National Institute for Health and Care Excellence

[IP770/3] – [Endobronchial valve insertion to reduce lung volume in emphysema]

IPAC date: October 2017

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 NHS Professional	**1.2 & 1.3**	"I would like to congratulate the authors of these guidelines on their hard work. I fully support the guidelines. I have a couple of comments 1. I believe the core members of an emphysema MDT should be defined i.e chest physician, radiologist, thoracic surgeon and respiratory nurse 2. As endobronchial valve insertion is an alternative to surgery, then NICE should comment on patient selection for surgery or valves, and the potential benefits and disadvantages of each method. Failure to take into account the above two points could potentially lead to insertion of Endobronchial valves in hospitals without thoracic surgery input, and patients being denied lung volume reduction surgery which may give superior results in some case or worse results in others.	Thank you for your comments. The Consultee agrees with point 1.2 of the guidance but suggests a different wording. The Consultee agrees with section 1.3 of the guidance but suggests that more specific patient selection criteria should be added. The Committee has decided to change 1.2 of the guidance to addresses the Consultee request.
2	Consultee 2 NHS Professional	**2.2**	"""Certain therapies ...may be particularly useful..."" is probably overstating the evidence. Suggest ""Other lung volume reduction approaches under clinical investigation include lung volume reduction coils, airway sealants and bronchoscopic thermal vapour ablation.""" I would like to draw attention to the UK Lung Volume Register - a national database for lung volume reduction procedures. **http://www.isrctn.com/ISRCTN16371361**	Thank you for your comments. The Consultee disagrees with the wording in the "current treatments" section of the guidance. The Committee has changed the wording in section 2.2 of

				the guidance to address the Consultee request. A committee comment has been added “At consultation the committee was informed that there is a UK lung volume reduction trial and national database for lung volume reduction procedures into which suitable patients undergoing Endobronchial valve insertion could be entered.”
3	Consultee 3 Professional Organisation		There is significant variation in outcome (including exercise capacity and quality of life) and complications (including pneumothorax and death) across the included studies. This may in part reflect patient selection and technical issues. Overall the improvement in exercise capacity is modest, but notably with a clinically and statistically significant improvement in quality of life. The meta-analysis for umbrella valves showed a trend for higher mortality in the intervention arm: mortality OR= 4.95, 95% CI 0.85 to 28.94, p=0.076. It is quite plausible that the difference in mortality would have reached statistical significance had the sample size been larger. In light of the above, inclusion of more explicit selection criteria within the recommendations and a requirement for reporting of baseline characteristics and clinical outcomes for all patients by all centres is justified. Recommendation 1.1 refers to standard arrangements for clinical governance and audit. There is an existing UK national register for lung volume procedures for COPD; the committee may wish to consider making participation mandatory (all patients, all centres).	Thank you for your comments. The Consultee agrees with the main recommendation. The Committee makes recommendations on conditions for the safe use of a procedure including training standards, consent, audit and clinical governance. Its guidance is advisory and does not mandate implementation in the NHS. It is the clinicians’ responsibility to make arrangements for clinical governance, consent and audit. A committee comment has been added “At consultation the committee was informed

				that there is a UK lung volume reduction trial and national database for lung volume reduction procedures into which suitable patients undergoing Endobronchial valve insertion could be entered.”
4	Consultee 3 Professional Organisation		"Recommendation 1.4 We strongly support limiting the procedure to lobes without collateral ventilation. Consider inclusion of additional selection criteria. Consider including a recommendation regarding the nature and duration of follow up, including assessment of symptoms, exercise capacity (6MWT), lung function and complications.	Thank you for your comments. The consultee agree with point section 1.4 of the guidance.
5	Consultee 3 Professional Organisation		"Section 3.2 Consider rewording â€œ1 or more for each segment of the lung to be treatedâ€□. This is unclear and could be interpreted as implying that every segment in a lung is treated. This is incorrect. Every segment within a lobe is treated (but not all lobes in the lung are).	Thank you for your comments. The consultee disagrees with the wording in section 3.2 of the guidance. The Committee considered this comment but decided not to change the guidance.
6	Consultee 3 Professional Organisation		Section 4.1 and 4.2: Please review the meta-analysis data. If reporting FEV1 % it is important that it is clear whether this refers to a relative or absolute change from baseline. The MCID for FEV1 is stated as an absolute lung volume in millilitres (100 ml). We acknowledge that a lower value may be appropriate in very severe disease, however to allow comparison to other interventions it would be useful to compare FEV1 change compared to baseline between arms in ml if the data are available.	Thank you for your comments. Data in sections 4.1 and 4.2 are taken directly from the published papers and represent a percentage change from baseline. Further analysis from NICE is not possible.
7	Consultee 4		To Whom It May Concern,	Thank you for your comments.

	Company		Please accept the attached file as comments related to the NICE Interventional procedure consultation document, July 2017, Endobronchial valve insertion to reduce lung volume in emphysema, posted August 25, 2017 for comment. Thank you. Sincerely, [redacted] **NICE IPG on endobronchial valves for lung volume reduction comments to draft guidance 19Sept2017 FINAL.docx** [redacted] thanks NICE for the opportunity to comment on the Interventional procedures draft guidance on *Endobronchial valve insertion to reduce lung volume in emphysema*. **Overall comments for consideration** [redacted] agrees with the evaluation, the conclusions and draft recommendations in this guidance document. The overview of the clinical literature is extensive and very clear. To further validate the conclusions and recommendations of the referenced draft document, [redacted] would like to inform NICE about the very recent publication of another randomized controlled trial (RCT) of the [redacted] Endobronchial Valve Treatment in Heterogeneous Emphysema (TRANSFORM) that further validates previous findings on the safety and efficacy of this procedure.	The Committee has decided to include this study in table 2.

			New evidence since the publication of the draft consultation document The Multicenter RCT of [redacted] Endobronchial Valve Treatment in Heterogeneous Emphysema (TRANSFORM) was published on line September 8, 2017, in the American Journal of Respiratory and Critical Care Medicine, Articles in Press (**https://doi.org/10.1164/rccm.201707-1327OC**). This publication confirms the findings in the consultation document; in emphysema patients with absence of collateral ventilation in the target lobe, endobronchial lung volume reduction with [redacted] valves improves lung function, dyspnea, exercise tolerance, and quality of life over current standard of care medical therapy with an acceptable safety profile. 97 patients deemed to be CV negative were included in the study and randomized (2:1) to receive either EBV ([redacted]) (n=65) or Standard of Care (SoC) (n=32). At 3 months, 55.4% of EBV and 6.5% of SoC subjects had a FEV1 improvement ≥12% from baseline (p<0.001). Improvements were maintained at 6 months: EBV 56.3% vs SoC 3.2% (p<0.001), with a mean change in FEV1 at 6 months of 20.7±29.6% and -8.6±13.0%, respectively. Between group differences for changes at 6 months were statistically and clinically significant: ΔEBV–SoC for RV -700ml; 6MWD +78.7m; SGRQ -6.5 points; mMRC Dyspnea score -0.6 points; BODE Index -1.8 points (all p<0.05). Safety: as observed in the other RCTs, pneumothorax was the most common adverse event. This RCT further confirms the conclusions in the draft guidance that current evidence on safety and efficacy of endobronchial valve insertion to reduce lung volume in emphysema is adequate in quantity and quality to support its use under standard arrangements for clinical governance, consent and audit.	

8	Consultee 4 Company	**2.2**	In addition, we submit suggestions for wording in sections 2, 3 and 4 of the document, as follows. • **Section 2.2** This section refers to the current treatment options for emphysema. The reference to "c*ertain therapies such as coiling, use of sealants and thermal ablation"* in the last sentence seems out of place given that these treatments have not yet been established as "standard" and exploratory clinical research with these procedures is still ongoing. We wonder whether the reference to these treatments in this guidance on the use of endobronchial valve insertion is appropriate at this time.	Thank you for your comments. The Consultee disagrees with section 2.2 of the guidance. The Committee has decided to change the wording of section 2.2 of the guidance to address the Consultee suggestions.
9	Consultee 4 Company	**3.2**	• **Section 3.2** We propose to remove the word "slightly" in the last sentence. We do not think the differences between the two types of valves are slight; in addition, this is a value judgment that does not really add any value to the description of the different valves.	Thank you for your comments. The Consultee disagrees with section 3.2 of the guidance. The Committee has decided to change the wording of section 3.2 to address the Consultee suggestions.
10	Consultee 4 Company	**4.1**	• **Section 4.1** In the literature, the umbrella-shaped valves are described as **Intra**bronchial valves or **IBV**. In order to avoid confusion, we suggest maintaining this differentiation throughout the text for the description of the valves: duckbill endobronchial valve (EBV) and umbrella-shaped intrabronchial valves (IBV). Thank you for your consideration. We again appreciate the opportunity to comment. Sincerely	Thank you for your comments. The Consultee disagrees with the wording used to refer to different EBVs used in section 4.1 of the guidance. The IP programme issues guidance on procedures rather than individual devices.
11	Consultee 5 Company		"We would like to emphasise the evidence regarding the REACH study (NCT01989182), which has been completed and its 6-months data was	Thank you for your comments.

			presented at the ERS international congress in London, UK, last year. See below for the abstract and reference. The REACH study is a multi-centre RCT that assessed the safety and effectiveness of the SVS (umbrella EBV) for severe emphysema. While a full manuscript is in progress for peer-review publication, we would recommend taking the results of this study in consideration in the present guidance document. Abstract: The REACH study, a randomized controlled trial assessing the safety and effectiveness of the Spiration Valve System intra-bronchial therapy for severe emphysema The REACH study is the first multicentre randomized controlled trial conducted in China assessing the safety and effectiveness of bronchial valve treatment for severe emphysema patients with complete fissures. The study objectives were target lobe volume reduction (TLVR) and significant improvement in lung function. 101 subjects, 66 treatment and 35 control, were enrolled at 12 study sites. Target lobe selection, based on visual HRCT identified an upper lobe in 55% and a lower lobe in 45% of patients. Treatment consisted of target lobe occlusion utilising the Separation Valve System ([redacted]). The control group received optimal medical management. 67% of patients at 6 months showed evidence of significant (TLVR). Mean TLVR in treatment patients was 779 ml at 6 months. Compared to control, the treatment group achieved a significant and clinically meaningful improvement in FEV1 at the 1, 3, and 6 month visits (16.8%, 14.2%, 20.7%, respectively) with a responder rate of approximately 60% at these time periods. Significant improvements were also observed for quality of life measures and 6MWT. There were 24 serious adverse events in the treatment group consisting primarily of acute COPD exacerbations (12) and pneumothorax (5). There was one control and no treatment group deaths. In conclusion, this is the first multicentre study comparing bronchial valve therapy to medical arm control that has met its primary effectiveness end point and demonstrated sustained clinically meaningful benefit with	Conference abstracts are not normally considered adequate to support decisions on efficacy and are not generally selected for presentation in the overview, unless they contain important safety data.

			acceptable adverse events for severe emphysema patients selected only by HRCT. Reference: Li S et al. The REACH study, a randomized controlled trial assessing the safety and effectiveness of the Spiration Valve System endobronchial therapy for severe emphysema. ERS International Congress, London 2016." "We would like to point out that the most important conclusion from the clinical development of valve therapy is the correct patient selection. In section 1.4 it is noted that the procedure should only be done to occlude volumes of the lung where there is no collateral ventilation, by clinicians with specific training in doing the procedure. The latest evidence on [redacted] Valve System (umbrella EBV) shows clinical and functional effectiveness with low adverse event rate (see our comment No.1) Based on the above, we would invite the committee to note the latest clinical studies focusing on the correct patient population exhibit positive outcomes regardless of the device used. "	