Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 11/1/24**
(See policy history boxes for previous effective dates)

Title: Transplant-Lung and Lobar Lung

Description/Background

Solid organ transplantation offers a treatment option for patients with different types of endstage organ failure that can be lifesaving or provide significant improvements to a patient's quality of life.[1] Many advances have been made in the last several decades to reduce perioperative complications. Available data supports improvement in long-term survival as well as improved quality of life particularly for liver, kidney, pancreas, heart, and lung transplants. Allograft rejection remains a key early and late complication risk for any organ transplantation. Transplant recipients require life-long immunosuppression to prevent rejection. Patients are prioritized for transplant by mortality risk and severity of illness criteria developed by Organ Procurement and Transplantation Network and United Network of Organ Sharing.

Lung Transplant

To date, 53,486 transplants were performed in the United States procured from 53,233 deceased donors and 253 living donors.[2] Lung transplants were the fourth most common procedure.

End-stage lung disease may be the consequence of a number of different etiologies. The most common indications for lung transplantation are chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), cystic fibrosis (CF), alpha-1 antitrypsin deficiency and idiopathic pulmonary arterial hypertension (IPAH). Before consideration for transplant, patients should be receiving maximal medical therapy, including oxygen supplementation, or surgical options, such as lung volume reduction surgery for chronic obstructive pulmonary disease. Lung or lobar lung transplantation is an option for patients with end-stage lung disease despite these measures.

A lung transplant refers to single-lung or double-lung replacement. In a single-lung transplant, only one lung from a deceased donor is provided to the recipient. In a double-lung transplant, both the recipient's lungs are removed and replaced by the donor's lungs. In a lobar transplant, a lobe of the donor's lung is excised, sized appropriately for the recipient's thoracic dimensions and transplanted. Donors for lobar transplant have primarily been living-related donors, with one lobe obtained from each of two donors (e.g., mother and father) in cases for which bilateral transplantation is required. There are also cases of cadaver lobe transplants.

Potential recipients who are 12 years of age and older are ranked according to the Lung Allocation Score (LAS).[3] Patients 12 years of age and older receive a score between 1 and 100 based on predicted survival after transplantation reduced by predicted survival on the waiting list; the LAS takes into consideration the patient's disease and clinical parameters. Waiting list incorporates the Lung Allocation Score, geography, and blood type classifications. Children under the age of 12 receive a priority for lung allocation. Under this system, children under 12 with respiratory lung failure and/or pulmonary hypertension who meet criteria are considered "priority 1" and all other candidates in the age group are considered "priority 2." A lung review board (LRB) has authority to adjust scores on appeal for adults and children.

Regulatory Status

Solid organ transplants are a surgical procedure and, as such, are not subject to regulation by the U.S. Food and Drug Administration (FDA).

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation Title 21, parts 1270 and 1271.Solid organs used for transplantation are subject to these regulations.

Medical Policy Statement

The safety and effectiveness of lung or lobar lung from a living or deceased donor transplantation and retransplantation has been established. It may be considered a useful therapeutic option for carefully selected adults, children and adolescents with irreversible, progressively disabling, primary or secondary end-stage pulmonary disease. It is a useful therapeutic option for individuals meeting selection criteria.

Lung or lobar lung transplantation and retransplantation is considered experimental/investigational in all other situations.

Inclusionary and Exclusionary Guidelines

Note: Final patient eligibility for transplant is subject to the judgment and discretion of the requesting transplant center.

Inclusions:

Indications for lung, lobar lung transplantation and retransplantation include, but are not limited to, irreversible, chronic lung diseases for which there is no further medical or surgical therapy available and survival is limited. The most common illnesses which may result in irreversible, progressively disabling, primary or secondary end-stage pulmonary disease include but are not limited to:

- Alpha-1 antitrypsin deficiency
- Asbestosis
- Benign hypertensive heart disease without congestive heart failure
- Bilateral bronchiectasis
- Bronchiolitis obliterans
- Bronchopulmonary dysplasia
- Chronic airway obstruction, not elsewhere classified
- Chronic obstructive pulmonary disease
- Chronic respiratory conditions due to fumes and vapors
- Chronic respiratory disease arising in the perinatal period
- Coal workers' pneumoconiosis
- Congenital bronchiectasis
- Cystic fibrosis with meconium ileus (double lung transplanted)
- Cystic fibrosis without mention of meconium ileus (double lung transplanted)
- Eisenmenger's syndrome
- Emphysema
- Eosinophilic granuloma
- Idiopathic pulmonary fibrosis
- Idiopathic fibrosing alveolitis
- Interstitial pulmonary fibrosis
- Lung involvement in other diseases classified elsewhere
- Lymphangiomyomatosis
- Neoplasm of uncertain behavior of trachea, bronchus and lung
- Other chronic bronchitis
- Other deficiencies of circulating enzymes
- Other emphysema
- Other specified disorders of metabolism
- Pneumoconiosis due to other inorganic dust
- Pneumoconiosis due to other silica or silicates
- Pneumoconiosis, unspecified
- Pneumonopathy due to inhalation of other dust
- Postinflammatory pulmonary fibrosis
- Primary pulmonary hypertension
- Pulmonary fibrosis
- Pulmonary embolism and infraction
- Pulmonary hypertension due to cardiac disease
- Recurrent pulmonary embolism

- Sarcoidosis
- Scleroderma
- Systemic sclerosis
- Tuberculosis fibrosis of lung
- Ventricular septal defect

Potential Contraindications for Transplant:

Potential contraindications are subject to the judgment of the transplant center:

- Known current malignancy, including metastatic cancer;
- Recent malignancy with high risk of recurrence;
- History of cancer with a moderate risk of recurrence;
- Untreated systemic infection making immunosuppression unsafe, including chronic infection;
- Other irreversible end-stage disease not attributed to heart or lung disease[a];
- Stable systemic disease that could be exacerbated by immunosuppression;
- Psychosocial conditions or chemical dependency affecting ability to adhere to therapy .

Policy specific:

- Coronary artery disease not amenable to percutaneous intervention or bypass grafting, or associated with significant impairment of left ventricular function[a]; or
- Colonization with highly resistant or highly virulent bacteria, fungi, or mycobacteria.

[a] Some patients may be candidates for combined heart and lung transplantation

The consideration for risk-reducing procedure (e.g., CABG) performed at the same time as the organ transplant is a consideration based on the medical consultation review.

Lung Specific Guidelines

Bilateral lung transplantation is typically required when chronic lung infection disease is present, i.e., associated with cystic fibrosis and bronchiectasis. Some, but not all, cases of pulmonary hypertension will require bilateral lung transplantation. Bronchiolitis obliterans is associated with chronic lung transplant rejection, and thus may be the etiology of a request for lung retransplantation.

Individuals must meet United Network for Organ Sharing (UNOS) guidelines for lung allocation score greater than zero.

All transplants must be prior authorized through the Human Organ Transplant Program.

Exclusions:

Lung and lobar lung transplants and retransplantations are considered investigational in all other situations.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

32850	32851	32852	32853	32854	32855
32856	S2060	S2061			

Other codes (investigational, not medically necessary, etc.):

N/A

Rationale

Potential Contraindications to Transplantation

Malignancy

Malignancies are common after lung transplantation, with 21% and 40% of patients reporting 1 or more malignancies at 5 and 10 years post transplantation, respectively.[4] Skin cancer occurred most frequently, and lymphoproliferative disorders were the malignancies most associated with morbidity post transplantation.

Human Immunodeficiency Virus Infection

Current OPTN policy permits human immunodeficiency virus (HIV)-positive transplant candidates. The 2020 US Public Health Service guideline also allows for transplantations in HIV-positive recipients with proper screenings and effective regimens for HIV infections.[5] In 2022, the US Public Health Service published updated guidance for testing transplant candidates aged less than 12 years of age.[6] They recommended that children less than 12 years of age who have received postnatal infectious disease testing are exempt from repeat pretransplant HIV, HBV, and HCV testing during hospital admission for transplant surgery.

The British HIV Association and the British Transplantation Society (2017) updated their guidelines on kidney transplantation in patients with HIV disease.[7] These criteria for adding a patient to the waitlist may be extrapolated to other organs:

- Adherent with treatment, particularly antiretroviral therapy
- Cluster of Differentiation 4 count greater than 100 cells/mL (ideally >200 cells/mL) for at least 3 months
- Undetectable HIV viremia (<50 HIV-1 RNA copies/mL) for at least 6 months
- No opportunistic infections for at least 6 months
- No history of progressive multifocal leukoencephalopathy, chronic intestinal cryptosporidiosis, or lymphoma.

Other Infections

Infection with *Burkholderia cenocepacia* is associated with increased mortality in some transplant centers, a factor that may be considered when evaluating the overall risk of transplant survival.[8] Two articles have evaluated the impact of infection with various species of *Burkholderia* on outcomes for lung transplantation for cystic fibrosis. In a study by Murray et

al (2008), multivariate Cox survival models were applied to 1026 lung transplant candidates and 528 transplant recipients.[9,] Of the transplant recipients, 88 were infected with *Burkholderia*. Among transplant recipients infected with *B. cenocepacia,* only those infected with nonepidemic strains (n=11) had significantly greater posttransplant mortality than uninfected patients (HR , 2.52; 95% CI, 1.04 to 6.12; p=.04). Transplant recipients infected with *Burkholderia gladioli* (n=14) also had significantly greater posttransplant mortality than uninfected patients (HR , 2.23; 95% CI, 1.05 to 4.74; p=.04). When adjustments for specific species or strains were included, the Lung Allocation Scores of *Burkholderia multivorans*-infected transplant candidates were comparable with uninfected candidate scores, and scores for patients infected with nonepidemic *B. cenocepacia* or *B. gladioli* were lower. In a smaller study of 22 patients colonized with *Burkholderia cepacia* complex who underwent lung transplantation in 2 French centers, Boussaud et al (2008) reported that the risk of death by univariate analysis was significantly higher for the 8 patients infected with *B. cenocepacia* than for the other 14 colonized patients (11 of whom had *B. multivorans*).[10]

An analysis of international registry data by Yusen et al (2016) found that non-cytomegalovirus (CMV) infection is a major cause of mortality within 30 days of a lung transplant in adults.[11] A total of 655 (19%) of 3424 deaths after transplants between 1990 and 2015 were due to non-CMV infection. Only 3 (0.1%) of the deaths were due to CMV infection.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

LUNG TRANSPLANTATION FOR END-STAGE PULMONARY DISEASE

Clinical Context and Test Purpose

The purpose of lung transplantation in individuals who have end-stage pulmonary disease is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following **PICOs** were used to select literature to inform this review.

Populations
The relevant population of interest is individuals with end-stage pulmonary disease.

Before consideration for transplant, patients should be receiving maximal medical therapy, including oxygen supplementation, or surgical options, such as lung volume reduction surgery for chronic obstructive pulmonary disease (COPD).

Interventions
The therapy being considered is a lung transplant.

Comparators
The following practice is currently being used to make decisions about reducing the risk of end-stage pulmonary disease: medical management.

Outcomes
The general outcomes of interest are overall survival and treatment-related adverse events (e.g., immunosuppression, graft failure, surgical complications, infections, cardiovascular complications, malignancies).

Registry Studies
Paraskeva et al (2018) analyzed survival rates of adolescent lung transplant recipients using data from the International Society for Heart and Lung Transplantation Registry.[12] Patients between 10 and 24 years old represented 9% of the registry data (n=2319) and they were compared with both old and young cohorts. Overall survival in the adolescent cohort was 65% at 3 years, which was similar to that observed in adults between 50 and 65 years of age, but significantly lower than 3-year survival rate among the pediatric subgroup (73%; p=0.006) or adults 25 to 34 years old (75%; p<0.001) and 35 to 49 years old (71%; p<0.001). Within the adolescent group, patients between 15 and 19 years of age had the poorest survival rates at 3 years (59%) compared with 10- to 14-year old patients (73%) and 20- to 24-year old year patients (66%,) (both p<0.001). The registry study was biased toward inclusion of North American data and potential data entry errors or missing data. There were no data reported on the cause of mortality, differences in regimens, or rates of graft dysfunction between the groups.

The Registry of the International Society for Heart and Lung Transplantation (ISHLT) contains data from 49,453 adult recipients who received lung transplantation (including lung retransplantation) through June 2015, at 134 transplant centers.[11] A total of 55,795 lung transplants were performed, of which 53,522 (95.9%) were primary transplants and 2273 (4.1%) were retransplants. The overall median survival of patients who underwent lung transplantation was 5.8 years. Estimated unadjusted survival rates were 89% at 3 months, 80% at 1 year, 65% at 5 years, and 32% at 10 years. Patients who survived a year after primary transplantation had a median survival of 8.0 years. In the first 30 days after transplantation, the major reported causes of mortality were graft failure (24.5%) and non-cytomegalovirus (non-CMV) infections (19.1%) while non-CMV infections became the major cause of death for the remainder of the first year. Beyond the first year, the most common reported causes of mortality were obstructive bronchiolitis/bronchiolitis obliterans syndrome (OB/BOS), graft failure, and non-CMV infections. Beyond 10 years post-transplant, the major

causes of mortality were OB/BOS (21.5%), non-CMV infection (16.5%), and nonlymphoma malignancy (13.7%).

The International Society for Heart and Lung Transplantation Registry contains a total of 2229 pediatric lung transplants performed through 2014.[13] Most transplants (73%) were done in older children between the ages of 11 and 17 years. Median survival in children who underwent lung transplantation was 5.4 years, similar to survival in adults (mean survival, 5.7 years). However, median survival in children was lower (2.2 years) than in adults (5.6 years) for single-lung transplants.

In 2010, Thabut and colleagues reported on a comparison of patients undergoing single- and double-lung transplantation for idiopathic pulmonary fibrosis.[14] A retrospective review was conducted of 3,327 patients with data in the United Network for Organ Sharing (UNOS) registry. More patients underwent single-lung as compared to double-lung transplant (64.5 vs. 35.5%, respectively). Median survival time was greater for the double-lung group at 5.2 years (95% confidence interval [CI], 4.3 to 6.7 years) versus 3.8 years (95% confidence interval [CI], 3.6 to 4.1 years; p<0.001). After adjustment for baseline differences, however, survival times were not statistically different. The authors concluded that overall survival did not differ between the two groups: single-lung transplants offered improved short-term survival but long-term harm, whereas double-lung transplant increased short-term harm but was associated with a long-term survival benefit. In 2014, Black et al reported on LAS and single versus double lung transplant in 8778 patients (8050 had an LAS<75 and 728 had an LAS ≥75).[5] A significant decrease in survival was seen in single-lung transplant patients with a high LAS compared with double-lung transplant patients with a high LAS, even though operative morbidity was higher (p<0.001). Yu et al (2019) compared double-lung with single-lung transplantations for outcomes of survival, pulmonary function, surgical indicators, and complications in a meta-analysis of 30 studies (n=1980 recipients of single-lung transplants and n=2112 recipients of double-lung transplants).[9] Overall survival, in-hospital mortality, and postoperative complications besides bronchiolitis obliterans syndrome were similar between the 2 groups. Recipients of double-lung transplants had lower rates of bronchiolitis obliterans syndrome, better postoperative lung function, improved long-term survival, while recipients of single-lung transplants spent less time in surgery, postoperative intensive care unit, and postoperative hospital stay.

In 2010, Yusen and colleagues reviewed the effect of the Lung Allocation Score (LAS) on lung transplantation by comparing statistics for the period before and after its implementation in 2005.[17] Other independent changes in clinical practice, which may affect outcomes over the same period of time, include variation in immunosuppressive regimens, an increased supply of donor lungs, changes in diagnostic mix, and increased consideration of older recipients. Deaths on the waiting list declined following implementation of the LAS system, from approximately 500 per 5,000 patients to 300 per 5,000 patients. However, it is expected that implementation of the LAS affected patient characteristics of transplant applicants. One-year survival post-transplantation did not improve after implementation of the LAS system: patient survival data before and after are approximately 83%. Long-term survival data are not yet available for comparison. In 2014, Shafii et al reported on a retrospective evaluation of the LAS and mortality in 537 adults listed for lung transplantation and 426 who underwent primary lung transplantation between 2005 and 2010.[11] Patients on the waitlist who had a higher LAS had a higher rate of mortality (p<0.001). In the highest quartile of LAS, ranging from 47 to 95, within 1 year of listing, there was a 75% mortality rate. Higher LAS was also associated with early post-

transplant survival (p=0.05) but not late post-transplant survival (p=0.4). When other predictive factors of early mortality were accounted for, pretransplant LAS was not independently related to post transplant mortality (p=0.12).

Section Summary: Lung Transplant for End-Stage Pulmonary Disease
International registry data on a large number of patients receiving lung transplantation (>50,000) found relatively high patient survival rates (89% at 3 months, 80% at 1 year, 65% at 5 years, 32% at 10 years). In patients who survived a year, median survival was 8 years. After adjusting for potential confounding factors, survival did not differ significantly after single- or double-lung transplant. A subgroup analysis of an international registry study found decreased survival for adolescent patients, especially between 15 and 19 years of age, who received lung transplantation but the study was limited by inclusion bias and lack of data on mortality, differences in treatment regimens, and rates of graft dysfunction.

LOBAR LUNG TRANSPLANTATION FOR END-STAGE PULMONARY DISEASE

Clinical Context and Test Purpose
The purpose of lobar lung transplantation in individuals who have end-stage pulmonary disease is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following **PICOs** were used to select literature to inform this review.

Populations
The relevant population of interest is individuals with end-stage pulmonary disease.
Before consideration for transplant, patients should be receiving maximal medical therapy, including oxygen supplementation, or surgical options, such as lung volume reduction surgery for COPD .

Interventions
The therapy being considered is a lobar lung transplant. Lobar lung transplantation is provided in a hospital setting with specialized staff and equipment to perform the surgical procedure and provide postsurgical intensive care.

Comparators
The following practice is currently being used to make decisions about end-stage pulmonary disease: medical management.

Outcomes
The general outcomes of interest are overall survival and treatment-related adverse events (e.g., immunosuppression, graft failure, surgical complications, infections, cardiovascular complications, malignancies).

Systematic Reviews
In 2017, Eberlein et al reported on a systematic review of studies on lobar lung transplantation from deceased donors.[20] Reviewers identified 9 studies comparing outcomes after lobar lung or lung transplant, all of which were single-center retrospective cohort studies. Seven studies were conducted in Europe and one in Australia and one in North America. One-year survival reported in individual studies ranged from 50% to 100% after lobar lung transplant and from

72% to 88% after conventional lung transplant. In a pooled analysis of data from 8 studies, lobar lung transplant recipients (n=284) had a significantly higher risk of 1-year mortality than lung transplant recipients (n=2777) (relative risk [RR], 1.85; 95% CI, 1.52 to 2.25; p<0.001; I^2=0%).

Retrospective Studies

Several studies have reported on lobar lung transplants from living donors. In 2005, Barr and colleagues reported on experience performing living donor lobar lung transplants in the U.S.[21] Ninety patients were adults and 43 were children. The primary indication for transplantation (86%) was cystic fibrosis. At the time of transplantation, 67% of patients were hospitalized and 20% were ventilator dependent. Overall recipient actuarial survival at 1-, 3- and 5-years was 70%, 54% and 45%, respectively. There was not a statistically significant difference in actuarial survival between adults and children who underwent transplantation. Moreover, survival rates were similar to the general population of lung transplant recipients. The authors also reported that rates of postoperative pulmonary function in patients surviving more than 3 months post-transplant were comparable to rates in cadaveric lung transplant recipients.

In 2015, Date et al reported on a retrospective study comparing 42 living-donor lobar lung transplants and 37 cadaveric lung transplants.[22] Survival rates at 1 and 3 years were not significantly different between the groups (89.7 and 86.1% vs. 88.3 and 83.1%, respectively, p=0.55), despite living-donor lobar lung transplant patients having poorer health status preoperatively. In 2012, a program in Japan reported on 14 critically ill patients who had undergone single living-donor lobar lung transplants; there were 10 children and 4 adults.[23] Patients were followed for a mean 45 months. The 3-year survival rate was 70% and the 5-year survival was 56%. Severe graft dysfunction occurred in 4 patients. Mean forced vital capacity (FVC) was found to be lower in patients experiencing severe graft dysfunction compared with the other patients, mean FVC was 54.5% and 66.5%, respectively. The authors stated that this suggests size mismatching in the patients with severe graft dysfunction.

In 2014 Slama et al reported on a comparison of outcomes in 138 cadaveric lobar lung transplants (for size discrepancies) to 778 patients who received cadaveric whole-lung transplants, 239 of whom had downsizing by wedge resection of the right middle lobe and/or the left lingula.[24] Survival in the lobar lung transplant group at 1 and 5 years was 65.1% and 54.9% versus 84.8% and 65.1% in the whole lung and downsized by wedge resection group (p<0.001). The lobar lung transplantation group experienced significantly inferior early postoperative outcomes, but in patients who were successfully discharged, survival rates were similar to standard lung transplantation (p=0.168).

Section Summary: Lung Lobar Transplant for End-Stage Pulmonary Disease

There are fewer data on lung lobar transplants than on whole-lung transplants. The available data reported in case series has suggested reasonably similar survival outcomes, and lung lobar transplants may be the only option for patients unable to wait for a whole-lung. A 2017 systematic review found 1-year survival rates in the available published studies ranging from 50% to 100%.

LUNG OR LOBAR RETRANSPLANTATION WHEN MEETING CRITERIA FOR A LUNG TRANSPLANT

Clinical Context and Test Purpose

The purpose of lung retransplantation in individuals who have had a prior lung or lobar transplant and who meet criteria for a lung transplant is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following **PICOs** were used to select literature to inform this review.

Populations
The relevant population of interest is individuals receiving a lung retransplant after failing a prior lung or lobar transplant and who would be eligible for a lung transplant.

Interventions
The therapy being considered is lung or lobar retransplantation. Lobar lung retransplantation is provided in a hospital setting with specialized staff and equipment to perform the surgical procedure and provide postsurgical intensive care.

Comparators
The following practice is currently being used to make decisions about treating those whose lung or lobar transplant has failed and would still be considered as meeting eligibility criteria for an initial transplant: medical management.

Outcomes
The general outcomes of interest are overall survival and treatment-related adverse events (e.g., immunosuppression, graft failure, surgical complications, infections, cardiovascular complications, malignancies). See the Potential Contraindications section for detailed discussion.

Case Series
Registry data and case series reports have demonstrated favorable outcomes with lung retransplantation in certain populations, such as in patients who meet criteria for initial lung transplantation.[4,25,26]

Biswas Roy et al (2018) published a single-center retrospective study comparing survival outcomes in 29 patients who received retransplantation for chronic lung allograft dysfunction with 390 patients receiving a primary lung transplant at the same center.[27] Patients receiving retransplantation had significantly higher use of extracorporeal membrane oxygenation support for severe primary graft dysfunction (p=0.019) and underwent cardiopulmonary bypass and re-exploration for bleeding (p=0.019) more frequently than patients receiving primary transplantation (p=0.029). At 1-year follow-up, 89.7% of primary transplant patients were living, as were 89.2% of retransplantation patients. At 5-year follow-up, a greater percentage of the retransplantation group had survived, compared with the primary transplantation group (64.3% vs. 58.2%), although the difference was not statistically significant. While high LAS and extended hospital length of stay were both identified as independent mortality risk factors, retransplantation was not (hazard ratio, 1.58; 95% CI, 0.31 to 8.08; p=0.58). Study limitations included its single-center, retrospective design, the potential selection bias for younger patients, and the small size of the retransplantation group. Further, follow-up data at 3 and 5 years were incomplete for some patients and patients who were refused retransplantation were not considered in the analyses. However, for appropriately selected patients,

retransplantation after chronic lung allograft dysfunction resulted in 1- and 5-year survival rates comparable to those seen after primary lung transplantation.

Registry Studies
The Organ Procurement and Transplantation Network has reported data on lung transplants performed between 2008 and 2015.[28] Patient survival rates after repeat transplants were lower than primary transplants, but a substantial number of patients survived. For example, 1-year patient survival was 87.9% (95% CI, 87.2% to 88.7%) after a primary lung transplant and 76% (95% CI, 70.9% to 80.2%) after a repeat transplant. Five-year patient survival rates were 55.9% (54.7% to 57.2%) after a primary lung transplant and 33.8% (28.5 to 39.1%) after repeat transplant.

The International Society for Heart and Lung Transplantation Registry contains data on 2273 retransplantation patients performed through June 2015 (4.4% of lung transplantations).[11] The major causes of death in the first 30 days after retransplantation were graft failure and non-CMV infection, followed by multiorgan failure, cardiovascular causes, and technical factors related to the transplant procedure. Beyond the first year, the most common reported causes of mortality were OB/BOS, graft failure, and non-CMV infections.

Section Summary: Lung or Lobar Retransplant
Data from registries and case series have found favorable outcomes with lung retransplantation in patients who meet criteria for initial lung transplantation. Given the exceedingly poor survival without retransplantation of patients who have exhausted other treatments, evidence of a moderate level of post-transplant survival is sufficient in this patient population.

SUMMARY OF EVIDENCE
For individuals who have end-stage pulmonary disease who receive lung transplantation, the evidence includes case series and registry studies. Relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. International registry data on a large number of patients receiving lung transplantation (>50,000) found relatively high patient survival rates, especially among patients who survived the first year post transplant. After adjusting for potential confounding factors, survival did not differ significantly after single- or double-lung transplant. Lung transplantation may be the only option for some patients with end-stage lung disease. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have end-stage pulmonary disease who receive lobar lung transplantation, the evidence includes case series and systematic reviews. Relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. There are less data on lung lobar transplants than on whole-lung transplants, but several case series have reported reasonably similar survival outcomes between the procedures, and lung lobar transplants may be the only option for patients unable to wait for a whole-lung transplant. A 2017 systematic review found 1-year survival rates in the available published studies ranging from 50% to 100%. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have a prior lung or lobar transplant who meet criteria for a lung transplant who receive a lung or lobar lung retransplant, the evidence includes case series and registry

studies. Relevant outcomes are overall survival, change in disease status, treatment-related mortality and morbidity. Data from registries and case series have found favorable outcomes with lung retransplantation in patients who meet criteria for initial lung transplantation. Given the exceedingly poor survival without retransplantation of patients who have exhausted other treatments, evidence of a moderate level of post-transplant survival is sufficient in this patient population. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

PRACTICE GUIDELINES AND POSITION STATEMENTS

International Society for Heart and Lung Transplantation

Initial Transplant

In 2021, the International Society for Heart and Lung Transplantation published updated consensus-based guidelines on the selection of lung transplant candidates.[29]
"Lung transplantation should be considered for adults with chronic, end-stage lung disease who meet all the following general criteria:

1. High (>50%) risk of death from lung disease within 2 years if lung transplantation is not performed.
2. High (>80%) likelihood of 5-year post-transplant survival from a general medical perspective provided that there is adequate graft function."

The guideline also notes risk factors to be considered in the evaluation of transplant candidates, along with pediatric and disease-specific considerations.

Retransplant

In 2021, guideline update briefly addressed lung retransplantation, with the consensus statement noting that "The outcomes after re-transplants are inferior compared to first lung transplants, particularly if the re-transplant is done within the first year after the original transplant or for patients with restrictive allograft syndrome (RAS) [...] In the pre-transplant evaluation of such patients, particular emphasis should be focused on understanding the possible reasons for the graft failure, such as alloimmunization, poor adherence, gastroesophageal reflux, or repeated infections".[29]

American Thoracic Society et al

Evidence-based recommendations from the American Thoracic Society and 3 international cardiac societies were published in 2011.[30] For appropriately selected patients with idiopathic pulmonary fibrosis, the group et al recommended lung transplantation (strong recommendation, low-quality evidence). An update to this document was published in 2015 in which the committee did not make a recommendation regarding single versus bilateral lung transplantation in patients with idiopathic fibrosis.[31] The committee stated that "it is unclear whether single or bilateral lung transplantation is preferential for long-term outcomes".

In 2014, the American Thoracic Society published guidelines on the management of bronchiolitis obliterans syndrome in lung transplant recipients in conjunction with the International Society for Heart and Lung Transplantation and the European Respiratory Society.[33] The guideline recommends referral to a transplant surgeon to be evaluated for

retransplantation for end-stage bronchial obliterans syndrome that is refractory to other therapies.

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT00177918	Prospective evaluations of infectious complication in lung transplant recipients	600	Dec 2025
NCT06218758	Prediction Model for PPCs in Patients Undergoing Lung Transplantation Using Machine Learning	214	Dec 2025
NCT05581745	A2 to O Lung Transplants	10	Dec 2032
Unpublished			
NCT00905463	Analysis of prognosis and patients reported outcomes in lung transplant candidates	272	Mar 2022

NCT: national clinical trial

Government Regulations

National:

Lung transplantation is covered under Medicare when performed in a facility that is approved by Medicare as meeting institutional coverage criteria.[34] The Centers for Medicare and Medicaid Services have stated that under certain limited cases, exceptions to the facility-related criteria may be warranted if there is justification and the facility ensures safety and efficacy objectives.

Local:

There is no local coverage determination for lung transplant.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Transplant Heart
- Transplant Heart-Kidney (Combined)
- Transplant Heart-Lung (Combined)
- Transplant Heart-Liver (Combined)
- Transplant Kidney
- Transplant Liver
- Transplant Liver-Kidney (Combined)
- Transplant-Pancreas

- Transplant Small Bowel and Liver/Multivisceral (Combined)
- Transplant-Small Bowel (Isolated)

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through July 2024, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
5/1/02	5/1/02	5/1/02	Joint policy established
12/5/03	12/5/03	1/16/04	Routine maintenance
2/28/05	2/28/05	2/2/05	Routine maintenance
9/1/06	7/10/06	7/6/06	Routine maintenance
9/1/07	7/1/07	7/22/07	Routine maintenance
11/1/08	8/19/08	10/30/08	Routine maintenance
11/01/09	8/18/09	8/18/09	Routine maintenance
9/1/12	6/12/12	6/19/12	Routine maintenance; Policy reformatted to mirror BCBSA medical policy.
3/1/14	12/10/13	1/6/14	Routine maintenance. Policy status unchanged. Additional references added.
9/1/15	6/19/15	7/16/15	Routine maintenance. Added rationale and references including information regarding lung retransplantation. Policy status unchanged.
9/1/16	6/21/16	6/21/16	Routine policy maintenance. No change in policy status.
9/1/17	6/20/17	6/20/17	Routine policy maintenance. No change in policy status.
9/1/18	6/19/18	6/19/18	Updated rationale, added references 2, 3, 9 and 17. Deleted references 25-33. No change in policy status.
11/1/19	8/20/19		Routine policy maintenance, no change in policy status.
11/1/20	8/18/20		Minor revisions to exclusion section to align with other transplant policies. Routine policy maintenance, no change in policy status.
11/1/21	8/17/21		Routine policy maintenance, added reference #9. No change in policy status.

11/1/22	8/16/22		Routine policy maintenance, added reference 31. No change in policy status.
11/1/23	8/15/23		Routine policy update. Asterisk changed to superscript a and then defined in inclusion/exclusion section. Vendor managed: N/A (ds)
11/1/24	8/26/24		Routine policy maintenance, added to inclusion/exclusion section and MPS. Title changed to Transplant-Lung and Lobar Lung. Vendor managed: N/A (ds)

Next Review Date: 3rd Qtr. 2025

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN: 6/1/99	Revised: 10/25/00, 4/16/02
BCBSM: 11/4/96	Revised: N/A

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: TRANSPLANT-LUNG AND LOBAR LUNG

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered, policy guidelines apply For an approved, preauthorized transplant, BCN will cover the necessary hospital, surgical, lab and X-ray services for a non-member donor under the BCN member's certificate, unless the non-member donor has coverage for such services. This also includes solid organ donor procurement fees. Donor travel, meals and lodging expenses are *not* covered unless the BCN member has a rider that covers such services. BCN does NOT cover expenses incurred by a BCN member for donating bone marrow, stem cells or a solid organ (e.g., kidney, liver lobe, lung lobe) to a non-BCN member. The donor services would be considered not medically necessary for the BCN member.
BCNA (Medicare Advantage)	Covered, policy guidelines apply, must be a Medicare approved facility For an approved, preauthorized transplant, BCNA will cover the necessary hospital, surgical, lab and X-ray services for a non-member donor under the BCNA member's certificate, unless the non-member donor has coverage for such services. Donor travel, meals and lodging expenses are covered.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

Note: Services related to the transplant, except evaluation services, will not be authorized until the transplant itself is approved.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.

- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.