

Bronchiolitis Obliterans Syndrome after Lung Transplantation: Economic Burden

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Background

The economic burden of BOS

- Bronchiolitis obliterans syndrome (BOS) is a common complication of lung transplantation, affecting nearly 50% of lung transplant recipients who survive five years after transplantation and nearly 80% of those who survive ten years after transplantation (ISHLT Registry; Kulkarni JSHLT, 2019)
- BOS appears most frequently after lung transplantation as a manifestation of chronic lung allograft dysfunction (CLAD) and is the most common CLAD phenotype, accounting for nearly 50% to 70% of CLAD cases (Khush et al., JHLT, 2020)
- BOS is the leading cause of death for patients who survive at least one year after transplant
- The impact of BOS on healthcare resource use (HRU) and costs is not well understood.
- The goal of this study was to quantify the economic burden of BOS in the US using real-world data

Methods

Methods

ICD9 and ICD10 Diagnosis codes used to identify BOS patients

Study patients meeting BOS criteria

BOS does not have a specific diagnosis code. Therefore, we developed an algorithm to identify likely BOS patients, building on ICD9 and ICD10 diagnosis codes for serious respiratory illness typically used for BOS

The first step of the analysis was to identify patients with lung transplantation with at least one of the diagnosis codes

Data source

IQVIA PharMetrics+ a nationally representative commercial claims database. Data contain enrollment, demographic and claims data for individuals with commercial insurance, including hospitalizations, outpatient hospital visits, physician and other office visits, home health visits, laboratory and imaging tests and prescription drugs. Extract contains all claims for patients with at least one claim for lung transplant from 1/1/2006-9/30/2018

ICD9	ICD10	BOS Diagnosis Code List
1	0	491.8-Other chronic bronchitis
1	0	491.9-Unspecified chronic bronchitis
1	0	516.34-Respiratory bronchiolitis interstitial lung disease
0	1	J42-Unspecified chronic bronchitis
0	1	J84.115-Respiratory bronchiolitis interstitial lung disease
1	0	516.8-Other specified alveolar and parietoalveolar pneumonopathies
0	1	J84.09-Other aveolar and parieto-aveolar conditions
1	0	515-Post inflammatory pulmonary fibrosis
0	1	J84.89-Other specified interstitial lung disease
0	1	J41.8-Mixed simple and mucopurulent chronic bronchitis

Methods

Additional criteria for patient inclusion

- The next step was to identify patients who met additional criteria consistent with BOS
- Patients had to meet all criteria to be included in the study

<i>Inclusion Criteria</i>
<i>Patients with a lung transplant</i>
<i>At least one diagnosis code used for BOS after transplantation at least 12 months after transplant.</i>
<i>At least 1 additional dx used for BOS dx 2 or more months from index-BOS dx</i>
<i>Index BOS diagnosis was not used as diagnosis before transplantation unless there was a 6+ month period with no evidence of that diagnosis code</i>
<i>Patients had at least 1 CT scan, 1 lung biopsy or 2+ bronchoscopies within 60 days of each other</i>

Outcomes

Settings for healthcare encounters

Healthcare encounters were organized by setting of care
 Costs for encounters were costs paid to providers by insurers
 Mean costs per patient per month were calculated overall and by setting of care

Healthcare resource setting	
Inpatient admission without ICU stay	<i>All inpatient admissions that do not include ICU admissions during hospital stay</i>
Inpatient admission with ICU stay	<i>Any inpatient admission that also included an ICU admission</i>
ED visit	<i>Emergency department visits that didn't lead to an inpatient admission</i>
Lab/Radiology test	<i>All pathology, lab, and radiology visits, regardless of place of service.</i>
Evaluation & Management visits	<i>Office visits. This includes office visits that occur in independent freestanding facilities and office visits in an outpatient hospital setting</i>
Outpatient hospital visits and surgeries	<i>All other services that would take place in an outpatient hospital such as ambulatory surgery</i>
Other outpatient	<i>All other outpatient services that do not fall into the categories listed above</i>
Pharmacy	<i>Prescription medications</i>

Statistical analyses

All analyses reflect costs and HRU starting at least 1 year after lung transplantation

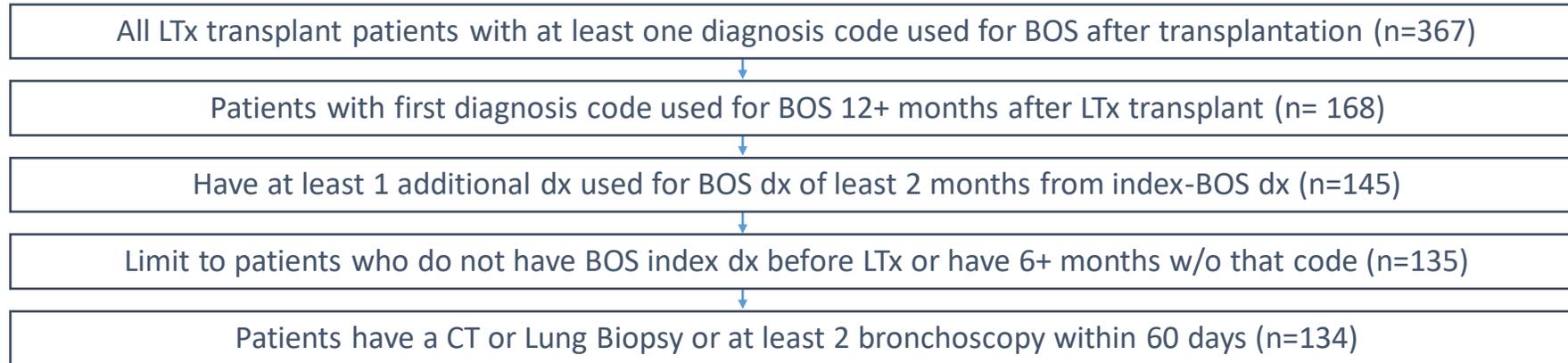
- **All cause costs pre and post BOS index diagnosis**
 - *Purpose:* Evaluate the impact of BOS diagnosis on costs
- **All cause costs per patient by HRU severity**
 - *Purpose:* Evaluate costs associated with increasingly intensive healthcare resource use (e.g., inpatient admissions, ICU stays)

Results

Results: Study Patients

Algorithm to identify BOS patients, absent a BOS specific ICD9 or ICD10 diagnosis code

Lung Transplantation-BOS Patient Attrition



There were 367 patients with a lung transplantation with at least one of the diagnosis codes used for BOS

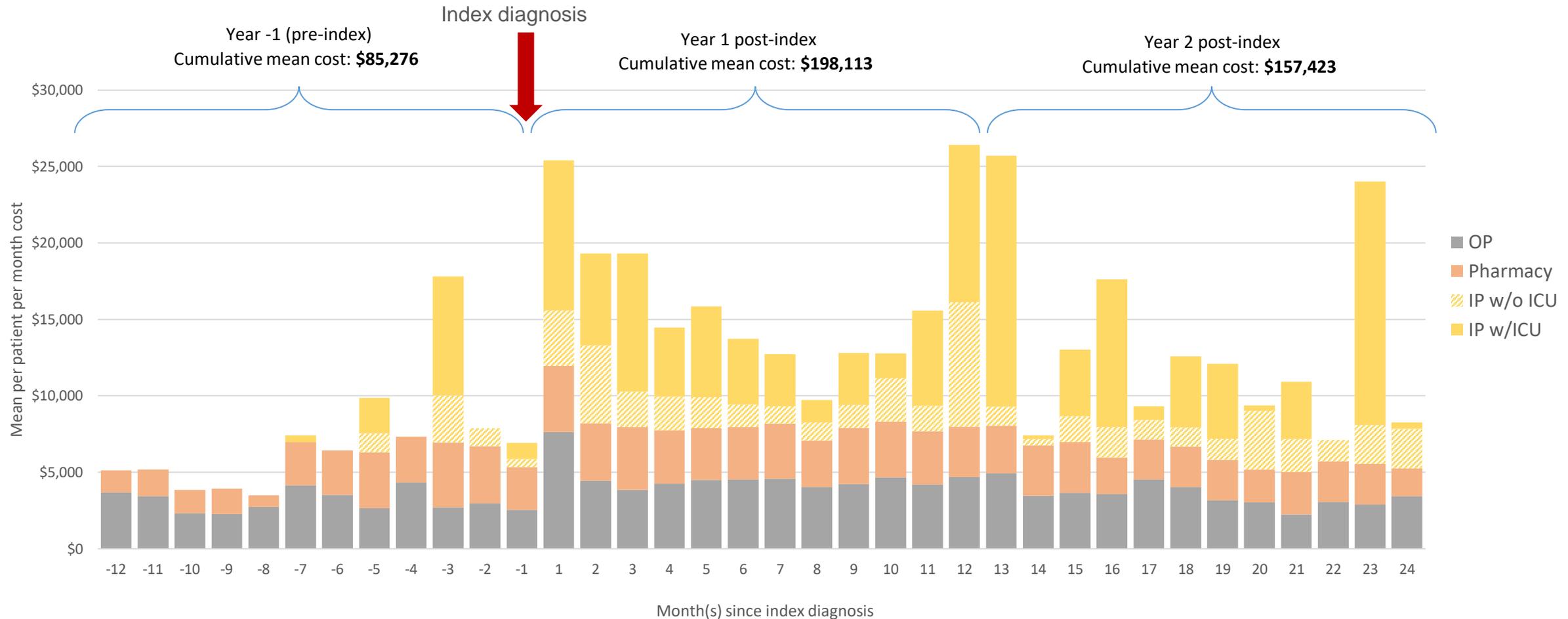
We applied additional criteria to exclude patients who were unlikely true BOS patients

Inclusion/exclusion criteria were discussed and validated with literature and clinical experts

There were **134** patients that met the inclusion/exclusion criteria for patients who develop BOS following lung transplantation

Costs increase dramatically after BOS diagnosis

Costs increased substantially after index diagnosis, with dramatically higher costs for inpatient admissions with ICU stays. Pharmacy and outpatient costs remained relatively stable before and after diagnosis.



In most severe BOS patients, ICU drives excess costs

Costs for patients, stratified by intensity of HRU

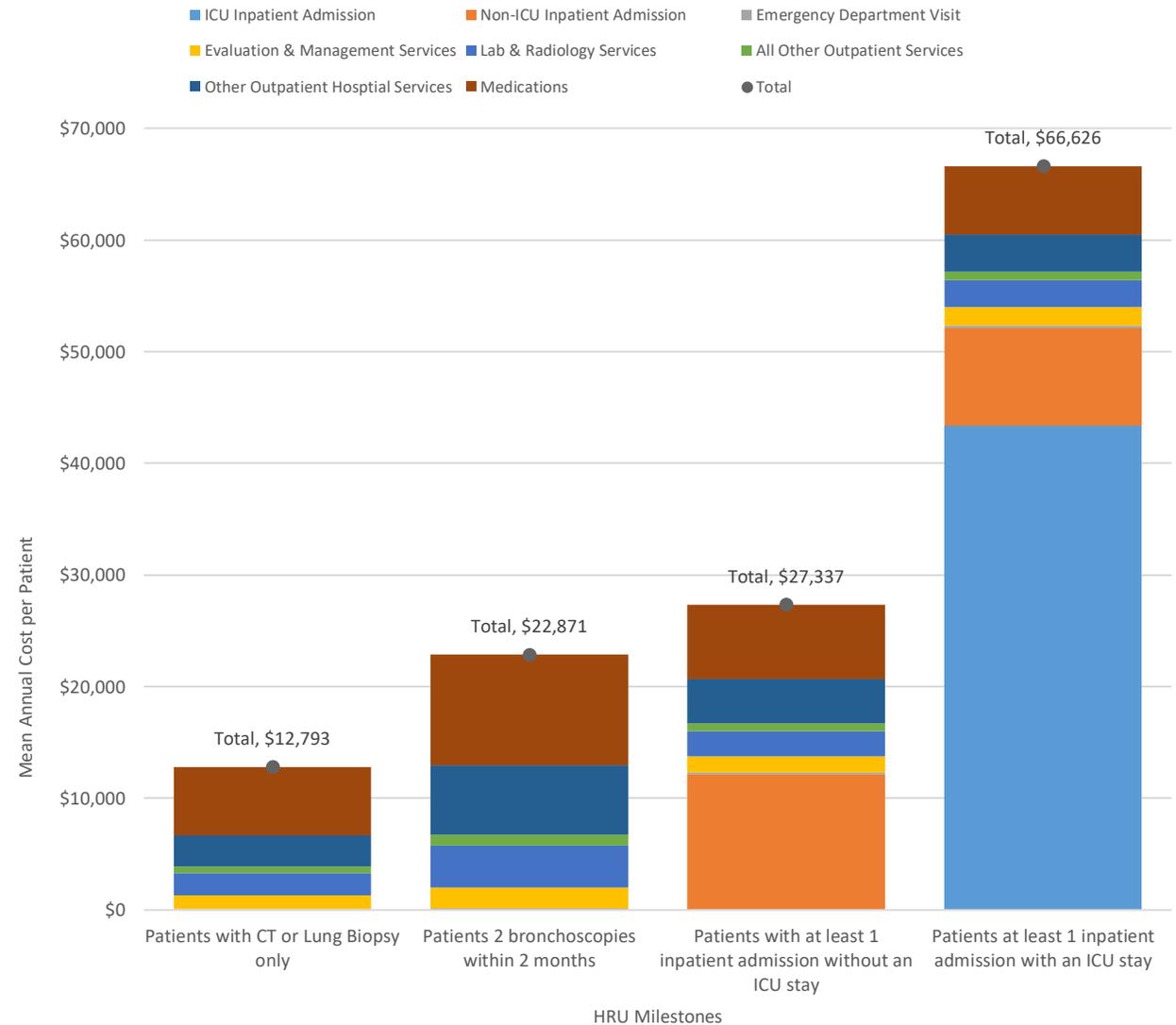
Costs overall and by setting of care based on healthcare service use

Starting 1 year after LTx, study patients were followed over time with health care utilization and costs collected on a monthly basis and averages projected annually.

Increasing levels of HRU intensity

- Patient has had a CT or lung biopsy but no hospitalizations
- Patients has had at least 2 bronchoscopies within 2 months but no hospitalizations
- Patient has had at least 1 inpatient admission without an ICU stay
- Patient has had at least 1 inpatient admission with an ICU stay

Projected average cost per patient per year by type of healthcare used



Would disease progression (CLAD) impact HRU intensity?

- CLAD progression is determined by patient FEV1 levels
- Claims data do not include clinical testing results
- As an exploratory analysis using a model, expected healthcare utilization patterns for BOS patients were based on increasingly intensive HRU
- HRU intensity was a proxy for CLAD stages (CLAD estimated)



Progression stage (CLAD) 1

- First CT scan or lung biopsy

Progression stage (CLAD) 2

- At least 2 bronchoscopies within 2 months

Progression stage (CLAD) 3

- First inpatient admission following CLAD 1 or CLAD 2

Progression stage (CLAD) 4

- First ICU admission following CLAD 1 or CLAD 2

Exploratory analysis

Average cost per patient per month by HRU setting and Progression Stage

Progression Stage (CLAD)	ICU Inpatient Admission	Non-ICU Inpatient Admission	Emergency Department Visit	Evaluation & Management Services	Lab & Radiology Services	All Other Outpatient Services	Other Outpatient Hospital Services	Medications	Total per patient per month by stage	Total per patient per year by stage
1	\$0	\$0	\$6	\$101	\$168	\$50	\$229	\$512	\$1,066	\$12,793
2	\$0	\$0	\$10	\$158	\$310	\$83	\$519	\$826	\$1,906	\$22,871
3	\$0	\$1,012	\$14	\$120	\$187	\$59	\$332	\$554	\$2,278	\$27,337
4	\$3,614	\$728	\$19	\$139	\$200	\$62	\$280	\$510	\$5,552	\$66,626
Total per patient per month by setting	\$3,614	\$1,740	\$50	\$518	\$866	\$253	\$1,360	\$2,402	\$10,802	\$129,624
Total per patient per year by setting	\$43,368	\$20,880	\$600	\$6,216	\$10,392	\$3,036	\$16,320	\$28,824	\$129,624	

Discussion and Conclusions

Discussion and Conclusions

- BOS after lung transplantation imposes a large economic burden on healthcare systems and patients
- Hospitalizations and ICU stays are key drivers of high costs in BOS patients
- To the extent that more advanced CLAD stages are characterized by more intensive healthcare resource use, the burden of BOS would be expected to increase substantially in patients in later CLAD stages
- Early diagnosis and therapies aimed at slowing disease progression may reduce economic burden associated with BOS .

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Disclosures

- Dr. Boerner is an employee of Breath Therapeutics, a Zambon company
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- Dr. Sheshadri is a member of the University of Texas MD Anderson Cancer Center, Department of Pulmonary Medicine
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Appendix