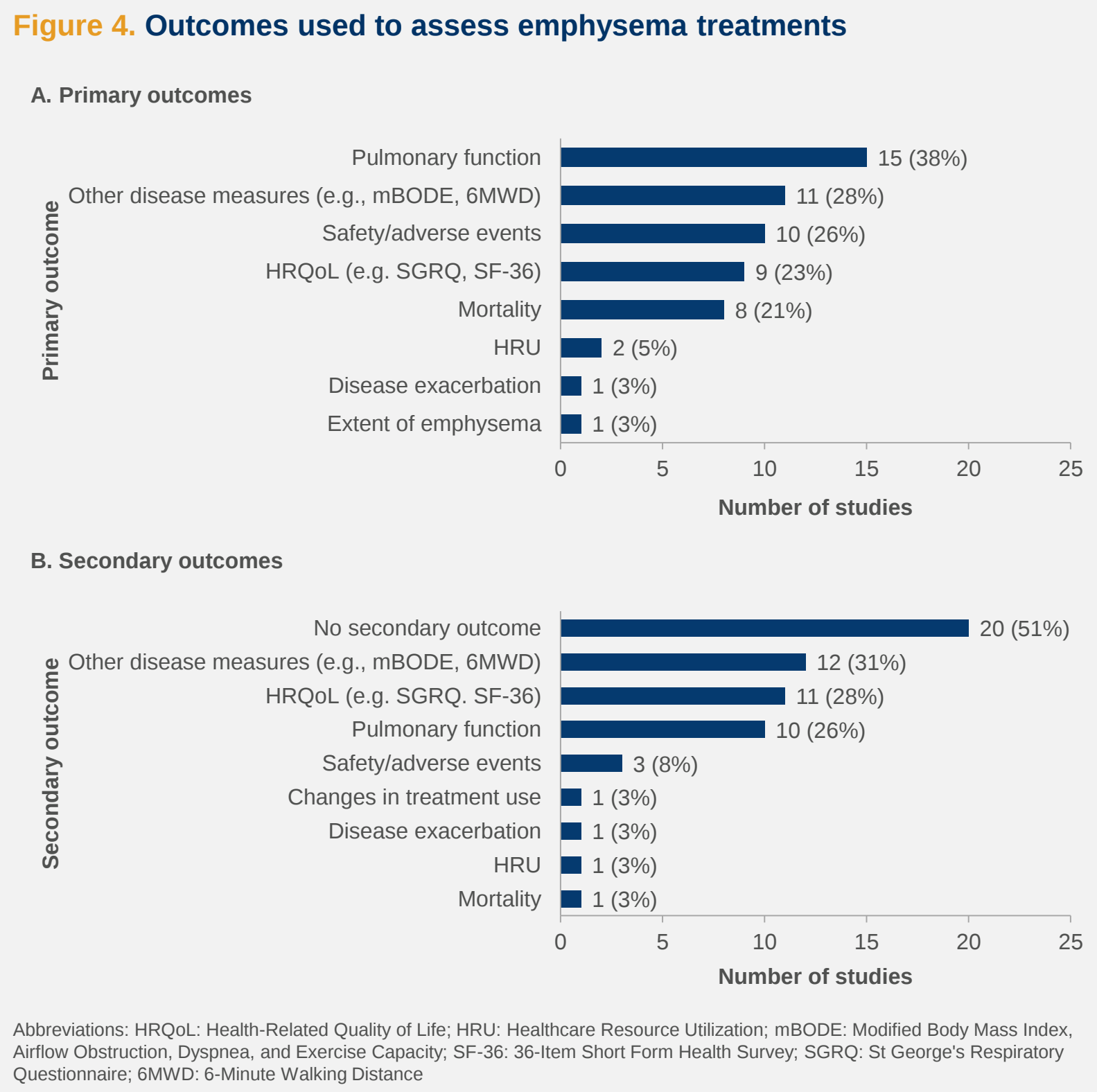
- Of the 84 studies included, 39 studies (46%) reported emphysema treatments
- The mean/median age ranged from 49 to 70 years; the proportion of males ranged from 25% to 85%; More emphasis on moderate-to-severe emphysema patients
- Most studies (82%, n=32) were clinical trials (sample sizes ranged from 7 to 1,218 patients); the remaining studies were observational studies (15%, n=6) using registry data, inpatient/claims databases, and surveys; and meta-analysis (3%, n=1)
- About half of studies identified emphysema via visual assessment of CT or high-resolution CT scans (49%, n=19); one study using a claims database identified patients using diagnosis codes for COPD; the remaining studies (49%, n=19) did not specify how emphysema was identified

Outcomes of included studies

- Nearly half of studies of procedures (n=32) described valve treatment (47%, n=15) and more than one-fourth described lung volume reduction surgery (28%, n=9) (**Figure 3**)
- Pharmacological treatments included inhaled tiotropium, other long-acting muscarinic antagonists (LAMAs), alpha-1-proteinase inhibitor, and sildenafil



- The most frequently assessed primary and secondary outcomes were pulmonary function, other disease measures including functional status, and measures of health-related quality of life (HRQoL) (**Figure 4**)



Studies reporting disease progression

Characteristics of study design and population

- Of the 84 studies included, 7 studies (8%) reported disease progression
- The mean age ranged from 58 to 64 years; the proportion of males ranged from 44% to 74%
- The majority of the studies (86%, n=6) were prospective cohort studies with one exception (14%, n=1) being a retrospective cohort study using a claims database
- Most studies (71%, n=5) identified emphysema via visual assessment of CT scans; one study (14%) identified patients using COPD diagnosis codes and one (14%, n=1) did not specify how emphysema was identified

Outcomes of included studies

- The included 7 studies described a total of 6 measures of disease progression, which were primarily clinical measures (n=4 studies, reporting 4 types of clinical measures) (**Table 2**)
 - Other studies measured progression through HRQoL or healthcare resource utilization (HRU) (n=1 each)

Table 2. Summary of measures of disease progression		
Disease Progression Measure* (n=7 studies)		
Clinical	Extent of emphysema (n=3)	Change in percentage of emphysema on CT (n=1) Lung density decline (n=2)
	Blood-based biomarker (n=1)	CD31+ endothelial microparticles
	Pulmonary function (n=1)	Change in FEV1
	Exercise capacity (n=1)	Change in 6MWD
	HRQoL (n=1)	Change in SGRQ-C score
Other	HRU (n=1)	Frequency of COPD hospitalizations

Abbreviations: CT: Computed Tomography; CD31: Cluster of Differentiation 31; FEV1: Forced Expiratory Volume in 1 Second; HRQoL: Health-Related Quality of Life; HRU: Healthcare Resource Utilization; SGRQ-C: St. George's Respiratory Questionnaire Validated for COPD; 6MWD: 6-Minute Walking Distance

*The studies are not mutually exclusive and may report more than one disease progression measure

Studies reporting economic burden of emphysema

Characteristics of study design and population

- Of the 84 studies included, 6 studies (7%) reported economic burden
- The age range of patients included in these studies varied from 18 to 80+ years; the proportion of males varied from 46% to 64%
- Most studies (67%, n=4) were patient surveys; the remaining used clinical trial or claims data (33%, n=2) (**Table 3**)
- Emphysema was identified by self-reported diagnosis (33%, n=2) or diagnosis codes for COPD (17%, n=1); the remaining studies (50%, n=3) did not specify how emphysema was identified

Outcomes of included studies

- The economic outcomes varied from costs of pulmonary rehabilitation to COPD-related healthcare costs and HRU (**Table 3**)
- None of the studies specifically examined the emphysema population; rather, the study populations more broadly included COPD patients or a subset of emphysema population

Table 3. Overview of studies related to the economic burden of emphysema		
Data Source	Population studied	Outcome Measures
Patient survey (n=4)	COPD patients	HRU only (emergency room visits and hospitalizations)
	COPD patients with AATD in a disease management program	HRU only (physician visits, emergency room visits and hospitalizations)
	Emphysema patients with AATD receiving or not receiving AAT augmentation therapy	Direct and indirect cost (years of life gained and estimated health service expenditures per year of life gained)
	Cancer patients with chronic conditions, including emphysema	Direct and indirect cost and HRU (total medical expenditures and productivity loss)
Clinical trial (n=1)	Emphysema patients undergoing lung volume reduction surgery	Cost of pulmonary rehabilitation
Claims database (n=1)	COPD patients identified by diagnosis codes treated with fluticasone propionate/salmeterol combination vs. anticholinergic bronchodilators	Direct COPD-related medical and pharmacy costs

Abbreviations: AAT: Alpha-1-Antitrypsin; AATD: Alpha-1-Antitrypsin Deficiency; COPD: Chronic Obstructive Pulmonary Disease; HRU: Healthcare Resource Utilization

CONCLUSION

- 84 studies were reviewed; 42% reported emphysema risk factors, 46% reported current treatments, 8% reported disease progression, and 7% reported economic burden
- Emphysema treatments and risk factors were well documented
 - However, the methodological differences and the variety of risk factors examined hinder identification of the most important risk factors
- There remains a gap in understanding of emphysema disease trajectories and patterns of progression
 - None of the studies described unique emphysema progression phenotypes
- The specific economic burden of emphysema in the US remains undocumented
 - The few retrospective claims database studies included in this review identified patients with broader COPD diagnosis codes and did not attempt to assess the added burden of emphysema
- A study limitation is the targeted search strategy used; expanding the search to other countries, other languages, and/or a wider time period may help identify additional evidence and support findings only reported by one or a few studies
- Future studies are needed to better understand patterns of progression and economic burden in emphysema patients

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