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Appendix I

Electronic Search Strategies

RCTs - Medline 1976-1998 (on Ovid)

- 1 Emphysema/
- 2 Lung diseases/
- 3 Airway obstruction/
- 4 Pulmonary emphysema/
- 5 Emphysema\$.tw.
- 6 or/1-6
- 7 Pneumonectomy/
- 8 Exp surgery lung/
- 9 Lung/su
- 10 Thoracotomy/
- 11 Surgical stapling/
- 12 Laser surgery/
- 13 Lung\$ and volume\$ and reduc\$ and surg\$.tw.
- 14 or/7-13
- 15 randomized controlled trial.pt.
- 16 controlled clinical trial.pt.
- 17 randomized controlled trials/
- 18 random allocation/
- 19 double blind method/
- 20 or/15-19
- 21 clinical trial.pt.
- 22 Exp clinical trials/
- 23 (clinl\$ adj trial\$.ti,ab.
- 24 ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj25 (blind\$ or mask\$)).ti,ab.
- 25 placebos/
- 26 placebo\$.ti,ab.
- 27 research design/
- 28 or/21-27
- 29 6 and 14
- 30 20 or 28
- 31 29 and 30
- 32 Limit 31 to human

RCTs - Embase 1976-1998 (via Datastar)

- 1 Emphysema.de.
- 2 Lung-emphysema
- 3 Obstructive-airway-disease
- 4 Lung-disease
- 5 Chronic-obstructive-lung-disease
- 6 Airway-obstruction
- 7 Emphysema\$
- 8 1 or 2 or 3 or 4 or 5 or 6 or 7
- 9 Lung-surgery

-
- 10 Lung-resection
 - 11 Thoracotomy
 - 12 Suturing-method
 - 13 Laser-surgery
 - 14 Lung\$2 and volume\$2
 - 15 Reduc\$ and surgery
 - 16 14 and 15
 - 17 9 or 10 or 11 or 12 or 13 or 14 or 16
 - 18 8 and 17
 - 19 18 and human.de.
 - 20 Clinical-trial
 - 21 Randomized-controlled-trial
 - 22 20 or 21
 - 23 19 and 22

Other analytical studies - Medline 1976-1998 (on Ovid)

- 1 Emphysema/
- 2 Lung diseases/
- 3 Airway obstruction/
- 4 Pulmonary emphysema/
- 5 Emphysema\$.tw.
- 6 or/1-6
- 7 Pneumonectomy/
- 8 Exp surgery lung/
- 9 Lung/su
- 10 Thoracotomy/
- 11 Surgical stapling/
- 12 Laser surgery/
- 13 Lung\$ and volume\$ and reduc\$ and surg\$.tw.
- 14 or/7-13
- 15 6 and 14
- 16 Prospective studies/
- 17 Comparative study/
- 18 Exp case control studies/
- 19 Cohort studies/
- 20 (Case and control).tw.
- 21 Cohort.tw.
- 22 or/16-21
- 23 15 and 22
- 24 Limit 23 to human

Other analytical studies - Embase 1976-1998 (via Datastar)

- 1 Emphysema.de.
- 2 Lung-emphysema
- 3 Obstructive-airway-disease
- 4 Lung-disease
- 5 Chronic-obstructive-lung-disease
- 6 Airway-obstruction

-
- 7 Emphysema\$
 - 8 1 or 2 or 3 or 4 or 5 or 6 or 7
 - 9 Lung-surgery
 - 10 Lung-resection
 - 11 Thoracotomy
 - 12 Suturing-method
 - 13 Laser-surgery
 - 14 Lung\$2 and volume\$2
 - 15 Reduc\$ and surgery
 - 16 14 and 15
 - 17 9 or 10 or 11 or 12 or 13 or 14 or 16
 - 18 8 and 17
 - 19 18 and human.de.
 - 20 Case and control
 - 21 Cohort
 - 22 Prospective\$
 - 23 20 or 21 or 22
 - 24 19 and 23

Cost studies - Medline 1993-1998 (on Ovid)

- 1 Cost allocation/
- 2 Cost benefit analysis/
- 3 Cost control/
- 4 Cost of illness/
- 5 Cost savings/
- 6 Costs and costs analysis/
- 7 Models, economic/
- 8 or/1-7
- 9 Emphysema/
- 10 Lung diseases/
- 11 Airway obstruction/
- 12 Pulmonary emphysema/
- 13 Emphysema\$.tw.
- 14 Pneumonectomy/
- 15 Thoracotomy/
- 16 Surgical stapling/
- 17 Lung\$ and volume\$ and reduc\$ and surg\$.tw.
- 18 or/9-17
- 19 8 and 18
- 20 Lung diseases obstructive/rh
- 21 Lung diseases obstructive/th
- 22 Exercise therapy/
- 23 Respiratory therapy/
- 24 or/20-23
- 25 8 and 24

Appendix II

Contacts and Local Clinical Experts

Dr. Sherwood Burge, Respiratory Physician, Birmingham Heartlands Hospital

Karen Hammond, Respiratory Research Nurse, Birmingham Heartlands Hospital

Nicky Harvey, Physiotherapist, Birmingham Heartlands Hospital

Paul Jones, Respiratory Physician, St George's Hospital, London

Paul Kind, Health Economist, Centre for Health Economics, University of York

Amanda Lambert, NHSE, West Midlands Regional Office

Dr Martin Miller, Respiratory Physician, University Hospital, Birmingham

Jean Peters, Research Co-ordinator, Trent Institute for Health Services Research

Francisco Pozo, Respiratory Physician, Hospital Universitario, Madrid, Spain

Mr. Rajesh, Thoracic Surgeon, Birmingham Heartlands Hospital

Jo Walsworth-Bell, Public Health Physician (Retired)

Martin Wildman, Research Registrar in Respiratory Medicine, Birmingham Heartlands Hospital

George Young, GP, Hall Green, Birmingham

Appendix III

Inclusion and Exclusion Criteria

	Inclusion	Exclusion
Population	Patients with diffuse, severe emphysema with significant functional limitation, despite maximum medical therapy.	Patients with large isolated emphysematous bullae in the presence of normal underlying compressed lung.
Intervention	Lung volume reduction surgery (reduction pneumoplasty or pneumectomy) defined as multiple lung resections and/or plications of diseased lung tissue to reduce lung volume. The following techniques and approaches were all included: open or closed procedure, unilateral or bilateral procedure; laser ablation, stapling or both.	The excision of localised giant bullae.
Outcomes	Studies were included irrespective of which outcomes they addressed. Ideally, they would address clinical and physiological outcomes and should provide data on morbidity and mortality rates associated with the procedure.	Studies which only considered short-term outcomes i.e. those with less than three months follow-up. Studies which primarily examined the mechanism of effect of LVRS as opposed to the effectiveness of the intervention in improving patients symptoms, leading to the measurement of inappropriate and non-clinically important outcomes.
Duplication	When several series emerged chronologically from the same source only the largest and most recent series was included.	Studies were excluded if they had clearly originated from the same source and there were indications that their analysis included some or all of the same patients.
Quality Criteria - pertaining to potential sources of bias		
Selection bias	A consecutive case series; cases studied represented all those treated or were shown to have been selected in an unbiased way or were shown not to be significantly different from the total number treated.	A selected case series; cases studied were a sub-group of those treated with no detail provided as to how they were selected or cases studies were a sub-group of those treated with no evidence to show that they were not significantly different from the total number treated
Attrition bias	Losses to follow-up of $\leq 25\%$ or adequate management of losses to follow-up e.g. demonstration that they were not significantly different from total population; inclusion in the final analysis; or sensitivity analyses NB. When losses to follow-up arose due to cases in the series not reaching a given follow-up point studies were included if they treated cases on whom data was available as a cohort with results presented for that discrete cohort before and after the intervention.	Losses to follow-up $> 25\%$ and inadequate management of losses to follow-up
Detection bias	Prospective study design; study states that it was conducted prospectively or outcomes of interest were clearly measured before and after the intervention using predefined criteria.	Retrospective study design; study states that it was conducted retrospectively or outcomes of interest were clearly not measured before and after the intervention using predefined criteria.

Appendix IV

Validity Assessment Criteria

Checklist for the critical appraisal of case series.

Case studies and case series tend to fall fairly low in the hierarchy of evidence relative to other study designs such as RCTs and CCTs. However, in certain situations evidence from this type of research may be all that is available, particularly when the intervention of interest is in the early stages of its development or, conversely, when its effectiveness has been well established in the absence of well-conducted RCTs. Situations where case series are likely to provide valid information tend to be those where the natural history of the condition is understood and it is clear that cases who are untreated will have a poor prognosis. For situations where the prognosis of untreated cases is not known the information from case series is less helpful.

The purpose of this checklist to help the reader identify the strengths and weaknesses of a given case series in order that they may apply its results within certain limits as they are defined. It is important at the outset, however to note a couple of points;

- reliable and validated search strategies for primary study designs other than RCTs and CCTs are not yet available, hence the impact of retrieval and publication bias in reviews of case series is completely unknown and should be acknowledged
- it is also possible that unbiased estimates of effect from case series may be contained within other study designs (e.g. each group within a comparative study may constitute a case series in its own right) and this should always be considered

Finally, it is important to stress that this checklist is a guide only. Appraisers may find that what constitutes acceptable assessment criteria may vary between situations and additional criteria specific to the subject area will often be required.

1. Was the study conducted prospectively?

Can be difficult to assess, but if the outcomes are clearly measured before and after the intervention, and criteria are clearly defined for the measurement of outcomes *a priori* it is highly probable that this was the case.

Information required

A description within the methods section describing the timing of the relevant events with respect to the initiation of the study, i.e. were cases selected for inclusion in the study before the results of the outcome of interest were known by the investigators.

Assessment Criteria

Ideal - Study states that it is conducted prospectively

Acceptable - Evidence that all key outcomes were measured before and after the intervention using clear criteria defined *a priori*.

Unacceptable - Study states that it was conducted retrospectively or it clearly does not measure key outcomes before and after the intervention

OR

no information.

2. Was the method of selection of cases identified and appropriate?

Again this is not always clear but if the case series has been selected from a wider population of cases treated it is important to assess whether this has been done in an unbiased way.

Information required

Detail within the methods or results section on the numbers treated and the numbers included in the case series and, if they are different, how cases were selected for inclusion and whether they were representative of the wider population.

Assessment Criteria

Ideal - Study states that a consecutive series of cases was included in the study.

Acceptable - Evidence that cases were selected for inclusion in an unbiased way or evidence that the characteristics of the included cases were not significantly different from those of the treated population.

Unacceptable - Clear evidence from the numbers that the included cases were a sample of those treated with no detail on the selection process or evidence that they were significantly different from the total population treated.

OR

no information.

3. Was the duration and completeness of follow-up reported and was it adequate?

Detail on losses to follow-up and deaths will usually be available. A particular problem in case series is that frequently only small subgroups of cases have reached given follow-up points which is potentially problematic if not handled carefully.

Information required

Numbers and characteristics of losses to follow-up and deaths.

Assessment Criteria

Ideal - Follow-up data on 80 - 100% of cases.

Acceptable - Adequate management of deaths and losses to follow-up such as detailing their characteristics, performing sensitivity analyses and/or including them in the final analysis

OR

If losses to follow-up are cases who have not yet reached a given follow-up point, are those for whom data is available treated as a cohort, with results presented for the cohort *only* before and after the intervention?

Unacceptable - Losses to follow up of over 20 - 25% particularly if they are unaccounted for.

OR

Follow-up data for a subgroup of patients followed up to a given point using baseline data for the whole series as a comparator

OR

no information.

Appendix V

Data Abstraction Form

DATA ABSTRACTION AND VALIDITY ASSESSMENT

AIM:

Numbers

Referred		Procedures
Evaluated		People
Treated		
Studied		
Followed up		

Consecutive	Yes/No	Prospective	Yes/No/Don't know
-------------	--------	-------------	-------------------

Follow up duration and completeness

Inclusion Criteria

Exclusion Criteria

Intervention

Unilateral	Bilateral	Both	Unclear
Laser	Stapling	Both	Unclear
Open			

Closed

Bovine Pericardial Strip Buttressing	Yes/No/Unclear
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Pulmonary Rehab Details -	Yes/No
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Experience/Setting

Outcomes

	Assessment	Subjectivity	Pre	Post1	Post2
FEV ₁					
Dyspnoea					
6MWD					
Mortality					
LOS					
ITU stay					
Suppl. O ²					

Appendix VI

Included Studies

1. Argenziano

Argenziano M, Thomashow B, Jellen PA et.al.

Functional comparison of unilateral versus bilateral lung volume reduction surgery.
Annals of Thoracic Surgery 1997;64:321-327

2. Bagley

Bagley PH, Davis SM, O'Shea M et.al.

Lung volume reduction surgery at a community hospital: program development and outcomes.

Chest 1997;111:1552-1559

3. Benditt

Benditt JO, Lewis S, Wood DE et.al.

Lung volume reduction surgery improves maximal O² consumption, maximal minute ventilation, O² pulse and dead space to tidal volume ratio during leg cycle ergometry.
American Journal of Respiratory and Critical Care Medicine 1997;156:561-566

4. Bousamra

Bousamra M, Haasler GB, Lipchik RJ et.al.

Functional and oximetric assessment of patients after lung reduction surgery.
Journal of Thoracic and Cardiovascular Surgery 1997;113:675-681

5. Cooper

Cooper JD, Patterson GA, Sunderesan RS et.al.

Results of 150 consecutive bilateral lung volume reduction procedures in patients with severe emphysema.

Journal of Thoracic and Cardiovascular Surgery 1996;112:1319-1329

6. Cordova

Cordova F, O'Brien G, Furukawa S et.al.

Stability of improvements in exercise performance and quality of life following bilateral lung volume reduction surgery in severe COPD.

Chest 1997;112:907-915

7. Criner

Criner GJ, O'Brien G, Furukawa S et.al.

Lung volume reduction surgery in ventilator dependent COPD patients.

Chest 1996;110:877-884

8. Daniel

Daniel TM, Chan BB, Bhaskar V et.al.

Lung volume reduction surgery. Case selection, operative technique and clinical results.

Annals of Thoracic Surgery 1996;223:526-531

9. Eugene^a

Eugene J, Dajee, Kayaleh R et.al.

Reduction pneumoplasty for patients with a forced expiratory volume in 1 second of 500 millilitres or less.

Annals of Thoracic Surgery 1996;223:526-531

10. Eugene^b

Eugene J, Ott R, Gogia H et.al.

Video-thoracic surgery for treatment of end-stage bullous emphysema and chronic obstructive pulmonary disease.

The American Surgeon 1995;61:934-936

11. Keller

Keller CA, Ruppel G, Hibbett A et.al.

Thoracoscopic lung volume reduction surgery reduces dyspnoea and improves exercise capacity in patients with emphysema.

American Journal of Respiratory and Critical Care Medicine 1997;156:60-67

12. Kotloff

Kotloff RM, Tino G, Bavaria JE et.al.

Bilateral lung volume reduction surgery for advanced emphysema: a comparison of median sternotomy and thoracoscopic approaches.

Chest 1996;110:1399-1406

13. Little

Little MD, Swain JA, Nino J et.al.

Reduction pneumoplasty for emphysema.

Annals of Surgery 1995;222:365-374

14. McKenna

McKenna RJ, Brenner M, Fischel R et.al.

Should lung volume reduction surgery be unilateral or bilateral?

The Journal of Thoracic and Cardiovascular Surgery 1996;112:1331-1339

15. Miller

Miller JI, Lee RB, Mansour KA.

Lung volume reduction surgery: Lessons learned.

Annals of Thoracic Surgery 1996;61:1464-1469

16. Scirbia

Scirbia FC, Rogers R, Keenan RJ et.al.

Improvement in pulmonary function and elastic recoil after lung volume reduction surgery for diffuse emphysema.

The New England Journal of Medicine 1996;334:1095-1099

17. Snell

Snell GI, Solin P, Weng Chin et. al.
Lung volume reduction surgery for emphysema.
Medical Journal of Australia 1997;167:529-532

18. Stammerberger

Stammerberger U, Thurnheer R, Bloch KE et.al.
Thoracoscopic bilateral lung volume reduction surgery for diffuse pulmonary
emphysema.
European Journal of Cardiothoracic Surgery 1997;11:1005-1010

19. Zenati

Zenati M, Keenan RJ, Sciurba FC et.al.
Role of lung volume reduction surgery in lung transplant candidates with pulmonary
emphysema.
Annals of Thoracic Surgery 1996;62:994-999

Excluded Studies [and main reasons for exclusion].

1. Bae KT, Slone RM, Gierada DS et.al.
Patients with emphysema: quantitative CT analysis before and after lung volume reduction surgery. Work in progress.
Radiology 1997;203:705-714
[reasons for exclusion: inappropriate outcomes]
2. Benditt JO, Woode DE, McCool FD et.al.
Changes in breathing and ventilatory muscle recruitment patterns induced by lung volume reduction surgery.
American Journal of Respiratory and Critical Care Medicine 1997;155:279-284
[reasons for exclusion: suspicion of duplication]
3. Bisingisser R, Zollinger A, Hauser M et.al.
Bilateral volume reduction surgery for diffuse pulmonary emphysema by video-assisted thoracoscopy.
Journal of Cardiovascular Surgery 1996;112:875-882
[reasons for exclusion: suspicion of duplication]
4. Bloch KE, Li Y, Zhang J et.al.
Effect of surgical lung volume reduction on breathing patterns in severe pulmonary emphysema.
American Journal of Respiratory and Critical Care Medicine 1997;156:553-560
[reasons for exclusion: suspicion of duplication]
5. Brenner M, Kayaleh RA, Milne EN et.al.
Thoracoscopic laser ablation of pulmonary bullae.
The Journal of Thoracic and Cardiovascular Surgery 1994;107:883-890
[reasons for exclusion: inadequate follow-up]
6. Brenner M, McKenna R, Gelb A et.al.
Objective predictors of response for staple versus laser emphysematous lung reduction.
American Journal of Respiratory and Critical Care Medicine 1997;155:1295-1301
[reasons for exclusion: inadequate follow-up]
7. Brenner M, McKenna RJ, Gelb AF et.al.
Dyspnoea response following bilateral thoracoscopic staple lung volume reduction surgery.
Chest 1997;112:916-923
[reasons for exclusion: inappropriate outcomes]
8. Colt HG, Ries AL, Brewer N et.al.
Analysis of chronic pulmonary disease referrals for lung volume reduction surgery.
Journal of Cardiopulmonary Rehabilitation 1997;17:248-252
[reasons for exclusion: inappropriate outcomes]

9. Connolly JE, Wilson A.
The current status of surgery for bullous emphysema.
The Journal of Thoracic and Cardiovascular Surgery 1989;97:351-361
[reasons for exclusion: inappropriate intervention]
10. Cooper JD Trulock EP, Triantafillou AN et.al.
Bilateral pneumectomy (volume reduction) for chronic obstructive pulmonary disease.
The Journal of Thoracic and Cardiovascular Surgery 1995;109:106-119
[reasons for exclusion: suspicion of duplication]
11. Cooper JD, Patterson GA.
Lung volume reduction surgery for severe emphysema.
Seminars in Thoracic and Cardiovascular Surgery 1996;8(1):52-60
[reasons for exclusion: suspicion of duplication]
12. Cooper JD.
Extended indications for median sternotomy in patients requiring pulmonary resection.
Annals of Thoracic Surgery 1978;26:413-420
[reasons for exclusion: suspicion of duplication]
13. Cooper J, Patterson GA.
Lung volume reduction surgery for emphysema.
Chest Surgery Clinics of North America 1995;5:815-831
[reasons for exclusion: inappropriate intervention]
14. Delarue NC, Woolf DE, Sanders FG.
Surgical treatment for pulmonary emphysema.
Canadian Journal of Surgery 1977;20:222-230
[reasons for exclusion: inappropriate intervention]
15. Fischel RJ, McKenna RJ, Peters H.
Thoracoscopic lung volume reduction surgery.
Surgical Rounds 1996;19:272-278
[reasons for exclusion: suspicion of duplication]
16. Fitzgerald MX, Keelan PJ, Cugell DW et.al.
Long-term results of surgery for bullous emphysema.
Journal of Thoracic and Cardiovascular Surgery 1974;68:566-587
[reasons for exclusion: inappropriate intervention]
17. Fujita RA, Barnes GB.
Morbidity and mortality after thoracoscopic pneumoplasty.
Annals of Thoracic Surgery 1996;62:251-257
[reasons for exclusion: inappropriate outcomes]

18. Gaissert HA, Trulock EP, Cooper JD et.al.
Comparison of early results after volume reduction or lung transplantation for chronic obstructive pulmonary disease.
Journal of Thoracic and Cardiovascular Surgery 1996;111:296-307
[reasons for exclusion: retrospective analysis]
19. Gelb AF, Brenner M, McKenna RJ et.al.
Lung function 12 months following emphysema resection.
Chest 1996;110:1407-1414
[reasons for exclusion: inappropriate outcomes]
20. Gelb AF, Zamel N, McKenna RJ et.al.
Mechanism of short-term improvement in lung function following emphysema resection.
American Journal of Respiratory and Critical Care Medicine 1996;154:945-951
[reasons for exclusion: inadequate follow-up]
21. Gelb AF, McKenna RJ, Brenner M et.al.
Contributions of lung and chest wall mechanics following emphysema resection.
Chest 1996;110:11-17
[reasons for exclusion: suspicion of duplication]
22. Gierada DS, Sloane RM, Bae KT et.al.
Pulmonary emphysema: comparison of preoperative quantitative CT and physiologic index values with clinical outcome after lung volume reduction surgery.
Radiology;1997:235-242
[reasons for exclusion: inappropriate outcomes]
23. Goldstraw P, Petrou M.
The surgical treatment of emphysema. The Brompton Approach.
Chest Surgery Clinics of North America 1995;5:777-796
[reasons for exclusion: inappropriate intervention]
24. Hazelrigg SR, Boley TM, Naunheim KS et.al.
Effect of bovine pericardial strips on air leak after stapled pulmonary resection.
Annals of Thoracic Surgery 1997;63:1573-1575
[reasons for exclusion: inappropriate outcomes]
25. Hazelrigg S, Boley T, Henkle J et.al.
Thoracoscopic laser bullectomy: a prospective study with three-month results.
The Journal of Thoracic and Cardiovascular Surgery 1996;112:319-327
[reasons for exclusion: inadequate follow-up]
26. Ingenito EP, Evans RB, Loring SH et.al.
Relation between pre-operative inspiratory lung resistance and the outcome of lung reduction surgery for emphysema.
The New England Journal of Medicine 1998;338:1181-1185
[reasons for exclusion: not a consecutive case series]

27. Iwa T, Watanabe Y, Fukatani G.
Simultaneous bilateral operations for bullous emphysema by median sternotomy.
The Journal of Thoracic and Cardiovascular Surgery 1981;81:732-737
[reasons for exclusion: inappropriate intervention]
28. Keenan RJ, Landreneau RJ, Sciurba FC et.al.
Unilateral thoracoscopic surgical approach for diffuse emphysema.
The Journal of Thoracic and Cardiovascular Surgery 1996;111:308-316
[reasons for exclusion: inadequate follow-up]
29. Krucylak PE, Naunheim KS, Keller CA et.al.
Anaesthetic management of patients undergoing video-assisted lung reduction for
treatment of end-stage emphysema.
Journal of Cardiothoracic and Vascular Anaesthesia 1996;10:850-853
[reasons for exclusion: inappropriate outcomes]
30. Lewis RJ, Caccavale RJ, Sisler GE.
VATS-Argon beam coagulator treatment of diffuse end-stage bilateral bullous disease
of the lung.
Annals of Thoracic Surgery 1993;55:1394-1399
[reasons for exclusion: inadequate follow-up]
31. Martinez FJ, Montes de Oca, Whyte RI et.al.
Lung volume reduction surgery improves dyspnoea, dynamic hyperinflation and
respiratory muscle function.
American Journal of Respiratory and Critical Care Medicine 1997;155:1984-1990
[reasons for exclusion: not a consecutive case series]
32. McKenna RJ, Fischel RJ, Brenner M et.al.
Combined operations for lung volume reduction surgery and lung cancer.
Chest 1996;110:885-888
[reasons for exclusion: suspicion of duplication]
33. McKenna RJ, Fischel RJ, Brenner M et. al.
Use of the Heimlich valve to shorten hospital stay after lung reduction surgery for
emphysema.
Annals of Thoracic Surgery 1996;61:1115-1117
[reasons for exclusion: inappropriate outcomes]
34. Naunheim KS, Keller CA, Krucylak PE et.al.
Unilateral VATS lung reduction.
Annals of Thoracic Surgery 1996;61:1092-1098
[reasons for exclusion: suspicion of duplication]
35. O'Donnell DE, Webb KA, Bertley JC et.al.
Mechanisms of relief of exertional breathlessness following unilateral bullectomy and
lung volume reduction surgery in emphysema.
Chest 1996;110:18-27
[reasons for exclusion: inappropriate intervention]

36. Roue C, Mal H, Sleiman C et.al.
Lung volume reduction in patients with severe diffuse emphysema.
Chest 1996;110:28-34
[reasons for exclusion: retrospective analysis]
37. Rubin JW, Finney NR, Borders BM et.al.
Intrathoracic biopsies, pulmonary wedge resection and management of pleural disease: Is video assisted closed chest surgery the approach of choice?
American Surgeon 1994;60:860-864
[reasons for exclusion: inappropriate intervention]
38. Slone RM, Gierada DS.
Radiology of pulmonary emphysema and lung volume reduction surgery.
Seminars in Thoracic and Cardiovascular Surgery 1996;8(1):61-82
[reasons for exclusion: inappropriate outcomes]
39. Slone RM, Pilgram TK, Gierada DS et.al.
Lung volume reduction surgery: comparison of preoperative radiological features and clinical outcome.
Radiology 1997;204:685-693
[reasons for exclusion: inappropriate outcomes]
40. Suga K, Nishigauchi K, Matsunaga N.
Three-dimensional surface displays of perfusion SPET in the evaluation of patients with pulmonary emphysema for thoracoscopic lung volume reduction surgery.
Nuclear Medicine Communications 1997;18:25-32
[reasons for exclusion: inappropriate intervention]
41. Swanson SJ, Mentzer SJ, DeCamp MM et.al.
No-cut thoracoscopic lung plication: a new technique for lung volume reduction surgery.
Journal of the American College of Surgeons 1997;185:25-32
[reasons for exclusion: inadequate follow-up]
42. Szekely LA, Oelberg DA, Wright Cameron et.al.
Preoperative predictors of operative morbidity and mortality in COPD patients undergoing bilateral lung volume reduction surgery.
Chest 1997;111:550-558
[reasons for exclusion: retrospective analysis]
43. Teschler H, Stamatis G, el-Raouf Farhat AA et.al.
Effect of surgical lung volume reduction on respiratory muscle function in pulmonary emphysema.
European Respiratory Journal 1996;9:1779-1784
[reasons for exclusion: inappropriate outcomes]
44. Triantafillou AN.
Anaesthetic management for bilateral volume reduction surgery.
Seminars in Thoracic and Cardiovascular Surgery 1996;8(1):94-98
[reasons for exclusion: inappropriate outcomes]

45. Tschernko EM, Wisser W, Wanke T et.al.
Changes in ventilatory mechanics and diaphragmatic function after lung volume reduction surgery in patients with COPD.
Thorax 1997;52:545-550
[reasons for exclusion: suspicion of duplication]
46. Tschernko EM, Wisser W, Hofer S.
The influence of lung volume reduction surgery on ventilatory mechanics in patients suffering from severe chronic obstructive pulmonary disease.
Anaesthesia and Analgesia 1996;83:996-1001
[reasons for exclusion: inappropriate outcomes]
47. Wakabayashi A, Brenner M, Kayaleh RA et.al.
Thoracoscopic carbon dioxide laser treatment of bullous emphysema.
Lancet 1991;337:881-883
[reasons for exclusion: retrospective analysis]
48. Wakabayashi A.
Thoracoscopic laser pneumoplasty in the treatment of diffuse bullous emphysema.
Annals of Thoracic Surgery 1995;60:936-942
[reasons for exclusion: retrospective analysis]
49. Wakabayashi A.
Unilateral thoracoscopic laser pneumoplasty of diffuse bullous emphysema.
Chest Surgery Clinics of North America 1995;5:833-850
[reasons for exclusion: retrospective analysis]
50. Wang SC, Fischer KC, Slone RA et.al.
Perfusion scintigraphy in the evaluation for lung volume reduction surgery: correlation with clinical outcome.
Radiology 1997;205:243-248
[reasons for exclusion: inappropriate outcomes]
51. Weder W, Schmidt RA, Russi EW.
Thoracoscopic lung volume reduction surgery for emphysema.
International Surgery 1996;81:229-234
[reasons for exclusion: suspicion of duplication]
52. Weder W, Thurnheer R, Stammberger U et.al.
Radiologic emphysema morphology is associated with outcome after lung volume reduction.
Annals of Thoracic Surgery 1997;64:313-319
[reasons for exclusion: inappropriate outcomes]
53. Wisser W, Tschernko E, Senbaklavaci O et.al.
Functional improvement after volume reduction: sternotomy versus videoendoscopic approach.
Annals of Thoracic Surgery 1997;63:822-828
[reasons for exclusion: retrospective analysis]

54. Yusef RD, Trulock EP, Pohl MS et.al.
Results of lung volume reduction surgery reduction in patients with emphysema.
Seminars in Thoracic and Cardiovascular Surgery 1996;8:99-109
[reasons for exclusion: suspicion of duplication]
55. Yusef RD, Lefrak SS.
Evaluation of patients with emphysema for lung volume reduction surgery.
Seminars in Thoracic and Cardiovascular Surgery 1996;8(1):83-93
[reasons for exclusion: suspicion of duplication]
56. Zenati M, Keenan RJ, Landreneau RJ et.al.
Lung reduction as a bridge to lung transplantation in pulmonary emphysema.
Annals of Thoracic Surgery 1995;59:1581-1583
[reasons for exclusion: inappropriate intervention]

Appendix VII

Characteristics of Included Studies

CHARACTERISTICS OF INCLUDED STUDIES						
Study Reference	Study Design Strengths and Weaknesses (n=sample size)	Criteria for Entry to Study		Intervention	Outcomes	Additional Information
		Inclusion	Exclusion			
Argenziano	Consecutive case series within a controlled comparison. n=92 75% reached the 3-6 month follow-up point and were treated as a discrete cohort with 96% follow-up. No information on assessment of outcome.	Hyperinflation. Poor diaphragmatic excursion. Pulmonary perfusion and ventilation deficits. Significant functional disability.	Morbid obesity. Chronic bronchitis. Excessive sputum production. Metastatic cancer. Continued or recent smoking. Less than severe functional disability.	Stapling with BPS buttressing. Bilateral and unilateral. Mainly open procedures.	Pulmonary function tests. Morbidity and mortality. Dyspnoea.	Baseline data - unclear when this was obtained. Setting/experience - part of a 2 year programme at Columbia-Presbyterian Medical Centre, New York, USA. NB. Population includes some very ill cases.
Bagley	Consecutive case series. n=55 82% followed up for three months. No information on assessment of outcome	Advanced emphysema unhappy with the limits imposed by the disease. Small amounts of airways inflammation. Recent completion of a pulmonary rehabilitation programme. RV >150% of predicted. PA systolic pressure < 50mmHg. Smoking cessation for at least 1 year.	Recent high dose steroid use. Other active medical problems.	Stapling with BPS buttressing. Bilateral via median sternotomy. 8 weeks pulmonary rehabilitation pre-op.	Pulmonary function tests. 6 MWD Chronic Respiratory Diseases Questionnaire.	Baseline data - 6MWD and subjective data obtained post-rehabilitation. Pulmonary function test baseline data collected at various points particularly for very ill cases. Setting/experience - early experience in a 320 bed community hospital in the USA. NB. Results presented as numbers of patients achieving a significant improvement post-operatively.
Benditt	Consenting cases of a consecutive series - included cases studied compared to those excluded and shown not to be significantly different. N=21 (of 47) 100% follow-up to 3 months. No information on assessment of outcome.	Evidence of emphysema on CT scan. Severe airflow limitation. FEV ₁ >15% and <35% of predicted. TLC >120% RV >150% Air trapping and hyperinflation. Smoking cessation for at least 3 months.	Aged > 75 years. Excessive daily sputum production. Significant co-morbidity.	Stapling with BPS buttressing. Bilateral via median sternotomy.	Pulmonary function tests to ATS standards.	Baseline data - no detail on when this was obtained. Setting/experience - part of a year long programme at the University of Washington in Seattle, USA.

LVRS for COPD

Bousamra	Consecutive case series. n=45 93% followed up to 3 months. No information on assessment of outcome.	Marked hyperexpansion. Heterogeneous emphysema. Large residual volume. Significant trapped gas volume.	Previous major thoracic surgery. Prominent component of bronchospasm. Copious sputum production or congestive cardiac failure. Inability to undertake pulmonary rehabilitation.	Mainly stapling. Bilateral via median sternotomy or thoracotomy. Pulmonary rehabilitation 6 weeks pre-op continuing post-op.	Pulmonary function tests. Dyspnoea - Mahler index (follow-up inadequate). 6MWD (follow-up inadequate). Mortality and morbidity.	Baseline data - obtained pre and post rehabilitation. Setting/experience - first 45 cases treated at the Medical College of Wisconsin Hospitals, USA.
Cooper	Consecutive case series. n=150 67% followed up to 6 months; 37% to 1 year; and 13% to 2 years; all treated as discrete cohorts. No information on assessment of outcome.	Emphysema with hyperinflation and heterogeneity. Marked physiological impairment (FEV ₁ < 35% of predicted). Marked restriction in activities of daily living despite maximal medical therapy. Aged < 75 years. Acceptable nutritional status (70% to 130% of ideal body weight). Ability to participate in vigorous pulmonary rehabilitation programme. No co-existing major medical problems that would significantly increase operative risk. Willingness to undertake risk of morbidity and mortality associated with the procedure. Smoking cessation for at least 6 months.	Diffuse disease with no target areas. Insufficient thoracic distension advanced age or associated medical problems. FEV ₁ too good. Pleural disease. Better suited to lung transplantation. PA carbon dioxide >55mmHg in association with other problems. Marked kyphosis.	Stapling with BPS buttressing. Bilateral via median sternotomy. 6 weeks pulmonary rehabilitation pre-op.	Pulmonary function tests. Exercise testing 6 MWD Morbidity and mortality. Dyspnoea - Mahler index and MMRC. Quality of life - Nottingham Health Profile and SF36.	Baseline data - generally obtained pre-and post rehab but presented separately. Setting/experience - the most recent results of a large programme at Washington University, Missouri, USA, which commenced in 1993.
Cordova	Consecutive case series. n=69 25 patients reached 3 months with 100% follow up and were treated as a discrete cohort. No information on assessment of outcome.	New York Heart Association class iii-iv. Evidence of airflow obstruction and hyperinflation by pulmonary function studies. (i.e. post-bronchodilator FEV ₁ 30% of predicted) FRC or TLC >120% of predicted. Discrepancy between helium dilution and FRC body box determination of lung volumes by >500ml. Documented hyperinflation on chest radiograph. Diffuse emphysema documented on CT scan. Ventilation-perfusion mismatch documented in planned resected lung by VQ scan.	Patients with severe and refractory hypoxaemia. Severe hypercapnic respiratory failure requiring mechanical ventilation. Presence of severe cardiovascular disease. Presence of severe pulmonary hypertension (mean PA pressure >500Hg). Severe debilitated state with total body weight <70% of ideal. Presence of significant extrapulmonary end-organ dysfunction expected to limit survival. Psychosocial dysfunction. Continued smoking.	Stapling. Bilateral via median sternotomy. All patients underwent pulmonary rehabilitation for 8 weeks pre-op and 3 months post-op.	Pulmonary function tests to ATS Standards. Exercise testing. 6MWD Quality of life - Sickness Impact Profile.	Baseline data - measurements were obtained after pulmonary rehabilitation. Setting/experience- first 25 cases of 69 treated in a 2-year programme at Temple University Hospital, Philadelphia, USA.

Criner	Consecutive case series. n=3 100% followed up for at least 3 months. No information on assessment of outcome.	Severe COPD and respiratory failure. Ventilator dependent. Poor mobility. Severe hypercapnia & cor pulmonale.	Not stated.	Stapling. Bilateral via thorotomy or Sternotomy. No pulmonary rehabilitation.	Pulmonary function tests to ATS standards. Arterial blood gas analysis. Bedside maximum inspired pressure & ventilation.	Baseline data - obtained 1-4 months prior to intubation (not available for one subject). Setting/experience - part of a 2 year programme at Temple University Hospital Philadelphia, USA. NB. All very ill cases.
Daniel	Consecutive case series. n=26 65% followed up to three months but treated as a discrete cohort (n=17). No information on assessment of outcome.	Diagnosis of COPD. No smoking for more than 1 month. Aged <75 years. FEV ₁ between 15% and 35% of predicted. PA carbon dioxide < 55mmhg. Prednisone dosage < 20 mg daily. PA pressure <55mmhg by echocardiogram. Commitment to pre & post-operative supervised pulmonary rehabilitation for 6 weeks.	Previous thoracotomy or pleurodesis. Symptomatic coronary heart disease, chronic asthma or bronchitis.	Stapling with BPS buttressing. Bilateral via median sternotomy. Pulmonary rehabilitation pre and post op for 6 weeks.	Pulmonary function tests quality of life - tool not stated.	Baseline data - no information as to when baseline measurements were obtained. Setting/experience - 1 year experience at the University of Virginia, USA.
Eugene ^a	Consecutive case series. n=44 91% followed up to 3 months and 86% followed up to 6 months. No information on assessment of outcome.	Severely impaired pulmonary function (FEV ₁ <0.5L). Lifestyle limiting dyspnoea. Reduced pulmonary function FEV ₁ 20-40% predicted. Residual volume >250% predicted. Hyperexpansion. Diffuse bullous emphysema. Target areas.	Advanced age. Hypercarbia. Irreversible pulmonary hypertension. Prior operation or thoracic deformities. Significant co-morbidity. Poor patient compliance.	Stapling with BPS buttressing and laser. Unilateral and bilateral. Via thoracoscopy and median sternotomy. No pre-op pulmonary rehabilitation (40 patients underwent rehab post op).	Pulmonary function tests. Dyspnoea - Borg and MMRC scores.	Baseline data- no information on when baseline data were obtained. Setting/experience - part of an 18 month experience at the Western Medical Centre, Anaheim, California, USA. NB. All very ill cases.
Eugene ^b	Consecutive case series. n=28 100% followed up to 3 months. No information on assessment of outcome.	Dyspnoea severely impairing lifestyle. Inability to work or self care. No improvement on maximal medical management. Bullous or diffuse emphysema with hyperinflation on CT scan. Markedly low FVC and FEV ₁ and high lung volumes.	Not stated.	Laser and/or stapling with BPS buttressing. Unilateral. Via thoracoscopy. No information on pulmonary rehabilitation.	Pulmonary function tests. Dyspnoea - tool not stated.	Baseline data - no information. Setting/experience - early experience (Nov 1993 - July 1994) at the Western Medical Centre, Anaheim and the University of California, Irvine, USA.
Keller	Consecutive case series. n=25 100% followed up to 6 months. No information on assessment of outcome.	Established diagnosis of diagnosis of severe emphysema. Significant air trapping. Impaired diffusion capacity. Demonstrated distinct target areas for surgical resection. Ventilation/perfusion mismatch.	Coronary heart disease or left ventricular failure. Chronic bronchitis. Severe hypercapnia (PA carbon dioxide >55mmHg). Significant PA hypertension (mean >35mmHg).	Stapling. Unilateral. Via thoracoscopy. Pre-op pulmonary rehabilitation for at least 6 weeks.	Pulmonary function tests. Dyspnoea - Mahler Index. Exercise testing. 6 MWD. (all to ATS standards)	Baseline data - measurements obtained after pulmonary rehabilitation. Setting/experience - first 25 cases in a series of 75 at St Louis University, Missouri, USA.

<p>Kotloff</p>	<p>Consecutive case series within a controlled comparison.</p> <p>Thoracoscopic procedure n=40 89% followed up for 3-6 months.</p> <p>Closed procedure n=80 81% followed up for 3-6 months.</p> <p>No information on assessment of outcome.</p>	<p>FEV₁ 20-30% of predicted. Severe hyperinflation. RV >200% of predicted. Heterogeneous disease. Large zones of hypoventilated and hypoperfused lung on VQ scan.</p>	<p>Giant bullectomy. PA carbon dioxide >50mmHg PA systolic pressure >50mmHg Continued smoking. Body weight over or under 20% of ideal. Prior surgery or pleurodesis. Significant bronchospasm with wide fluctuations in FEV₁. Copious daily sputum production. Poor functional status.</p>	<p>Stapling with BPS buttressing. Bilateral (some staged). Via median sternotomy or thoracoscopy. 6 weeks pulmonary rehabilitation pre and post-op.</p>	<p>Pulmonary function tests. Exercise testing. 6MWD. Mortality and morbidity.</p>	<p>Baseline data - obtained after pulmonary rehabilitation.</p> <p>Setting/experience - part of a programme at the University of Pennsylvania, USA (duration not stated).</p>
<p>Little</p>	<p>Consecutive case series. N=55 51% followed up to 3 months and treated as a discrete cohort. No information on assessment of outcome.</p>	<p>Diffuse emphysema. Cessation of smoking.</p>	<p>Severe bronchitis. Carbon dioxide retention >50mmHg. Congestive cardiac failure or cor pulmonale. End stage COPD. Inability to ambulate. FEV₁ <35% predicted despite pulmonary rehabilitation.</p>	<p>Mixed - mainly laser. Unilateral via thorascopy. But, includes some open procedures and 3 resection of giant bullae. No routine pulmonary rehabilitation although some did 6 weeks pre-op.</p>	<p>Pulmonary function tests. 6MWD. Dyspnoea.</p>	<p>Baseline data - when pulmonary rehabilitation was undertaken baseline data was obtained after this.</p> <p>Setting/experience - part of a wider programme at the University of Nevada, USA.</p>
<p>McKenna</p>	<p>Consecutive case series within a controlled comparison. n=166 87% followed up for 6-12 months. No information on assessment of outcome.</p>	<p>Marked symptoms despite maximal medical management. Hyperexpansion of the thorax and flattening of the diaphragm chest x-ray. Severe heterogeneous emphysema on CT scan.</p>	<p>Current smoking. Aged >80 years. Severe carbon dioxide retention PA carbon dioxide >55mmHg. Severe heart disease. History of cancer in the last 5 years. Ventilator dependency. Presence of a lung mass. Prior thoracic surgery.</p>	<p>Stapling with BPS buttressing. Unilateral or bilateral. Thorascopic. Pulmonary rehab not routine pre-op but all underwent this for 2-3 weeks post-op.</p>	<p>Mortality and morbidity. Pulmonary function tests. Dyspnoea - MMRC Steroid and oxygen dependence.</p>	<p>Baseline data - unclear when this was obtained.</p> <p>Setting/experience - results of a year long programme at the Lung Centre, Chapman Medical Centre, California, USA.</p>
<p>Miller</p>	<p>Consecutive case series. n=53 84% followed up to 6 months. No information on assessment of outcome.</p>	<p>Advanced generalised emphysema. No bullae over 5cm. Failure of maximum medical therapy. No significant coronary heart disease or psychiatric problems. No life threatening illness. The ability to perform pulmonary rehabilitation. Smoking cessation for 6 months. Steroid dosage >15mg a day. No generalised osteoporosis.</p>	<p>Predominately bullous emphysema. Smoking. Too good physiologic state. Significant coronary heart disease. PA pressure >35mmHg. Inability to participate in pulmonary rehabilitation. Steroid dosage >15mg a day. Use of multiple psychiatric drugs. Significant bronchitis or asthma. Previous pulmonary operation or sclerosis. Age <75. FEV₁ <30% of predicted. PA carbon dioxide < 50mmHg. PA oxygen > 40mmHg on room air.</p>	<p>Stapling with BPS buttressing. Bilateral. Via median sternotomy. 6 weeks pulmonary rehabilitation pre-op and post-op.</p>	<p>Pulmonary function tests. Dyspnoea - tool not stated. 6MWD.</p>	<p>Baseline data - no information on when baseline measurements were obtained.</p> <p>Setting/experience - early results of an 18 month programme at Emory University Medical School, Georgia, USA.</p>

Sciurba	Consecutive case series. n=20 100% followed up to 3 months. Outcome assessment by trained independent assessor.	Diffuse emphysema on the CT scan.	Giant bullae. Dominant bronchiectasis, chronic bronchitis or clinical cor pulmonale. Systolic PA pressure >50mmHg. Severe epistaxis or inability to tolerate oesophageal balloon placement. Severe dyspnoea despite maximal medical therapy. Clinically stable for 1 month pre-study. FEV ₁ < 0.5 and RV >140% predicted after bronchodilators.	Laser and stapling. Unilateral and bilateral. Open and closed procedures. No information on pulmonary rehabilitation.	6MWD (standardised). Dyspnoea - Mahler index. Pressure/volume relations. Elastic recoil.	Baseline data - obtained 1-4 weeks pre-op. Setting/experience - first 20 cases in the University of Pittsburgh, USA programme from October 1994 to February 1995.
Snell	Consecutive case series. n=20 95% followed up to 3 months. No information on assessment of outcome.	Diagnosis of emphysema in patients receiving optimal management. Bronchodilator FEV ₁ < 40% predicted. RV > 150% of predicted. Apical functionless emphysematous lung on CT and VQ with relative preservation of basal lung function.	Inability to complete pulmonary rehabilitation. Aged > 75 years. Body mass index < 16kg/m ² or 27kg/m ² . Previous thoracotomy or extensive pleural disease. Alpha 1 antitrypsin deficiency, bronchiectasis or asthma. Tobacco use within the last 3 months. Other major medical illness including psychiatric disorders. Prednisolone dosage >10mg/day. PA carbon dioxide >55mmHg or PA oxygen <45mmHg on air. 6 MWD < 150m. PA pressure > 50mmHg.	Stapling with BPS buttressing. Bilateral. Via median sternotomy. 8 weeks pulmonary rehabilitation pre-op.	Pulmonary function tests. 6MWD. Dyspnoea - MMRC score.	Baseline data - used best results obtained pre-op. Setting/experience - early experience in Australia. September 1995 to February 1997.
Stammerberger	Consecutive case series. n=42 85% followed up to 3 months. 69% to 6 months (data not included). No information on assessment of outcome.	Severe COPD. FEV ₁ <35% predicted. Considerable hyperinflation - TLC >130% and RV >200%. Flattened diaphragm. High motivation. No smoking for 6 months. No further improvement possible on medical management.	Aged > 75 years. PA carbon dioxide > 55mmHg. Diffusing capacity for carbon monoxide <20% of predicted. Bronchiectasis, acute broncho-pulmonary infection, neoplastic disease with a life expectancy of 2 years or psychiatric disturbance. Significant coronary heart disease or marked pulmonary hypertension (mean PA pressure 30mmHg).	Stapling. Bilateral via thoracoscopy. No systematic pulmonary rehabilitation.	Pulmonary function tests. 6MWD Dyspnoea - MMRC scale.	Baseline data - no information. Setting/experience - results of experience in Switzerland which began in Jan 1994 to Sept 1996. NB. 12MWD results halved to give 6MWD.

Zenati	Consecutive case series. N=35 86% followed up to 3 months. No information on assessment of outcome.	Patients who met the criteria for LVRS and lung transplantation. End stage diffuse emphysema. Severely impaired quality of life despite maximal medical therapy. Post bronchodilator FEV ₁ < 30% predicted. Disabling dyspnoea at <50 yards walking.	PA pressure > 55mmHg. Smoking within the last 3 months. Large bullae with underlying compressed lung on CT. Morbid obesity > 1.5 lean body weight. Unstable coronary heart disease. End-stage cancer. Non-ambulatory. Ventilator dependent. Previous thoracic surgery.	Laser and stapling with BPS buttressing. Bilateral and unilateral. Open and closed. No pulmonary rehabilitation.	Pulmonary function tests. 6MWD. Dyspnoea - Mahler index and Borg scale.	Baseline data - no information. Setting/experience - 18 month experience at Pittsburgh Medical Centre, USA from July 1994 to December 1995.
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Abbreviations use in table:

6MWD	six minute walking distance
CT	computerised tomography
VQ	ventilation perfusion
BPS	bovine pericardial strips
FRC	fixed residual capacity
RV	residual volume
FVC	forced vital capacity
PA	pulmonary artery
FEV ₁	forced expiratory volume in 1 second
TLC	total lung capacity
MMRC	modified Medical Research Council
ATS	American Thoracic Society

Appendix VIII

Results of all included studies for mortality, length of stay, dyspnoea, QOL and supplemental O²

Study Ref.	Deaths	QOL	Dyspnoea	Supplemental O ²	Mean LOS (days)
Argenziano	6/92 < 30 d. (6%) 8/86 > 30 d. (9%) Overall 14/92 (15%)		MRC score pre 4.1 ± 0.8 post 1.7 ± 1.3		
Bagley	3/55 hospital (5%) 3/52 home (6%) overall 11%	Mean change on CRQ Fatigue - 3.16 [p0.0001] Emotional function - 4.84 [p0.0031] Mastery - 3.61[p0.0005]	Mean change on CRQ score 5.84 [p0.0001]	Pre 41/55 (74%) v. Post 25/42 (60%)	overall 18[6-76] elective 16[6-76] urgent 33[16-56]
Bousamra	3/45 hospital (7%) 2/42 home (5%) overall 9%			Continuous; Pre 18/45 (40%) Post 3/37 (8%) On exertion; Pre 9/45 (20%) Post 13/37 (35%) Overall; Pre 60% Post 43%	16
Cooper	6/150 <90d. (4%) 4/144 >90 d. (3%) overall 7%	SF36 n = 108 compared with 1 year ago; 78% much better 20% somewhat better 1% about the same 1% somewhat worse 0% much worse NHP areas where significant improvement occurred [p<0.05] at 6months; physical mobility energy vitality Areas of general improvement (not statistically significant) emotional reaction job or work	MRC score pre 2.8 v. post 1.2 Mahler Index pre 0.83 v. post 2.2	<u>6 months</u> Continuous; Pre 52% v. Post 16% [p0.001] Overall; Pre 92% v. Post 44% [p0.001] <u>1 year</u> Continuous; Pre 58% v. Post 16% Overall; Pre 92% v. Post 51% <u>2 years</u> Continuous; Pre 26% v. Post 0% Overall; Pre 84% v. Post 32%	13.5 (median 10) Last 50 cases - 10 (median 7)

		looking after home or home life sex life interests and hobbies; enjoyment of holidays sleep physical functioning general health social functioning mental health			
Cordova	0/25	mean Sickness Impact Profile scores for 76% Pre 7 Post 18 p<0.0002 Physical scores 4 v. 13 p<0.008 Psychosocial scores 4 v. 11 p<0.02			
Criner	0/3				
Daniel	1/17 day 12 (6%)	79% expressed a marked improvement 17% somewhat better 4% worse		Continuous; Pre 7/17 (41%) v. Post 1/17 (6%) On exertion; Pre 2/17 (12%) v. Post 6/17 (35%) Overall; Pre 9/17 53% v. 7/17 41%	13.6 (range 6-48)
Eugene ^a	1/44 day 15 (2%) 2/43 days 40&50 (5%) 2/41 days 46&90 (5%) 3/39 <9 m. (8%) 4/36 <2 y. (11%) overall 27%		34/38 reported a subjective improvement Borg pre 7.6 v. post 4.65 [p<0.01] MMRC pre 3.9 v. post 2.35 [p<0.01]	Continuous; Pre 80% v. Post 45% [p<0.01]	12
Eugene ^b	0/28 hospital 3/28 home (11%)		22/28 (78.6%) reported a subjective improvement.	Pre 82% v. Post 60.3%	
Keller	0/25		BDT to TDI functional impairment mean increase from 1.0 (SD 6.3) to 1.72 (SD 0.7) magnitude of effort mean increase from 1.16 (SD 0.54) to 2.12 (SD 0.8) magnitude of task mean increase from 1.20 (SD 0.57) to 2.28 (SD 0.7) mean transitional focus score		median 7days

LVRS for COPD

			(overall) 6.12 (SD 2) from BDI of 3.36 (SD 1.47)		
Kotloff ^{MS}	5/80 < 30 d. (6%) 6/75 > 30 d. (8%) 11/80 > overall (14%)				22 (4-229)
Kotloff ^{VATS}	1/40 < 30 d. (2%)				simultaneous 15 (4-117) staged 25 (12-63) overall 20 (4-117)
Little	3/55 overall (5%)				12.9 (SD 1.4)
McKenna	5/166 < 30 d. (3%) 14/166 > 30 d. to 1 y.(8%) 17/166 overall (10%)		MMRC Pre-2.9 post 1.9 (<0.0001)	94/166 to 48/166	11.4 ± 1.1 unilateral 10.9 ± 1.1 bilateral 11.1 ± 1.1 overall
Miller	3/53 hospital (6%) [1 early day 9 2 late days 36&59] 2/50 home (4%) [days 50&67] overall 9%		36/40 significant improvement 3/40 no change 1/40 worse	Pre 47/53 (88%) v. Post 7/40 (17%)	range 10-59 days
Sciurba	0/20		TDI n=18 5.1 (SD 1.8) [p<0.001]		
Snell	1/20 day 28 (5%)		MRC score pre 2.1 (SD 0.8) v. post 3.4 (SD 0.5) [p<0.001]		17 (8-45)
Stammerberger	0/42 <30days 3/40 > 30days (7%)		MRC score pre 3.5 (SD 0.7) post 1.6 (SD 1.0)		13 (SD 5.5)
Zenati	0/35		BDI 0.9 (SD 0.4) TDI 1.65 (SD 0.6) Borg Pre 3.71 (SD 1.8) v. Post 2.4 (SD 1.2) [p<0.02]	On exertion; Pre 29/35 83% v. Post 14/30 46%	18 (SD 10)

Appendix IX

Probability Estimates for Decision Tree Chance Nodes

Options	Probability Estimate	Cumulative Probability
LVRS/early death v. survival	0.03 (v. 0.97)	0.03
LVRS/late death v. survival	0.1 (v. 0.9)	0.097
LVRS/survive/improvement	0.70	0.611
LVRS/survive/no improvement	0.30	0.262
No LVRS/early death v. survival	0 (v. 1)	0
No LVRS/late death v. survival	0.4 (v. 0.6)	0.4
No LVRS/survive/improvement	0	0
No LVRS/survive/no improvement	1	0.6

Mortality rates

Mortality rates for the intervention were obtained from the included studies. The IQR for early mortality (<30 days or hospital deaths) was 0-6%, and for late mortality (\geq 30 days or home deaths) was 1-8%.

The annual mortality rate for a population with a given FEV₁ of <0.75 litre has been estimated as 30%,^a and for a population with an FEV₁ <30% of predicted as around 10%, which declines rapidly with age. For example, a patient aged < 60 with an FEV₁ 40-49% of predicted (Stage II COPD) has a predicted mortality of around 25%.^b (Advanced age is, however, currently a contra-indication for LVRS.) A conservative estimate of the probability of death in 1 year *without* the intervention is thus around 0.2, or 0.4 over 2 years.

The probability of early death for patients *not* undergoing the procedure is clearly 0, and the natural history of COPD is such that all patients will continue to decline making the probability of improvement without the intervention also 0.

Subjective Improvements

Estimates for the probabilities of improvement were obtained from those included studies which measured subjective improvement in some way and from objective data on supplemental oxygen use.

Cooper recorded data using the SF36 collected data on 108 patients of whom,
 compared with 1 year ago;
 78% were much better
 20% were somewhat better
 1% were about the same
 1% were somewhat worse
 0% were much worse

^a American Thoracic Society. Standards for the diagnosis and care of patients with chronic pulmonary disease. *American Journal of Respiratory and Critical Care Medicine* 1995;152(suppl.):S77-S120

^b The COPD Guidelines Group of the Standards of Care Committee of the British Thoracic Society. BTS Guidelines for the Management of Chronic Obstructive Pulmonary Disease. *Thorax* 1997; 52 (suppl. 5): S1-S28

In the study by Daniel 79% expressed a marked improvement, 17% were somewhat better and 4% were worse.

Around 66% of those requiring oxygen either on exertion or continuously did not require it after the procedure

A conservative estimate of the probability of improvement after the intervention is probably somewhere around **0.7**.

The calculation of the cumulative probabilities derived from the decision model for all outcomes is outlined below.

Cumulative Probabilities as derived from the Decision Tree.

1. LVRS

Product	Probability of early death	Probability of late death	Probability of outcome
0.03	0.03		early death
0.097	0.97	0.1	late death
0.611	0.97	0.9	0.7 improvement
0.262	0.97	0.9	0.3 no improvement

2. Medical Management

Product	Probability of early death	Probability of late death	Probability of outcome
0	0		early death
0.4	1	0.4	late death
0	1	0.6	0 improvement
0.6	1	0.6	1 no improvement

Appendix X

Utility Analysis

EQ-5D

No good quality data on quality of life based on the EQ-5D was identified. Unpublished data from a small pilot study of the effectiveness of LVRS^a suggests that typical candidates for the operation will have a starting EQ-5D of around **37** and a post-operative EQ-5D of between **64** and **88**. Given the limitations of this study and supporting information (outlined below) obtained from other relevant studies, the point estimates for EQ-5D were taken as **40** pre-operatively and **70** post-operatively. Patients who got worse either post-operatively or through general deterioration were assigned a utility score of **30**. Other data from this study cross-checked against the results of the review suggested that the populations were similar.

Staging and LVRS

The table below summarises the basis for the American Thoracic Society system for COPD.

American Thoracic Society staging system for COPD^b

Stage I	FEV ₁ of >49% of predicted
Stage II	FEV ₁ of 35-49% of predicted
Stage III	FEV ₁ of <35% of predicted

The results of the FEV₁ for the included studies suggests that most patients eligible for LVRS can be crudely classified as having Stage III COPD (mean FEV₁ 26% of predicted) and will move post-operatively to Stage II (mean FEV₁ 37% of predicted). Although this information was used partially as the basis for the utility estimates, its limitations, particularly in relation to the poor correlation between physiological and functional outcomes, should be borne in mind (see text of report).

SGRQ and EQ-5D

The table below summarises the SGRQ scores and FEV₁ data for studies which collected data on both outcomes. In addition, results linking EQ-5D data with FEV₁ data or SGRQ data are also presented. The mean SGRQ score for Stage II COPD was 53 (±9). For ease of analysis the mean SGRQ score for Stage II (post-operative patients) was assumed to be around 50. Jones and colleagues have estimated that an intervention which is moderately or very effective will result in an 8-12 point change in SGRQ score.^c Donald and colleagues have shown that a change in 6MWD

^a SchARR Intervention surgery for heterogeneous emphysema in Leicester and Sheffield (ISLAS study) : cost-effectiveness, quality of life and physiological benefits for patients. University of Sheffield. December 1998

^b American Thoracic Society. Standards for the diagnosis and care of patients with chronic pulmonary disease. *American Journal of Respiratory and Critical Care Medicine* 1995; 152(suppl.): S77-S120

^c Jones PW, Issues concerning health-related quality of life in COPD. *Chest* 1995;107(Supplement):187S-193S

of 48 metres is equivalent to a clinical improvement where patients described themselves as “a little bit better”.^a Given that the mean improvement in the included studies was 80 metres, it can be assumed that the intervention is moderately effective. This would therefore bring about a change in SGRQ of around 10 points. Using this information and that from the table, the SGRQ of Stage III COPD (pre-operative patients) is assumed to be around 60. Additional, unpublished data^b suggests that patients with an SGRQ of 78 will have an EQ-5D score of 56, and in the study by Harper and colleagues an SGRQ of 65 equates with a EQ-5D of 53.^c Based on this Stage III patients with a SGRQ of around 60 are assumed to have an EQ-5D of 50. Stage II patients can be assumed to have an EQ-5D of 60.

^a Donald A, Redelmeier, Ahmed M Interpreting small differences in functional status: the six minute walk test in chronic lung disease patients. *American Journal of Critical Care Medicine* 1997;155:1278-1282

^b Wildman MJ, Groves J Lenaghan J et.al. Hospital mortality, functional capacity, health related quality of life and acute physiology in 242 patients hospitalised with exacerbations of chronic obstructive pulmonary disease. Unpublished.

^c Harper R, Brazier JE, Waterhouse JC et.al. Comparison of outcome measures for patients with chronic obstructive pulmonary disease (COPD) in an outpatient setting. *Thorax* 1997;52:879-887

Summary of SGRQ and EQ-5D scores and FEV₁ data by COPD stage for identified studies which collected data on both outcomes.

Study	Mean FEV ₁	SGRQ	EQ-5D
Stage I >49%			
Ferrer ^a	n/a	34	
Stage II 35-49%			
Wedzicha ^b	36%	58	
Osman ^c	39%	53	
Okubadejo ^d	42%	55	
Eiser ^e	46%	47	
Harper ^f	47%	65	52.4
Ferrer ⁱ	n/a	42	
Wildman ^g		77.7	56.0
Stage III <35%			
Ferrer ^a		55	

The table below summarises the utilities assigned to each of the key outcomes in the model for the SGRQ and the EQOL

Summary of utility estimates for key outcomes in the Decision Model.

Outcomes	Stage	SGRQ	EQOL
LVRS/survive/improvement	II	50	70
LVRS/survive/ no improvement/worse	III	60	40/30
LVRS/early mortality	n/a	0	0
LVRS/die late	n/a	0	0
no LVRS/die	n/a	0	0
no LVRS/survive/improvement	II	50	70
no LVRS/survive/no improvement	III	60	40

^a Ferrer M, Alonso J, Morera J et.al. Chronic obstructive pulmonary disease stage and health-related quality of life. *Annals of Internal Medicine* 1997; 127(12):1072-1079

^b Wedzicha JA, Bestall JC, Garrod R et.al. Randomized controlled trial of pulmonary rehabilitation in severe chronic obstructive pulmonary disease patients, stratified with the MRC dyspnoea scale. *European Respiratory Journal* 1998;12:363-369

^c Osman IM, Godden DJ, Friend JA and Douglas JG. Quality of life and hospital re-admission in patients with chronic obstructive pulmonary disease. *Thorax* 1997;52(1):67-71

^d Okubadejo AA, Jones PW and Wedzicha JA, Quality of life in patients with chronic obstructive pulmonary disease and severe hypoxaemia. *Thorax* 1996; 51:44-47

^e Eiser N, West C, Evans S et.al. Effects of psychotherapy in moderately severe COPD: a pilot study. *European Respiratory Journal* 1997;10:1581-1584

^f Harper R, Brazier JE, Waterhouse JC et.al. Comparison of outcome measures for patients with chronic obstructive pulmonary disease (COPD) in an outpatient setting. *Thorax* 1997;52:879-887

^g Wildman MJ, Groves J Lenaghan J et.al. Hospital mortality, functional capacity, health related quality of life and acute physiology in 242 patients hospitalised with exacerbations of chronic obstructive pulmonary disease. Unpublished.

Calculation of QALY's using the EQ-5D

1. LVRS/survive/improvement	1 week @ 0.3	= 0.005769	
	1 week @ 0.4	= 0.007692	
	1 week @ 0.5	= 0.009615	
	1 week @ 0.6	= 0.011538	
	<u>100 weeks @ 0.7</u>	<u>= 1.346154</u>	
	Total	1.380769	
2. LVRS/survive/no improvement	1 week @ 0.3	= 0.005769	
	<u>103 weeks @ 0.4</u>	<u>= 0.792308</u>	
	Total	0.798077	
	OR		
	104 weeks @ 0.3	= 0.6	
3. LVRS/early death	2 weeks @ 0.3	= 0.011538	
	OR		
	1 week @ 0.3	= 0.005769	
	<u>1 week @ 0.4</u>	<u>= 0.007692</u>	
	Total	0.013462	
4. LVRS/late death	1 week @ 0.3	= 0.005769	
	1 week @ 0.4	= 0.007692	
	1 week @ 0.5	= 0.009615	
	1 week @ 0.6	= 0.011538	
	<u>48 weeks @ 0.7</u>	<u>= 0.646154</u>	
	Total	0.680769	
		OR	
	1 week @ 0.3	= 0.005692	
	<u>51 weeks @ 0.4</u>	<u>= 0.392308</u>	
	Total	0.398077	
	OR		
	52 weeks @ 0.3	= 0.3	
5. no/LVRS/early death	2 weeks @ 0.4	= 0.015385	
6. no/LVRS/late death	52 weeks @ 0.4	= 0.4	
	OR		
	52 weeks @ 0.3	= 0.3	
7. no LVRS/survive/improve	1 week @ 0.4	= 0.007692	
	1 weeks @ 0.5	= 0.009615	
	1 week @ 0.6	= 0.011538	
	<u>101 weeks @ 0.7</u>	<u>= 1.359615</u>	
	Total	1.388462	
8. no LVRS/survive/no improvement	104 weeks @ 0.4	= 0.8	
	OR		
	104 weeks @ 0.3	= 0.6	

Appendix XI

Cost Analysis

A full breakdown of individual unit costs and their sources, is presented in the table below. These unit costs form the basis of the cost estimates for different events and treatment options in the management of COPD.

Individual unit costs and their sources in the management of COPD

UNIT	Number/Price	COST (£'S)	SOURCE	DATE
Intervention				
LVRS	total per case	6200	Shropshire HA	1998
District Nurse	daily visit for 2 weeks	490	PSSRU ^a	1997
Total	@ £35 each	6690		
Maximum Medical Management (MMM)				
(all over 1 year)				
Ventolin Inhaler	2 per month @ £2.30	55		
Atrovent Inhaler	2 per month @ £4.21	101		
Phyllocontin Continus	2 per month @ £3.29	79		
Becloforte Inhaler	2 per month @ £23.10	554	MIMS ^b (COPD guidelines, validated by local practitioner)	
Serevent Inhaler	2 per month @ £28.60	686		
Total drug costs		1475		1998
Oxygen Concentrator	15 hours per day	800	DeVilbiss Healthcare	1998
GP visits	1 per month @ 30 each	360	PSSRU [†]	1997
Outpatient Appointment	2 per year @ £52 each	104	PSSRU [†]	1997
Total		2739		
Pulmonary Rehabilitation				
	per 8 week course	500	estimate from existing research ^{c,d} (validated by local practitioner)	1998
Emergency Admission				
GP visit	(at 1 per year)			
Ambulance Transfer	1 @ £30	30	PSSRU [†] and Acute Care 96 ^e	1996/97
A/E attendance	1 @ £163	163		
Inpatient Days	1 @ £178	178		
	10 @ 195	1950		
Total		2321		
Death		2321	rough equivalent to emergency admission.	1996/97

^a Netten A and Dennett J Unit costs of health and social care. PSSRU, University of Kent at Canterbury, 1997

^b MIMS (Monthly Index of Medical Specialities) Haymarket Publishing Services Limited, London, 1998

^c Tjep BL Disease management of COPD with pulmonary rehabilitation. Chest 1997;112(6):1630-56

^d Reina-Rosenbaum R, Bach JR, and Penek J The cost/benefits of outpatient-based pulmonary rehabilitation. Arch of Phys Med Rehabil 1997;78:240-244

^e Acute Care 96. Healthcare Resource Groups National Statistics 1995/96. CHKS Limited, Alcester, Warwickshire, 1996

The table below summarises the cost estimates over one year for the main treatment options and events which might occur in a population of people with severe COPD, derived from the unit costs outlined above.

Cost estimates for the main treatment options and events.

Treatment/event	Cost Estimate	Comments
LVRS	£6690	
MMM - Maximum Medical Management	£2739	
RMM - Reduced Medical Management	£1960	MMM minus 50% steroids, 50% O ²
PR - Pulmonary Rehabilitation	£500	one course
EA - Emergency Admission	£2321	
Death	£2321	Except early post-LVRS deaths

The total costs for each outcome in the decision tree over 2 years were estimated using different combinations of treatment options and events, generating best and worst case estimates where appropriate. These calculations are presented below.

Calculation of cost estimates for main outcomes.

1. LVRS/early death	Year 1	LVRS	6690	
		<u>PRx1</u>	<u>500</u>	
				7190
2. LVRS/late death	Year 1	LVRS	6690	
		PRx2	1000	
		MMM	2739	
		<u>Death</u>	<u>2321</u>	
				12750
		OR		
	Year 1	LVRS	6690	
		PRx2	1000	
		RMM	1960	
		<u>Death</u>	<u>2321</u>	
				11971
3. LVRS/survive/improvement	Year 1	LVRS	6690	
		PRx2	1000	
		RMM	1960	
	Year 2	RMM	1960	
		<u>PRx1</u>	<u>500</u>	
				12110
		OR		
	Year 1	LVRS	6690	
		PRx2	1000	
		MMM	2739	
	Year 2	MMM	2739	
		<u>PR x1</u>	<u>500</u>	
				13668

4. LVRS/survive/no improvement	Year 1	LVRS	6690
		PRx2	1000
		MMM	2739
	Year 2	MMM	2739
		PRx1	500
<u>EAx1</u>		<u>2321</u>	
		15989	
5. no LVRS/early death	Year 1	Death	2321
6. no LVRS/late death	Year 1	PRx1	500
		MMM	2739
		<u>Death</u>	<u>2321</u>
			5560
7. no LVRS/survive/improvement	Year 1	PRx1	500
		RMM	1960
	Year 2	PRx1	500
		<u>RMM</u>	<u>1960</u>
			4920
8. no LVRS/survive/no improvement	Year 1	PRx1	500
		MMM	2739
		EA x1	2321
	Year 2	PRx1	500
		MMM	2739
		<u>EA</u>	<u>2321</u>
			11120

Appendix XII

Cost-Utility Analysis

Total expected cost of LVRS:	£13041
Total expected QALY's for LVRS:	1.09 EQ-5D

Total expected cost of Medical Management:	£8896
Total expected QALY's for Medical Management:	0.64 EQ-5D

Thus;

Additional cost of LVRS over Medical Management:	£4145 without carer
Additional QALY's gained :	0.45

Additional cost per QALY gained:	$£4145/0.45 = £9211$
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Appendix XIII

Sensitivity Analysis

IHQL

No data was available which facilitated estimates of IHQL for COPD patients. Estimates in this instance were made using the 3-dimensional classification based on knowledge about patients before and after LVRS obtained from descriptions in the literature and informal discussion with and observation of individual cases. The key sources were;

A review of LVRS described a group of patients who pre-operatively were dependent on others for all their activities of daily living, the majority of which were required continuous supplemental oxygen.^a

Similarly, Cooper describes a pre-operative population who are unable to shower or bathe, get dressed alone or leave the house without great difficulty. Again, most require continuous supplemental oxygen.^b

A patient who had undergone the operation at a local thoracic surgery unit described his pre-operative state as being very similar to those above. In addition, he described troublesome pain and stiffness in his limbs and chest. One year post-operatively he was able to perform all his own activities of daily living, no longer required supplemental oxygen and even undertook light DIY and gardening jobs around the house.^c

The information within the included studies for dyspnoea and supplemental oxygen are useful indicators for improvements in quality of life after the intervention. Interpretation of the dyspnoea results indicates that in all series patients experienced significant improvements in their degree of dyspnoea. The mean post-operative score for the MMRC scale of 1.8, places patients almost midway on a scale where 0 equates to dyspnoea only on strenuous exertion and 4 equates to life-limiting dyspnoea which prevents the patient from leaving the house or dressing. Most patients scored between 3 and 4 before the intervention. This implies considerable improvements in quality of life suggesting that post-operatively the majority of patients would be able handle their own activities of daily living, get out and about more easily and even undertake light jobs around house and garden.

The results for supplemental oxygen present a slightly conflicting picture. In those studies which collected this data, around 50% of cases still required supplemental oxygen. For about 20% this was required continuously and for the other 30%, only on exertion. This data, suggests that relative improvements in dyspnoea may

^a Lavell D and Higgins V, Lung Surgery. When less is more. Registered Nurse 1995;July:40-45

^b Cooper J, The history of surgical procedures for emphysema. Annals of Thoracic Surgery 1997;63:132-319

^c Personal communication

overestimate absolute improvements. Nevertheless it is the relative improvements which are probably the most important as far as quality of life improvements are concerned.

Finally, the relationship between anxiety and depression and COPD is well-documented.^a SGRQ scores of around 50 are associated with clinically significant depression.

On this basis, using the IHQL 3-dimensional classification, typical health states for baseline, improved and deteriorated patients might be as follows;

Baseline (Stage III COPD) - 0.648 (D6P3E3)

Disability - Confined to chair, therefore can only get out with assistance. Can only do the lightest of tasks e.g. switch on the TV. Can feed self, but needs help with all other self care activities. Very limited ability to perform role functions.

Discomfort (Physical) - Moderate pain.

Distress (Emotional) - Moderate distress: anxious and depressed most of the time, but happy and relaxed some of the time.

Deterioration - 0.498 (D7P3E4)

Disability - Confined to bed. Needs help with all self-care activities. Minimal ability to perform role functions.

Discomfort (Physical) - Moderate pain.

Distress (Emotional) - Moderate distress: anxious and depressed most of the time, but happy and relaxed some of the time.

Post-operative (Stage II COPD) - 0.861 (D4P2E2)

Disability - Able to get around house and do lighter physical work. Some difficulty in getting around community due to weakness or other physical limitations. Can perform all self-care activities. Ability to perform role functions limited.

Discomfort (Physical) - Slight pain.

Distress (Emotional) - Slight distress: happy and relaxed most of the time, but anxious and depressed some of the time.

^a Eiser N, West C, Evans S et.al. Effects of psychotherapy in moderately severe COPD: a pilot study. European Respiratory Journal 1997;10:1581-1584

Calculation of QALY's using the IHQL

1. LVRS/survive/improvement	1 week @ 0.50	= 0.009615
	1 week @ 0.65	= 0.0125
	<u>102 weeks @ 0.86</u>	= 1.686923
	Total	1.709038
2. LVRS/survive/no improvement	1 week @ 0.50	= 0.009615
	<u>103 weeks @ 0.65</u>	= 1.2875
	Total	1.297115
	OR	
	104 weeks @ 0.50	= 1.0
3. LVRS/early death	2 weeks @ 0.65	= 0.025
	OR	
	1 week @ 0.50	= 0.009615
	<u>1 week @ 0.65</u>	= 0.0125
	Total	0.022115
4. LVRS/late death	1 week @ 0.50	= 0.009615
	1 week @ 0.65	= 0.0125
	<u>50 weeks @ 0.86</u>	= 0.826923
	Total	0.849038
	OR	
	1 week @ 0.50	= 0.009615
	<u>51 weeks @ 0.65</u>	= 0.6375
	Total	0.647115
	OR	
	52 weeks @ 0.50	= 0.5
5. no/LVRS/early death	2 weeks @ 0.65	= 0.025
6. no/LVRS/late death	52 weeks @ 0.65	= 0.65
	OR	
	52 weeks @ 0.50	= 0.5
7. no LVRS/survive/improve	2 weeks @ 0.65	= 0.025
	<u>102 weeks @ 0.86</u>	= 1.686923
	Total	1.711923
8. no LVRS/survive/no improvement	104 weeks @ 0.65	= 1.3
	OR	
	104 weeks @ 0.50	= 1.0

Carer costs

The cost of the carer represents an attempt to quantify and incorporate the costs of "care". It is acknowledged that in many instances this will not be quantifiable in terms of monetary costs to the NHS, and often these costs will be borne by other sectors.

Carer (untrained)	1 hour per day @ £8 per hour	2920	PSSRU ^a	1997
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Incorporating carer costs into the model gives a total cost for Maximum Medical Management of £5695. The costs for each outcome are as for those in Appendix XI substituting this cost (£5695) for that of Maximum Medical Management without carer costs (£2739).

Cost Utility Analysis

Total expected cost of LVRS:	£14857 with carer	£13041 without carer
Total expected QALY's for LVRS:	1.09 EQ-5D	1.44 IHQL

Total expected cost of Medical Management:	£13568 with carer	£8896 without carer
Total expected QALY's for Medical Management:	0.64 EQ-5D	1.04 IHQL

Thus;

Additional cost of LVRS over Medical Management:	£1289 with carer	£4145 without carer
Additional QALY's gained :	0.45	0.4

Additional cost per QALY gained:	EQ-5D with carer	£1289/0.45 = £2864
	EQ-5D without carer	£4145/0.45 = £9211
	IHQL without carer	£4145/0.4 = £10362

^a Netten A and Dennett J Unit costs of health and social care. PSSRU, University of Kent at Canterbury, 1997

Appendix XIV

List of Abbreviations

LVRS	Lung Volume Reduction Surgery
COPD	Chronic Obstructive Pulmonary Disease
EQ-5D	EuroQol
QALY	Quality Adjusted Life Year
BTS	British Thoracic Society
FEV ₁	Forced Expiratory Volume in 1 second
CO ₂	Carbon Dioxide
QOL	Quality of Life
AHCPR	Agency for Health Care Policy and Research
ARIF	Aggressive Research Intelligence Facility
IHQL	Index of Health Related Quality of Life
IQR	Inter-quartile Range
VATS	Video-assisted Thoracic Surgery
MS	Median Sternotomy
6MWD	6 Minute Walking Distance
CRQ	Chronic Respiratory Disease Questionnaire
SF36	Short Form 36
SIP	Sickness Impact Profile
MMRC	Modified Medical Research Council
BDI	Baseline Dyspnoea Index
TDI	Transitional Dyspnoea Index
BFS	Baseline Focal Score
TDS	Transitional Focal Score
SMD	Standardised Mean Difference
SGRQ	St. George's Respiratory Disease Questionnaire
VC	Slow Vital Capacity
FRC	Functional Residual Capacity
TLCO	Diffusing Capacity for Carbon Monoxide or Gas Transfer Factor