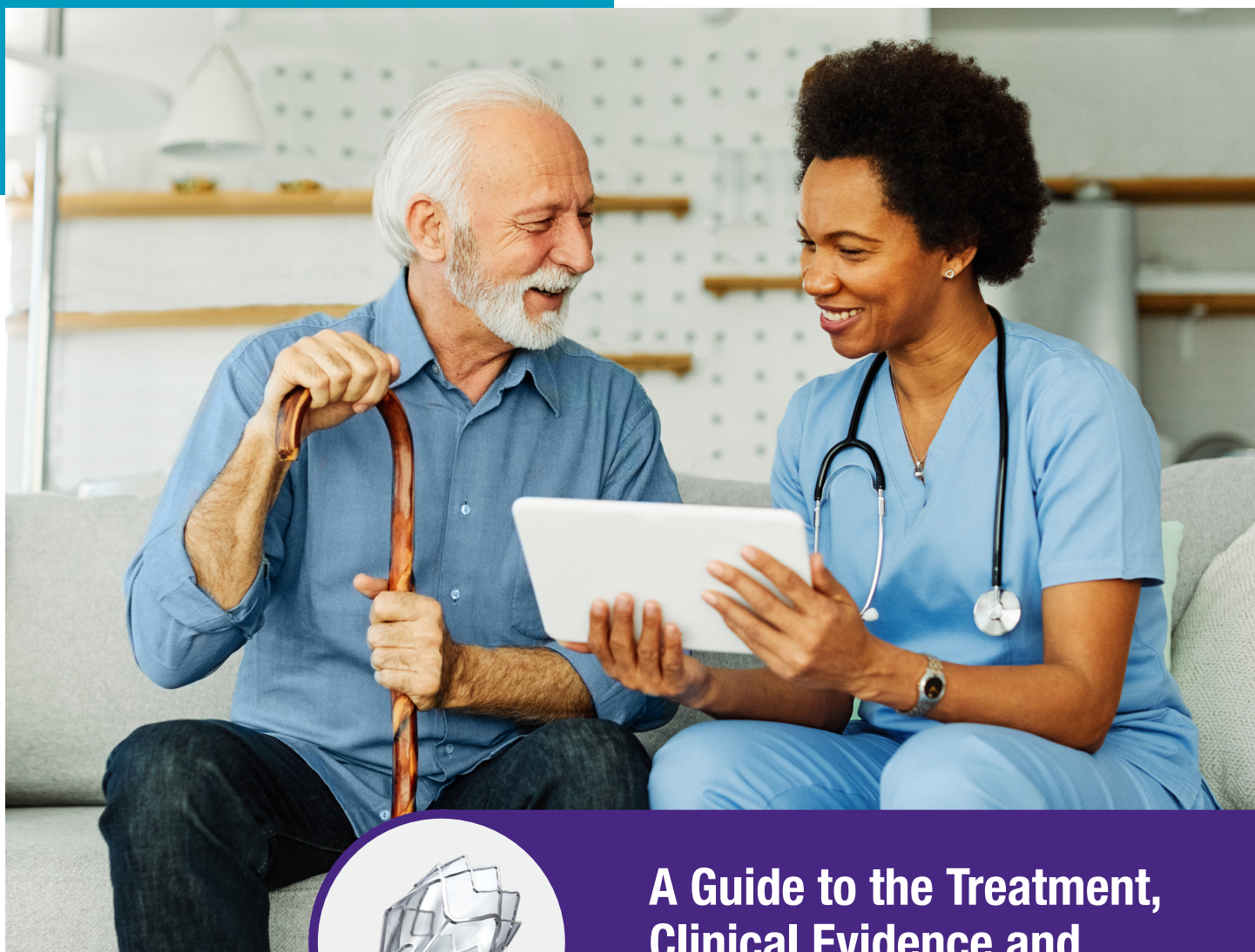


Zephyr[®] Endobronchial Valve

A Proven Treatment for Breathlessness Due to Severe COPD/Emphysema



**A Guide to the Treatment,
Clinical Evidence and
Patient Selection**



zephyr[®]
by pulmonx

Do You Have Severe COPD/Emphysema Patients Like These?

Meet a Few Severe COPD/Emphysema Patients Treated with Zephyr® Valves

Cindy, 56-year-old



Before Zephyr Valve Treatment:

- Basic tasks are difficult
- No appetite
- Anxious all the time
- Missing kids' activities and special moments

“The Zephyr Valves allowed me to feel like a normal person again.”

After Zephyr Valve Treatment:

- Back to doing housework and going to the gym
- Able to travel to daughter's bowling tournaments
- Can stand and walk to the bathroom with no problem

Mike, 65-year-old



Before Zephyr Valve Treatment:

- Several ER trips
- Pneumonia twice
- 4 liters of oxygen 24/7 for two years
- Had to retire early

“About six weeks after having my Zephyr Valves, I had my ‘ah-ha’ moment and knew that this worked for me when I was able to play badminton in the yard with my granddaughter on the 4th of July without oxygen.”

After Zephyr Valve Treatment:

- On less oxygen right away; now only needed for sleeping
- Hikes and walks hilly roads
- Works in garden 5-6 hours a day

Karen, 62-year-old



Before Zephyr Valve Treatment:

- Gave up active lifestyle (cheerleading coach, gymnastics teacher, swim instructor)
- “Closet user” of oxygen
- Worried about future with grandkids

“I’ve been cleared to scuba dive again, but I am most excited to be able to swim with my grandkids this summer. I am so blessed with a big loving family, and I am just grateful to be feeling well again so we can enjoy our time together.”

After Zephyr Valve Treatment:

- Feels like not just surviving, but now living
- Back on the go 2 months after procedure
- Infrequent oxygen use

Darryl, 67-year-old



Before Zephyr Valve Treatment:

- Felt trapped at home
- No longer able to enjoy passions like road trips and concerts
- Couldn’t catch his breath and began restricting normal activities

“After I got out of the hospital, it took about two weeks for me to feel the benefit of the valves. Now that I can breathe easier, I really have a new lease on life. I’ve added a trip to New Orleans to my bucket list — I’ve never been, and I think I would really enjoy it now.”

After Zephyr Valve Treatment:

- Enjoys being outside
- Re-engaged with friends and family
- Works out at gym 3x week

Zephyr® Endobronchial Valves: Most Studied. Most Proven. Most Used Valves for Severe COPD/Emphysema.¹

The Zephyr Endobronchial Valve is a clinically-proven bronchoscopic treatment for patients with severe COPD/emphysema who suffer from dyspnea despite optimized medical therapy.

The **2025 GOLD Report** summarized the following patient benefits reported in clinical studies on Endobronchial Valve (EBV) Treatment for severe COPD/emphysema:²

- **Improved FEV₁, 6MWD, and health status** at 6 and 12 months*
- **Improved survival** after successful treatment (4 retrospective studies)
- **Decreased exacerbations**
- **Decreased respiratory failure** episodes

Complications of the Zephyr Endobronchial Valve treatment can include, but are not limited to, pneumothorax, worsening of COPD symptoms, hemoptysis, pneumonia, dyspnea and, in rare cases, death.

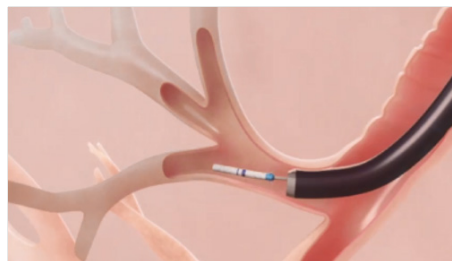


Zephyr Valves Improve Lung Function by Treating Hyperinflation

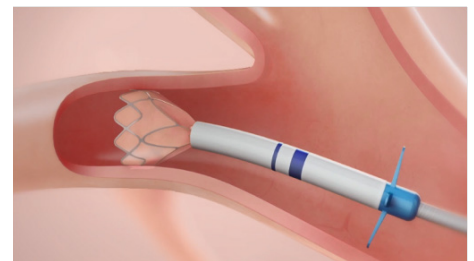
Zephyr Valves are one-way valves that are intended to treat hyperinflation. They are placed into the major airways of a diseased lobe via bronchoscopy, allowing trapped air to escape and preventing new air from entering. The lobe will deflate, allowing the rest of the lung to expand and the diaphragm to rise.³⁻⁶



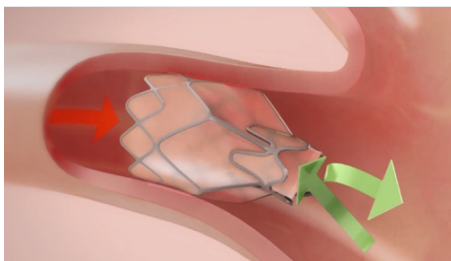
1 Bronchoscope introduced into lungs of patient with diseased, hyperinflated lobe



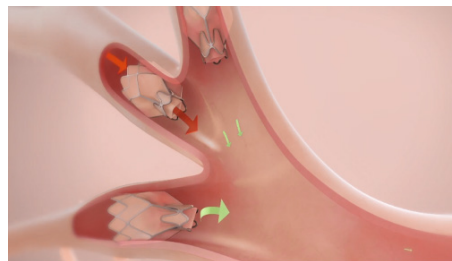
2 Delivery catheter advanced into target lobe through bronchoscope



3 Valve size chosen in one step procedure and delivered to seal target airway



4 Zephyr Valve allows trapped air to escape but not to re-enter



5 Typically 3-5 Zephyr Valves delivered to fully occlude diseased lobe



6 Hyperinflation in target lobe is reduced, improving lung function and breathlessness

*Quality and quantity of data rated "Evidence Level A"

Consider Zephyr® Endobronchial Valves for All Patients with Severe COPD/Emphysema

Patients with varying levels of symptom burdens can benefit from Zephyr Valve treatment. There is no need to restrict this treatment for only patients with the most severe symptoms.

Many physicians report that they see more benefit in patients who are just beginning to limit their activities due to breathlessness. They recommend evaluating patients earlier to avoid a situation where patients are too sick to qualify.

Spectrum of qualifying symptom burden

Profiles of Patients who Qualified for Zephyr Valve Treatment			
mMRC	2	3	4
Shortness of Breath	On activity	On activity & at rest	Continuous
Activity Level	Limiting activities	Difficulty with activities of daily living	Inability to perform many activities of daily living
Oxygen Therapy	None	As needed	Continuous
Quality of Life Challenges	Difficulty keeping up with family and friends	Breathless even walking short distances; limited daily activities	Reliance on help for everyday activities

Ask Your Patients How COPD/Emphysema Is Affecting Their Quality of Life

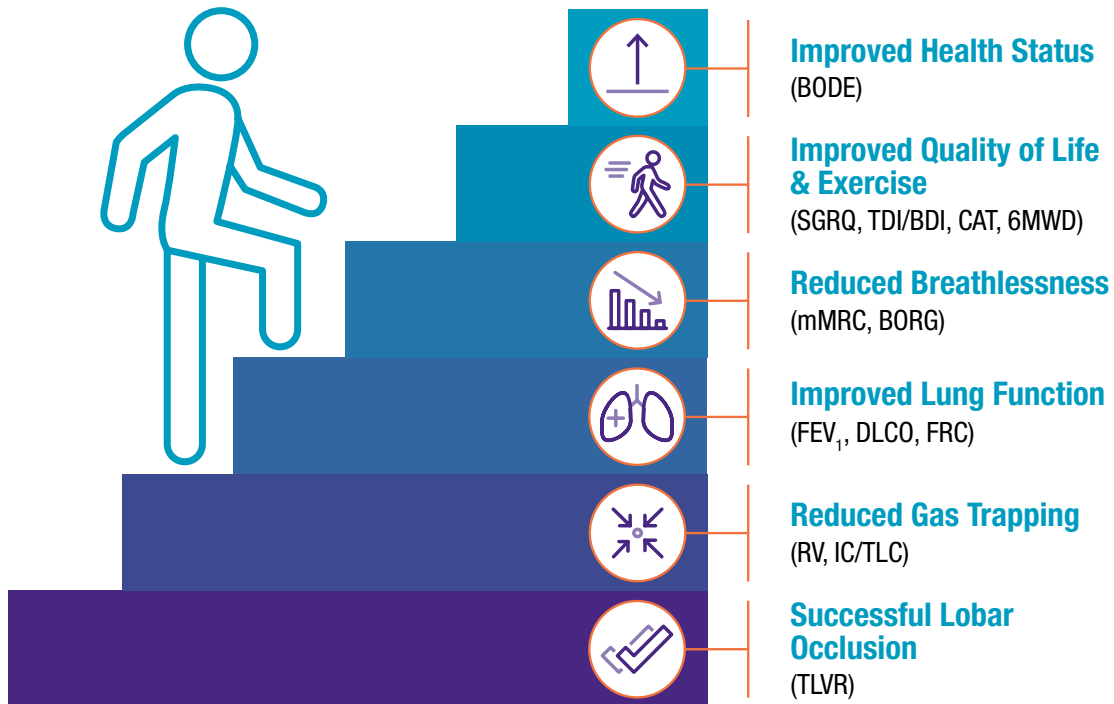
Asking these questions at clinic visits may help patients better communicate about how breathlessness is impacting their quality of life:

- What activities could you do last year that are no longer possible?
- How often do you have to stop to catch your breath?
- Do you need help in order to do your regular chores and activities?
- Are you able to leave the house and go places without assistance?

Real Benefits that Make a Difference in Patients' Lives

Zephyr® Valve Treatment Leads to Improved Health Status³

Patients treated with Zephyr Valves **experienced clinical benefits and improved quality of life** when compared to patients who were on medications alone.³



Breathe Easier

Be less short of breath with increased lung function.³



Have More Freedom

Do more things on their own like bathing, cooking, and cleaning.³



Enjoy Life More

Have more energy and get back to their favorite hobbies and socializing.³



Feel More Confident

When leaving home and living life.³

Help Your Patients with Severe COPD/Emphysema Achieve a Better Quality of Life with Zephyr Valves

Patient Benefits Proven in Four Randomized Controlled Trials

Consistent Outcomes Across 4 Randomized Controlled Trials in Patients Without Collateral Ventilation³⁻⁶

RCT	Design	Sample size & follow-up period	Difference Zephyr® Valve vs. Control Groups (ITT)		
			LUNG FUNCTION (FEV ₁ %)	EXERCISE CAPACITY (6MWD)	QUALITY OF LIFE (SGRQ)
LIBERATE³	2:1 Randomization Heterogenous only Multicenter	n=190 12 months	18.0% p<0.001	39 m p=0.002	-7.1 pts p=0.004
TRANSFORM⁴	2:1 Randomization Heterogenous only Multicenter	n=97 6 months	29.3% p<0.001	79 m p<0.001	-6.5 pts p=0.031
IMPACT⁵	1:1 Randomization Homogenous only Multicenter	n=93 6 months	16.3% p<0.001	28 m p=0.016	-7.5 pts p<0.001
STELVIO⁶	1:1 Randomization Heterogenous & Homogenous Single center	n=68 6 months	17.8% p=0.001	74 m p<0.001	-14.7 pts* p<0.001

*Completed Cases, all other values listed are ITT population

Reversible Procedure

While the majority of Zephyr Valve patients do achieve a positive benefit, if a patient does not favorably respond to treatment, the procedure can be reversed by removing the valves via bronchoscopy.

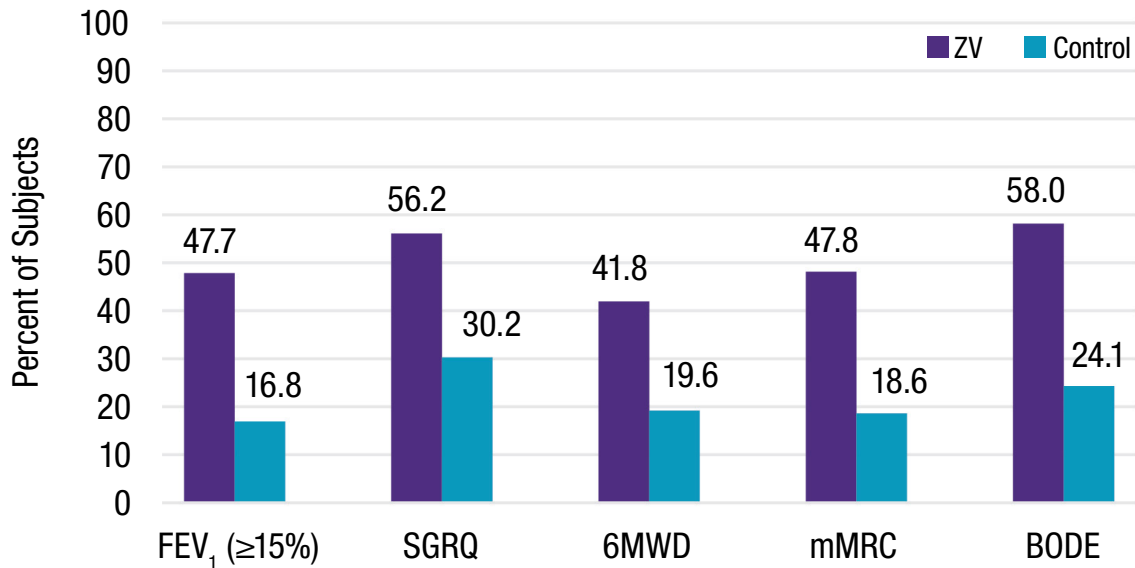
Potential Risks

The major significant side effect associated with the Zephyr Valve procedure in the short-term is pneumothorax, which occurs in approximately one-third of patients. Targeted lobar deflation can cause inflation of the ipsilateral lobe, which can result in a tear of the already compromised parenchymal tissue of the emphysematous ipsilateral lobe, resulting in pneumothorax. In the LIBERATE clinical study, subjects experiencing a pneumothorax attained the same level of benefit over the long-term as those without pneumothorax. Patients remain in the hospital at least 3 nights after the procedure in order to monitor this or any other potential side effect. Zephyr Valve Treating physicians and their staff are trained to recognize the signs and symptoms and to treat a pneumothorax.

Other complications of Zephyr Endobronchial Valve treatment can include, but are not limited to worsening of COPD symptoms, hemoptysis, pneumonia, dyspnea, and in rare cases, death.

Zephyr® Valve Body of Clinical Evidence

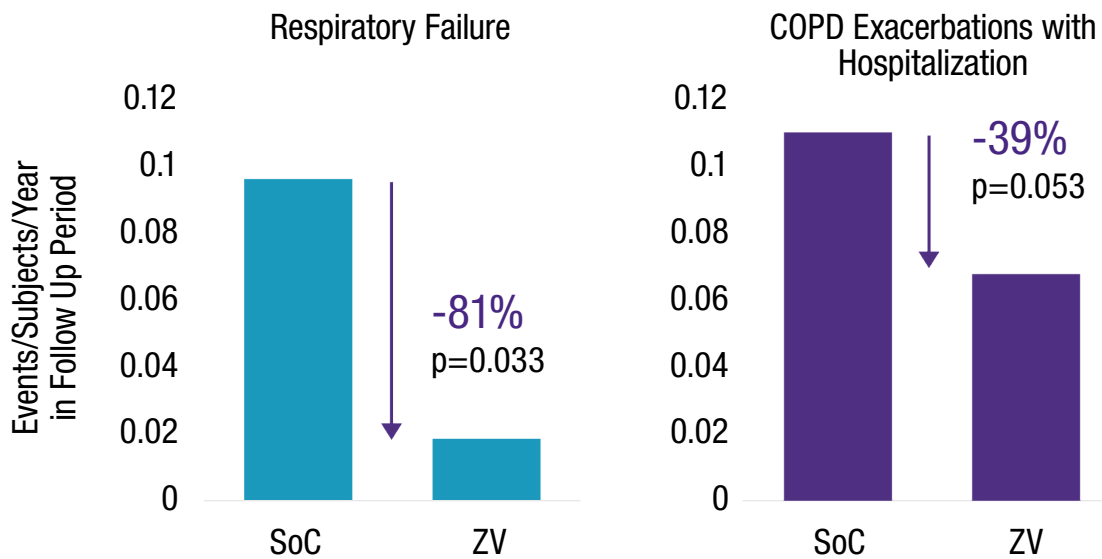
Zephyr Valve Responder Rates 12 Months After Treatment³ Randomized Controlled Trials Primary & Secondary Endpoints



Responders were those that met the MCID improvement for each endpoint.

FEV₁: ≥15%, SGRQ Score: ≥ -4 points, 6MWD: ≥25 meter, mMRC: ≥ -1 points, BODE Index: ≥ -1 point

Indications of Lower Long-Term Respiratory Serious Adverse Events Following Zephyr Valve Treatment³



SoC = Standard of Care Treatment, ZV = Zephyr Valve Treatment

Long-term follow up was the period 45 days post-treatment through the end of the 1-year study period

Potential Impact on Survival

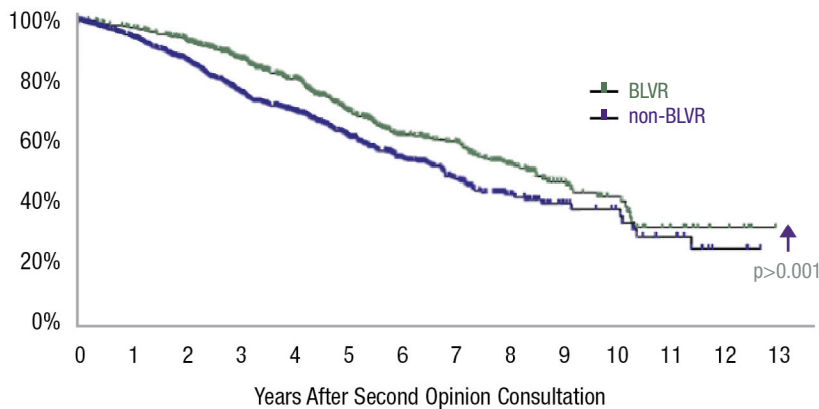
In a first-of-its-kind study, researchers examined the survival rate of severe COPD/emphysema patients undergoing Bronchoscopic Lung Volume Reduction (BLVR) vs. patients who were *evaluated* for BLVR but *not treated*.

This single-center, non-randomized, retrospective analysis included 1,471 patients.

The study found that patients treated with BLVR:⁷

- Had a statically significant survival rate of 1.7 years longer than the non-treated group
- Were 41% less likely to die over the course of the study

Retrospective Analysis of Long-Term Survival Following Bronchoscopic Lung Volume Reduction (BLVR) Treatment



The study authors concluded: “BLVR treatment was found to be an independent predictor of survival when adjusting for other survival-influencing factors such as age, gender, or severity of disease.”

In the study described above, the BLVR group comprised 483 patients and the non-BLVR group comprised 988 patients. Of the BLVR group, 73% of patients received BLVR with Zephyr® Valves and 27% received endobronchial coils [a technology that is not approved in the United States]. Reprinted with permission of Respiratory Medicine. Copyright © 2022 Respiratory Magazine

Potential Impact on Exacerbations

Exacerbations drive the progression of COPD, resulting in lower quality of life and higher mortality. Clinical research suggests that treatment with Endobronchial Valves reduces the number of moderate and severe exacerbations in patients with severe emphysema.

A single-center retrospective analysis of 129 patients treated with Endobronchial Valves examined the number of exacerbations before and after Endobronchial Valve Treatment.

The primary endpoint of the study was the number of exacerbations one year after Endobronchial Valve Treatment compared to one year before. Below is a summary of these results.⁸

Clinical Outcomes 1 Year After Treatment Compared to 1 Year Before Treatment

PATIENT GROUP	Sample Size	Moderate to Severe Exacerbations Year Before Treatment	Moderate to Severe Exacerbations First Year After Treatment	Decrease in Exacerbation Rate (Percent)
All patients who received Endobronchial Valve Treatment	n=129	2.5 ± 2.2	1.8 ± 2.2 p=0.009	-32%
Patients who received Endobronchial Valve Treatment and had complete lobar atelectasis	n=41	2.8 ± 2.0	1.4 ± 1.8 p<0.001	-50%

The study authors concluded treatment with Endobronchial Valves “appears promising to reduce the exacerbation rate in COPD patients, especially when the full treatment benefit of complete lobar atelectasis is achieved.”

Medications Alone Cannot Achieve the Same Benefits

Patients treated with the Zephyr® Valve in addition to medications, as compared to patients on medication alone, were able to:³

- Return to a more active lifestyle
- Feel less shortness of breath
- Walk longer distances
- Have more energy
- Feel more confident leaving their home

The **2025 GOLD Report** states that **hyperinflation** is clinically relevant in patients with COPD and contributes to dyspnea, impaired exercise capacity, increased hospitalizations, respiratory failure, and increased mortality.²

Unlike medical treatments that only mildly improve shortness of breath symptoms, Zephyr Valves target the **root cause of breathlessness** – releasing trapped gasses that cause hyperinflation. They can provide a greater benefit than medications alone.³⁻⁶

Clarifying Treatment Pathways for COPD

Even on optimal medical management, patients with severe COPD and emphysema may continue to experience breathlessness. It's important to treat the source of their symptoms, as well as any conditions that elevate their risk of exacerbations.

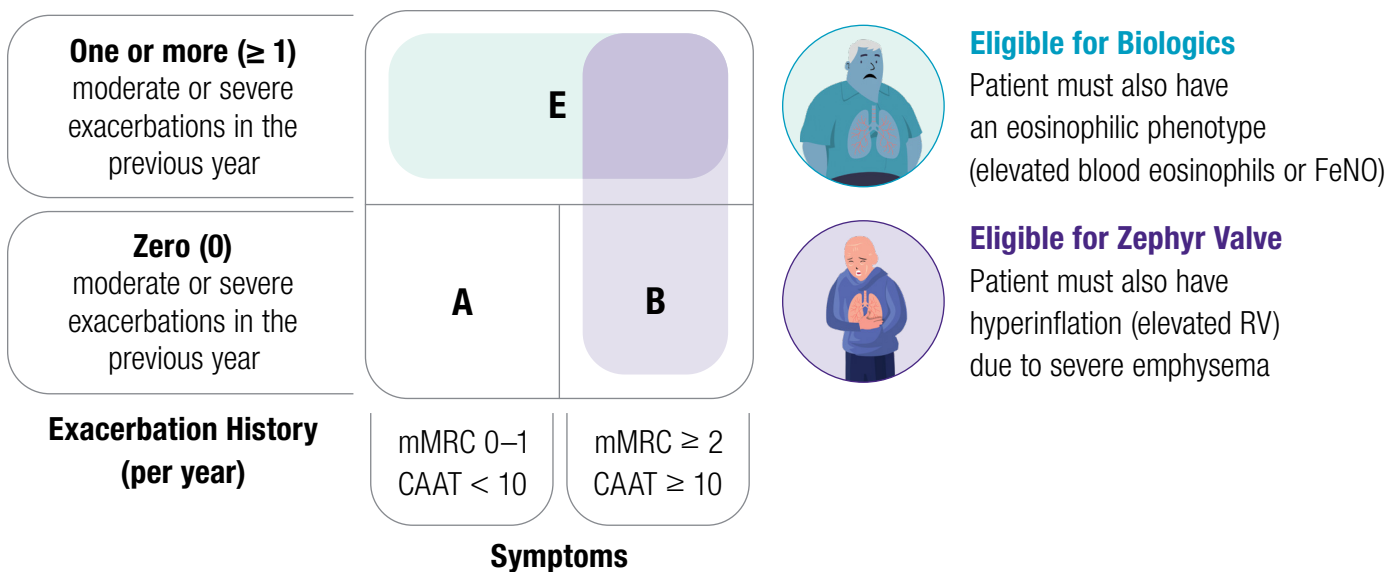
A complementary approach.

Zephyr Endobronchial Valves and biologics address distinct pathophysiological aspects of severe COPD/emphysema, making them complementary rather than competing treatment options.

Both therapies target different patient phenotypes and accomplish different goals. Biologics reduce inflammation over time, leading to reduced exacerbation rates and a modest benefit in lung function,^{9,10} whereas valves reduce hyperinflation by reducing gas trapping and improving breathing mechanics resulting in global improvement (lung function, exercise capacity and quality of life).³

This approach aligns well with the recommendations from GOLD regarding risk mitigation and symptom management.

GOLD* COPD A, B, E Assessment Tool



*Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2026 Report.

Patient Eligibility Criteria for Zephyr® Valve Treatment

If shortness of breath is not controlled with medical management, patients may qualify for Zephyr Valves based on the following:

Clinical Presentation

- Severe COPD/emphysema
- Shortness of breath upon activity or rest
- Limited in daily functions
- Dissatisfied with activity level and quality of life

Medical History

- Full medical treatment for COPD
- Periods of stable and/or unstable COPD
- Persistent COPD symptoms
- History of smoking
- Usage of supplemental oxygen not required

Diagnosis and Symptoms	<ul style="list-style-type: none"> • Diagnosis of emphysema confirmed by CT • Breathless despite optimal medical management
Evidence of Obstruction	Spirometry: FEV ₁ 15-50% predicted, post-bronchodilator
Evidence of Hyperinflation (not required, can be assessed after referral)	Residual Volume ≥ 150% predicted (by Body Plethysmography only)
Smoking Status	Non-smoking or willing to quit smoking

Zephyr Valves have been clinically proven to be effective in:

- Patients with heterogeneous and homogeneous emphysema⁵
- Upper lobe and lower lobe predominant emphysema³

Contraindications¹¹

- Patients for whom bronchoscopic procedures are contraindicated
- Patients with evidence of active pulmonary infection
- Patients with known allergies to Nitinol, Nickel, Titanium, or Silicone
- Patients who have not quit smoking
- Patients with large bullae encompassing greater than 30% of either lung

Warnings¹¹

The Zephyr Valve should be used with caution and only after careful consideration in patients with:

- Prior lung transplant, LVRS, median sternotomy or lobectomy
- Congestive heart failure (left ventricular ejection fraction <45%); myocardial infarction
- FEV₁ < 15% of predicted value

Zephyr® Valve Treatment Screening Protocols

A common way to identify patients who may qualify for Zephyr Valves is to prospectively review the PFT tests for all severe COPD/emphysema patients.

Step 1: Prospective PFT Screening

Patients with the following characteristics could be flagged as meeting the baseline criteria for the Zephyr Valve Treatment:

- **Evidence of Severe Obstruction**
 - $FEV_1 \leq 50\%$ predicted (spirometry)
- **Evidence of Hyperinflation**
 - Body Plethysmography: $RV \geq 150\%$ predicted
 - Nitrogen Washout Lung Volumes are not recommended****
 - Imaging: Chest X-ray: Flattened diaphragm
 - HRCT: Evidence of emphysematous tissue

Step 2: Qualifying and Counseling Patients

Patients who meet Step 1 criteria should be further examined to determine if they meet the other Zephyr Valve eligibility criteria:

- Confirmed diagnosis of severe COPD/emphysema
- $6MWD = 100-500m$ or $328-1640ft$
- Non-smoking or willing to quit smoking

Zephyr Valve Patient Education & Clinical Resources

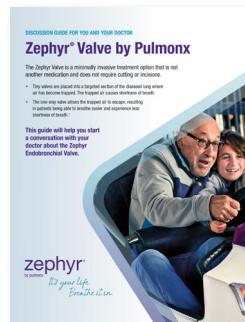
Patient and clinical education resources, including print materials, videos, real-world stories, programs, and webinars are available at pulmonx.com.



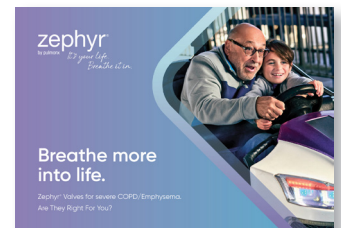
Patient Brochure



Patient-Doctor Discussion Guide



Patient Information Card



*Gas dilution PFT tests, like Nitrogen Washout or Helium Dilution, have been shown to underestimate TLC & RV because only communicating gas volume is measured in these tests. In the presence of severe airflow obstruction, TLC can be underestimated by a gas dilution method by as much as 3 liters.¹²⁻¹⁴

New Recommendation from GOLD: Simultaneously Screen for Both COPD & Lung Cancer

The United States Preventative Service Task Force (USPSTF) recommends annual screening to diagnose lung cancer for people aged 50-80 years with a 20 pack-year smoking history.¹⁵

GOLD now recommends that patients being screened for lung cancer should also simultaneously be screened for COPD.

Studies show that when patients undergoing lung cancer screening are also evaluated for COPD symptoms and given spirometry:²

- **57% were found to have COPD**
 - **68%-73% have emphysema**
 - **67% have undiagnosed COPD, and 50% of these patients were symptomatic**



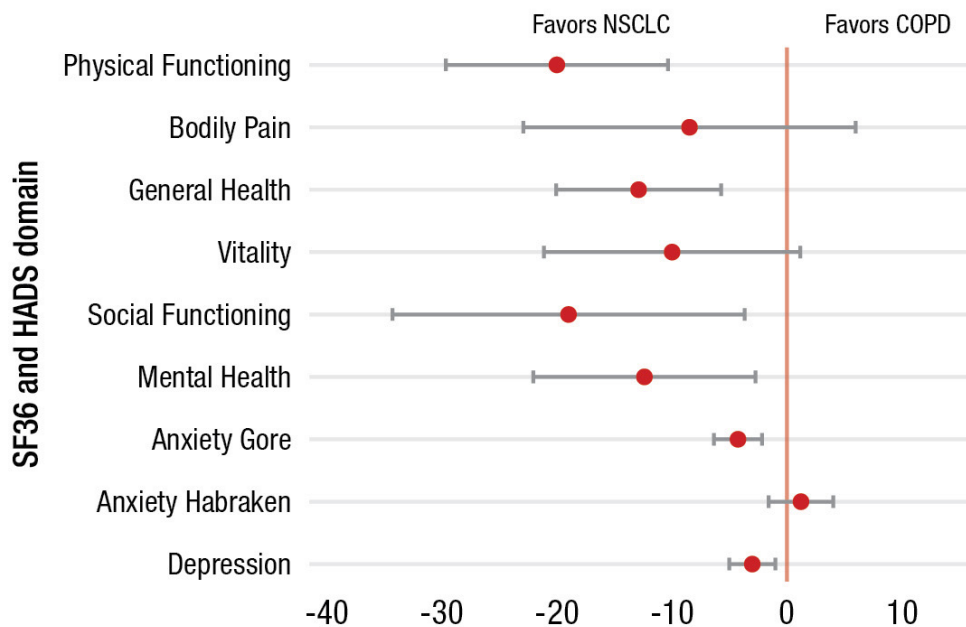
Patients with emphysema and a $FEV_1 \leq 50\%$ predicted may qualify for Zephyr® Valves, and could benefit from a full evaluation to see if they meet the other eligibility criteria.

COPD Patients' Quality of Life Worse than End-Stage Lung Cancer¹⁶

Lung cancer and COPD share common risk factors and a similar patient profile. Both are terrible diseases that worsen quality of life and shorten survival.

A clinical study found that end-stage (GOLD IV) COPD patients have comparable or worse health-related quality of life (HRQOL) scores than end-stage, non-small cell lung cancer patients.

Differences in Health-Related Quality of Life Scores. End-Stage COPD vs End-Stage NSCLC Patient Groups. (95% CI)



Difference between COPD and NSCLC patients with 95% CI

Globally Recognized. Broad Insurance Coverage.

Endobronchial Valve Treatment is a **part of the standard of care** for severe COPD/emphysema.



2025 Report

The **2025 GOLD Report** summarized the following patient benefits reported in clinical studies on Endobronchial Valve (EBV) Treatment:²

- **Improved FEV₁, 6MWD, and health status** at 6 and 12 months*
- **Improved survival** after successful treatment (4 retrospective studies)
- **Decreased exacerbations**
- **Decreased respiratory failure** episodes

Endobronchial valves are included in national and global guidance documents such as:

- UpToDate
- Global Initiative for Chronic Obstructive Lung Disease (GOLD)
- National Institute for Health and Care Excellence (NICE)
- German Respiratory Society (DGP)
- Austrian Society for Pneumology (OGP)
- National Health Care Institute of the Netherlands (Zorginstituut Nederland)
- Milliman Care Guidelines (MCG)

Zephyr® Valves Have Broad Coverage

More than 90% of patients nationwide are under policies with positive coverage or under plans that are not restricting access.**

- Medicare is covering patients who qualify
- >95% of patients with commercial insurance are securing coverage***

*Quality and quantity of data was rated “Evidence Level A.”

**Pulmonx data on file; assuming patients meet medical criteria for BLVR.

***Pulmonx Patient Reimbursement Support Program experience through the prior authorization process, for cases where patients opted in.

Zephyr Valves are approved by the Food and Drug Administration (FDA). Providers should contact their individual payers prior to performing the Zephyr Valve procedure for information on coverage.

The information is subject to change without notice because of complex and frequently changing laws, regulations, rules, and policies.

For reimbursement information, please visit: bit.ly/4aipqRl.



Zephyr® Valve Treating Centers

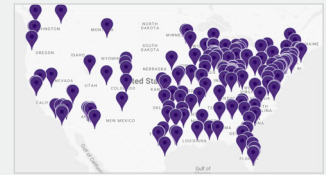
Diagnostic Testing

Once the patient is referred to the Zephyr Valve Treating Center, the clinical team may confirm patient eligibility with additional testing that may include:

- Full pulmonary function testing
- 6-minute walk test
- High resolution CT scan with specialized protocols
- Echocardiogram
- Arterial blood gas
- Perfusion testing

While these tests are typically performed at the hospital-based treating center, it may be possible to perform some of these diagnostics locally. Physicians should confirm protocols by contacting the treating center prior to ordering any tests.

Patients are seen in the post-procedure timeframe by the Zephyr Valve treating physician, but they also may return to their PCP or the physician who sent them for consultation.

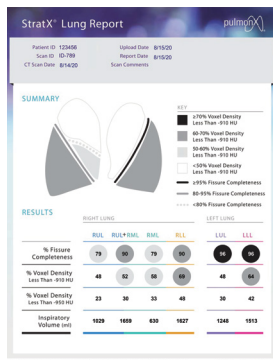


To find a Zephyr Valve Treating Center, please visit: pulmonx.com/zephyr-centers



Assess Patient Eligibility and Likelihood of Success

The Zephyr Valve Treating Center will use the following technologies to assess whether a patient may benefit from Zephyr Endobronchial Valves.



StratX® Lung Analysis Report:*

CT analysis presents information on emphysema destruction, fissure completeness, and lobar volume to help identify target lobes for Zephyr Valve treatment. Patients with fissure completeness scores are reviewed for collateral ventilation,** to confirm that they may be good candidates for Zephyr Valve treatment.



Chartis® Pulmonary Assessment System:

Immediately prior to the Zephyr Valve procedure, a Chartis System assessment is performed via bronchoscopy to confirm the absence of collateral ventilation.**

*Pulmonx's LungTraX Detect CT and StratX Reports help present information from CT scans analyzed by FDA-cleared software (Thirona's LungQ, K232412) for quantitative assessment of lung structure and function to support clinical decision making, diagnosis and follow-up. LungTraX Detect CT assists healthcare providers with visualizing this LungQ data, which may suggest the presence of emphysema. Refer to Thirona's indications for use here: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K232412>

**Collateral ventilation happens when the fissure structure between lobes is not solid and air can pass through from one lobe to another. Patients who are positive for collateral ventilation (CV+) will not benefit from Zephyr Valves.

Important Safety Information: The Pulmonx Zephyr® Endobronchial Valves are implantable bronchial valves indicated 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. The Zephyr Valve is contraindicated for: Patients for whom bronchoscopic procedures are contraindicated; those with evidence of active pulmonary infection; known allergies to Nitinol (nickel-titanium) or its constituent metals (nickel or titanium); known allergies to silicone; or with large bullae encompassing greater than 30% of either lung; Patients who have not quit smoking. The Zephyr Valve should be used with caution and only after careful consideration in treating patients with: Prior lung transplant, LVRS, median sternotomy, lobectomy, or pleurodesis on the target lung side; Congestive heart failure or recent myocardial infarction; FEV1 <15% of predicted value. Use is restricted to a trained physician. Prior to use, please reference the Zephyr Endobronchial Valve System Instructions for more information on indications, contraindications, warnings, all precautions, and adverse events.

Caution: Federal law restricts this device to sale by or on the order of a physician.

Important Safety Information: The Chartis® System is indicated for use by bronchoscopists during a bronchoscopy in adult patients with emphysema, a form of Chronic Obstructive Pulmonary Disease (COPD), in a bronchoscopy suite. The system, composed of the Chartis Catheter and Chartis Console, is designed to measure pressure and flow in order to calculate resistance to airflow and quantify collateral ventilation in isolated lung compartments. The Chartis Catheter is used through the working channel of a bronchoscope and connects to the Chartis Console. The Chartis Console is capital equipment that is reusable and displays the patient information. The Chartis System is contraindicated in the presence of active infection or major bleeding diathesis. There are no known interfering substances. Use is restricted to a trained physician. Prior to use, please reference the Chartis System Instructions for Use/ User Manual for more information on indications, contraindications, warnings, all precautions, and adverse events.

Caution: Federal law restricts this device to sale by or on the order of a physician.

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