7.01.128	Bronchial Valves		
Original Policy Date:	September 27, 2013	**Effective Date:**	August 1, 2024
Section:	7.0 Surgery	**Page:**	Page 1 of 29

Policy Statement

I. Bronchial valves are considered **investigational** in **all** situations including, but not limited to:
   A. Treatment of prolonged air leaks
   B. Treatment for individuals with chronic obstructive pulmonary disease or emphysema

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Coding
See the Codes table for details.

Description

Bronchial valves are synthetic devices deployed with bronchoscopy into ventilatory airways of the lung to control airflow. They have been investigated for use in individuals who have prolonged bronchopleural air leaks and in individuals with lobar hyperinflation from severe or advanced emphysema.

Related Policies

- Lung Volume Reduction Surgery for Severe Emphysema
- Outpatient Pulmonary Rehabilitation

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

In October 2008, the Spiration® IBV Valve System (Spiration) was approved by the U.S. Food and Drug Administration (FDA) through the humanitarian device exemption (H060002) process for use in controlling prolonged air leaks of the lung or significant air leaks that are likely to become prolonged air leaks following lobectomy, segmentectomy, or lung volume reduction surgery. An air leak present on postoperative day 7 is considered prolonged unless present only during forced exhalation or cough. An air leak present on day 5 should be considered for treatment if it is: (1) continuous, (2) present during the normal inhalation phase of inspiration, or (3) present on normal expiration and

accompanied by subcutaneous emphysema or respiratory compromise. Use of the Intrabronchial Valve System is limited to 6 weeks per prolonged air leak. FDA product code: OAZ.

Two bronchial valve systems are FDA approved for treatment of patients with severe emphysema. In June 2018, FDA granted the Zephyr Valve system breakthrough device status with expedited approval for the bronchoscopic treatment of adult patients with hyperinflation associated with severe emphysema in regions of the lung that have little to no collateral ventilation. In December 2018, FDA approved the Spiration Valve System for adult patients with shortness of breath and hyperinflation associated with severe emphysema in regions of the lung that have evidence of low collateral ventilation. FDA product code: NJK.

Table 1. Bronchial Valve Systems Approved by FDA

Device	Indication	Manufacturer	Location	Date Approved	HDE/PMA No.
IBV® Valve System	To control prolonged air leaks of the lung, or significant air leaks that are likely to become prolonged air leaks, following lobectomy, segmentectomy, or lung volume reduction surgery	Spiration, Inc	Redmond, WA	10/24/08	H060002
Spiration® Valve System	For adult patients with shortness of breath and hyperinflation associated with severe emphysema in regions of the lung that have evidence of low collateral ventilation	Spiration, Inc	Redmond, WA	12/03/18	P180007
Zephyr® Endobronchial Valve System	For the bronchoscopic treatment of adult patients with hyperinflation associated with severe emphysema in regions of the lung that have little to no collateral ventilation	Pulmonx Corporation	Redwood City, CA	06/29/18	P180002

FDA: Food and Drug Administration, HDE: human device exemption; PMA: premarket approval application.

Rationale

Background

Pulmonary Air Leaks

Proper lung functioning depends on the separation between the air-containing parts of the lung and the small vacuum-containing space around the lung called the pleural space. When air leaks into the pleural space, the lung is unable to inflate, resulting in hypoventilation and hypoxemia; this condition is known as a pneumothorax. A pneumothorax can result from trauma, high airway pressures induced during mechanical ventilation, lung surgery, and rupture of lung blebs or bullae, which may be congenital or a result of chronic obstructive pulmonary disease (COPD).

Emphysema

Emphysema, a form of COPD, is a progressive, debilitating disease characterized by irreversible destruction of alveolar tissue. This destruction results in reduced elastic recoil, progressive hyperinflation and gas trapping with patients experiencing chronic dyspnea, limited exercise tolerance, and poor health-related quality of life. In emphysematous COPD, diseased portions of the lung ventilate poorly, cause air trapping, and hyperinflate, compressing relatively normal lung tissue. The patterns and degree of emphysema heterogeneity (i.e., the extent and distribution of air space enlargements) can be measured using computed tomography (CT) density as an indicator for tissue

destruction. The most diseased portions of lung can then potentially be targeted for lung volume reduction procedures. In homogeneous emphysema, there is minor or no regional difference in disease within or between lobes of the lung.

In the United States, prevalence of COPD varies widely by state, with the estimated prevalence in 2019 ranging from <4.5% in California, Colorado, Hawaii, Massachusetts, Minnesota, and Utah to >9% in Alabama, Arkansas, Kentucky, and West Virginia.[1,] In 2018, chronic lower respiratory disease, primarily COPD, was the fourth leading cause of death in the United States.[2,] COPD mortality has decreased among Americans overall but this decline has not been observed in all sociodemographic groups. An analysis of COPD mortality between 2004 and 2018 found that African American women were the only sociodemographic group to have had an increase in COPD mortality, with an annual percent change (APC) of 1.3% (95% confidence interval [CI], 0.9% to 1.6%), compared to a decrease in men (APC -1.2%; 95% CI -1.5% to -0.9%), and no change for women overall.[3,]

The Global Initiative for Chronic Obstructive Lung Disease, or GOLD, system is commonly used to categorize patients with emphysema according to severity.[4,] Stages of airflow limitation are based on the FEV1), or the amount of air a person can force out in 1 second after taking a deep breath. Patients with an FEV1 of less than 50% of their predicted value are considered to have severe airflow limitation. Patients are also grouped in the GOLD system according to categories of risk of having an exacerbation. These groups are based on number and type of exacerbations per year and self-reported symptoms such as breathlessness.

Table 2. Classification of Disease Severity

Stages of Airflow Limitation	Severity Grouping
• GOLD 1 (mild): FEV1 ≥80% predicted • GOLD 2 (moderate): 50% ≤ FEV1 <80% predicted • GOLD 3 (severe): ○ 30% ≤ FEV1 <50% predicted • GOLD 4 (very severe): FEV1 <30% predicted	**Group A: low risk** 0 to 1 exacerbation per year, not requiring hospitalization, fewer symptoms **Group B: low risk** 0 to 1 exacerbation per year, not requiring hospitalization, more symptoms **Group C: high risk** ≥2 exacerbations per year, or 1 or more requiring hospitalization, fewer symptoms **Group D: high risk** ≥2 exacerbations per year, or 1 or more requiring hospitalization, more symptoms

FEV1: forced expiratory volume in 1 second; GOLD: Global Initiative for Chronic Obstructive Lung Disease.

Bronchial Valves

Bronchial valves are synthetic devices deployed with bronchoscopy into ventilatory airways of the lung to control airflow. During inhalation, the valve is closed, preventing air flow into the diseased area of the lung. The valve opens during exhalation to allow air to escape from the diseased area of the lung. They have been investigated for use in patients who have prolonged bronchopleural air leaks and in patients with lobar hyperinflation from severe or advanced emphysema.

When used to treat persistent air leaks from the lung into the pleural space, the bronchial valve theoretically permits less air flow across the diseased portion of the lung during inhalation, aiding in air leak closure. The valve may be placed, and subsequently removed, by bronchoscopy.

The use of bronchial valves to treat emphysema is based on the improvement observed in patients who have undergone lung volume reduction surgery. Lung volume reduction surgery involves excision of peripheral emphysematous lung tissue, generally from the upper lobes. The precise mechanism of clinical improvement for patients undergoing lung volume reduction has not been firmly established.

However, it is believed that elastic recoil and diaphragmatic function are improved by reducing the volume of the diseased lung. Currently, and at the time the clinical trials were designed, very few lung volume reduction procedures were performed. The procedure is designed to relieve dyspnea and improve functional lung capacity and quality of life; it is not curative. Medical management remains the most common treatment for a majority of patients with severe emphysema.

In early trials of bronchial valves for treatment of emphysema, absence of collateral ventilation (pathways that bypass the normal bronchial airways) was associated with better outcomes, presumably because patients with collateral ventilation did not develop lobar atelectasis (collapse). In subsequent trials, patients were selected for absence of collateral ventilation, and it is current practice for patients to be assessed for the presence of collateral ventilation prior to undergoing the procedure. Collateral ventilation is measured by the Chartis System, which requires bronchoscopy, or as a surrogate, CT scanning to assess the completeness of fissures. After 45 days post-procedure, residual volume can provide information on whether lung volume reduction has been achieved successfully.

Literature Review

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 1 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 (RCT) 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.

Treatment of Pulmonary Air Leaks

Clinical Context and Therapy Purpose

The purpose of placing bronchial valves in patients who have pulmonary air leaks is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with pulmonary air leaks.

Interventions

The therapy being considered is the placement of bronchial valves. A bronchial valve is a device that permits one-way air movement. During inhalation, the valve is closed, preventing air flow into the diseased area of the lung. The valve opens during exhalation to allow air to escape from the diseased area of the lung. When used to treat persistent air leak from the lung into the pleural space, the bronchial valve theoretically permits less air flow across the diseased portion of the lung during inhalation, aiding in air leak closure. The valve may be placed, and subsequently removed, by bronchoscopy.

Comparators

The following practices are currently being used:

- Inserting a chest tube (tube thoracostomy) and employing a water seal or one-way valve to evacuate air collected in the pleural space and prevent it from reaccumulating;
- Lowering airway pressures by adjusting the mechanical ventilator;
- Using autologous blood patches; and
- Performing a thoracotomy with mechanical or chemical pleurodesis.

Outcomes

The general outcomes of interest, in addition to overall survival, are a reduction in symptoms (e.g., pneumothorax) and improvements in functional outcomes. Placement of bronchial valves requires an inpatient surgical procedure. Bronchial valves can be utilized for up to 6 weeks to effect resolution of a persistent pulmonary leak.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Review of Evidence

Case Series

No RCTs or comparative observational studies were identified. Only case series and case reports are available.

In the largest case series, Travaline et al (2009) reported on 40 patients treated at 17 sites in the United States and Europe.[5,] The Zephyr Endobronchial Valve (EBV) was used. All patients in the series had prolonged pulmonary air leak (mean duration, 119 days; median, 20 days). The most common comorbidities were cancer and chronic obstructive pulmonary disease (COPD). After valve placement, 19 (47.5%) patients had complete resolution of the acute air leak, 18 (45%) had a reduction in air leak, 2 (5%) had no change, and no data were available for 1 patient. The mean time from valve placement to chest tube removal was 21 days (median time, 7.5 days). Six patients experienced adverse events related to valve placement, including valve expectoration, moderate oxygen desaturation, initial malpositioning of a valve, pneumonia, and *Staphylococcus aureus* colonization. The length of follow-up varied, ranging from 5 to 1109 days. At last follow-up, 16 patients had died, though none of the deaths was attributed to the valve or the implantation procedure.

Firlinger et al (2013) studied 13 patients with persistent, continuous air leak (i.e., having an intrathoracic chest tube for >7 days despite conservative and/or surgical therapy) in Austria.[6,] Spiration valves were used in 9 patients and Zephyr valves in 4 patients. Ten (77%) of 13 patients were considered responders, defined as successful chest tube removal without need for further intervention. The Spiration IBV (intrabronchial valve) was used in 6 of 10 responders and all 3 nonresponders.

Gillespie et al (2011) reported on a case series of 7 patients with pulmonary air leaks treated with Spiration IBV.[7,] The median duration of air leaks in the 7 patients before valve placement was 4 weeks (range, 2 weeks to 5 months). One patient had a second valve implanted due to an additional air leak. Complete air leak cessation occurred in 6 of 8 procedures after a mean duration of 5.2 days. The other 2 procedures resulted in a reduction of air leak. There were no operative or postoperative complications attributed to the bronchial valves. The valves were removed in 5 of the 7 patients at a

mean of 37 days after placement (range, 14 to 55 days). Valves were not removed from a patient who entered hospice care or the patient who underwent 2 procedures because the patient declined removal.

The Humanitarian Device Exemption approval of the IBV Valve required a post-approval study (PAS). The PAS was a prospective observational study to collect safety information about the IBV Valve System for the treatment of prolonged air leak. Eligible subjects were enrolled into the study on the day of valve treatment. The subjects were monitored after treatment until discharge from the hospital (a minimum of 1 night stay after the procedure). After discharge, the subjects were seen by the investigator for assessment of air leak status as clinically indicated. Valves were to be removed after the air leak was resolved. If the air leak was not resolved, the valves were to be removed no longer than 6 weeks after device placement and other options were to be considered. A summary of the U.S. Food and Drug Administration (FDA) PAS is provided in Table 3.

Table 3. Summary of IBV Valve PAS

Study	Countries	Sites	Dates	Participants	SAEs	Findings Regarding Air Leak Resolution
H060002 / PAS001 Prospective Cohort Study	US	11	2009-2014	39 post IBV valve placement for prolonged air leak	2[1]	32/39 per protocol follow-up: 2/32: no response 30/32: positive response 11/30: complete resolution 19/30: improvement

Source: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?c_id=249&t_id=367937
IBV: Intrabronchial valve; PAS: Post-Approval Study; SAE: serious adverse event.
[1] AE: One systolic arrest secondary to hypercapnia resolved prior to IBV placement and one mucus impaction of a bronchial valve

Section Summary: Treatment of Pulmonary Air Leaks

Data on the Spiration IBV are limited to reports of the first patients submitted to the Food and Drug Administration for the Humanitarian Device Exemption for use for prolonged air leaks as well as the results of the PAS completed in 2014. Other reports are small series of heterogeneous patients. There are no comparative data with alternatives. This evidence is inadequate to determine the impact of this technology on the net health outcome.

Treatment of Severe or Advanced Emphysema

Clinical Context and Therapy Purpose

The purpose of placing bronchial valves in individuals who have severe or advanced emphysema with little or no collateral ventilation between target and ipsilateral lobe is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with severe/advanced emphysema with little or no collateral ventilation between target and ipsilateral lobe who remain symptomatic despite optimal medical management.

Emphysema, a form of COPD, is a progressive, debilitating disease characterized by irreversible destruction of alveolar tissue. This destruction results in reduced elastic recoil, progressive hyperinflation, and gas trapping with patients experiencing chronic dyspnea, limited exercise tolerance, and poor health-related quality of life.

Bronchial valves would be considered for patients at Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 3 or 4 (severe or very severe).

Interventions

The therapy being considered is the placement of bronchial valves. Bronchial valves are synthetic devices deployed with a flexible bronchoscope into the airways of the lung. The devices use a one-way valve to achieve an atelectasis (collapse) of the lobe, allowing air to escape while blocking airflow into the treated lobe. Valves are designed to prevent air inflow during inspiration but to allow air and mucus to exit during expiration. This is intended to result in a reduction in lung volume and hyperinflation in the targeted area. Endobronchial valve insertion is done with the patient under sedation or general anesthesia. Several valves may be needed. Bronchial valves can be removed or replaced using bronchoscopy.

Comparators

Alternatives for the treatment of severe emphysema include medical management, lung volume reduction surgery, and lung transplantation.

GOLD lists the following components of optimal medical management for severe emphysema:[4,]

- Smoking cessation
- Individualized pharmacological therapy
- Assessment of inhaler technique
- Pulmonary rehabilitation (exercise training, health education, breathing techniques)
- Influenza and pneumococcal vaccinations
- Oxygen therapy
- Palliative approaches to symptom control (treat dyspnea, support nutrition, address panic, anxiety, depression, and fatigue)

Outcomes

The general outcomes of interest, in addition to overall survival, are a reduction in symptoms, functional outcomes, quality of life, and treatment-related morbidity.

Relevant health outcomes include COPD exacerbations, mortality, and adverse events (e.g., pneumothorax, pneumonia, and respiratory failure). Efficacy outcomes include measures of lung function, physical function, and quality of life (Table 4).

Improvement in lung function after use of bronchial valves as part of multimodality pulmonary care should be assessed at 6 months after insertion.

Table 4. Efficacy Outcome Measures

Measure	Description	Clinically Meaningful Difference
FEV1	• Volume of air a person can force out in 1 second after taking a deep breath • Not an objective of COPD management, but frequently used by regulatory authorities to interpret treatment efficacy in COPD trials • Used to categorize severity of airflow limitation	15% improvement • 100 to 140 mL increase
SGRQ	• Measures quality of life in patients with emphysema • Scores range from 0 to 100, with higher scores indicating a worse quality of life	4-point decrease (improvement)
6-Minute Walk Test	• Distance a person can walk in 6 minutes • Measures physical function	Increase of 25 to 30 meters

Measure	Description	Clinically Meaningful Difference
	• Healthy subjects can walk 400 to 700 meters	

COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 second; SGRQ: St. George Respiratory Questionnaire.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Review of Evidence
Zephyr Valve

Randomized Controlled Trials

Seven RCTs have evaluated the Zephyr valve in patients with severe emphysema (Table 5). Only a single trial (BELIEVER) used a sham procedure as a comparator; the rest were open-label and compared the Zephyr valve to standard medical care, typically optimal medical care as described in the GOLD guidelines. The VENT trial included patients with collateral ventilation, but subgroup analyses of patients with collateral ventilation were reported. The IMPACT (A Multicentre, Prospective, Randomized, Controlled, One-way Crossover Investigation of Endobronchial Valve (EBV) Therapy vs. Standard of Care (SoC) in Homogeneous Emphysema) trial included patients with homogeneous emphysema distribution and the other trials were limited to those with heterogeneous emphysema. The BELIEVER trial was limited in that it only had a 3-month follow-up duration. The other trials followed patients for 6 or 12 months. In IMPACT, participants in the standard of care arm were crossed over to the Zephyr valve arm if eligible after completing 6 months of follow-up. Eberhardt et al (2021) reported randomized results up to 6 months and single-arm results at 12 months.[8,]

A post hoc analysis of the 2 earliest trials (Endobronchial Valve for Emphysema Palliation Trial (VENT) EU 2012 and VENT US 2010) showed better response rates in participants who had intact fissures. As a result, the newer trials altered their inclusion criteria to only select participants with intact fissures, thereby lowering the chance of selecting participants who had collateral ventilation, which resulted in better functional outcomes.[9,]

The trials showed statistically and clinically significant improvements in FEV1 (Table 6). Both response and mean change were significantly higher in the valve group in all the trials that measured this outcome. This was consistent and clinically meaningful, but there was some imprecision, with wide confidence intervals in some of the trials. On the St. George Respiratory Questionnaire (SGRQ), there was no significant in the sham controlled study, while the open-label trials consistently showed a better outcome in the valve group.

The incidence of COPD exacerbations requiring hospitalization reported in the trials is shown in Table 7. In the immediate post-procedure period, more patients who received the intervention experienced a COPD exacerbation. However, at later time points, the incidence was lower among patients who received the valve. For example, in the LIBERATE (Lung Function Improvement After Bronchoscopic Lung Volume Reduction with Pulmonx Endobronchial Valves Used in Treatment of Emphysema) trial, the mean difference up to 45 days was 3.0% (95% confidence interval [CI], -4.1% to 10.1%), compared to 7.69% (95% CI, -5.99% to 21.38%) from day 46 up to 12 months.

Mortality and adverse event results are detailed in Table 8. The number of deaths was low and studies were not powered to detect a difference in events between groups. The most common serious adverse event was pneumothorax, which occurred in up to 27% of patients.

Table 5. Summary of Key RCT Characteristics- Zephyr Valve

Trial	Countries	Sites	Dates	Participants	Interventions		Duration
LIBERATE, Criner et al (2018)[10, 11,] **NCT01796392**	US and other	31	2013-2016	Heterogeneous emphysema and little to no collateral ventilation 91.6% White, 5.8% Black, 2.6% other race 46.8% male	Zephyr valve (n=128)	Standard care (n=62)	12 months
TRANSFORM, Kemp et al (2017)[12,] **NCT02022683**	Europe	17	2014-2016	Heterogeneous emphysema and no collateral ventilation Race and ethnicity not reported 59.8% male	Zephyr valve (n=65)	Standard care (n=32)	6 months
IMPACT, Valipour et al (2016)[13,] Eberhardt et al (2021)[8,] **NCT02025205**	Austria, Germany, Netherlands	15	2014-2016	Homogenous emphysema and no collateral ventilation Race and ethnicity not reported 38.7% male	Zephyr valve (n=43)	Standard care (n=50)	6 months
STELVIO, Klooster et al (2015)[14,] **NTR2876 (Netherlands)**	Netherlands	1	NR	Severe emphysema and no collateral ventilation Race not reported 32.4% male	Zephyr valve (n=34)	Standard care (n=34)	6 months
BELIEVER HI-FI, Davey et al (2015)[15,] **ISRCTN04761234**	England	1	2012-2013	Heterogeneous emphysema and intact interlobar fissures Race and ethnicity not reported 62.0% male	Zephyr valve (n=25)	Sham procedure (n=25)	3 months
VENT EUROPE, Herth et al (2012)[16,] **NCT00129584**	Multiple European	23	2005-2009	Severe heterogenous emphysema 99.4% White 71.9% male	Zephyr valve (n=111, 44 with complete fissure)	Standard care (n=60, 19 with complete fissure)	12 months

Trial	Countries	Sites	Dates	Participants	Interventions		Duration
VENT US, Sciurba et al (2010)[17], NCT00129584	US	31	2004-2006	Severe heterogenous emphysema 97.2% White 82.4% male	Zephyr valve (n=220)	Standard care (n=101)	6 months

NCT: National Clinical Trial; NR: Not reported; RCT: randomized controlled trial.

Table 6. RCTs of the Zephyr Valve- Efficacy Results

Study (Publication Date)	FEV1 Responders (>15% Increase from Baseline[1])	FEV1 - Mean Change	SGRQ Responders (>4-point decrease from baseline)	SGRQ - Mean Change	6-MInute Walk Distance - Responders (>25 meters increase from baseline)	6-MInute Walk Distance - mean change, meters
LIBERATE (2018)						
Number analyzed	190	190	190	190	190	190
Zephyr valve	47.7%	17.2%	56.2%		41.8%	
Standard care	16.8%	-0.8%	30.2%		19.6%	
Difference (95% CI)	31.5% (18.9% to 44.1%)	17.96% (9.84% to 26.09%)	25.6% (11.3% to 39.9%)	-7.05 (-11.84 to -2.27)	22.8% (9.8% to 35.9%)	39.31 (14.64 to 63.98)
p-value	<.001	<.001	NR	.004	NR	<.002
TRANSFORM (2017)						
Total N	97	97	97	97	97	97
Zephyr valve	56.3%		61.7%		52.4%	36.2
Standard care	3.2%		34.4%		12.9%	-42.5
Difference (95% CI)	53.1% (NR)	0.23 L (0.14 to 0.32)	27.3% (NR)	-6.5 (-12.4 to -0.6)	39.5% (NR)	78.7 (46.3 to 111.0)
P-value	<.001	<. 001	.042	.031	.001	<.001
IMPACT (2016 and 2021)						
Total N	93	93	84	84	92	92
Zephyr valve	30.2%	11.54%	63.9%	-6.84	45.2%	21.3
Standard care	10.0%	-4.73%	31.3%	0.63	22.0%	-7.1
Difference (95% CI)	20.2% (NR)	16.3% (NR)	32.8% (NR)	-7.51 (NR)	23.2% (NR)	28.3 (NR)
P-value	.014	<.0001	.003	<.0001	.018	.016
STELVIO (2015)						
Total N	68	NR	68	NR	68	68
Zephyr valve	59.0%	NR	79%	NR	59%	60 (35 to 85)
Standard care	24.0%	NR	33%	NR	6%	-14 (-25 to -3)
Difference (95% CI)	35.0% (NR)	NR	46% (NR)	NR	49% (NR)	74 (47 to 100)
P-value	0.001	NR	NR	NR	<.001	.001
BELIEVER HI-FI (2015)						
Total N	43	43	43	43	NR	43
Zephyr valve	47%	24.8%	58%		NR	*Median, IQR:* 25 (7 to 64)
Sham	4%	3.9%	46%		NR	*Median, IQR:* 3 (-14 to 20)
Difference (95% CI)	43.2% (19.4% to 67.0%)	20.9% (4.3% to 37.5%);	12.1% (-17.8% to 41.9%)	-9.64 (-14.09 to -5.20)	NR	NR
p-value	.0022	.033	NR	.36	NR	.0119
VENT Europe						
Total N	NR	63	NR	63	NR	63

Study (Publication Date)	FEV1 Responders (>15% Increase from Baseline[1])	FEV1 - Mean Change	SGRQ Responders (>4-point decrease from baseline)	SGRQ - Mean Change	6-MInute Walk Distance - Responders (>25 meters increase from baseline)	6-MInute Walk Distance - mean change, meters
Zephyr valve	NR	15%	NR	-6.0	NR	13%
Standard care	NR	-2%	NR	3.0	NR	10%
Difference (95% CI)	NR	17% (NR)	NR	3.0 (NR)	NR	3% (NR)
p-value	NR	.04	NR	.09	NR	.80
VENT US[2]						
Total N	321	NR	321	NR	321	NR
Zephyr valve	23.5%	NR	23.5%	NR	25.3%	NR
Standard care	10.7%	NR	10.7%	NR	17.8%	NR
Difference (95% CI)	6.8 (NR)	NR	12.8%	NR	7.5% (NR)	NR
p-value	.02	NR	.02	NR	.25	NR

[1]Responder definition was >10% in STELVIO and >12% in IMPACT and TRANSFORM.
CI: confidence interval; FEV1: forced expiratory volume in 1 second; IQR: interquartile range; NR: not reported; RCT: randomized controlled trial; SGRQ: St. George Respiratory Questionnaire.

Table 7. COPD Exacerbations in RCTs of the Zephyr Valve

Study	Time Point	Zephyr vs Control
LIBERATE	0 days to 46 days	7.8% vs. 4.8% Difference 3.0% (95% CI -4.1% to 10.1%)
	> 46 days to 12 months	23.0% vs. 30.6% Difference 7.69% (95% CI -5.99% to 21.38%)
TRANSFORM	0 days to 30 days	4.6% vs. 0%
	> 30 days to 6 months	4.6% vs. 6.3%
IMPACT	0 days to 30 days	14.0% vs. 1.0% p=.046
	31 days to 6 months	18.6% vs. 20.0%; p=1.00
STELVIO	0 days to 6 months	12% vs. 6%; p=.67
BELIEVER	0 days to 3 months	20.0% vs. 12.0%; p=.70
VENT EU	0 days to 3 months	11.7% vs. 10.0%; p=.80
	> 3 months to 12 months	Data NR (NS)
VENT US	0 days to 90 days	7.9% vs. 1.1%; p=.03
	3 months to 12 months	10.3% vs. 9.2%; p=.84

CI: confidence interval; COPD: chronic obstructive pulmonary disease; NR: not reported; NS: nonsignificant; RCT: randomized controlled trial.

Table 8. Mortality and Serious Adverse Events in RCTs of the Zephyr Valve

Study	Time Point	Mortality (Zephyr vs Control)	Serious Adverse Events (Zephyr vs Control)
LIBERATE	0 days to 46 days	3.1% vs. 0% Difference 3.1% (95% CI 0.11% to 6.1%)	39.8% vs. 4.8%
	>46 days to 12 months	0.8% vs. 1.6%	38.5% vs. 50.0%
TRANSFORM	0 days to 30 days	1.5% vs. 0%	38.5% vs. 3.1%
	>30 days to 6 months	0% vs. 0%	15.4% vs. 9.4%
IMPACT	0 days to 30 days	0 vs. 0	44.2% vs. 1.0%; p<.001
	31 days to 6 months	0 vs. 2 (4.0%)	34.9% vs. 26.0%; p=.269
STELVIO	0 days to 6 months	1 vs. 0	67.6% vs. 14.7%
BELIEVER	0 days to 3 months	2 vs. 0	% patients NR
VENT EU	0 days to 3 months	1 (0.9%) vs. 1 (1.7%); p=1.00	% patients NR
	>3 months to 12 months	5 (4.5%) vs. 3 (5.0%)	% patients NR
	0 days to 12 months	6 (5%) vs. 4 (7%)	% patients NR

Study	Time Point	Mortality (Zephyr vs Control)	Serious Adverse Events (Zephyr vs Control)
VENT US	0 to 90 days	2 (0.9%) vs. 0 (0%)	4.2% vs. 0%
	3 months to 12 months	6 (2.8%) vs. 3 (3.4%); p=.72	6.1% vs. 4.6%
	0 days to 6 months	6 (2.8%) vs. 0 (0%); p=.19	6.1% vs. 1.2%; p=.08
	0 days to 12 months	3.7% vs. 3.5%; p=.88	10.3% vs. 4.6%; p=.17

CI: confidence interval; NR: not reported; RCT: randomized controlled trial.

Tables 9 and 10 summarize the design and conduct limitations of the Zephyr valve RCTs. Because they included patients with collateral ventilation, the VENT trials are no longer representative of the intended use of the device. BELIEVER is limited by its 3-month follow-up duration. A major limitation in most of the trials was a lack of blinding, which could have influenced performance on measures of lung function, exercise tolerance (e.g., it might have affected clinicians' coaching of patients and/or the degree of effort exerted by patients), and patient-reported measures of symptoms and quality of life. Most studies were too small to detect differences between groups on important health outcomes such as mortality and COPD exacerbations. Five of 7 trials were conducted outside of the U.S. Three of 7 trials did not report race or ethnicity data on participants. In the 3 trials that reported race, 91.7% to 99.4% of participants were White. Therefore, it is uncertain if their results would be generalizable to the U.S. population.

Table 9. RCTs of the Zephyr Valve- Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
LIBERATE					
TRANSFORM	4. unable to determine; race of participants not reported			6. Used >12% in FEV for response	
IMPACT	4. unable to determine; race of participants not reported				
STELVIO	4. unable to determine; race of participants not reported			6. Used >10% for FEV1 response	
BELIEVER HI-FI	4. unable to determine; race of participants not reported				1,2 three months only
VENT Europe	3. included patients with collateral ventilation; 4. 97.2% white				
VENT US	3. included patients with collateral ventilation; 4. 99.4% White				.

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4. Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 10. RCTs of the Zephyr Valve- Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
LIBERATE		1, 2 not blinded				
TRANSFORM		1, 2 not blinded				
IMPACT		1, 2 not blinded				
STELVIO		1, 2 not blinded		6 Not ITT for some outcomes		3. confidence intervals not reported for some outcomes
BELIEVER HI-FI						
VENT Europe		1, 2 not blinded			3 smaller than the a priori estimate	3. confidence intervals not reported for some outcomes
VENT US		1, 2 not blinded				

ITT: intent to treat.
The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Systematic Reviews

Multiple systematic reviews with meta-analyses have assessed the use of the Zephyr valve system for patients with severe emphysema.[9,18,19,20,] Authors of all of these reviews came to similar conclusions: In patients with severe emphysema and low collateral ventilation, RCTs provide evidence of clinically meaningful benefit for bronchial valves compared to standard medical management on short-term measures of lung function, exercise tolerance, and quality of life, but these benefits should be measured against the greater risk of serious adverse events compared to usual care.

A recent and relevant good methodological quality meta-analysis was conducted by LaBarca et al in 2019.[20,] The remainder of this section focuses on this review. La Barca et al (2019) included all 7 RCTs of the Zephyr valve but excluded from quantitative meta-analyses the 2 RCTs that included patients

with collateral ventilation (VENT EU and VENT US). Two independent reviewers assessed the risk of bias of the included studies, and the quality of the overall body of evidence was ranked using the GRADE approach. Prespecified efficacy outcomes were change in FEV1, change in SGRQ; change in 6-minute walk test distance, and change in residual volume. The safety analysis included assessment of all-cause mortality and pneumothorax. The reviewers also conducted subgroup analyses based on length of follow-up (3 months vs. 6 months or longer), heterogeneous versus homogeneous emphysema distribution, and study comparator (standard of care vs. sham valve). Results are summarized in Table 12. Meta-analyses found statistically and clinically significant improvements with the Zephyr valve in FEV1, residual volume, 6-minute walk distance, and SGRQ, but with an increased risk of adverse events. The certainty of evidence was rated high only for SGRQ and risk of pneumothorax. Certainty of the evidence for the other efficacy outcomes was downgraded due to risk of bias from lack of blinding, and non-primary outcomes. Certainty of the evidence was rated low for overall mortality because it was not a primary outcome and the estimate had wide confidence intervals.

Table 11. Systematic Review and Meta-Analysis of the Zephyr Valve-Characteristics

Study	Search end date	RCTs	Participants	N (Range)	Duration
LaBarca et al (2020)[20,]	Oct 2018	7 (5 included in meta-analyses; excluded studies in patients with collateral ventilation)	Adult patients (mean age range 59.7 to 65.3 years); mostly COPD stage IV; without collateral ventilation measured by the Chartis system; optimal medical management according to GOLD recommendations;	498 (50 to 190)	3 to 12 months

COPD: chronic obstructive pulmonary disease; GOLD: Global Initiative for Chronic Obstructive Lung Disease; RCT: randomized controlled trial.

Table 12. Meta-analysis of RCTs of the Zephyr Valve- Results[20,]

Outcome	Pooled Result (95% CI)	Heterogeneity	Certainty of the Evidence (reasons for downgrading)
Change in Residual Volume, mL (mean difference)	−0.57 (−0.76 to −0.39)	I^2 = 37%; p =.18	Not assessed
Change in FEV1, mL (mean difference)	20.74% (15.68 to 25.79)	I^2 = 25%; p =.25	Moderate (risk of bias regarding blinding of participants and personnel in most studies)
Change in 6-min walk distance, meters (mean difference)	53.10 (34.72 to 71.49)	I^2 = 54%; p =.07	Low (high heterogeneity between studies despite subgroup analysis, non-primary outcome) Note: An erratum published in 2021 with corrected data found heterogeneity was no longer significant for this outcome, but the Certainty of Evidence rating was not changed
Change in SGRQ score (mean difference)	-8.42 (-10.86 to -5.97)	I^2 = 6%; p =.37	High
Pneumothorax (relative risk)	6.32 (3.74 to 10.67)	I^2 = 25%; p =.25	High
Overall Mortality (relative risk)	1.26 (0.50 to 3.15)	I^2 = 25%; p =.25	Low (non-primary outcome, wide CI)

CI: confidence interval; FEV1: forced expiratory volume in 1 second.; RCT: randomized controlled trial; SGRQ: St. George Respiratory Questionnaire.

Randomized Controlled Trial of Zephyr Valve Compared to Lung Volume Reduction Surgery

The CELEB study was an RCT comparing the Zephyr valve to LVRS in individuals with severe emphysema at 5 centers in the UK (Table 13). The primary outcome was the between group

difference in the i-BODE index from baseline to 12 months post procedure. i-BODE is a composite measure of disease severity made up of 4 components: the incremental shuttle walk test, body mass index, FEV1, and the Medical Research Council (MRC) dyspnea score. The instrument is scored from 0 to 10, with 10 indicating greater severity. The study authors do not cite a MCID threshold for the i-BODE, but calculated the sample size to detect a 1.5-point difference between groups, based on a previous study that reported an association between change in BODE score 3 months post-LVRS and survival at 5 years. Secondary outcomes were health status as assessed by the COPD Assessment Test (CAT) score, patient experience of physical activity assessed using the clinic visit PROactive Physical Activity in COPD (c-PPAC) score, change in residual volume, and change in fat-free mass index.

Of 163 individuals screened, 88 were eligible and randomized. The most common reason for ineligibility was evidence of collateral ventilation. A total of 80 individuals received treatment (34 LVRS, 46 BV). Six who were randomized to LVRS, and 1 who was randomized to the BV group decided against having the procedure post-randomization and exited the trial prior to treatment.

There was no statistically significant difference between groups on the primary outcome (Table 14), or on any of the 4 individual components of the composite measure (Table 15). Notably, the magnitude of change from baseline for both groups on the i-BODE was below the 1.5-point difference considered by the study investigators to be sufficiently clinically important. Of 4 secondary outcomes reported, only the CAT differed significantly between groups, and favored the LVRS arm with a magnitude of difference above the MCID threshold of 2 points (mean difference from baseline -6 [2 to 9]).

Other health outcomes are shown in Table 16. More participants in the BV group required additional procedures post-intervention, including 4 (8.5%) who went on to LVRS. There were 2 additional procedures required in the LVRS group; 1 participant returned to surgery for BV insertion due to a prolonged air leak and 1 had a redo thoracotomy and wash out of a hemothorax. There were 7 repeat procedures in the BV group requiring the participant to undergo a further bronchoscopy; 4 related to pneumothoraces with 2 requiring surgical chest drains and 2 undergoing blood pleurodesis. Two participants had valves removed and 1 participant had valves removed and re-placed before undergoing a LVRS. Three further participants in the BV arm crossed over into the LVRS arm due to no symptomatic benefit. There was 1 death in the BV group (procedure related) and 1 death in the LVRS group (not considered procedure related). Participants undergoing BV placement were required to remain as inpatients for a minimum of 3 days post-procedure in case of pneumothorax. Of those who had a pneumothorax, 9 (81.8%) occurred while still an inpatient post procedure, median (IQR) time to onset 2 (30) days and drain was removed after a median (IQR) 10 (12) days. The median (IQR) number of days with a chest drain post LVRS was 8.0 (11.0).

The study had several limitations that decrease confidence in its results (Tables 17 and 18). Lack of blinding of participants increases the potential for bias on outcomes requiring participant effort or self-reported experience of symptoms, although outcome assessors were blinded and participants were instructed not to reveal their allocation. Because it was designed to assess comparative effectiveness of bronchial valves and LVRS, the trial does not address existing gaps in the evidence on bronchial valves compared to medical management, the comparison of interest for this evidence review. The use of an endpoint not used in previous BV trials and the absence of outcomes that were primary endpoints in previous trials (such as the 6-minute walk test and the SGRQ) limits comparisons of the trial's results to the existing body of evidence. Additionally, the rationale for the choice of a composite endpoint was not clear. There is evidence of selective reporting of outcomes in that the published protocol lists the EQ-5D-5L as a secondary endpoint to be assessed, but this measure is not mentioned in the results publication and the reason for its absence is not addressed.[21,] Given that the CAT score (a measure of health status) showed a statistically and clinically significant benefit for LVRS over BVs, additional comparative information on quality of life, if measured, would help to inform the assessment of whether the benefits of bronchial valves outweigh its demonstrated

risks. Bronchial valves are proposed as a less invasive, and therefore safer, alternative to LVRS. However, participants who receive bronchial valves in the CELEB trial had more repeat procedures (including subsequent LVRS) than those who received LVRS and there was 1 procedure-related death in the BV group. Finally, the trial was limited by a high loss to follow-up: only 21 of 34 (61.8%) participants who received LVRS and 28 of 46 who received BVs (60.9%) had complete data on the primary outcome. The authors note that follow-up was interrupted due to the COVID-19 pandemic and some in-person research visits were missed as they were not possible or considered unsafe in this vulnerable group.

Table 13. RCT of Bronchial Valves Compared to Lung Volume Reduction Surgery (CELEB) - Study Characteristics

Trial	Countries	Sites	Dates	Participants	Interventions		Duration of Followup
Buttery et al (2023)[22,]	UK	5	2016-2019	N = 8848% female, mean (SD) age 64.6 (7.7) years All participants were required to have undergone a course of Pulmonary Rehabilitation within the 12 months preceding trial enrollment and underwent bronchoscopy to confirm absence of collateral ventilation. 87 (98.9%) White, 1 (1.1%) Middle Eastern	LVRS N = 41 randomized 34 received treatment	Bronchial Valves (Zephyr) N = 47 randomized 46 received treatment	12 months

LVRS: lung volume reduction surgery; RCT: randomized controlled trial.

Table 14. RCT of Bronchial Valves Compared to Lung Volume Reduction Surgery- Efficacy Results (Primary and Secondary Outcomes)

	Primary Outcome	Secondary Outcomes, Mean Change from Baseline to 12 months				
Buttery et al (2023)[22,]	**i-BODE mean change from baseline to 12 months (95% CI)**	**Health Status (CAT Score, 95% CI)**	**Health Related Quality of Life (EQ-5D-5L)**	**Residual Volume % predicted (95% CI)**	**Fat-free Mass (kg/m²)**	**Patient experience of Physical activity (PROactive Physical Activity in COPD instrument,(95% CI))**
N analyzed	49 (21 LVRS/28 BV)		Not reported			
LVRS	-1.10 (1.44)	-7 (-11 to -1)		-36.1 (-54.1, to -10)	-0.79 (-3.67 to 1.44)	+18.3 (17.3)
Bronchial Valves	-0.82 (1.61)	-1 (-3 to 3)		-30.1 (-53.7 to -9)	0.46 (-1.84 to 1.89)	+16.1 (16.9)

	Primary Outcome	Secondary Outcomes, Mean Change from Baseline to 12 months			
Difference (95% CI)	-0.27 (-0.62 to 1.17)	-6 (2 to 9)	2.7 (-25.4 to 19.1)	0.98 (-1.25 to 3.20)	-2.2 (-15.8 to 11.4)
p-value	.54	.005	.81	,39	.74

CI: confidence interval. LVRS: lung volume reduction surgery.

Table 15. RCT of Bronchial Valves Compared to Lung Volume Reduction Surgery- Efficacy Results- Components of Composite Primary Outcome

	Mean Change from Baseline to 12 Months			
Buttery et al (2023)[22,]	BMI (kg/m^2)	FEV1 % predicted	MRC Dyspnea score	ISWT (m)
LVRS	0.10 (SD 1.83)	1.1 (SD 9.1)	-0.65 (SD 0.89)	27.9 (SD 60.7)
Bronchial Valves	0.74 (SD 1.57)	4.5 (SD 6.8)	-0.33 (SD 0.97)	-4.8 (SD 73.8)
Difference (95% CI)	0.64 (-0.27 to 1.56)	3.4 (CI -0.8 to 7.6)	-0.32 (-0.80 to 0.16)	-32.7 (-71.0 to 5.5)
P-value	.16	.11	.19	.09

BMI: body mass index; CI: confidence interval; FEV1: forced expiratory volume in 1 second; ISWT: incremental shuttle walk test; LVRS: lung volume reduction surgery; MRC: medical Research Council; RCT: randomized controlled trial.

Table 16. RCT of Bronchial Valves Compared to Lung Volume Reduction Surgery- Other Health Outcomes and Adverse Events

Study	Mortality at 12 months	COPD exacerbations requiring hospitalization at 3 months	Adverse Events
Buttery et al (2023)[22,]			
LVRS	1 death 44 days post-procedure, complications related to the procedure	3/34 (8.8%)	Most common complication was subcutaneous emphysema (29.3%) 2 individuals required at least 1 further bronchoscopy or procedure 1 individual crossed over to bronchial valves
Bronchial Valves	1 death 5 months post-procedure, acute COPD exacerbation, not procedure related	5/46 (10.9%)	Most common complication was pneumothorax (30.4%) 8 individuals required at least 1 further bronchoscopy or procedure 4 individuals crossed over to LVRS

COPD: chronic obstructive pulmonary disease; RCT: randomized controlled trial.

Table 17. RCT of Bronchial Valves Compared to Lung Volume Reduction Surgery- Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Buttery et al (2023)[22,]			Comparator was LVRS	Rationale for choice of composite primary outcome measure unclear	

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4. Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 18. RCT of Bronchial Valves Compared to Lung Volume Reduction Surgery - Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Buttery et al (2023)[22,]		1. participants not blinded, outcome assessment blinded	2. Quality of life on EQ-5L was measured but not reported.	1. high loss to follow-up: 21/34 (61.8%) who received LVRS and 28/46 (60.9%) who received BV had data on the primary outcome (i-BODE at 12 months)		

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Spiration Valve

Randomized Controlled Trials

Three RCTs of the Spiration valve in patients with emphysema have been published.[23,24,25,] One used a sham control and 2 were open-label. Tables 19 to 22 summarize the characteristics and results of these trials.

EMPROVE (A Prospective, Randomized, Controlled Multicenter Clinical Study to Evaluate the Safety and Effectiveness of the Spiration® Valve System for the Single Lobe Treatment of Severe Emphysema) was an open-label trial of 172 patients with severe emphysema and no collateral ventilation. Twelve-monthresults were published in a peer-reviewed journal in 2019;[25,] results were previously available as part of the Spiration Premarket Approval (PMA) application.[26,]Efficacy results at 6 months (the timepoint for the primary endpoint, change in FEV1) are summarized in Table 20. Patients who received the Spiration valve had improvements in lung function and quality of life compared to usual care, but there was no significant difference between groups in exercise capacity. Thoracic serious adverse events, the primary safety outcome, were more frequent in the Spiration group (31.0% vs. 11.9%), primarily due to a 12.4% incidence of serious pneumothorax (Table 22). Criner et al reported 24-month results from EMPROVE in 2023.[27,] Of the 172 participants enrolled, 114 were evaluable at 24 months: 80 (81.6%) of the treatment group and 34 (77.3%) of the control group. Between the 12-month visit and 24-month visit, 10 participants died (8 intervention and 2 control) and 15 additional withdrew (7 intervention, 8 control). Change from baseline in FEV1 remained significantly improved in the treatment group compared to control group through 24 months (P =.01; data reported graphically only). The FEV1 responder rate (15% or greater improvement from baseline) at 24 months did not differ between groups (19.7% treatment vs 13.3% control; P =.57). Acute exacerbations of COPD at the 24-month follow-up occurred in 13.7% (14 of 102) and 15.6% (7 of 45) of individuals in the treatment and control groups, respectively (P =.80). One individual in the intervention group and none in the control group experienced a pneumothorax during the 12- to 24-month follow-up period. Significant improvements were maintained through 24 months on some, but not all, measures of quality of life; however confidence in these results is limited due to the study's lack of blinding.

Significant differences were maintained on the SGRQ (P =.03) and the mMRC dyspnea scale (P =.001), but mean SF-36 PCS scores were not significantly different between groups (P =.06).
The REACH (The Spiration Valve System for the Treatment of Severe Emphysema) trial found improvements in FEV1, 6-minute walk test, and SGRQ. The sham-controlled IBV Valve (A Prospective, Randomized, Controlled Multicenter Clinical Trial to Evaluate the Safety and Effectiveness of the IBV® Valve System for the Treatment of Severe Emphysema) trial showed statistically significant results favoring the Spiration valve, but confidence intervals were wide and the study authors concluded that the trial did not obtain clinically meaningful results.[23,].

Table 19. Summary of Key RCT Characteristics-Spiration Valve

Trial	Countries	Sites	Dates	Participants	Interventions		Duration
					Active	Comparator	
EMPROVE [25,26,] **NCT 01812447[27,]**	US and Canada	31	2013-2017	Severe emphysema without collateral ventilation Race not reported 53.5% male	Spiration valve (n=113)	Standard care (n=59)	24 months Primary outcome was FEV1 change at 6 months
REACH, Li et al (2018) [24,] NCT01989182	China	12	2013-2017	Severe emphysema and intact interlobular fissures 100% Asian 99% male	Spiration valve (n=72)	Standard care (n=35)	6 months
IBV Valve, Wood et al (2014)[23,] NCT00475007	US	36	2007-2017	Emphysema, airflow obstruction, hyperinflation, and severe dyspnea Race not reported 57% male	Spiration valve (n=142)	Sham procedure (n=135)	6 months

IDE: Investigational Device Exemption; NCT: National Clinical Trial; NR: Not reported; RCT: randomized controlled trial.

Table 20. RCTs of the Spiration Valve- Efficacy Results

Study	FEV1 Responders (>15% Increase from Baseline)	FEV1 Mean Change, liters	SGRQ Responders (>4-point decrease from baseline)	SGRQ Score Mean Change	6-MInute Walk Distance-Responders (>25 meters increase from baseline)	6-MInute Walk Distance-Mean change, meters
EMPROVE[25,26,]						
Total N	156	156	136	136	150	150
Spiration valve	36.8%	NR	50.5%	-5,8	32.4%	NR
Standard care	10.0%	NR	22.0%	3.7	22.9%	NR
Difference (95% CI)	25.7% (12.7% to 38.7%)	0.101 (0.060 to 0.141)	28.6% (12.4% to 44.8%)	-9.5 (-14.4 to -4.7)	9.4% (-5.5% to 24.4%)	Difference 6.9

Study	FEV1 Responders (>15% Increase from Baseline)	FEV1 Mean Change, liters	SGRQ Responders (>4-point decrease from baseline)	SGRQ Score Mean Change	6-MInute Walk Distance-Responders (>25 meters increase from baseline)	6-MInute Walk Distance-Mean change, meters
						(-14.2 to 28.2)
p-value	NR	NR	NR	NR	NR	NR
REACH [24,]						
Total N	NR	NR	NR	NR	NR	NR
Spiration valve	48%	0.09 (95% CI 0.16 to 0.05)	NR	-8.39 (95% CI -12.69 to -4.08)	NR	20.82 (95% CI -0.58, 42.22)
Standard Care	13%	-0.24 (95% CI -0.14, -0.07)	NR	2.11 (95% CI -3.87, 8.08)	NR	-15.58 (95% CI -40.12, 8.96)
Difference (95% CI)	35% (NR)	NR	NR	NR	NR	NR
p-value	.001	.001	NR	.007	NR	NR
IBV Valve[23,]						
Total N	NR	250	254	277	NR	NR
Spiration valve	NR	-0.07 (SD 0.17)	32.2%	2.15 (16.36)	NR	-24.02
Sham	NR	0.00 (SD 0.16)	39.8%	-1.41 (11.26)	NR	-3.0
Difference	NR	(-0.11, -0.02)	7.6% (-4.15% to 19.39%)	(0.04, 7.07)	NR	-21.02 (-38.84 to -2.44)
p-value	NR	NR	NR	NR	NR	NR

CI: confidence interval; FEV1: forced expiratory volume in 1 second; NR: not reported; RCT: randomized controlled trial; SGRQ: St. George Respiratory Questionnaire.

Table 21. COPD Exacerbations in RCTs of the Spiration Valve

Study	Time Point	Spiration vs Control
EMPROVE	0 to 6 months	16.8% vs. 10.2% Difference 6.6% (95% CI -5.1% to 16.0%)
	>6 to 12 months	13.6% vs. 8.5% Difference 5.1% (95% CI -7.4% to 14.2%)
	>12 months to 24 months	13.7% vs 15.6%; P =.80
REACH	0 to 6 months	19.7% vs. 24.2%
IBV Valve	0 to 6 months	4.9% vs. 1.5% Difference 3.4% (95% CI -0.5 to 7.9%)

CI: confidence interval; COPD: chronic obstructive pulmonary disease; RCT: randomized controlled trial.

Table 22. Mortality and Serious Adverse Events in RCTs of the Spiration Valve

Study	Time Point	Mortality Spiration vs Control	Serious Adverse Events Spiration vs Control
EMPROVE	0 to 6 months	5.3% vs. 1.7%; Difference 3.6% (95% CI -1.7% to 8.9%)	31.0% vs. 11.8%; 19.1% (95% CI 5.9% to 29.7%)
	>6 to 12 months	3.9% vs. 6.4%	21.4% vs. 10.6%; 10.7% (95% CI 3.0% to 21.2%)
	>12 months to 24 months	7.8% vs 4,4%; P =.72	27.5% vs 15.6%; P =.41
REACH	0 to 6 months	0% vs. 3.0%	44.3% vs. 24.2%
IBV Valve	0 to 6 months	4.2% vs. 0.7%; Difference 3.5% (95% CI 0.2% to 7.5%)	14.1% vs. 3.7%; 10.4% (95% CI 4.0% to 17.1%)

CI: confidence interval; RCT: randomized controlled trial.

Tables 23 and 24 summarize the design and conduct limitations of the Spiration valve RCTs. A major limitation was a lack of blinding, which could have influenced performance on measures of lung function, exercise tolerance (e.g., it might have affected clinicians' coaching of patients and/or the degree of effort exerted by patients), and patient-reported measures of symptoms and quality of life. One trial was conducted in China and the 2 trials conducted in the U.S. did not report data on race. Therefore it is uncertain if the study results would be generalizable to the U.S. population.

Table 23. RCTs of the Spiration Valve- Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
EMPROVE	4. unable to determine; race of participants not reported				
REACH	4. 100% male				
IBV Valve	4. unable to determine; race of participants not reported				

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4. Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 24. RCTs of the Spiration Valve- Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
EMPROVE		1, 2 not blinded				
REACH		1, 2 not blinded				
IBV Valve						

The evidence limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Prospective Cohort Study

Hartman et al (2021) conducted a prospective cohort study to investigate patient satisfaction and patient-specific treatment goals among individuals who received bronchial valves for treatment of severe emphysema at 1 hospital in The Netherlands.[28,] Patient satisfaction was measured by a questionnaire administered 1 year after valve placement. Patient-specific goals were measured using

the Dutch patient-specific complaint (PSC) questionnaire. In this questionnaire, patients reported their 3 most personally desired post-treatment goals and used a numeric rating scale (0 to 10) to score the level of disability per goal before and 1 year after treatment. Lung function, exercise capacity, dyspnea severity, and quality of life were also measured before treatment and at 1-year follow-up. Of 134 patients who underwent bronchial valve placement prior to January 1, 2019, 109 (81.3%) completed the patient-satisfaction questionnaire, 88 (65.7%) completed the PSC questionnaire at baseline and follow-up, and 94 (70.1%) returned to the hospital for a follow-up visit at 1 year. Reasons for loss to follow-up in 40 patients were bronchial valve removed (16 patients), died (n=5), comorbidity (n=5), revision at that time (n=3), lung volume reduction surgery (LVRS) or lung transplant (n=2), and other (n=9). The PSC-questionnaire score significantly improved 1 year after bronchial valve treatment, from 23.7 to 17.1 points (mean decrease of 6.5 points; p=.001) and an improvement in the PSC-questionnaire sum score was significantly associated with a larger improvement in FEV1, residual volume, exercise capacity, dyspnea severity, and quality of life. Seventy-five percent of the patients who completed the questionnaire were satisfied or very satisfied with the treatment and 11% were unsatisfied or very unsatisfied. Just over half of the questionnaire respondents (52.6%) were satisfied or very satisfied with the reduction in their symptoms after treatment, and 24.9% were unsatisfied or very unsatisfied. For the question of whether the treatment satisfied their expectations (range 1 to 5), the mean score was 3.29 (standard deviation 1.43). Most of those who completed the questionnaire (91.4%) would recommend the treatment to other patients. This study was limited by its uncontrolled design and relatively high loss to follow-up (29.9%), but it provides information on outcomes important to patients that could be used to guide future research.

Section Summary: Severe or Advanced Emphysema

In individuals with severe or advanced emphysema with little or no collateral ventilation between target and ipsilateral lobe, RCTs provide evidence of clinically meaningful benefit for bronchial valves compared to standard medical management on measures of lung function, exercise tolerance, and quality of life. However, confidence in these results is low due to study limitations including a lack of blinding and wide confidence intervals around estimates of effect. Across studies, there was an increased risk of serious procedure-related adverse events compared to usual care, including pneumothorax occurring in up to 27% of patients. Results at 24 months have been published from one RCT (EMPROVE), with evaluable data from 114 of 172 participants (66.3%). Between the 12-month visit and 24-month visit, 10 participants died (8 intervention and 2 control). Change from baseline in FEV1 remained significantly improved in the treatment group compared to control group through 24 months, but the FEV1 responder rate (15% or greater improvement from baseline) at 24 months did not differ between groups (19.7% treatment vs 13.3% control; P =.57). Acute exacerbations of COPD at the 24-month follow-up occurred in 13.7% (14 of 102) and 15.6% (7 of 45) of individuals in the treatment and control groups, respectively (P =.80). Significant improvements were maintained through 24 months on some, but not all, measures of quality of life. A RCT (CELEb) that compared bronchial valves to LVRS in 80 individuals found no statistically significant difference between treatment groups on the primary outcome (change from baseline to 12 months on the iBODE instrument, -0.27 (-0.62 to 1.17; P =.54). Notably, the magnitude of change from baseline for both groups on the i-BODE was below the 1.5-point difference considered by the study investigators to be sufficiently clinically important. The trial was limited by lack of participant blinding, high loss to followup, choice of a composite primary outcome, and evidence of selective outcome reporting. More participants in the bronchial valve group required additional procedures post-intervention, including 4 (8.5%) who went on to LVRS. In a prospective cohort study of patient-reported outcomes 1 year following treatment, 74.8% were satisfied with the treatment , 52.6% were satisfied with the reduction in their symptoms after treatment , and 91.4% said they would recommend the treatment to others. Confidence in these findings is limited by the study's uncontrolled design and high loss to follow-up (29.9%). The potential benefits of the procedure do not outweigh the demonstrated harms.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

Global Initiative for Chronic Obstructive Lung Disease (GOLD)

The 2023 GOLD publication makes the following statements on lung volume reduction interventions:[4,]

- "In selected patients with heterogeneous or homogenous emphysema and significant hyperinflation refractory to optimized medical care, surgical or bronchoscopic modes of lung volume reduction (e.g., endobronchial one-way valves, lung coils or thermal ablation) may be considered."
- "In select patients with advanced emphysema refractory to optimized medical care, surgical or bronchoscopic interventional treatments may be beneficial."

National Institute for Health and Care Excellence (NICE)

In December 2017, NICE issued the following recommendations on endobronchial valve insertion to reduce lung volume in emphysema:[29,]

1.1Current evidence on the safety and efficacy of endobronchial valve insertion to reduce lung volume in emphysema is adequate in quantity and quality to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit.

1.2Patient selection should be done by a multidisciplinary team experienced in managing emphysema, which should typically include a chest physician, a radiologist, a thoracic surgeon and a respiratory nurse.

1.3Patients selected for treatment should have had pulmonary rehabilitation.

1.4The procedure should only be done to occlude volumes of the lung where there is no collateral ventilation, by clinicians with specific training in doing the procedure.

NICE guidance on the diagnosis and management of COPD (2018, updated 2019) included the following recommendations on lung volume reduction procedures:[18,]

Offer a respiratory review to assess whether a lung volume reduction procedure is a possibility for people with COPD when they complete pulmonary rehabilitation and at other subsequent reviews, if all of the following apply:

- they have severe COPD, with FEV1 less than 50% and breathlessness that affects their quality of life despite optimal medical treatment
- they do not smoke
- they can complete a 6-minute walk distance of at least 140 m (if limited by breathlessness).

At the respiratory review, refer the person with COPD to a lung volume reduction multidisciplinary team to assess whether lung volume reduction surgery or endobronchial valves are suitable if they have:

- hyperinflation, assessed by lung function testing with body plethysmography **and**
- emphysema on unenhanced CT chest scan **and**
- optimised treatment for other comorbidities.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some ongoing and unpublished trials that might influence this review are listed in Table 25.

Table 25. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01796392[a]	Lung Function Improvement After Bronchoscopic Lung Volume Reduction With Pulmonx Endobronchial Valves Used in Treatment of Emphysema (LIBERATE)	190	Apr 2024 (post approval study, 5-year extension)
NCT04186546[a]	Zephyr Valve Registry (ZEVR)	150	Dec 2026
NCT04302272[a]	The Spiration Valve System (SVS) Post-Market Registry Study for Severe Emphysema	150	Apr 2028

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Documentation for Clinical Review

Please provide the following documentation:

- History and physical and/or consultation notes including:
  - Reason for endobronchial valve use
  - Documentation of FDA HDE process and approval

Post Service (in addition to the above, please include the following):

- Operative report(s)

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	31647	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, when performed, assessment of air leak, airway sizing, and insertion of bronchial valve(s), initial lobe
	31648	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with removal of bronchial valve(s), initial lobe
	31649	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with removal of bronchial valve(s), each additional lobe (List separately in addition to code for primary procedure)
	31651	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, when performed, assessment of air leak, airway sizing, and insertion of bronchial valve(s), each additional lobe (List separately in addition to code for primary procedure[s])
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
09/27/2013	BCBSA Medical Policy adoption
06/30/2015	Policy revision with position change
08/01/2016	Policy revision without position change
08/01/2017	Policy title change from Endobronchial Valves Policy revision without position change
08/01/2018	Policy revision without position change

Effective Date	Action
08/01/2019	Policy revision without position change
08/01/2020	Annual review. No change to policy statement. Literature review updated
08/01/2021	Annual review. No change to policy statement. Literature review updated.
08/01/2022	Annual review. Policy statement and literature review updated.
08/01/2023	Annual review. No change to policy statement. Policy guidelines and literature review updated.
08/01/2024	Annual review. No change to policy statement. Policy guidelines and literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local

standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Bronchial Valves 7.01.128 **Policy Statement:** I. Bronchial valves are considered **investigational** in **all** situations including, but not limited to: A. Treatment of prolonged air leaks B. Treatment for individuals with chronic obstructive pulmonary disease or emphysema	**Bronchial Valves 7.01.128** **Policy Statement:** I. Bronchial valves are considered **investigational** in **all** situations including, but not limited to: A. Treatment of prolonged air leaks B. Treatment for individuals with chronic obstructive pulmonary disease or emphysema