

# **Clinical Commissioning Policy Proposition:**

**Lung volume reduction by  
surgery or endobronchial valve  
for severe emphysema in adults**

Reference: NHS England 1622



**Prepared by NHS England Specialised Services Clinical Reference Group for  
Specialised Respiratory Services**

Published by NHS England, in electronic format only.

FOR CONSULTATION

## Contents

1	Executive Summary .....	4
	Equality Statement .....	4
	Plain Language Summary .....	4
2	Introduction .....	7
3	Proposed Intervention and Clinical Indication .....	7
4	Definitions .....	8
5	Aims and Objectives .....	8
6	Epidemiology and Needs Assessment .....	8
7	Evidence Base.....	9
8	Proposed Criteria for Commissioning .....	11
9	Proposed Patient Pathway .....	14
10	Proposed Governance Arrangements.....	15
11	Proposed Mechanism for Funding .....	16
12	Proposed Audit Requirements.....	16
13	Documents That Have Informed This Policy Proposition.....	16
14	Date of Review .....	17
15	References .....	18

# 1 Executive Summary

## Equality Statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

## Plain Language Summary

### **About Lung volume reduction by surgery or endobronchial valve for emphysema**

Lung volume reduction (LVR) is an approach which removes the worst affected areas of the diseased lung so that the healthier parts can work better. By removing the enlarged lung air spaces that occur in emphysema less air is trapped so that breathing is more efficient and comfortable. There are two National Institute for Health and Care Excellence (NICE) approved procedures for LVR. One involves surgery to cut out part of the diseased lung; the other is to insert a valve or valves into the airways to stop air from getting into the diseased parts of the lungs.

### **About current treatments**

Emphysema is one of a group of long-term lung diseases that form Chronic Obstructive Pulmonary Disease, or COPD. In emphysema, there is damage to the air sacs in the lungs which can lead to them becoming over inflated, making it difficult to breathe. Other symptoms of emphysema include coughing, tiredness and weight loss. Clinicians use the terms heterogenous or homogenous emphysema to describe whether there is a target area of the lung that can be treated with LVR. The

greater the clarity of the target area the better the outcome of the treatment is.

Homogenous means there is no target area, heterogeneous means there is.

Current treatments for emphysema include practical advice (such as stopping smoking, exercise training and breathing retraining), inhalers that act on the lung airways, steroids, oxygen treatment and lung transplant.

### **About the new treatment**

There are currently two procedures for LVR which are undertaken in clinical practice. These two treatments have the most robust evidence and clinical experience to identify the patients who will gain the most benefit from treatment.

### **LVR through surgery (LVRS)**

LVRS is undertaken by keyhole surgery under a general anaesthetic. The surgeons make two or three small openings in the chest wall to access the lung. The worst affected part of the lung is shaved off. The lung is then re-inflated with small tubes left in the opening or openings to re-expand the lung.

### **LVR through endobronchial valve (EBV) technique**

Under a general anaesthetic or sedation, a thin flexible tube with a camera on the end (bronchoscope) is moved through the patient's nose or mouth into the lungs. Small, one-way valves (duckbill type) are passed through the tube and placed in the diseased parts of the lungs. The valves stop air from getting into the diseased parts of the lungs when breathing in, but allow air and mucus out when breathing out. Several valves may be inserted.

In carefully selected patients with severe emphysema, these two treatments have the potential to improve lung function and quality of life. Both treatments need the involvement of a multi-disciplinary clinical team (MDT) to determine who will benefit from either treatment.

## **What we have decided**

NHS England has carefully reviewed the evidence to treat emphysema with LVR.

We have concluded that there is enough evidence to consider making treatments with both surgery and endobronchial valves available in centres with an experienced multidisciplinary team (MDT).

We have also concluded that in line with NICE IPG157 coils and other novel technologies should remain within the research setting. The proposed pathway by assessment through an MDT would enable patients with emphysema not suitable for surgery or valves to be able to access ongoing research studies with these alternative developing therapies in line with the research recommendation in NICE IPG517.

## 2 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to routinely commission LVR.

This document also describes the proposed criteria for commissioning, proposed governance arrangements and proposed funding mechanisms.

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether LVR will be routinely commissioned will be made by NHS England following a recommendation from the Clinical Priorities Advisory Group.

## 3 Proposed Intervention and Clinical Indication

**Background** – severe emphysema at the end of maximal medical therapy remains debilitating, leading to a reduction in the quality of life, increased use of healthcare resources and eventually premature death. Currently, LVR treatments are carried out in England but patient access is variable. Access to different techniques is also variable and can depend on individual operator preference.

**Signs and symptoms** – breathlessness, reduction in exercise capacity, weight loss, hyperinflated chest, bronchospasm, chronic cough, infective exacerbations, impairment in quality of life.

**Existing treatment** – **smoking cessation**, bronchodilating inhalers, corticosteroid inhalers, systemic steroids, pulmonary rehabilitation, supplemental oxygen therapy, domiciliary non-invasive ventilation, lung transplant.

**Proposed intervention** – LVR by surgery or endobronchial valve insertion after assessment by a specialist MDT.

**Rationale** – by excising non-functioning lung tissue or by causing collapse of poorly functioning emphysematous lung tissue, a reduction in lung volume produces a

change in chest wall mechanics enabling more efficient respiration. This reduces the sensation of breathlessness and improves exercise capacity, quality of life and mortality in carefully selected individuals.

## 4 Definitions

Emphysema is one of a group of lung conditions known as COPD. It affects the air sacs at the end of the airways in the lungs. They break down and the lungs become baggy and full of holes which trap air.

LVRS is an operation which removes the worst affected areas of the lung so that the healthier parts can work better. By removing the enlarged air spaces, less air is trapped so that breathing is more efficient and comfortable.

EBV is a procedure where small, one-way valves are placed in the airways of the diseased parts of the lungs. The valves stop air from getting into the diseased parts of the lungs when breathing in but allow air and mucus out when breathing out. Lung volume is therefore reduced and enables more efficient and comfortable breathing.

## 5 Aims and Objectives

This policy proposition considered: LVR for symptomatic severe pulmonary emphysema by either surgery or endobronchial valve placement.

The objectives were to:

1. Establish a policy proposition for the appropriate use of these procedures in correctly selected patients discussed by a multidisciplinary team.
2. Ensure equitable access to these selection processes and treatments across England.

## 6 Epidemiology and Needs Assessment



Emphysema is one of the presentations of COPD. COPD is one of the leading causes of morbidity and mortality in the world. There are around 835,000 people currently diagnosed with COPD in the UK and an estimated 2,200,000 people with COPD who remain undiagnosed, which is equivalent to 13% of the population of England aged 35 and over (Mindell et al 2011).

It is the second most common cause of emergency admission to hospital and is one of the most costly diseases in terms of acute hospital care in England (Department of Health 2011). There is a four-fold variation in non-elective admissions across England, and readmission rates vary by up to five times in different parts of the country. Over 15% are only diagnosed when they present to hospital as an emergency. 15% of those admitted to hospital with COPD die within three months and around 25% die within a year of admission. Over 50% of people currently diagnosed with COPD are under 65 years of age. 24 million working days are lost each year from COPD with £3.8 billion lost through reduced productivity.

Of the medical therapies used in management, only smoking cessation has been shown to modify the natural history of the condition. Oxygen therapy is associated with survival benefit. Emphysema is often associated with other conditions that need assessment and effective interventions in a holistic care approach, e.g. about 40% also have heart disease, and significant numbers have depression and/or anxiety disorder.

Accurate data on the number of individuals in England who would be potentially eligible for LVR are lacking. Clark et al (2014) made the assumption that if 10% of people with COPD have severe or very severe disease and of these 15% meet the criteria for LVR, this would make approximately 14438 eligible individuals in England.

## 7 Evidence Base

NHS England has concluded that there is sufficient evidence to support a proposal

for the routine commissioning of this treatment for the indication.

### **Evidence Review: LVR using video assisted thoracoscopic surgery (VATS) for severe emphysema**

#### **Summary of Results**

- The results suggest that VATS is an effective intervention for improving Quality of Life (QoL), exercise capacity and lung function in patients with severe emphysema in the short-term. Uncertainty remains about the risk of death and serious complications associated with the surgery.
- It is unclear whether there is a difference in effectiveness and safety between VATS and open surgery as the majority of results were statistically non-significant and most studies included both approaches. Only one study compared VATS and open surgery. However, results would suggest if there are any differences between the approaches, they are likely to be relatively small. Hospital stay was shorter for VATS and costs appear lower, although the costs reported are from over ten years ago and from a US setting.
- Overall, the results should be treated with caution as the included trials were relatively small. In addition, a couple of the trials were unbalanced in respect to known prognostic factors at baseline which may have introduced bias. Finally, the trials comparing VATS to medical management had short follow-up times of up to 12 months before cross-over, so the long-term effectiveness of VATS is not known although its utilisation in the previous reported open surgery studies with longer follow up should be noted.

### **Evidence Review: LVR by Endobronchial Valves for Severe Emphysema**

#### **Summary of Results**

- Results on a range of measures suggests that duckbill type valves provide significant meaningful benefit to patients in terms of lung function, exercise capacity and QoL, despite issues such as heterogeneity and lack of blinding in most studies. Evidence relating to some of these outcome measures indicates there is a greater benefit in patients with heterogeneous emphysema, patients

without CV to the target lobe and those where lobar occlusion is complete, although patients with homogenous emphysema with heterogeneous perfusion may benefit too. However, risk benefits need to be carefully appraised when making individual patient decisions and the fact that cost-effectiveness is not clear.

- Umbrella type valves appear to have a negative effect or no effect on these outcome measures. However, this may be due to the strategy tested rather than the type of valve, as the strategy in the two RCTs was partial occlusion of bronchi bilaterally without accounting for CV status, whereas in the duckbill valve trials it was complete occlusion of the most damaged areas of lung in those without collateral ventilation.

## **8 Proposed Criteria for Commissioning**

The evidence reviews show that LVR by either surgical technique or endobronchial valves show evidence of effectiveness. Patients need to undergo an assessment by a LVR MDT to determine the most appropriate intervention. This is an essential part of the service and no patients undergoing LVR should do so without discussion at an LVR MDT. They ensure the selection criteria are met; assess which technique is most suited to the individual patient (based on anatomy and physiology) and assess the individual risk and whether LVR is appropriate at that time. The appropriate member then discusses the conclusions of the MDT with the patient to enable informed consent. An LVR MDT should consist of a surgeon, COPD physician, interventional bronchoscopist, radiologist, and specialist nurse as a minimum, with appropriate administrative support.

Patients with a limited life expectancy or multiple co-morbidities who do not meet eligibility criteria should not be referred for consideration at the LVR MDT given the early complication rate. Referrals should come from secondary care clinicians currently involved in the care of the patient.

## Referral to LVR MDT

To be eligible for MDT assessment and considered for treatment the following criteria **should** be met.

### Referral Criteria

- Evidence of symptomatic hyperinflation due to emphysema with impaired quality of life. Medical Research Council (MRC) Dyspnoea Scale 3 or more
- Non-smoker at least 4 months
- **Completion of a Pulmonary Rehabilitation programme within last 12 months**
- Forced Expiratory Volume in one second (FEV1) 20-40% predicted
- Carbon Monoxide Diffusion Capacity (DLCO) > 20% predicted
- Residual Volume (RV) :Total Lung Capacity(TLC) > 55
- RV> 150%
- pCO<sub>2</sub><7KPa (partial pressure of carbon dioxide)
- Body Mass Index (BMI)> 18,

Patients unsuitable for referral to the LVR MDT include those with:

- Severe co-morbidities such as renal, hepatic or cardiac failure
- Severe progressive disease including disseminated malignancy
- Type 2 Respiratory Failure
- Severe pulmonary hypertension

### MDT assessment

The MDT will require additional information on the following criteria to inform their decision making regarding the appropriateness of LVR and the preferred method.

- The use of quantitative lung perfusion scans and high-resolution computer tomography (HRCT) to determine the distribution of emphysema in either upper or lower lobes as target areas for volume reduction
- **The greater the clarity of target areas the greater the outcome from**

#### **treatment.**

- An assessment of exercise ability, either shuttle walk test (SWT) or 6 minute walking distance (6MWD) to determine the required fitness for LVR or the need for further pulmonary rehabilitation
- The calculation of predicted procedural risk using published indices of body mass index, airflow obstruction, dyspnoea, exercise capacity index (BODE) and Glenfield risk scoring (Greening, *et al* 2017)

Those thought suitable for LVR with appropriate physiology and target areas should proceed to bronchoscopy assessment to determine the presence of collateral ventilation between lobes which would exclude EBV. In cases with poorly defined fissures CT software can be used as an adjunct to estimate the likelihood of collateral ventilation.

Either the St George's Respiratory questionnaire or the COPD Assessment Test (CAT) score should be measured as a baseline Quality of Life assessment.

#### **Exclusion criteria**

The main reasons for the MDT to determine that LVR is clinically inappropriate are:

- Lack of suitable target areas
- Excessive risk. Risk of morbidity and mortality after LVRS is related to the severity of the emphysema as measured by absolute FEV1 and predicted Diffusion Lung Capacity (DLCO) and the patient's nutritional status as measured by BMI. (Greening *et al* 2017) There is no evidence of effectiveness of LVR in patients with hypercapnia.

#### **Eligibility Criteria for LVR Intervention :**

##### **LVRS (method to be determined after MDT assessment)**

- Upper lobe heterogeneous emphysema
- RV:TLC >60, TLCO >20, BMI >18
- Collateral ventilation and low exercise capacity
- Predominantly apical disease with collateral ventilation and low exercise

capacity

- Lower lobe heterogeneous emphysema with collateral ventilation

Patients with collateral ventilation should be fully informed of the individualized risk of LVRS and treatment undertaken in those consenting.

Patients with previous thoracic surgery may be considered and should be fully informed of the individualized risk of LVRS and treatment undertaken in those consenting.

#### **EBV**

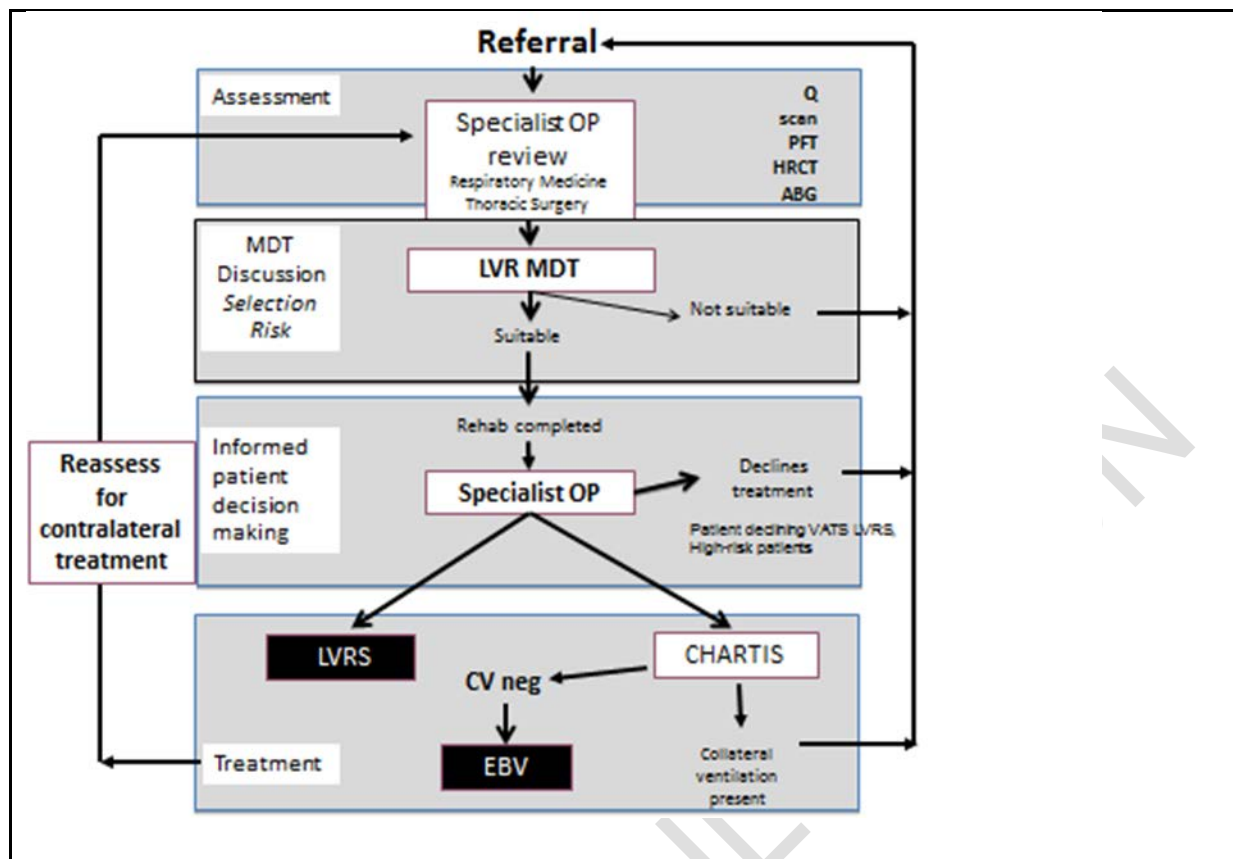
- Upper or lower lobe heterogeneous emphysema without collateral ventilation.
- RV >180%, TLC >20, BMI >18.
- Previous thoracic surgery

#### **LVRS or EBV:**

- Upper or lower lobe heterogeneous emphysema without collateral ventilation.
- RV > 180% and/or RV:TLC >60, TLC >20, BMI >18

Patient choice is of key importance and careful explanation of the potential treatment risks and benefits of both procedures must be given.

## **9 Proposed Patient Pathway**



## 10 Proposed Governance Arrangements

NICE guidance should be followed.

**EBV should not be carried out as a day case procedure.**

All future EBV procedures must be entered into the UK Lung Volume Registry (UKLVR).

LVRs procedures are already entered into the Society for Cardiothoracic Surgery's Audit. Outcomes for complications and 30 day mortality are published.

A dashboard of quality measures is to be developed and linked to the Thoracic Surgery Adults Service Specification 170016/S.

Commissioned LVR services should be delivered by thoracic services, respiratory services and interventional bronchoscopy services working together through a joint MDT.

Provider organisations must register all patients using prior approval software and

ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

## 11 Proposed Mechanism for Funding

A prior approval system will be implemented to ensure appropriate case selection.

LVRs and EBV are both within tariff so will be identified and paid for through standard coding methodology.

NICE IPG517 states that coils and other novel technologies should currently remain within the research setting and so will not be funded by NHS England.

## 12 Proposed Audit Requirements

National data collection process for commissioned services with outcome data and benchmarking and production of an annual national report.

Each commissioned service will produce an annual report regarding patients assessed and those treated but also those considered. This should be available to commissioners.

All interventions should be entered into the relevant national register.

EBV procedures must be entered into the UK Lung Volume Registry (UKLVR).

LVRs procedures must be entered into the Society for Cardiothoracic Surgery Audit.

## 13 Documents That Have Informed This Policy Proposition

This document updates and replaces

An Outcomes Strategy for Chronic Obstructive Pulmonary Disease (COPD) and Asthma in England <https://www.gov.uk/government/publications/an-outcomes-strategy-for-people-with-chronic-obstructive-pulmonary-disease-copd-and-asthma->



[in-england 2011](#)

Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017.

Gold Standards Framework [www.goldstandardsframework.org.uk](http://www.goldstandardsframework.org.uk) 2017

Greening NJ, Vaughan P, Oey I, Steiner MC, Morgan MD, Rathinam S, Waller DA 2017. Individualised risk in patients undergoing lung volume reduction surgery: the Glenfield BFG score. *European Respiratory Journal* 49: 1601766

NICE Lung volume reduction surgery for advanced emphysema 2005 (IPG114)

National Institute for Health and Care Excellence (NICE) Interventional Procedures Programme. 2013. Endobronchial valve insertion to reduce lung volume in emphysema Interventional procedures guidance [IPG600]. NICE. December 2017. <https://www.nice.org.uk/guidance/ipg600>

NICE Insertion of endobronchial nitinol coils to improve lung function in emphysema 2015 (IPG 517)

Sridhar Rathinam,, Inger Oey, Mick Steiner, Tom Spyt, Mike D. Morgan and David A. Waller 2014. The role of the emphysema multidisciplinary team in a successful lung volume reduction surgery programme *European Journal of Cardio-Thoracic Surgery* 1-6

## 14 Date of Review

This document will lapse upon publication by NHS England of a clinical commissioning policy for the proposed intervention that confirms whether it is routinely or non-routinely commissioned.

## 15 References

### LVR using open surgery for severe emphysema

- Fishman AI, Martinez F, Naunheim K, Piantadosi S, Wise R, Ries A *et al.* 2003. A randomized trial comparing lung volume-reduction surgery with medical therapy for severe emphysema. *New England Journal of Medicine*. 348(21):2059–73.
- Hillerdal G, Lofdahl CG, Strom K, Skoogh BE, Jorfeldt L, Nilsson F *et al.* 2005. Comparison of Lung Volume Reduction Surgery and Physical Training on Health Status and Physiologic Outcomes - A Randomized Controlled Clinical Trial. *Chest*. 128:3489–3499.
- Jones PW, Beeh KM, Chapman KR, Decramer M, Mahler DA, Wedzicha JA. 2014. Minimal Clinically Important Differences in Pharmacological Trials. *American Journal of Respiratory and Critical Care Medicine*. 189:250–255.
- McKenna RJ, Benditt JO, DeCamp M, Deschamps C, Kaiser L, Lee SM *et al.* 2004. Safety and efficacy of median sternotomy versus video-assisted thoracic surgery for lung volume reduction surgery. *Journal of Thoracic & Cardiovascular Surgery*. 127(5):1350–60.
- Miller JD, Berger RL, Malthaner RA, Celli BR, Goldsmith CH, Ingenito EP *et al.* 2005. Lung Volume Reduction Surgery vs Medical Treatment for Patients with Advanced Emphysema. *Chest*. 127:1166–1177.
- Miller JD, Malthaner RA, Goldsmith CH, Goeree R, Higgins D, Cox PG *et al.* 2006. A randomized clinical trial of lung volume reduction surgery versus best medical care for patients with advanced emphysema: A two-year study from Canada. *Annals of Thoracic Surgery*. 81(1):314-21.
- Naunheim KS, Wood DE, Mohsenifar Z, Sternberg AL, Criner GJ, DeCamp MM *et al.* 2006. Long-term follow-up of patients receiving lung-volume-reduction surgery versus medical therapy for severe emphysema by the National Emphysema Treatment Trial Research Group. *The Annals of Thoracic Surgery*. 82(2):431-43.
- Ramsey SD, Berry K, Etzioni R, Kaplan RM, Sullivan SD, Wood DE. 2003. Cost effectiveness of lung-volume-reduction surgery for patients with severe emphysema. *The New England Journal of Medicine*. 348(21):2092–102.
- Ramsey SD, Shroyer AL, Sullivan SD, Wood DE. 2007. Updated evaluation of the cost-effectiveness of lung volume reduction surgery. *Chest*. 131(3):823–32.
- van Agteren JEM, Carson KV, Tiong LU, Smith BJ. 2016. Lung volume reduction surgery for diffuse emphysema. *Cochrane Database of Systematic Reviews*. 2016, Issue 10.
- van Agteren JEM, Hnin K, Grosser D, Carson KV, Smith BJ. 2017. Bronchoscopic lung volume reduction procedures for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2017, Issue 2.

### Evidence Review: LVR using video assisted thoracoscopic surgery for severe emphysema

Clarenbach CF, Sievi NA, Brock M, Schneider D, Weder W, Kohler M. 2015. Lung volume reduction surgery and improvement of endothelial function and blood pressure in patients with chronic obstructive pulmonary disease. A randomized controlled trial. *American Journal of Respiratory and Critical Care Medicine*. 192(3):307–14.

Goldstein RS, Todd TR, Guyatt G, Keshavjee S, Dolmage TE, van Rooy S *et al*. 2003. Influence of lung volume reduction surgery (LVRS) on health related quality of life in patients with chronic obstructive pulmonary disease. *Thorax*. 58:405–10.

ISRCTN Registry. 2016. CELEB: Lung volume reduction in COPD - surgery vs endobronchial valves (ISRCTN19684749). April 2016. ISRCTN Registry. <https://doi.org/10.1186/ISRCTN19684749>. (accessed 19 February 2018).

Jones PW, Beeh KM, Chapman KR, Decramer M, Mahler DA, Wedzicha JA. 2014. Minimal Clinically Important Differences in Pharmacological Trials. *Am J Respir Crit Care Med*. 189:250–255.

McKenna RJ, Benditt JO, DeCamp M, Deschamps C, Kaiser L, Lee SM *et al*. 2004. Safety and efficacy of median sternotomy versus video-assisted thoracic surgery for lung volume reduction surgery. *Journal of Thoracic & Cardiovascular Surgery*. 127(5):1350–60.

Mineo TC, Ambrogi V, Pompeo E, Elia S, Mineo D, Bollero P, Nofroni I. 2004. Impact of lung volume reduction surgery versus rehabilitation on quality of life. *Eur Respir J*. 23:275–280.

Naunheim KS, Wood DE, Mohsenifar Z, Sternberg AL, Criner GJ, DeCamp MM *et al*. 2006. Long-term follow-up of patients receiving lung-volume-reduction surgery versus medical therapy for severe emphysema by the National Emphysema Treatment Trial Research Group. *The Annals of Thoracic Surgery*. 82(2):431–43.

van Agteren JEM, Carson KV, Tiong LU, Smith BJ. 2016. Lung volume reduction surgery for diffuse emphysema. *Cochrane Database of Systematic Reviews*. 2016, Issue 10.

van Agteren JEM, Hnin K, Grosser D, Carson KV, Smith BJ. 2017. Bronchoscopic lung volume reduction procedures for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2017, Issue 2.

Wouters EFM. 2005. Minimal Clinically Important Differences in COPD: Body Mass Index and Muscle Strength. COPD: *Journal of Chronic Obstructive Pulmonary Disease*. 2:149–155

### **Evidence Review: LVR by Endobronchial Valves for Severe Emphysema**

Brown MS, Kim HJ, Abtin FG, Strange C, Galperin-Aizenberg M, Pais R, *et al*. 2012. Emphysema lung lobe volume reduction: effects on the ipsilateral and contralateral lobes. *Eur Radiol*. 22(7):1547-55.

Eberhardt R, Gompelmann D, Schuhmann M, Reinhardt H, Ernst A, Heussel CP, *et al*. 2012. Complete unilateral vs partial bilateral endoscopic lung volume reduction in patients with bilateral lung emphysema. *Chest*. 142(4):900-8.

Hartman JE, Klooster K, Slebos DJ, Ten Hacken NH. 2016. Improvement of physical activity after endobronchial valve treatment in emphysema patients. *Respir Med*. 117:116-21.

Kemp SV, Slebos DJ, Kirk A, Kornaszewska M, Carron K, Ek L, *et al.* 2017. A Multicenter RCT of Zephyr(R) Endobronchial Valve Treatment in Heterogeneous Emphysema (TRANSFORM). *Am J Respir Crit Care Med.* 2017 Sep 08.

Pietzsch JB, Garner A, Herth FJ. 2014. Cost-effectiveness of endobronchial valve therapy for severe emphysema: a model-based projection based on the VENT study. *Respiration.* 88(5):389-98.

van Agteren JEM, Hnin K, Grosser D, Carson KV, Smith BJ. 2017. Bronchoscopic lung volume reduction procedures for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews.* 2017, Issue 2.

Wang Y, Lai TW, Xu F, Zhou JS, Li ZY, Xu XC, *et al.* 2017. Efficacy and safety of bronchoscopic lung volume reduction therapy in patients with severe emphysema: a meta-analysis of randomized controlled trials. *Oncotarget.* 29;8(44):78031-43.

END