NHS England

Evidence Review:

Robotic assisted lung resection for primary lung cancer

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Prepared by	Turnkey Clinical Evidence Review Team on behalf of NHS England Specialised Commissioning

Contents

1. Introduction

The appropriate treatment for lung cancer depends on the type of cancer, how far it has spread and how good one's general health is. The treatment of lung cancer is a rapidly developing field. Existing surgical techniques include Video Assisted Thoracoscopic Surgery (VATS) and open thoracotomy. VATS is an evolving minimally invasive technique that is increasingly applied in situations where traditional open thoracotomy has long been used for lung resections. VATS may have a number of benefits over open thoracotomy including smaller incisions, less blood loss, fewer complications and faster recovery times. However, VATS has not been widely adopted by the surgical community. In 2013/14 30% of resections for primary lung cancer were performed by VATS (SCTS Return 2013/14) in part due to the steep learning curve. Thus the majority of patients currently receive open thoracotomy.

Robotic Assisted Thoracoscopic Surgery (RATS) is an alternative minimally invasive operation platform with a number of potential benefits including 3DHD vision affording 360 degree vision of the whole of the inside of the chest, a fully articulated arm which allows more complex operations in tight spaces and greater ease of use for the surgeon due to the better ergonomics.

2. Summary of results

Overall the quality of evidence to address the clinical effectiveness questions around the use of RATS in treatment of lung cancer is limited as the predominant sources of evidence are single-centre case series reports. There are no large cohorts or randomised control trials (RCTs) comparing RATS and alternative thoracic surgery techniques. Systematic reviews and meta-analysis identified in the literature are limited by the quality and type of studies available.

In summary, robotic lobectomy is a feasible, safe, technically reproducible and oncologically sound surgical treatment for early-stage lung cancer. There may be advantages in cancer upstaging, reduced length of stay, complications, blood loss and earlier recovery. Disadvantages include capital costs, the learning curve for the team, and the lack of tactile feedback. Early experiences suggest that the learning curve is approximately 20 cases for experienced surgeons. There was no evidence relating outcome to volume of cases per surgeon or centre.

Learning curve:

The literature has suggested that it takes surgeons 18-20 cases (Brooks et al, 2015) and approximately one year learning time to go from maximally invasive techniques to minimally invasive robotic techniques which is primarily related to the positioning of trocars in the chest wall, accessibility of the appropriate surgical tools, ability to determine the use of correct robotic arms, and understanding the patient positioning (Brooks et al, 2015). Additional learning aspects of robotic-assisted thoracic lobectomy were cited as the loss of tactile senses, the increased time of the procedure, and the need for a surgical assistant to fire the stapler. A stapler that the surgeon can use has been developed and is expected to be introduced soon.

Safety and peri-operative outcomes:

Safety and perioperative outcomes in relation to this evidence review are defined as operation times, length of stay, conversion to open procedures, estimated blood loss, rates of morbidity and mortality.

A systematic review of twelve observational studies including one multi-institutional retrospective review of 325 consecutive patients that looked at long term outcomes, concludes that RATS is a safe surgical option for lobectomy, thymectomy and mediastinal node resection in early stage lung cancers (Brooks et al, 2015). A recent meta-analysis of perioperative morbidity data from eight observation studies did not find any significant difference in perioperative morbidity rates (RR, 1.02; 95% CI, 0.94-1.10; P=0.605) between RATS and VATS for lung cancer. There was no significant difference in overall perioperative mortality rates (RR, 0.28; 95% CI 0.06-1.25; P=0.095) based on meta-analysis of data from four of the eight studies (Ye et al, 2015).

The operative complications for RATS were identified as
- Atelectasis (1-22%)
- Atrial Fibrillation (3-19%)
- Air Leak (3-13%)
- ARDS (1-13%)
- Pneumonia (1-5%)

Commonest complications were arrhythmias and air leaks.

Velez-Cubian et al, 2015 combined data taken from 23 studies identified in a literature search with a retrospective case series (n=208) from their own institution. Data taken from the literature was divided into two groups based on year of publication and the authors' own data was divided into an early series and a late series of procedures. In a solely descriptive analysis without statistical tests of comparisons, the authors described how mortality and morbidity rates were comparable in the first two groups.

Published Studies	**2005-2010**	**2011-2014**
Operative Time (mins)	150- 240	90-242 ns
Conversion Rates	0-19%	0-11% - *more difficult cases, larger tumours, advanced stages, patients with pre induction chemo
Mortality Rates	0-5%	0-2%
Morbidity Rates	11-39%	11-44%
Own Centre Data		
LOS (days)	3-11	2-6
Morbidity rates	43%	38%
Mortality rates	0.5%	0.2%
Operative Time	179	172
Conversion rates	9.6%	13% (*and also hybrid procedures)

Quality of Life outcomes:

There was limited evidence for impact on quality of life. Balduyck et al, 2011 reports that patients who underwent RATS returned to pre surgery levels of physical, role and social functioning sooner than those who underwent open sternotomy. Significant limitations in the study design prevent extrapolation of these findings beyond the study population.

Oncological outcomes:

Nodal upstaging is a surrogate measure of the quality of the surgery. Higher rates of nodal upstaging are preferred and the ability to assess more nodes provides a strong prognostic tool.

Several studies have reported that the open thoracotomy approach has higher mean total number of N2 lymph nodes retrieved than the VATS approach (Velez-Cubian et al, 2015). The rate of nodal upstaging for RATS (10.9%) appeared to be superior than for VATS and similar to thoracotomy data by clinical tumour stage. Velez-Cubian's own cohort had an overall 30% upstaging rate and a 19% nodal upstaging rate. Wilson et al, 2014 demonstrated upstaging in 33 out of 302 patients, however 2 year disease free survival and overall survival at 70.2% and 88% remained similar to VATS and Thoracotomy. Similar rates of lymph node upstaging and lack of an impact on 2 year disease free and overall survival was also shown by Lee et al, 2015. The inference is that RATS permits meticulous and detailed dissection and lymph node dissection that can improve early detection of metastatic disease. This more accurate staging will allow further appropriate adjuvant chemotherapy. A multi-centre study (Park et al, 2012) has also shown that RATS resulted in an overall 5-year survival for the group of 80%. By cancer stage there was 5 year survival of stage 1A cancers of 91%, 1B of 88% and 49% for all patients with stage II.

In Velez-Cubian et al, 2015 the oncological outcome was measured in terms of mediastinal nodal station dissection and upstaging rates. The oncological outcomes were not reported in the same comparative groups (literature review 2005-10; 2011-14) but instead a comparison was undertaken with the National Comprehensive Cancer Network (NCCN) database and one study identified by the authors. Mediastinal lymph node (LN) dissection and detection of occult mediastinal LN metastases were improved during robotic-assisted lobectomy for non-small-cell lung cancer, as demonstrated by an overall 30% upstaging rate, including a 19% nodal upstaging rate, in the cohort.

Published Studies	RATS (own centre data)	VATS (NCCN/NSLC database)	Open surgery (NCCN/NSLC) database
Assessment of mediastinal nodal stations			
Mean number of N2 LN stations dissected	3.7 +0.1	3.1 / 2.5	2.9 / 3.7
>3N2 LN dissected	98%	66%	58%
Individual N2 LNs retrieved	7.2 ± 0.3	2.5*	3.7*
Nodal upstaging rate			
cN0-to-pN2	8.2%	2.1-4.9%	1.9-5%
cN0-to-pN1	16.4%	8.8-15.9%	14.3-14.5%

*Damico TA et al, 2011

Cost effectiveness:

Data from US studies indicates open thoracotomy remains the most costly out of the three options with longer hospitalisation, intensive care and respiratory therapy use. The cost of RATS increases the minimal invasive surgery (VATS) cost by 3000 to 4500 USD per case. The key cost drivers of RATS were the capital costs, followed by cost of specific consumables (Swanson et al 2014, Deen et al 2014). Park et al, 2008 report further additional costs due to additional procedures undertaken for RATS cases. Current evidence is largely cost–comparisons of direct peri-operative costs. More studies are needed for evaluating the cost effectiveness and long term clinical benefit to the patients.

3. Research questions

What evidence is available on the clinical effectiveness of robot-assisted thoracic surgery compared to existing surgical techniques for lung resection?

What evidence is available on the cost effectiveness of robot-assisted thoracic surgery compared to existing surgical techniques for lung resection?

What is the impact of surgeon or centre volume on outcomes of robot-assisted thoracic surgery for lung resection?

4. Methodology

A review of published, peer reviewed literature has been undertaken based on the research questions set out in Section 3 and a search strategy agreed with the lead clinician and public health lead for this policy area. This has involved a PubMed search and search of the Cochrane database for systematic reviews, in addition to review of any existing NICE or SIGN guidance. The evidence review has been independently quality assured.

An audit trail has been maintained of papers excluded from the review on the basis of the inclusion and exclusion criteria agreed within the search strategy. The full list has been made available to the clinicians developing the policy where requested.

5. Results

A detailed breakdown of the evidence is included in the Appendix.

Appendix One

Level	Study design and			Outcomes					Reference	Other		
Level of evidence	Study design	Study size	Intervention	Category	Primary Outcome	Primary Result	Secondary Outcome	Secondary Result	Reference	Complications noted	Benefits noted	Comments
3	Case series	3015 patients across 24 studies	RATS	Clinical effectiveness of the intervention	Perioperative outcomes	Velez-Cubian et al 2015 combined data taken from 23 studies identified in a literature search with a retrospective case series (n=208) from their own institution. Data taken from the literature was divided into two groups based on year of publication, and the authors own data was divided into an early series and a late series of procedures. In a solely descriptive analysis without statistical tests of comparisons, the authors described how mortality and morbidity rates were comparable in the first two groups. Please see Evidence Review for detailed summary of results.	Oncological	The oncological outcomes were not reported in the same comparative groups (literature review 2005-10; 2011-14). The oncological outcome was measured in terms of mediastinal nodal station dissection and upstaging rates. Please see Evidence Review for detailed summary of results.	Velez-Cubian, Frank O.; Ng, Emily P.; Fontaine, Jacques P.; Toloza, Eric M.. Robotic-Assisted Videothoracoscopic Surgery of the Lung. Cancer Control 2015;102(1):40-49.	NA	Robotic assisted lobectomy surgery appears to be at least as safe as conventional videothoracoscopy . Benefits in decreased perioperative complications and shorter hospital length of stays have been demonstrated in the case series reviewed. Overall, the improved efficacy of lymph node dissection appears to be the key benefit of robotic technology.	This is a combined review of studies identified from literature and the data from authors' centre. Majority of studies included are retrospective case series. There are several limitations which impact the evidence quality including but not limited to: a. lack of systematic approach to comparison and presentation of data b. oncological outcome comparisons made as simple references with no further details such as comparability of population groups c. no attempt to adjust for potential confounders including site and complexity of procedure, surgical skills, etc

3	Other	1052	RATS	Safety of the intervention	Perioperative outcomes	On the basis of evidence tabled in the review, all twelve studies appear to conclude that RATS is a safe and effective surgical option for lobectomy/ mediastinal node resection/ thymectomy in early stage lung cancer. This included one multi-institutional retrospective review of 325 consecutive patients that looked at long term outcomes (Park et al 2012). Notably, Augustin et al 2011 showed in a case series that robot assisted treatment for early stage lung cancer is a reasonable and safe intervention with a 1 year survival rate of 100% for early stage cancer patients. The same authors reviewed 26 consecutive robotic-assisted and 26 consecutive conventional minimally invasive VATS lobectomies performed between July 2001 and July 2009 and found comparable perioperative outcomes, but a greater cost with no increase in clinical benefit to the patients (Augustin et 2013).	Learning curve	On the basis of evidence provided in the review, implementing a robotic assisted surgery programme is associated with a significant learning curve. Cerfolio et al 2011 conclude that the learning curve is approximately one year for a surgeon to go from maximally invasive techniques to minimally invasive robotic techniques, and this is primarily related to the positioning of trocars in the chest wall, accessibility of the appropriate surgical tools, ability to determine the use of correct robotic arms, and understanding the patient positioning. The main surgical disadvantages of robotic-assisted thoracic lobectomy was cited as the loss of tactile senses, the increased time of the procedure, and the need for a surgical assistant to fire the stapler. Meyer et al 2012 reported learning curve of 18 + 3 cases based on parameters of operative time, mortality, and surgeon comfort in a review of 185 cases.	Brooks, Paula. Robotic-Assisted Thoracic Surgery for Early-Stage Lung Cancer: A Review. AORN J 2015;21(4):409-414.	NA	-	Although this review is labelled a systematic review and its initial methodology conforms to this, it stops short and turns into a reporting of evidence from the including studies without any further analysis or conclusion. The studies included in the review are mostly case series. In view of the above limitations, the evidence has been rated at evidence level 3.
1+	Systematic	3379	RATS	Clinical effectiveness of the intervention compared to existing interventions	Perioperative outcomes	Meta-analysis of data on 3379 patients from 9 retrospective observational studies comparing RATS and VATS for lung cancer concluded the following: a. the overall perioperative morbidity rate was not significantly different between patients who underwent RATS when compared with patients who underwent VATS (RR, 1.02; 95% CI, 0.94–1.10; P = 0.605) (RR, 1.02; 95% CI, 0.94-1.10; P=0.605) with no significant heterogeneity across the studies. b. the overall perioperative mortality rate (data from 4 studies) was not significantly different between patients who underwent RATS when compared with patients who underwent VATS (RR, 0.28; 95% CI 0.06-1.25; P=0.095).	NA	-	Ye, Xiong; Xie, Liang; Chen, Gang; Tang, Ji-Ming; Ben, Xiao-Song. Robotic thoracic surgery versus video-assisted thoracic surgery for lung cancer: a meta-analysis. Interact Cardiovasc Thorac Surg 2015;():.	NA	RATS is comparable to VATS in terms of perioperative outcomes. VATS has been shown by RCTS to have improved outcomes compared with open thoracotomy for lung cancer.	This is a well conducted meta-analysis with evaluation of heterogeneity between studies, sensitivity analysis (for study inclusion and exclusion) and test for publication bias. The key limitation remain the lack of randomised control trials which reflects the state of the best clinical evidence available on the subject. There is potential for bias from variability in baseline patient characteristics, surgical skills and perioperative care. Longer term oncological outcomes were not considered.

3	Case series	331	RATS	Clinical effectiveness of the intervention	Perioperative outcomes	6.9% of procedures were converted to open thoracotomy. The median length of operations was 180 minutes, median length of stay was 4 days, an estimated blood loss during surgery was 47.85ml. The perioperative morbidity rate was 8.8% and 30 day mortality was 0.9%.	Oncological	All patients in the study underwent lymph node exploration. The mean number of lymph nodes excised was 5.34 (range 2-22) and the mean number biopsied was 4.8 (range 2-11).	Radkani, Pejman; Joshi, Devendra; Barot, Tushar; Williams, Roy F.. Robotic video-assisted thoracoscopic lung resection for lung tumors: a community tertiary care center experience over four years. Surg Endosc 2015;100(1):229-233; discussion 233-234.	NA	Study compares favourably with reported results in the literature and indicates advantage of lymph node dissection. There was no comparison with other surgical options.	This study described a case series of 331 patients who underwent RATS for early stage lung cancer by a single surgeon between 2009 and 2013.This is a retrospective case series without a comparable group of patients for control. The surgical learning curve has not been accounted for in the analysis.
2+	Cohort	211	RATS - Lobectomy	Clinical effectiveness of the intervention compared to existing interventions	Perioperative outcomes	The study reports a significantly longer operation time in the RATS group (161 min vs. 123 min p=0.02); no significant difference in length of stay 3 (1-11) for RATS vs 3 (1-33) for VATS. Significantly higher rate of morbidity in the VATS group 24% vs. 11% p = 0.05. No significant difference in perioperative mortality rate was observed.	Oncological	Median number of lymph nodes harvested was significantly higher in the RATS group 17 vs 11 p<0.001 in VATS. Nodal upstaging rate was 13.2% for RATS compared to 15.2% for VATS (p=0.72). When segregated by clinical T stage, nodal upstaging did not differ significantly between the two procedures. There were no significant difference in 2-year overall survival (RATS 95% vs VATS 88%, p = 0.40) and disease-free survival (93% vs 83%, p = 0.48).	Lee, Benjamin E.; Shapiro, Mark; Rutledge, John R.; Korst, Robert J.. Nodal Upstaging in Robotic and Video Assisted Thoracic Surgery Lobectomy for Clinical N0 Lung Cancer. Ann. Thorac. Surg. 2015;7(Suppl 2):S122-130.	NA	The study did not identify any significant differences in pathologic nodal upstaging, overall survival, or disease-free survival between a VATS and RATS approach for the treatment of clinically node-negative patients with lung cancer.	Retrospective study of 211 consecutive patients, split into two groups: those undergoing RATS (n= 53), VATS (n=158) with no significant difference in the tumour characteristics i.e. size, stage, location, histopathology between the two groups baring a higher proportion of males in the RATS subgroup. The following key limitations were identified in addition to study design: a. survival and disease free survival may be affected by a smaller RATS group with a shorter follow up period 36 months vs. 60 months. b. the study was not powered to identify differences in nodal upstaging.
3	Case series	13	RATS lobectomy	Clinical effectiveness of the intervention	Perioperative outcomes	There was one conversion to open surgery out of thirteen cases. Median operation time was 210 minutes, median length of stay was 5 days, an estimated blood loss of 33ml (range 25-150ml) and 2 cases with surgical complications.	Oncological	The median lymph node yield in 9 patients was 19 (11-40).	Kumar, Arvind; Asaf, Belal Bin; Cerfolio, Robert James; Sood, Jayshree; Kumar, Reena. Robotic lobectomy: The first Indian report. J Minim Access Surg 2015;20(3):304-309.	NA	The authors conclude: "Robotic lobectomy is feasible and safe. It appears to be oncologically sound surgical treatment for early-stage lung cancer. There appears no doubt that it offers certain advantages to the surgeon, but whether it translates into cost effective benefits to the patients, needs to be further evaluated by long term studies."	Very small sample size. Conclusion on safety is difficult to reach with such a small sample size.

2+	Cohort	99	RATS lung segmentectomies	Clinical effectiveness of the intervention compared to existing interventions	Perioperative outcomes	The only significant difference in perioperative outcomes was in terms of the mean operation time. The mean operating time for RATS was longer than the mean operation time for VATS [76 ± 23 (40–150) vs 65 ± 22 (30–120) min (P = 0.018)]. The mean duration of drainage was similar for RATS and VATS [3.53 ± 2.3 (1–10) days vs 3.98 ± 3.6 (1–21) (P = 0.90)], respectively. The duration of postoperative stay for RATS was 4.65 ± 1.94 (2–10) days and for VATS was 6.16 ± 4.7 (2–24) days (P = 0.39). The major morbidity and mortality rates were 24–23% and 0–1.5% for RATS and VATS (P = 0.57) and (P = 0.66), respectively.	NA	NA	Demir, Adalet; Ayalp, Kemal; Ozkan, Berker; Kaba, Erkan; Toker, Alper. Robotic and video-assisted thoracic surgery lung segmentectomy for malignant and benign lesions. Interact Cardiovasc Thorac Surg 2015;62(12):720-725.	Both RATS and VATS pulmonary segmentectomy operations were performed with similar morbidity and mortality rates. Although the duration of operation was longer in RATS, there is a tendency towards a shorter postoperative stay.	Minimally invasive surgery - VATS has been demonstrated to be preferable to open segmentectomy. This study shows no difference in outcomes when comparing between VATS and RATS, bar longer duration of RATS procedures.	Demir et al undertook a retrospective study of a consecutive series of patients. The outcomes were reviewed in 99 patients who underwent RATS (n=34) and VATS (n=65) lung segmentectomies. While the median age of the two groups was comparable, no other formal analysis of comparability between two patient groups was undertaken. Patients were selected for RATS or VATS according to their preferences.
3	Case series	21	RATS segmentectomy	Clinical effectiveness of the intervention	Perioperative outcomes	Toker et al 2014 published a case series of 21 patients in Turkey who underwent segmentectomy using RATS. Of these 15 were individuals with malignant lung disease. No conversions to open surgery were reported; the mean duration of operation was 84+/- 26 (40-150) min; the mean length of stay reported was 4+/- 1.4 [2-7] days. Four patients had post operative complications - all prolonged air leak. Pain scale visual analogue scale on postoperative day 2 and day 15 3.4-1.4; Mean FEV (ml) 2278+/-662 [1274-4870];	NA	Mean number of lymph nodes dissected from mediastinum (stations 2-9) - 14.3 [2-21]; the mean number of mediastinal stations dissected was 4.2 [2-6]	Toker, Alper; Ayalp, Kemal; Uyumaz, Elena; Kaba, Erkan; Demirhan, Ozkan; Erus, Suat. Robotic lung segmentectomy for malignant and benign lesions. J Thorac Dis 2014;6 Suppl 2():S211-216.	NA	The authors state that they have demonstrated that the robotic anatomic lung segmentectomy is a feasible and safe procedure with an acceptable operating time, adequate lymph node dissection, less pain and few complications.	Not a comparative study - only a descriptive case study. Comparison with the literature refers to better performance or similar performance to VATs without full evidence provided. Largely a discussion on the use of segmentectomy rather than the clinical effectiveness of using RATS.
3	Case series	302	RATS lobectomy	Clinical effectiveness of the intervention	Oncological	Two year overall survival was 87.6% and the disease free survival was 70.2%. The overall (pN1ppN2) rate of nodal upstaging was 10.9%. Hilar (pN1) disease was detected in 20 (6.6%) and mediastinal (pN2) disease was detected in 13 patients (4.3%). The authors compared the outcomes with three retrospective studies of open thoracotomy and VATS cases, and found that their results were similar to the VATS results. However, based on changes in cT staging in accordance with the AJCC seventh edition, the upstaging rates for RATS were reported as superior to VATS and comparable to open thoracotomy.	-	-	Wilson, Jennifer L.; Louie, Brian E.; Cerfolio, Robert J.; Park, Bernard J.; Vallières, Eric; Aye, Ralph W.; Abdel-Razek, Ahmed; Bryant, Ayesha; Farivar, Alexander S.. The prevalence of nodal upstaging during robotic lung resection in early stage non-small cell lung cancer. Ann. Thorac. Surg. 2014;20(2):93-98.	NA	The rate of robotic pathologic nodal upstaging for clinically stage I NSCLC appears to be superior to the VATS approach and similar to the open approach when compared by equivalent AJCC, seventh edition, clinical T stage.	Nodal upstaging is a surrogate for the completeness of nodal evaluation and thus the quality of the surgery with higher rates of nodal upstaging preferable. Limitations of the study besides its observational study design without an a comparison group include: a. potential confounding due to variability in surgical skills and inclusion of learning curve data in RATS group. b. short follow-up of two years.
3	Systematic	0	2 comparisons: VATS vs. Open thoracotomy; RATS for primary lung cancer	Clinical effectiveness of the intervention	Perioperative outcomes	The study results were tabulated without the benefit of much further analysis. The authors conclude that VATS for lung cancer is widely performed because the efficacy of this procedure has been well established. The authors were unable to verify that the merits of surgery using RATS surpass those of VATS as only a few comparative studies were available at the time of this analysis with data limited to perioperative and short-term results. The results from included studies were variable.	NA	NA	Nakamura, Hiroshige. Systematic review of published studies on safety and efficacy of thoracoscopic and robot-assisted lobectomy for lung cancer. Ann Thorac Cardiovasc Surg 2014;146(2):292-298.	NA	-	The methodology of systematic review including inclusion/ exclusion criteria, control for potential differences in the underlying patient population, stage of uptake of the technology etc. has not been provided. The findings of individual studies are tabled without much further analysis.

2+	Cohort	184	RATS	Cost effectiveness	Cost	There was no statistically significant difference in overall cost between VATS and open cases (Δ = $1,207) or open and robotic cases (Δ = $1,975). Robotic cases cost $3,182 more than VATS (p < 0.001) owing to the cost of robotic-specific supplies and depreciation. The main opportunities to reduce cost in open cases were the intensive care unit, respiratory therapy, and laboratories. Lowering operating time and supply costs would reduce costs for VATS and robotic cases.	NA	NA	Deen, Shaun A.; Wilson, Jennifer L.; Wilshire, Candice L.; Vallières, Eric; Farivar, Alexander S.; Aye, Ralph W.; Ely, Robson E.; Louie, Brian E.. Defining the cost of care for lobectomy and segmentectomy: a comparison of open, video-assisted thoracoscopic, and robotic approaches. Ann. Thorac. Surg. 2014;30(2):133-140.	NA	The authors conclude that costs are similar between open and minimally invasive techniques, however this is only true when capital depreciation of the robot and the robot specific supplies are removed from the total cost. VATS is the least expensive approach, and the findings challenge the view that open resection is more expensive than VATS. Shorter LOS for open resection than elsewhere in the literature.	The authors find no statistically significant difference in the costs of RATS and VATS cases once they remove the capital depreciation and robot specific supply costs. Retrospective study design makes it difficult to control for surgeon variability and patient selection.
2+	Case series	120	RATS Lobectomy	Clinical effectiveness of the intervention compared to existing interventions	Perioperative outcomes	For RATS vs initial VATS group, there was significant difference in the median length of stay (6 vs.9 days, p<0.001). In the RATS vs current VATS group there was no significant difference in the length of stay (6 vs. 7 days p = 0.085).	Oncological	RATS vs initial VATS: dissected lymph node number 22 (7-45) vs. 29 (15-56) p < 0.001. RATS vs. current VATs : dissected lymph node number 26 (12-46) p=0.006	Jang, Hee-Jin; Lee, Hyun-Sung; Park, Seong Yong; Zo, Jae Ill. Comparison of the early robot-assisted lobectomy experience to video-assisted thoracic surgery lobectomy for lung cancer: a single-institution case series matching study. Innovations (Phila) 2011;143(2):383-389.	NA	Outcomes of initial RATS are comparable to outcomes from initial VATS	The authors have tried to address the effect of recent adoption of the procedure in their study design by identifying cohorts of operations where the surgeon involved had a similar level of experience. The study is designed to match a case series of early RATS lobectomy experiences with early VATS lobectomy for lung cancer and a third group of more recent VATS procedures. Each of the three groups were composed of 40 patients. The mean age of patients in the initial RATS group was significantly higher (64.2 vs. 59.6 p=0.043 or 59.7 p=0.035) than in the other two groups, and the RATS group had significantly more later stage cancers than the initial VATS group (p=0.043) but in all other terms the groups were comparable. The study describes the work of a single surgeon which is both a strength (controls for variability in systematic approach to node assessment) and a weakness as this limits the generalisability of the study.

3	Case series	325	RATS Lobectomy	Clinical effectiveness of the intervention	Perioperative outcomes	Significant	Oncological	The median number of lymph node stations dissected was 5 (range, 2-8). Sixty-one (19%) patients had metastatic nodal disease, and 67 patients received adjuvant cytotoxic chemotherapy. At a median follow-up of 27 months, 32 (10%) patients had had recurrence, with 25 dead of their disease. Overall 5-year survival for the group was 80%. By cancer stage there was 5 year survival of stage 1A cancers of 91%, 1B of 88% and 49% for all patients with stage II.	Park, Bernard J.; Melfi, Franca; Mussi, Alfredo; Maisonneuve, Patrick; Spaggiari, Lorenzo; Da Silva, Ruy Kuenzer Caetano; Veronesi, Giulia. Robotic lobectomy for non-small cell lung cancer (NSCLC): long-term oncologic results. J. Thorac. Cardiovasc. Surg. 2012;91(3):e45-47.	NA	The authors conclude that RATS lobectomy is feasible and safe with a short chest tube duration and length of stay, as well as low major morbidity and in-hospital mortality rates. 5 year cancer survival rates consistent with VATS.	This is a large case series. Limitation include: a) retrospective review with potential sources of selection bias b) lack of controls for surgical skill and learning curve.
2-	Cohort	36	RATS	Clinical effectiveness of the intervention compared to existing interventions	Quality of Life measures	Quality of Life (QoL) scores were obtained using the Dutch version of the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)-C30 (cancer core questionnaire) and the EORTC QLQLC- 13 lung cancer-specific questionnaire module. Comprises five functional scales, three symptom scales and a global health/QoL scale. 1 month following surgery all QoL subscales had returned to baseline, except for increased pain in thoracic and shoulder pain in the first three months for RATS procedures. In the sternotomy cohort, there was a significant dips in physical functioning (66.3 vs. 81.5 p=0.001), role functioning (40.8 vs. 71.9 p=0.001), and social functioning 66.7 vs. 78.0 p=0.044) - not observed in the RATS cohort. Sternotomy patients showed a temporary 1-month increase in fatigue (p=0.003) and 3 month increase in thoracic pain (p=0.017) At 12 months neither procedure was significantly different from baseline in QoL scores.	NA	NA	Balduyck, Bram; Hendriks, Jeroen M.; Lauwers, Patrick; Mercelis, Rudy; Ten Broecke, Pieter; Van Schil, Paul. Quality of life after anterior mediastinal mass resection: a prospective study comparing open with robotic-assisted thoracoscopic resection. Eur J Cardiothorac Surg 2011;25(1):108-113.	NA	Following RATS for mediastinal tumours, patients can resume routine activities more quickly than patients who undergo standard sternotomy	There are some weaknesses in the study design. Firstly the sample size is small <50 combined. No randomisation, and there are different indications for whether the patient would receive sternotomy or RATS, with larger mediastinal masses reserved for open sternotomy. This could present a bias in individual's perceptions of pain/functioning post operatively. In the robotic arm there were lower response rates for various questionnaires, and although not significantly different from the response rate of the sternotomy patients, there was not discussion of follow up on non respondents.
0	Case series	325	RATS	Clinical effectiveness of the intervention	Oncological	Median follow up of 27 months, 280 patients were without evidence of disease and 32 recurred and 25 dead of the disease. Majority of recurrence were distant - 17 distant and 6 loco regional and distant. 9 were loco regional only. 5 yr survival was 80%. Stage 1 5yr survival was 91%, 1B 88%, II 49%.	Perioperative	Median operation time 206 min (110 to 383 min) No intraoperative deaths. Conversion rate to open 8%. Morbidity rate was 25.2%. Median number of lymph nodes dissected was 5 (2-8)	Park, Bernard J.. Robotic lobectomy for non-small cell lung cancer (NSCLC): Multi-center registry study of long-term oncologic results. Ann Cardiothorac Surg 2012;6(6):355-360.	NA	Feasible safe and oncologically sound treatment for early stage lung cancer with comparable results to conventional VATS - although not assessed in the article	Case series reviewed retrospectively. One benefit is the longer follow up than in other reports.

3	Case series	91	RATS	Safety of the intervention	Perioperative outcomes	Operating times decline to a plateau after about 20 operations. The median duration of the operation including robot setup and frozen section examination was 239 (range 85–411) minutes, 260 minutes in the first 18 patients and 221 minutes in the remaining 73 cases (P=0.01; Table 2). Median postoperative hospitalization was 5 (range 3–38) days, declining from 6 days in the first 18 cases to 5 days in the remaining 73 cases (P= 0.002). Conversion rate and number of complications reduced non-significantly from the first to the later series. Major complications occurred in 11% of the first 18 patients and only 4% of the later series.	-	NA	Veronesi, Giulia; Agoglia, Bernardo G.; Melfi, Franca; Maisonneuve, Patrick; Bertolotti, Raffaella; Bianchi, Paolo P.; Rocco, Bernardo; Borri, Alessandro; Gasparri, Roberto; Spaggiari, Lorenzo. Experience with robotic lobectomy for lung cancer. Innovations (Phila) 2011;16(1):173-177.	NA	The study suggests that about 20 operations are required for a surgeon experienced in major thoracic open resection but not VATS lobectomy to become competent in RATS. This finding is comparable to other studies in the literature.	Case series reviewed retrospectively.
3	Case series	269 open thoracotomy; 87 VATS and 12 RATS	RATS	Cost effectiveness	Average cost of surgery	The overall VATS group had a substantially less total average cost compared with the thoracotomy patients ($1479 versus $8368, difference of -$6889). This difference was even more pronounced when the VATS only group was analysed (-$7969) relative to thoracotomy. Use of RATS during VATS was associated with increased average cost of $3981 per procedure compared with VATS alone. RATS was still less costly than thoracotomy (-$3988).	Reason for access cost of RATS	RATS excess costs were largely on first day of hospitalisation. Analysis indicate two possible reasons for this: 1. Higher percentage of robotic patients underwent additional procedure (e.g. 92% of RATS cases had bronchoscopy compared with only 54% of all non-robotic cases. 25% of RATS cases required extensive lysis of adhesions versus only 3.5% of non-robotic lobectomy. 2. Expense of specialised instruments and certain disposables.	Park, Bernard J.; Flores, Raja M.. Cost comparison of robotic, video-assisted thoracic surgery and thoracotomy approaches to pulmonary lobectomy. Thorac Surg Clin 2008;147(3):929-937.	Not provided	The findings related to higher hospital costs associated with robotic surgery are consistent with similar studies.	The key limitations for this study include: 1. cross sectional design. 2. patient selection bias. 3. surgical and cost data from a single institution. 4. Disproportionately smaller number of RATS cases. Due to these limitations, the study findings need to be interpreted and generalised with caution.
2+	Cohort	15,502 VATS 96%, RATS 4%. After matching, 1,240 patients with equal number of RATS and VATS	RATS, Lobectomy, Wedge resection	Cost effectiveness	Cost, Operating room times, length of stay	Cost: The average cost of inpatient procedures with RATS was approx. $4,500 higher than VATS ($25,040.70 vs $20,476.58 (P =.0001)) for lobectomies and approx. $3,000 for wedge resections ($19,592.42 vs $16,600.13 (P =.0001)).	Complication rates (30 day and immediate peri-operative)	The odds of an event occurring were not significantly different for major and minor events in either group for both lobectomy and wedge resection.	Swanson, Scott J.; Miller, Daniel L.; McKenna, Robert Joseph; Howington, John; Marshall, M. Blair; Yoo, Andrew C.; Moore, Matthew; Gunnarsson, Candace L.; Meyers, Bryan F.. Comparing robot-assisted thoracic surgical lobectomy with conventional video-assisted thoracic surgical lobectomy and wedge resection: results from a multihospital database (Premier). J. Thorac. Cardiovasc. Surg. 2014;.	Refer secondary outcomes	The findings related to higher hospital costs associated with robotic surgery are consistent with similar studies.	To balance cohorts and mitigate the possibility of confounders and the large discrepancy in sample size between robotic and non-robotic procedures, patients were matched for age, gender, health status, insurance type using propensity scoring. After matching, a total of 1,240 patients remained; 590 lobectomies and 650 wedge resections with equal number of RATS and VATS in each group. Large patient population and data from multiple centres, sound statistical methodology are strengths of this study. The key challenge is the difference in cost and funding system between NHS and USA which will impact any direct comparison.

Appendix Two

Literature search terms

Assumptions / limits applied to search:	
Original search terms:	Robotics da Vinci
Updated search terms - Population	Lung Cancer Pulmonary Cancer Neoplasms Lung Pulmonary Neoplasms Lung tumour Lung tumor Lung tumours Lung tumors Non-small cell carcinoma lung
Updated search terms - Intervention	Robotic Robotics da Vinci Robotically-assisted Robotically assisted Robotic-assisted Robot assisted Robot-assisted Computer assisted Computer-assisted Remote Operations Telerobotics Lung Resection Lung Surgery Lung Surgeries Lobectomy Lobectomies Pneumonectomy Pneumonectomies Thoracic Surgery Thoracic Surgeries Thoracoscopic Surgery Thoracoscopic Surgeries Thoracoscopy Thoracoscopies
Updated search terms - Comparator	Open thoracotomy Video-assisted Video assisted VATS

Inclusion criteria	**General inclusion criteria**
	In order of decreasing priority, the following are included: 1. All relevant systematic reviews and meta-analysis in the last 5 years and those in 5-10 years period which are still relevant (e.g. no further updated systematic review available) 2. All relevant RCTs and those in the 5-10 years period which are still relevant (e.g. not superseded by a next phase of the trial/ the RCT is one of the few or only high quality clinical trials available) >>>> If studies included reach 30, inclusion stops here 3. All relevant case control and cohort studies, that qualify after exclusion criteria >>>> If studies included reach 30, inclusion stops here 4. All relevant non analytical studies (case series/ reports etc) that qualify after exclusion criteria >>>> If studies included reach 30, inclusion stops here 5. Expert opinion
	Specific inclusion criteria
	English language <5 years Title/Abstract 2 additional papers added as requetsed by PH lead: a. Park, Bernard J.; Flores, Raja M.. Cost comparison of robotic, video-assisted thoracic surgery and thoracotomy approaches to pulmonary lobectomy. Thorac Surg Clin 2008;147(3):929-937. b. Swanson, Scott J.; Miller, Daniel L.; McKenna, Robert Joseph; Howington, John; Marshall, M. Blair; Yoo, Andrew C.; Moore, Matthew; Gunnarsson, Candace L.; Meyers, Bryan F.. Comparing robot-assisted thoracic surgical lobectomy with conventional video-assisted thoracic surgical lobectomy and wedge resection: results from a multihospital database (Premier). J. Thorac. Cardiovasc. Surg. 2014;.
Exclusion criteria	**General exclusion criteria**
	Studies with the following characteristics will be excluded: 1. Do not answer a PICO research question 2. Comparator differs from the PICO 3. < 50 subjects (except where there are fewer than 10 studies overall) 4. No relevant outcomes 5. Incorrect study type 6. Inclusion of outcomes for only one surgeon/doctor or only one clinical site
	Specific exclusion criteria
	None