NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of insertion of endobronchial air valves for persistent air leaks

Treating persistent air leaks in the lungs by inserting valves into the airways

Persistent air leaks from the lungs can occur after chest surgery or injury, or because of underlying lung disease. Leakage of air into the area between the lung and rib cage can lead to collapse of the lung and difficulty breathing. To prevent this, a chest drain (a tube inserted through the skin and rib cage) may be temporarily used to remove the air. In some cases the air leak does not seal and alternative treatments are needed such as surgery or inserting a foam or gel to seal the leak.

Endobronchial valves are a possible treatment for patients with air leaks for whom the usual treatments have not worked or for those unable to have surgery.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in July 2012 and updated in November 2012.

Procedure name

- Insertion of endobronchial air valves for persistent air leaks

Specialist societies

- British Thoracic Society
- Royal College of Surgeons
- Royal College of Physicians

- Society for Cardiothoracic Surgery in Great Britain and Ireland

Description

Indications and current treatment

Leakage of air from the lungs into the pleural space can lead to collapse of the lung and difficulty in breathing. Persistent air leaks from the lungs can occur after thoracic operations or trauma, or because of underlying pulmonary disease.

Persistent air leaks may initially be treated with a temporary chest drain to remove the air from the pleural space. If air continues to leak from the lung, a surgical repair may be needed. Pleurodesis may be an alternative option.

What the procedure involves

Insertion of endobronchial valves for persistent air leaks aims to reduce or eliminate airflow through the leaks so that the rest of the lung can function normally. It may also allow the tissues around an air leak to heal so that the leak stops.

The procedure is done using flexible bronchoscopy with the patient under sedation or general anaesthesia. The area of air leak is identified by occluding suspected segments with a saline-filled balloon and monitoring the effect on the air leak. Once the correct segment or segments are identified, a one-way valve is inserted using a flexible catheter which is passed through the bronchoscope and inserted into the target airway.

More than 1 valve may be inserted during a procedure. Valves may be removed when the tear on the lung surface has sealed.

Different devices are available for this procedure.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to insertion of endobronchial valves for persistent air leaks. Searches were conducted of the following databases, covering the period from their commencement to 22 November 2012: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good-quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, an editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with persistent air leaks.
Intervention/test	Endobronchial air valves
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on 61 patients from 2 case series[1–2] and 6 case reports[3–8].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on insertion of endobronchial valves for persistent air leaks

Abbreviations used: COPD, chronic obstructive pulmonary disease; CT, computed tomography; EBV, endobronchial valve; IQR, interquartile range; IV, intravenous; VATS, video-assisted thoracic surgery

Study details	Key efficacy findings	Key safety findings	Comments
Travaline JM (2009)[1] **Case series** Australia, USA and Italy Recruitment period: 2002–07 Study population: patients with prolonged air leaks Duration of air leak before treatment: mean 119 days n = **40** Number of valves inserted: 116 Age: mean 60 years Sex: 63% male Patient selection criteria: not reported. Technique: Under conscious sedation (n=8), deep sedation (n=16) or general anaesthesia (n=16), balloon-tipped catheter was inserted into the lobar airway and the balloon was inflated to provide selective bronchial occlusions. Using a flexible catheter, a valve (Zephyr EBV: Emphasys) was passed through a bronchoscope and deployed at the targeted airway. Procedures were performed during more than 1 session in 3 patients. Follow-up: range 5–1109 days Conflict of interest/source of funding: One of the authors is a consultant for Pneum Rx.	Number of patients analysed: **40** **Resolution of air leak** Complete cessation of air leak was achieved in 48% (19/40) of patients, 45% (18/40) had a reduction and no change in 2 patients. In 1 patient, an immediate change in air leak was not reported. Time from insertion to chest tube removal (data available for 28 patients only): Median 7.5 days (IQR 3 to 29) Time from insertion of the valve to hospital discharge: Median 11 days (IQR 4 to 27) **Valve removal** 8/40 patients had their valves removed after cessation of air leak, and clinician elected to leave the valves in place for the remaining patients. Valves were in place for mean 66 days (range 7to 143 days) before removal.	**Death** No deaths were attributed to the valve or implantation of the valve. Death was reported in 40% (16/40) of patients (at 'last follow-up') and was attributed to the following: underlying disease (n=8), cancer (n=4), bronchiectasis (n=1), emphysema (n=1), respiratory failure (n=1) and sepsis (n=1). Complications were reported in 6 patients. It is unclear if only 1, or more than 1 patient experienced the following complications: • initial malposition of the valve (requiring deployment) • valve expectoration • moderate oxygen desaturation • pneumonia • methicillin-resistant *Staphylococcus aureus* colonisation after a second valve procedure • 'unspecified event'. Timing of complications was not reported.	**Follow-up issues**: • No loss to follow-up reported. **Study design issues**: • Multicentre study (15 centres). • Methods used to recruit patients not described. **Study population issues**: • Aetiologies of air leaks: of recurrent spontaneous pneumothorax (n=21), postoperative (n=7), iatrogenic (n=6), first-time spontaneous pneumothorax (n=21), bronchoscopic lung volume reduction (n=1), and trauma (n=1). • Before placement of a valve, 4 patients had other treatments: blood patch (n=3), wedge resection (n=1), and pleurodesis (n=1). • Primary comorbidities in patients included cancer (30%), COPD (30%) and pneumonia (7.5%).

Abbreviations used: COPD, chronic obstructive pulmonary disease; CT, computed tomography; EBV, endobronchial valve; IQR, interquartile range; IV, intravenous; VATS, video-assisted thoracic surgery

Study details	Key efficacy findings	Key safety findings	Comments
Gillespie CT (2011)[2] **Case series** USA Recruitment period: 2007–08 Study population: patients with alveolopleural fistula Duration of air leaks: persistent for a median of 4 weeks after therapeutic measures had failed n = **9 (10 procedures)** Number of valves inserted: 31 Age: median 58 years Sex: 57% male Patient selection criteria: not reported Technique: Under general anaesthesia flexible bronchoscopy was performed. The airway was identified using intermittent balloon occlusion. If reduction or cessation of air leakage was identified, a valve (Spiration IBV valve, Spriration Inc) was placed before additional airways were evaluated. Follow-up: unclear Conflict of interest/source of funding: Authors disclosed a financial relationship with Spiration Inc.	Number of patients analysed: **7 (8 procedures)** **Resolution of air leak** Complete cessation of air leak occurred in 6 of 8 procedures (mean 5.2 days). In 1 further patient, the air leak reduced from occurring with expiration to occurring only with cough (by day 27). Air leak resolved at 41 days after valve placement using a pleural tent. In 1 patient a reduced air leak returned after valve removal (15 days after procedure). Days after valve treatment to discharge: median 3 days (IQR 1 to 31) Days after valve treatment to chest tube removal (n=5): median 16 days (10 to 36) Valves were removed in 5 of 7 patients (mean 37 days after valve placement). One valve was not removed because of lung fibrosis (no adverse sequelae at follow-up to 36 months) and another because of patient going to a hospice.	There were no procedural or valve-related complications observed.	**Follow-up issues:** • Treatment with valves did not proceed in 2 of the 9 patients because the target airways could not be identified with catheter balloon occlusion. **Study design issues:** • Methods used to recruit patients not reported. **Study population issues:** • Aetiology: 3 patients presented with spontaneous pneumothorax and 4 occurred after an operation. **Other issues:** • Prior interventions included VATS wedge resection, pleurodesis, chest tubes and operation with muscle flap.

Abbreviations used: COPD, chronic obstructive pulmonary disease; CT, computed tomography; EBV, endobronchial valve; IQR, interquartile range; IV, intravenous; VATS, video-assisted thoracic surgery

Study details	Key efficacy findings	Key safety findings	Comments
Conforti S (2010)[3] **Case reports** Italy Recruitment period: Not known Study population: patients with post-operative persistent air leaks n = **4** Number of valves inserted: 6 Age: 28 years; 57 years; 60 years; 62 years. Sex: 50% males Patient selection criteria: not reported Technique: Flexible bronchoscopy was performed under local (n=2) or general anaesthesia (n=2). Air leak was identified using intermittent balloon occlusion and a valve (Zephyr EBV, Pulmonx) was placed. Follow-up: 6 months Conflict of interest/source of funding: None stated	Number of patients analysed: **4** **Resolution of air leak** Complete cessation of air leak occurred in all 4 patients (range: immediately to 2 days after valve placement). Days after valve treatment to chest tube removal: mean 4 days in 2 patients. **Resolution of pneumothorax** Re-expansion of the lung was reported in 3 patients (at 48 hours in 1 patient, at 6 months in another patient, and not reported for the third patient) **Discharge** Days after valve treatment to discharge: 2 weeks in 1 patient. One valve was removed in 1 patient and valves were still in place in 2 patients after 6 months**.**	Death: 25% (1/4) The death was because of pre-existing systemic infection from mediastinitis and not thought to be related to valve placement. There were no valve-related complications reported.	**Follow-up issues:** • Follow-up was only 2 weeks in 1 patient who died. **Study population issues:** • Three patients had air leak after an operation, 2 for adenocarcinoma, 1 for Fontan syndrome. One patient was originally operated on for persistent air leak because of bullous emphysema.

Abbreviations used: COPD, chronic obstructive pulmonary disease; CT, computed tomography; EBV, endobronchial valve; IQR, interquartile range; IV, intravenous; VATS, video-assisted thoracic surgery			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Anile M (2006)[4] **Case reports** Italy Recruitment period: none stated Study population: patients with persistent air leaks n = **3** Number of valves inserted: **4** Age: 29 years; 57 years; 82 years Sex: 1 male, 1 female, 1 not stated Patient selection criteria: none reported Technique: Flexible bronchoscopy under IV sedation. Valve (Zephyr EBV, Emphasys Medical Inc.) was inserted into the target bronchus. Follow-up: 6 months to 1 year in 2 patients, unclear in 1 patient Conflict of interest/source of funding: none stated	Number of patients analysed: **3** **Resolution of air leak** Complete resolution in all 3 patients. Time from valve placement to resolution: immediately to 24 hours. Time from valve placement to chest drain removal: 1 day and 1 week. **Resolution of pneumothorax** Complete resolution of pneumothorax reported in 2 patients (within a week for 1 patient and by 6 months in the other patient). Valves remained in place in 1 patient 6 months after the procedure and were not removed in 1 patient.	One death from disseminated disease (unrelated to valve placement). No infectious complications or granulations reported.	**Study population issues:** • Persistent air leaks after thoracocentesis (n=1), after VATS (1) and spontaneous pneumothorax (1).

Abbreviations used: COPD, chronic obstructive pulmonary disease; CT, computed tomography; EBV, endobronchial valve; IQR, interquartile range; IV, intravenous; VATS, video-assisted thoracic surgery

Study details	Key efficacy findings	Key safety findings	Comments
Toma TP (2007)[5] **Case reports** UK Recruitment period: not stated Study population: patients with persistent air leaks n = **2 (4 procedures)** Number of valves inserted: 7 Age: 32 years; 35 years Sex: 100% female Patient selection criteria: none stated Technique: Under general anaesthesia, flexible bronchoscopy was performed. The airway was identified using balloon occlusion and valve (EBV, Emphasys) was inserted. Follow-up: 22 months (1 patient) Conflict of interest/source of funding: Emphasys provided the valves free of charge and an unrestricted educational grant to Royal Brompton Hospital, but took no part in analysis of data or preparation of the manuscript.	Number of patients analysed: **2 (4 procedures)** **Resolution of air leak** Complete cessation of air leak occurred in 1 patient (2 hours after valve placement). Partial resolution of air leak occurred in the other patient. Chest drain was removed in 1 patient. **Symptom control** Ventilation improved in 1 patient. **Discharge** One patient was discharged a few weeks after valve placement. The valves were not removed.	**Death** Death in 1 patient (because of cardiorespiratory arrest after mucus plugging and new pneumothorax of the transplanted lung; patient died 5 days after the procedure). **Infection** An infection occurred in the residual pleural space in 1 patient. Reviewed 22 months after valve placement (treated by antibiotics). **Re-treatment** Treatment failure occurred in both patients. This needed a second valve insertion session after 48 hours (1 valve inserted in the first session, 3 valves in second session in both patients).	**Study population issues:** • 1 patient had a persistent air leak after a lung transplant for lymphangioleiomyomatosis. One patient had a bilateral pneumothorax after severe community-acquired pneumonia**.**

Abbreviations used: COPD, chronic obstructive pulmonary disease; CT, computed tomography; EBV, endobronchial valve; IQR, interquartile range; IV, intravenous; VATS, video-assisted thoracic surgery

Study details	Key efficacy findings	Key safety findings	Comments
Jenkins M (2011)[6] **Case report** UK Recruitment period: none stated Study population: patient with severe bullous emphysema n = **1** Number of valves inserted: 2 Age: 61 years Sex: male Patient selection criteria: none reported Technique: Under general anaesthesia, flexible bronchoscope was introduced through the endotracheal tube. Valves (Zephyr, Pulmonx) were inserted into the occluded segments. Follow-up: 5 months Conflict of interest/source of funding: not reported	Number of patients analysed: **1** **Resolution of air leak** Air leak ceased immediately after insertion. **Discharge** Patient was discharged after 3 days.	**Chest infection** Recurrent chest infection (needing admission to hospital) in the subsequent 5 months after the initial procedure. **Valve migration** The valves had migrated to the orifice of the basal segments of the left lower and right lower lobe (valves removed at 5 months). (valve migration was retrospectively confirmed on a chest X-ray at 2 months after insertion).	**Study population issues:** • Patient developed air leak after VATS, and treatment by chemical pleurodeses and thoracotomy (oversewing and application of glue to the staple line) had failed.

Abbreviations used: COPD, chronic obstructive pulmonary disease; CT, computed tomography; EBV, endobronchial valve; IQR, interquartile range; IV, intravenous; VATS, video-assisted thoracic surgery

Study details	Key efficacy findings	Key safety findings	Comments
Schiavon M (2011)[7] **Case report** Italy Recruitment period: none stated Study population: patient with severe COPD with unresolved pneumothorax n = **1** Number of valves inserted: 1 Age: 69 years Sex: male Patient selection criteria: none stated Technique: Flexible bronchoscopy under sedation and local anaesthesia. The airway was targeted using intermittent balloon occlusion, and valve (Zephyr, Pulmonx Corp.) was inserted. Follow-up: 4 weeks Conflict of interest/source of funding: Not reported	Number of patients analysed: **1** Number of valves inserted: **1** **Resolution of air leak** Complete cessation of air leak occurred (at 1 week). Chest drain was removed after a week. **Symptom control** Subjective improvement in dyspnoea. **Reduction of pneumothorax** Partial reduction of pneumothorax (on CT scan). **Discharge** The patient was discharged after 1 week.	**Death** The patient died 3 weeks after discharge from a myocardial infarction (unrelated to valve placement). **Atelecatasis** A partial atelectasis of the lower lobe (assessed on CT scan) was reported 'at follow-up' (no further details).	**Follow-up issues:** • Follow-up no longer than 4 weeks because of death of the patient.

Abbreviations used: COPD, chronic obstructive pulmonary disease; CT, computed tomography; EBV, endobronchial valve; IQR, interquartile range; IV, intravenous; VATS, video-assisted thoracic surgery			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Snell G (2005)[8] **Case report** Australia Study population: persistent bronchocutaneous fistula. n = **1** Number of valves inserted: **4** Age: 53 years Sex: Male Patient selection criteria: none reported Technique: Flexible bronchoscopy under general anaesthesia. Valves (Emphasys Medical, Inc.) were inserted into a proximal airway. Follow-up: 5 months Conflict of interest/source of funding: One author disclosed a financial relationship with Emphasys Medical Inc. Manufacturers provided financial and technical support.	Number of patients analysed: **1** **Resolution of air leak** Complete cessation occurred. **Discharge** Patient discharged on same day. **Other outcomes** Increased epithelialisation of fistula surface Reduced sputum production in fistula.	No complications reported	**Follow-up issues:** • Follow-up period unclear.

Efficacy

Resolution of air leak

A case series of 40 patients treated by insertion of endobronchial valves reported a complete cessation of air leak in 48% (19/40) of patients, partial cessation in 45% (18/40), and no change in 5% (2/40) (range of follow-up: 5–1109 days)[1].

A case series of 7 patients (8 procedures) treated by insertion of endobronchial valves reported a complete cessation of air leak in 75% (6/8) of procedures (mean 5 days after the procedure)[2].

In a study reporting 3 case reports, complete resolution of air leak was reported immediately after valve placement in 2 patients and within 24 hours in 1 patient[4].

Successful removal of chest drain

The case series of 40 patients reported successful chest drain removal in 28 patients (for whom data were available) at a median of 8 days after valve insertion[1].

The case series of 7 patients (8 procedures) reported successful removal of chest drains in 5 patients at a median of 16 days after valve insertion[2].

Resolution of pneumothorax

A case report of 4 patients treated by insertion of endobronchial valves reported a reduction in pneumothorax in 3 patients. Re-expansion of both lungs was reported within 2 days in 1 patient and at 6 months in another patient. Improvement of pneumothorax in 1 lung was reported in a third patient (timing unclear)[3].

The study with case reports of 3 patients treated by insertion of endobronchial valves reported complete lung expansion in 1 patient immediately after the procedure and a completely expanded lung on CT in another patient within 24 hours[4].

A case report of 1 patient reported partial regression of the pneumothorax at a follow-up CT scan (timing not reported)[7].

Resolution of breathlessness

The case report of 1 patient treated by insertion of endobronchial valves reported ‘subjective improvement in dyspnoea’ at follow-up (timing unclear)[7].

Treatment failure

In the case series of 7 patients, a reduced air leak returned after valve removal in 1 patient (15 days after the procedure)[2].

Safety

Valve migration

Valve migration was reported in a case report (retrospectively confirmed on chest X-ray taken 2 months after the procedure). The valve was removed at 5 months after the procedure[6].

Valve malpositioning

Initial malpositioning of the valve (needing redeployment) was reported in the case series of 40 patients (number of patients not stated and timing of event unclear)[1].

Valve expectoration

Expectoration of the valve was reported in the case series of 40 patients (number of patients not stated and timing of event unclear)[1].

Recurrent chest infection

Recurrent chest infection was reported in a patient in a case report at 5 months after the initial procedure (needing admission to hospital and subsequent removal of the 2 valves)[6].

Atelectasis

Partial atelectasis of the lower lobe was reported in a case report (reported 'at follow-up'; timing unclear; no further details)[7].

Validity and generalisability of the studies

- There are no comparative or long-term data.
- Evidence is from a small number of patients in case series and case reports.
- One study reported on a patient with a bronchocutaneous fistula.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

NICE is developing the following guidance (details available from the NICE website):

Insertion of endobronchial valves (with or without assessment for collateral ventilation) for lung volume reduction in emphysema. NICE interventional procedure guidance. Publication expected June 2013.

This is a review of Bronchoscopic lung volume reduction with airway valves for advanced emphysema. NICE interventional procedure guidance 318 (2009). Available from www.nice.org.uk/guidance/IPG318

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Dr Samuel Kemp, Dr Andrew Medford, Dr Kamlesh Mohan, Dr Pallav Shah (Royal College of Physicians); Mr Richard Milton and Mr Rajesh Shah (Society for Cardiothoracic Surgery in Great Britain and Ireland)

- Three Specialist Advisors have performed this procedure regularly,
  2 Specialist Advisors have performed the procedure at least once and
  1 Specialist Advisor has not performed this procedure.
- Two Specialist Advisors noted this was a novel procedure with uncertain safety and efficacy, 2 noted it was an established procedure and 2 noted it was a minor variation on an existing procedure.
- All Specialist Advisors noted that fewer than 10% of specialists are engaged in this area of work.
- Key efficacy outcomes are duration of air leak, reduction or resolution of air leak, reduction in hospital stay, reduction in intensive care/high-dependency unit stay, reduction in the use of non-invasive ventilation/intermittent positive pressure ventilation, mortality, improvement in health-related quality of life, volume of air leak, recurrence of air leak and pneumothorax.
- Adverse events reported in the literature are atelectasis, valve dislodgement or migration, recurrence of pneumothorax or air leak, procedure failure, haemoptysis, respiratory failure, distal infection or pneumonia, valve migration,

granulation tissue formation around valves, moderate oxygen desaturation, initial malpositioning of the valve needing redeployment, and methicillin-resistant *Staphylococcus aureus* (MRSA) infection after a second valve procedure.

- Anecdotal adverse events are procedure failure, haemoptysis, respiratory failure, distal infection or pneumonia, granulation tissue formation around valves, pneumothorax, death, chest infection and migration or dislodgement of valve.
- Theoretical adverse events are atelectasis, pneumonia, valve migration, recurrence of pneumothorax or air leak, respiratory failure, granulation tissue formation around valves, sore throat, mild or significant haemoptysis, valve displacement, dyspnoea, hypoxaemia, valve malposition, infection, bleeding, loss of effect and death.
- In terms of the number of patients eligible for treatment and use of resources, 4 Specialist Advisors noted that the potential impact of this procedure on the NHS would be minor and 1 noted that it would be moderate.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

- Ongoing trials:
  - NCT01451359: Endobronchial valves in persistent air leak; case series; Belgium; estimated enrolment: 15; estimated completion date: March 2013.

References

1. Travaline JM, McKenna RJ, De Giacomo T et al. (2009) Treatment of persistent pulmonary air leaks using endobronchial valves. Chest 136 (2): 355–60

2. Gillespie CT, Sterman DH, Cerfolio RJ et al. (2011) Endobronchial valve treatment for prolonged air leaks of the lung: a case series. Annals of Thoracic Surgery 91(1):270–3

3. Conforti S, Torre M, Fieschi S et al. (2010) Successful treatment of persistent postoperative air leaks following the placement of an endobronchial one-way valve. Monaldi Archives for Chest Disease 73(2):88–91

4. Anile M, Venuta F, De Giacomo T et al. (2006) Treatment of persistent air leakage with endobronchial one-way valves. Journal of Thoracic and Cardiovascular Surgery 132(3): 711–2

5. Toma TP, Kon OM, Oldfield W et al. (2007) Reduction of persistent air leak with endoscopic valve implants. Thorax Sep;62(9): 830–3

6. Jenkins M, Vaughan P, Place D, et al. (2011) Endobronchial valve migration. European Journal of Cardio-Thoracic Surgery Nov;40(5): 1258–60

7. Schiavon M, Marulli G, Zuin A et al. (2011) Endobronchial valve for secondary pneumothorax in a severe emphysema patient. Thoracic and Cardiovascular Surgeon 59(8): 509–10

8. Snell GI, Holsworth L, Fowler S et al. (2005) Occlusion of a bronchocutaneous fistula with endobronchial one-way valves. Annals of Thoracic Surgery 80(5): 1930–2

Appendix A: Additional papers on insertion of endobronchial valves for persistent air leaks

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Abu-Hijleh M, Blundin M. (2010) Emergency use of an endobronchial one-way valve in the management of severe air leak and massive subcutaneous emphysema. Lung 188(3):253–7.	n=1 Follow-up= unclear	Despite resolution of air leak patient had unrelated complications and died.	Larger studies included in table 2.
Alexander ES, Healey, TT, Martin DW et al. (2012) Use of endobronchial valves for the treatment of bronchopleural fistulas after thermal ablation of lung neoplasms. Journal of Vascular & Interventional Radiology 23(9):1236–40.	n=4 case reports Follow-up=2 months to 2 years	In 3 of the 4 patients, the pneumothoraces resolved after valve placement. One patient required further treatment with pleurodesis.	Outcomes reported in table 2.
Brichon PY, Poquet C, Arvieux C et al. (2012) Successful treatment of a life-threatening air leakage, complicating severe abdominal sepsis, with a one-way endobronchial valve. Interactive CardiovascularThoracic Surgery 15(4):779–80.	n=1 Follow-up=4 months	After valve placement, immediate cessation of air leakage and removal of extracorporeal membrane oxygenation was reported, thus avoiding a lower left lobectomy with myoplasty. Valves were removed 9 weeks after the procedure. Recovery of the lower lobe parenchyma without pleural sequelae was reported at 4 months after the procedure.	Larger studies included in table 2.
De Giacomo T, Venuta F, Diso D et al. (2006) Successful treatment with one-way endobronchial valve of large air-leakage complicating narrow-bore enteral feeding tube malposition. European Journal of Cardiothoracic Surgery 30(5):811–2.	n=1 Follow-up=5 days	Air leak resolved at 5 days.	Outcome reported in table 2.

Feller-Kopman D, Bechara R, Garland R et al. (2006) Use of a removable endobronchial valve for the treatment of bronchopleural fistula. Chest 130(1):273–5.	n=1 Follow-up=unclear	Resolution of air leak after repeat procedure.	Outcome reported in table 2.
Dooms CA, De Leyn PR, Yserbyt J et al. (2012) Endobronchial valves for persistent postoperative pulmonary air leak: Accurate monitoring and functional implications. Respiration 84(4):329–33.	n=1 Follow-up=3 weeks	1 day after valve placement there was no pneumothorax or atelectasis. Chest drain was removed within 72 hours. Visual Analogue Scale (VAS) dyspnoea score improved from 7 after valve placement to 3 after valve removal. Forced Expiratory Volume in 1 second ($FEV_{1)}$ reduced from 2.77 litres to 2.37 litres 1 day after the procedure.	Larger studies included in table 2.
El-Sameed Y, Waness, A, Al Shamsi I et al. (2012) Endobronchial valves in the management of broncho-pleural and alveolo-pleural fistulae. Lung 190(3):347–51.	n=4 case reports Follow-up=3 weeks to 4 months	Air leak ceased immediately in 2 patients, after 1 week in 1 patient and after 9 days in 1 patient.	Outcome reported in table 2.
Ferguson JS, Sprenger K, Van Natta T. (2006) Closure of a bronchopleural fistula using bronchoscopic placement of an endobronchial valve designed for the treatment of emphysema. Chest 129(2):479–81.	n=1 Follow-up=4 months	Immediate cessation of air leak and no recurrence of pneumothorax at follow-up.	Outcome reported in table 2.
Fischer W, Feller-Kopman D, Shah A et al. (2012) Endobronchial valve therapy for pneumothorax as a bridge to lung transplantation. Journal of Heart and Lung Transplantation 31(3):334–6.	n=1 Follow-up=unclear	Subsequent pneumothorax developed 3 days after insertion of endobronchial air valves.	Outcome reported in table 2.
Mahajan AK, Verhoef P, Patel SB et al. (2012) Intrabronchial valves a case series describing a minimally invasive approach to	n =3 case reports Follow-up=3 to 8 days	Resolution of air leak was reported immediately and 3 days after the procedure (transferred out of the intensive care unit and	Outcome reported in table 2.

bronchopleural fistulas in medical intensive care unit patients. Journal of Bronchology and Interventional Pulmonology 19(2): 137–41.		discharged).	
Mitchell KM, Boley TM, Hazelrigg SR. (2006) Endobronchial valves for treatment of bronchopleural fistula. Annals of Thoracic Surgery 81(3):1129–31.	n=1 Follow-up=unclear	Cessation of air leak was reported after placement of valves.	Outcome reported in table 2.
Santini M, Fiorelli A, Vicidomini G et al. (2010) Latrogenic air leak successfully treated by bronchoscopic placement of unidirectional endobronchial valves. Annals of Thoracic Surgery 89(6):2007–10.	n=1 Follow-up=1 month	Subjective improvement in dyspnoea and resolution of air leak after placement of valves. No pneumothorax recurrence at 1 month follow-up.	Outcome reported in table 2.
Schweigert M, Kraus D, Ficker JH et al. (2011) Closure of persisting air leaks in patients with severe pleural empyema-use of endoscopic one-way endobronchial valve. European Journal of Cardiothoracic Surgery 39(3):401–3.	n=2 Follow-up=unclear	Cessation of air leakage in both cases.	Outcome reported in table 2.
Yu WC, Yeung YC, Chang Y et al. (2009) Use of endobronchial one-way valves reveals questions on etiology of spontaneous pneumothorax: report of three cases. Journal of Cardiothoracic Surgery 4:63.	N=3 Follow up= 8 months	Following insertion of valves, cessation of air leak was reported in 2 patients and in another patient air leak resolved after 11 days. Valves were removed 6 to 10 days after insertion. None of the patients had recurrence at 8 months follow up.	Outcome reported in table 2.

Appendix B: Related NICE guidance for insertion of endobronchial valves for persistent air leaks

Guidance	Recommendations
Interventional procedures	**Bronchoscopic lung volume reduction with airway valves for advanced emphysema. NICE interventional procedures guidance 318 (2009) (currently under review)** 1.1 Current evidence on the efficacy of bronchoscopic lung volume reduction with airway valves for advanced emphysema shows some improvement in patient-reported quality of life outcomes but there is inadequate evidence of improvement based on objective outcomes of efficacy. There are no major safety concerns in the short term, but there is inadequate evidence on safety in the long term. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake bronchoscopic lung volume reduction with airway valves for advanced emphysema should take the following actions. •Inform the clinical governance leads in their Trusts. •Ensure that patients and their carers understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended. •Audit and review clinical outcomes of all patients having bronchoscopic lung volume reduction with airway valves for advanced emphysema (see section 3.1). 1.3 This procedure should be carried out only by clinicians with specific training and expertise in interventional bronchoscopy, who should perform their initial procedures with an experienced mentor. 1.4 NICE encourages further research into bronchoscopic lung volume reduction with airway valves for advanced emphysema. Research should take the form of studies that allow comparison with the natural history of the disease. The studies should define patient selection criteria. Outcome measures should include exercise tolerance, ventilation–perfusion (VQ) mismatch, quality of life and long-term safety. NICE is aware of current clinical trials involving this procedure, and may review the procedure on publication of further evidence.

Appendix C: Literature search for insertion of endobronchial valves for persistent air leaks

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	22/11/12	Issue 11 of 12, Nov 2012
Database of Abstracts of Reviews of Effects – DARE (CRD website)	22/11/12	Issue 11 of 12, Nov 2012
HTA database (CRD website)	22/11/12	Issue 11 of 12, Nov 2012
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	22/11/12	Issue 11 of 12, Nov 2012
MEDLINE (Ovid)	22/11/12	1946 to November Week 3 2012
MEDLINE In-Process (Ovid)	22/11/12	November 21, 2012
EMBASE (Ovid)	22/11/12	1974 to 2012 Week 46
CINAHL (NLH Search 2.0/EBSCOhost)	22/11/12	-

Trial sources searched on 18/07/2012:

- Current Controlled Trials metaRegister of Controlled Trials – mRCT
- Clinicaltrials.gov
- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database

Websites searched on 18/07/2012:

- National Institute for Health and Clinical Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference search
- General internet search

The following search strategy was used to identify papers in MEDLINE.

MEDLINE search strategy

1	(Endobronch* adj3 (valve* or tap* or control* or device* or prosthe* or Implant*)).tw.
2	EBV.tw.
3	(intrabronch* adj3 (valve* or tap* or control* or device* or prosthes* or implant*)).tw.
4	(Endoscop* adj3 (valve* or tap* or control* or device* or prosthes* or implant*)).tw.
5	or/1-4
6	Bronchoscopy/
7	Bronchoscop*.tw.
8	Bronchoscopes/
9	or/6-8
10	Pneumothorax/
11	Pneumothor*.tw.
12	Bronchial Fistula/
13	(bronchopleur* adj3 fistul*).tw.
14	(broncho* adj pleur* adj3 fistul*).tw.
15	((Persist* or pulmon* or lung* or respirat*) adj3 leak*).tw.
16	exp Pleural Disease/
17	((Pleur* or Bronch* or Lung*) adj3 Diseas*).tw.
18	((Pleur* or Bronch*) adj3 leak*).tw.
19	Bronchial Diseases/
20	or/10-19
21	5 and 9
22	Pulmonx.tw.
23	Zephyr.tw.
24	22 or 23
25	5 and 20
26	21 or 24 or 25
27	Animals/ not Humans/
28	26 not 27