The Cost of Chronic Lung Allograft Dysfunction (CLAD) in Lung Transplant (LTx) Recipients by Stage 0-4: A Claims Database Analysis

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BACKGROUND

- The United States had more than 2,700 lung transplants (LTx) performed in 2022.[1]
- Chronic lung allograft dysfunction (CLAD)-bronchiolitis obliterans syndrome (BOS) is the most common manifestation of LTx rejection, occurring in approximately 50% of LTx recipients within 5 years after transplant.[2]
- CLAD-BOS is a progressive, irreversible pulmonary disease where the immune system attacks airways in transplanted lungs leading to gradual occlusion and subsequent graft failure becoming the leading cause of death after the first post-LTx year.[2-3]
- Severity of CLAD-BOS is measured using CLAD stages 0-4 based on decreased forced expiratory volume in one second (FEV_1).[4]
- Estimation of the economic burden of CLAD-BOS is required for demonstrating the impact of new therapies and is challenging due to:
  - Absence of an International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) code prior to late 2023.
  - Requirement of FEV_1 data to identify CLAD-BOS staging with subsequent progression and the absence of this information within claims data.

OBJECTIVE

- To estimate direct medical costs in LTx patients with CLAD-BOS, stratified by CLAD stage, from the perspective of a US payer.

METHODS

STUDY DESIGN AND DATA SOURCE

- A retrospective cohort study was conducted using the IQVIA PharMetrics Plus™ commercial claims database, with fully adjudicated, de-identified medical and prescription drug claims for over 140 million individuals with commercial insurance coverage in the US.
- BOS diagnosis was assumed to occur within a minimum of 12 months post-LTx with patients followed for at least an additional 12 months after diagnosis until end of data availability or loss to follow-up.
- All study data were de-identified and thus no approval by an Institutional Review Board was required.

STUDY PATIENTS

- Underwent LTx between January 1, 2006, and September 30, 2018.
- Aged <65 years at the time of LTx.
- At least two diagnosis codes indicative of BOS ≥12 months after LTx. Because there was no ICD-10-CM diagnosis code for CLAD-BOS at the time the study was conducted, severe lung disease diagnosis codes were used as a proxy. These diagnoses included:
  - Chronic bronchitis (ICD-9-CM 491.8, 491.9; ICD-10-CM J41.8, J42.x)
  - Respiratory bronchiolitis interstitial lung disease (ICD-9-CM 516.34; ICD-10-CM J84.115)
  - Post-inflammatory pulmonary fibrosis (ICD-9-CM 515.x)
  - Other interstitial lung disease (ICD-10-CM J84.89)
  - Other alveolar and parietoalveolar pneumonopathies (ICD-9-CM 516.8; ICD-10-CM J84.09)
- No diagnosis codes suggestive of CLAD-BOS prior to LTx.
- Evidence of a computed tomography scan, lung biopsy, or at least 2 bronchoscopies ≤60 days apart.

OUTCOMES

- The primary outcome was total direct healthcare costs per patient per month (PPPM) following CLAD-BOS diagnosis, stratified by CLAD stage.
- Costs were stratified by categories including hospital admissions, outpatient services (outpatient hospital visits, office visits, laboratory and imaging tests, other outpatient encounters such as home health visits and urgent care), and prescription medications.

METHODS (Continued)

DATA ANALYSIS

- Mean monthly healthcare costs were calculated for each patient from presumptive CLAD-BOS diagnosis to end of follow-up and ranked from smallest to largest.
- The following cross-sectional distribution of CLAD stages, reflective of increasing mortality by stage, were used to segment the study population:
  - CLAD 0: 69.7%
  - CLAD 1: 30.8%
  - CLAD 2: 20.1%
  - CLAD 3: 6.7%
  - CLAD 4: 6.7%
- Study patients were assigned to CLAD stage using these percentages, with the lowest costs assigned and assumed to be CLAD 0 and the highest costs assigned and assumed to be CLAD 4.
- Mean monthly costs within each CLAD stage were calculated and stratified by cost type.
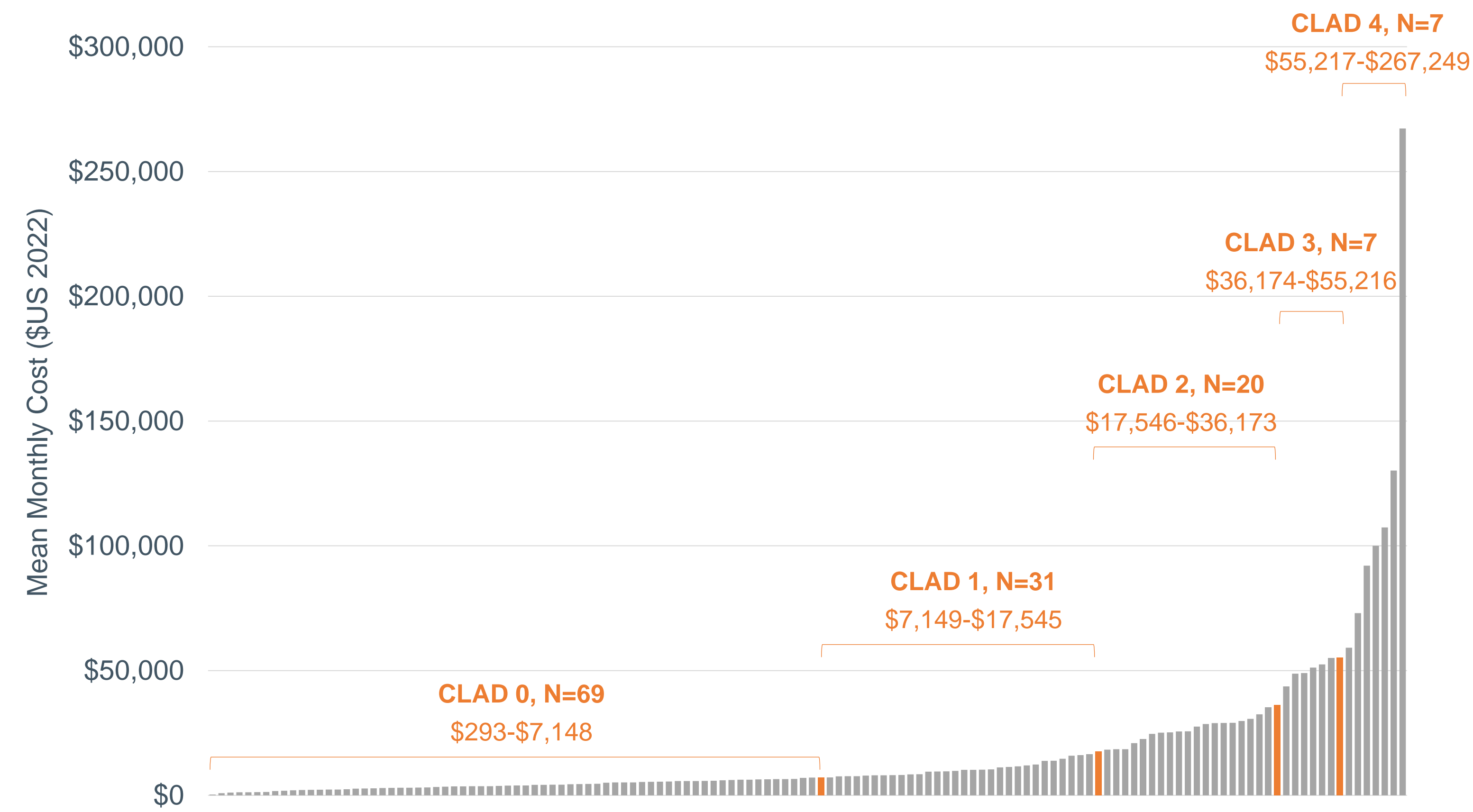- All costs were inflated to $US 2022 using the Consumer Price Index for Medical Care.

RESULTS

- A total of 134 patients met the inclusion criteria for this study.
- Patients were predominantly male (65%) with a mean age of 50.9 years (Table 1).
- Mean monthly costs over the post-BOS follow-up period ranged from $293 to $267,249 (Figure 1).
- After applying the cross-sectional distribution of CLAD stage to the patient sample (N=134), mean total monthly costs by CLAD stage ranged from $4,037 in CLAD 0 to $118,431 in CLAD 4 (Figure 2).
  - Outpatient and prescription costs increased through CLAD stages 0-4, except for CLAD 4 where a greater proportion of costs were attributed to inpatient admissions.
  - Inpatient admissions comprised 78% of inpatient costs and ranged from 34% in CLAD 1 to 91% in CLAD 4.

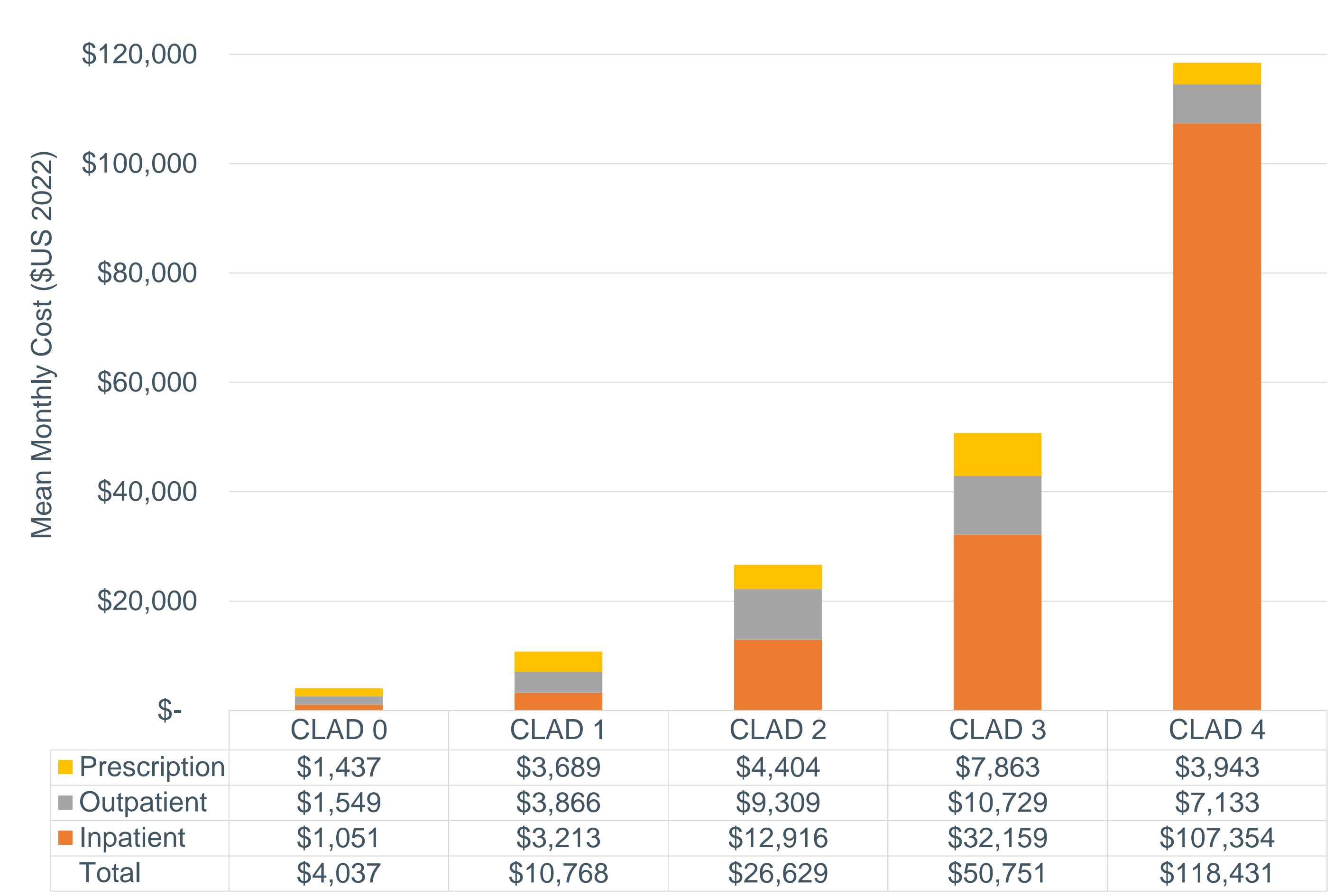### Table 1. Patient Characteristics

	N=134
Male, n (%)	87 (65)
Age (years), mean ± SD	50.9 ± 12.7
Geographic region, n (%)	
Midwest	45 (34)
Northeast	27 (20)
South	52 (39)
West	10 (7)
Type of benefit plan, n (%)	
Preferred provider organization	110 (82)
Health maintenance organization	15 (11)
Other	9 (7)
Charlson Comorbidity Index, mean ± SD	2.1 ± 1.5
Pulmonary comorbidities, n (%)	
Pulmonary fibrosis or interstitial lung disease	104 (78)
Pulmonary arterial hypertension	65 (49)
Bronchiectasis	40 (30)
Cystic fibrosis	27 (20)
Chronic obstructive pulmonary disease	21 (16)

Figure 1: Distribution of Per-patient Mean Monthly Cost

CLAD 0, N=69 $293-$7,148
CLAD 1, N=31 $7,149-$17,545
CLAD 2, N=20 $17,546-$36,173
CLAD 3, N=7 $36,174-$55,216
CLAD 4, N=7 $55,217-$267,249

RESULTS

Figure 2: Per-patient Mean Monthly Costs by CLAD Stage

	CLAD 0	CLAD 1	CLAD 2	CLAD 3	CLAD 4
Prescription	$1,437	$3,689	$4,404	$7,863	$3,943
Outpatient	$1,549	$3,866	$9,309	$10,729	$7,133
Inpatient	$1,051	$3,213	$12,916	$32,159	$107,354
Total	$4,037	$10,768	$26,629	$50,751	$118,431

LIMITATIONS

- Due to the lack of ICD-10 codes for BOS and the subsequent linkage to CLAD Stages 0-4, our study assumed a linear progression of costs from CLAD 0 through CLAD 4 which we cannot verify within claims data.
- Presumptive codes for BOS may overestimate/underestimate patients with the condition and may not represent the true CLAD-BOS patient population.

CONCLUSIONS

- This study fills a gap in the literature related to CLAD-BOS burden and provides value to estimate the economic impact of new therapies to prevent or treat CLAD-BOS.
- Monthly costs for patients with CLAD-BOS were substantial and further research into understanding costs by CLAD stage is warranted.
- Interventions aimed at treating CLAD-BOS may help decrease costs and provide benefit to patients.

REFERENCES

1. OPTN/SRTR 2022 Annual Data Report: Lung. Available at: https://srtr.transplant.hrsa.gov/annual_reports/2022/Lung.aspx. Accessed 19 March 2024.
2. Chambers DC, Cherikh WS, Goldfarb SB, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-fifth adult lung and heart-lung transplant report-2018; Focus theme: Multiorgan Transplantation. J Heart Lung Transplant 2018; 37(10):1169-1183.
3. Barker AF, Bergeron A, Rom WN, Hertz MI. Obliterative bronchiolitis. N Engl J Med. 2014;370(19):1820-1828.
4. Verleden GM, Glanville AR, Lease ED, et al. Chronic lung allograft dysfunction: Definition, diagnostic criteria, and approaches to treatment-A consensus report from the Pulmonary Council of the ISHLT. J Heart Lung Transplant 2019;38:493-503.

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