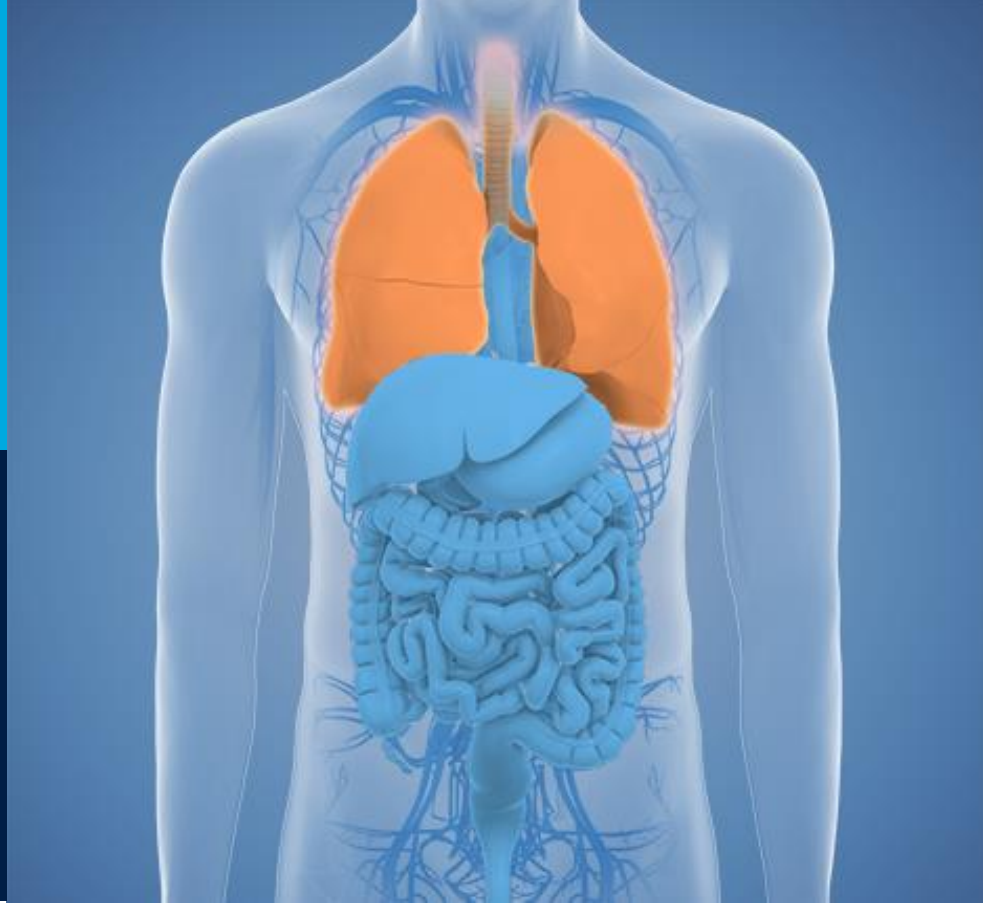

GLOBAL VALUE DOSSIER
FOR MINIMALLY INVASIVE SURGERY (MIS)
THORACIC SURGERY

Medtronic
Further, Together

Prepared by: **Jayne Smith-Palmer**

Ossian Health Economics and Communications, Bäumleingasse 20, 4051 Basel, Switzerland

Phone: +41 61 271 6214

E-mail: smith-palmer@ossianconsulting.com

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1. Video-assisted thoracic surgery (wedge, segmentectomy, lobectomy)

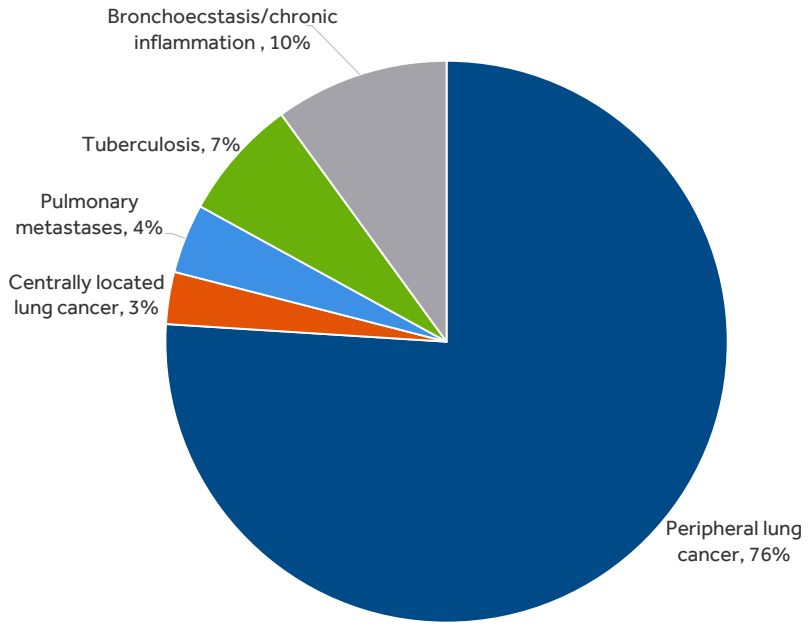
1.1. Overview of procedure

Video-assisted thoracic surgery (VATS) is used for both diagnostic and therapeutic procedures, with VATS procedures including wedge resections, segmentectomy, lobectomy, sleeve resections and pneumonectomy. VATS is becoming increasingly used for stage I and II non-small cell lung cancer (NSCLC) as well as in the treatment of spontaneous pneumothorax, biopsy and several benign conditions. The increased use of VATS in recent years has been partly attributed to improvements in optics and instrumentation and better anesthesia.[1] VATS is preferred to open surgery, especially for some populations including those with pulmonary compromise, advanced age or impaired wound healing. Relative contraindications to VATS include tumor >6 cm in diameter. A key benefit of VATS over open surgery is reduced post-operative pain and reduced trauma to the chest wall as VATS, or thoracoscopic surgery, utilizes small incisions rather than the long incision required in traditional thoracotomy.

One of the most common indications for VATS procedures is NSCLC, which is one of the most commonly occurring cancers in the US and Europe, with >220,000 new cases of lung cancer in the US in 2015[2] and >380,000 cases in Europe in 2008.[3] The use of VATS procedures in the US is continuing to increase at approximately 5% per year from an estimated 26,000 per year in 2005 to 43,000 per year in 2014.[1] Additionally, the economic burden associated with lung resections is substantial; in the US alone, the cost of lung resections is an estimated USD 1.9 billion per year.[4]

Typically, VATS procedures are performed with the patient in the lateral decubitus position with flexion of the operating table (to widen the intercostal spaces) and require general anesthesia with isolation of one lung and utilize three incisions including one utility incision (ranging from 4–10 cm in length, providing instrument access and through which the resected material is removed) and two for instrument access; however, some procedures can be performed using a single port. Lung cancer is the most common indication for major pulmonary resections with VATS (Figure 1-1); where the indication for VATS is lung cancer, hilar and mediastinal lymphadenectomy or node sampling are performed.

Figure 1-1 Indications for VATS major pulmonary resection in Russia

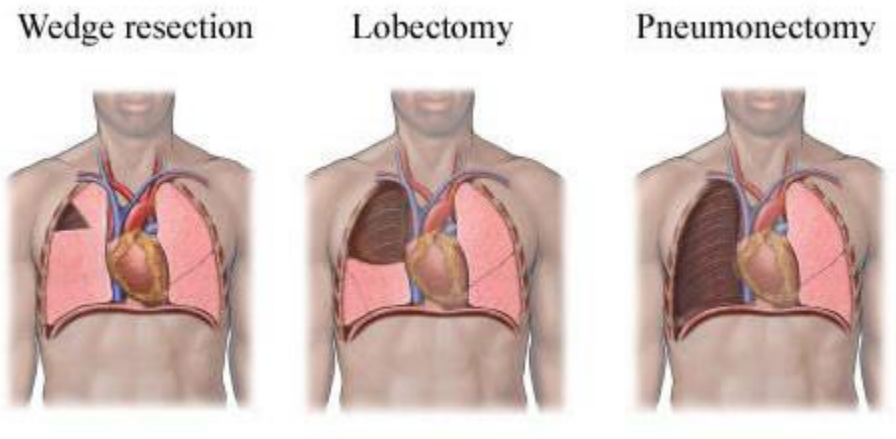


Source: Pischik 2014[5]

Wedge resection/segmentectomy

Indications for wedge resection include stage I NSCLC or solitary metastases (<3cm) in patients who would not tolerate a lobectomy (e.g. those with pulmonary hypertension or severe comorbid conditions) as well as indeterminate pulmonary nodules and benign disease (Figure 1-2).[1,6] VATS wedge resection involves three incisions with the camera port typically located at the seventh or eighth intercostal space. The most common resection technique is resection with mechanical endoscopic staplers. The removed tissue is extracted using a specimen sac. The final stages for both lobectomy and wedge resection is pleural lavage followed by the insertion of one or two chest drains into the pleural cavity via the port incisions; these are removed only when air leakage stops and fluid drainage is minimal.

Figure 1-2 Wedge resection (segmentectomy), lobectomy and pneumonectomy



Source: Colorado Cardiovascular Surgical Associates (available at: http://ccvsa.com/medical-surgical-procedures/thoracic-surgery)

Lobectomy

VATS lobectomy involves the removal of an entire lobe of the lung and is a relatively commonly performed procedure (Figure 1-2). Indications for lobectomy include stage I or II NSCLC in patients with sufficient pulmonary reserve to tolerate lobectomy as well as benign conditions such as granuloma, organized pneumonia, bronchiectasis, abscess and malformations.[6] VATS lobectomy typically utilizes three incisions; the hilar structures are dissected first, after which the pulmonary vessels and bronchi within the hilum are then dissected, most commonly using endoscopic staplers.

Pneumonectomy

Pneumonectomy is a rarely performed procedure and a relatively low proportion of pneumonectomy procedures are performed using VATS and involves the removal of the entire lung, making it the most extensive pulmonary resection, pneumonectomy is generally avoided if other procedures can be performed instead of pneumonectomy (Figure 1-2). One of the most common indications for VATS pneumonectomy is bronchial tumors that cannot be resected using sleeve lobectomy. Three incisions are typically used and soft tissues retracted at the access incision, this is followed by hilar dissection then dissection of the pulmonary vessels, the lung is then then extracted from the thoracic cavity through the utility port using a specimen sac.[7]

Sleeve lobectomy

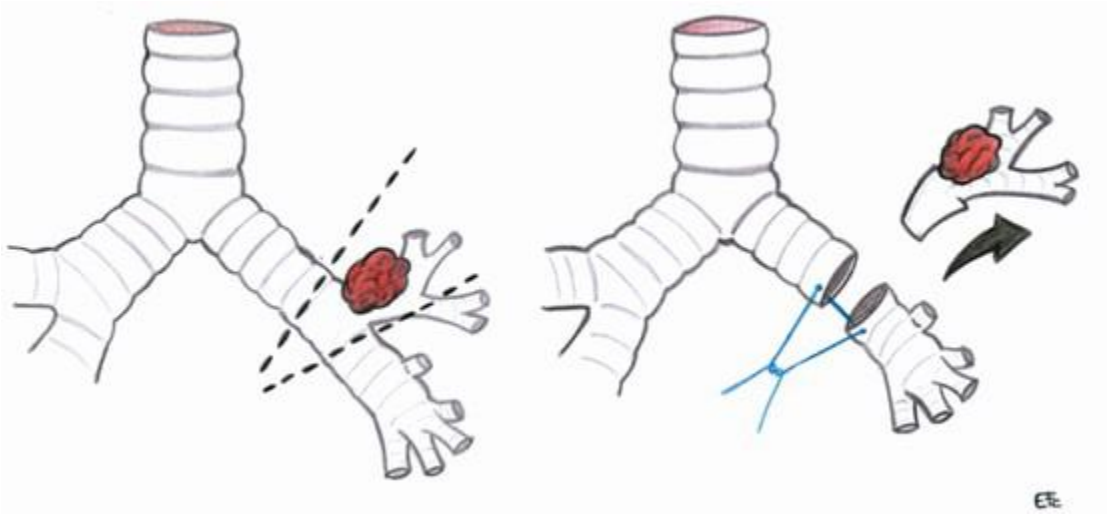
Sleeve lobectomy using VATS was first reported in 2002 but is not common and generally only performed by thoracic surgeons with considerable experience in VATS. Sleeve lobectomy is the most common bronchoplastic resection procedure, and involves circumferential airway resection and end-to-end anastomosis to join the remaining airways (Figure 1-3).[8] The most common indications for sleeve lobectomy are benign or low grade malignant neoplasms or stenoses involving the main or lobar bronchi. Sleeve lobectomy is also indicated for patients who have compromised cardiopulmonary function (FEV_1 <50%

predicted[1] and maximum voluntary ventilation <50% predicted value) to preserve lung parenchyma and avoid pneumonectomy.

Sleeve lobectomy may be performed for any lobe but the most common site for sleeve lobectomy is right upper lobe followed by the left upper lobe; left lobe sleeve resections are more technically challenging owing to the proximity of the aorta and left recurrent nerve.

The procedure begins with dividing hilar structures followed by identification and transection of the pulmonary vessels then bronchial resection and anastomosis. Possible complications following sleeve lobectomy include sputum retention, bronchovascular and bronchopulmonary fistula, and anastomotic failure.

Figure 1-3 Sleeve lobectomy



Source: Gonzalez-Rivas et al. 2014[9]

[1] FEV1; forced expiratory volume in 1 second

Guidelines on VATS

2007 Recommendations from the Consensus Statement of the International Society of Minimally Invasive Cardiothoracic Surgery[10]

For patients with clinical stage I non-small cell lung cancer (NSCLC) undergoing lung lobectomy

- VATS can be recommended to reduce overall postoperative complications (class IIa, level A evidence)
- VATS can be recommended to reduce pain and overall functionality over the short term (class IIa, level B evidence)
- VATS can be recommended to improve delivery of adjuvant chemotherapy delivery (class IIa, level B evidence)
- VATS can be recommended for lobectomy in clinical stage I and II NSCLC patients with no proven difference in stage-specific 5-year survival compared with open thoracotomy (class IIb, level B evidence)

2014 Recommendations from the Japanese Association for Chest Surgery

For patients with pneumothorax undergoing surgery[11]

- VATS is broadly indicated as surgery for pneumothorax
- VATS is judged to be less invasive, as it results in minimal post-operative pain, the periods of chest tube placement and hospitalization are short, and it shows a trend toward early realization of social integration
- There is no difference in terms of safety and complications between VATS and open thoracotomy
- As it is anticipated that VATS will result in a higher recurrence rate than open thoracotomy, it may be desirable to add a supplemental procedure during surgery

For patients with lung cancer[12]

- VATS lobectomy may be considered and applied for patients with clinical stage I NSCLC; however, well-established evidence is lacking (Recommendation grade: Level C1)
  VATS lobectomy by an experienced thoracic surgeon may be considered for patients with clinical stage I NSCLC
- VATS lobectomy is estimated to be less invasive
- VATS showed better or at least equivalent outcomes regarding intra- or postoperative complications compared with thoracotomy
- Long-term survival by VATS lobectomy is suggested to be at least equivalent, although there is lack of evidence

2013 Recommendations from the American College of Chest Physicians (ACCP) for the treatment of patients with stage I and II NSCLC[13]

Lobectomy: for patients with clinical stage I NSCLC, a minimally invasive approach such as VATS (thoracoscopy) is preferred over a thoracotomy for anatomic pulmonary resection and is suggested in experienced centers (Grade 2C)

1.2. Clinical and economic outcomes with VATS versus open thoracic surgery for pulmonary resection

Key findings

Clinical outcomes

- **Length of stay:** Studies show that in patients undergoing lobectomy VATS was consistently associated with a shorter LoS than open surgery (Figure 1-4), with this difference achieving statistical significance in several individual studies[28,30,33,34,36,3841,44,46,] and meta-analyses.[23,25]
- **Blood loss:** Mean (or median) blood loss was consistently and significantly lower with VATS lobectomy compared with open lobectomy in individual studies[38,46,50,51] (Figure 1-5) and meta-analyses[23,25]
- **Blood transfusion:** A lower proportion of patients undergoing VATS resection required blood transfusion compared with those undergoing open lung resection[32,38,39,44,46] in the majority of these the difference was significant[32,38,39,46]
- **Operating time:** VATS lobectomy was associated with significantly longer operating times than open lobectomy across several studies (Figure 1-6).[44,47] However, some studies showed operating times to be significantly shorted with VATS lobectomy compared with open lobectomy[38,50,51]
- **Surgical Site Infection:** In general, rates of SSI were similar for lobectomy performed as an open procedure or VATS;[28,39,46] one study reported a significantly lower incidence of SSI with VATS versus open lobectomy[35] (Figure 1-7)
- **Overall survival:** For patients undergoing lung resection for lung cancer, 5 year survival rates were similar for open and VATS resection (Figure 1-8)[27,40,41] One 2015 study[49] and two meta-analyses showed a significant survival benefit in favor of VATS[23,24]
- **Chest tubes:** Meta-analyses showed that the length of time chest tube drainage was required was significantly shorter with VATS than open lobectomy[23,25]; findings among individual studies were inconsistent, two reported a significant difference in favor of VATS[38,39] but four reported no significance difference[47,49,50,,51]
- **Post-operative pain:** Post-operative pain scores were lower with VATS versus open lung resection[42] and the proportion of patients requiring pain medication was also significantly lower[46]

Economic outcomes

- **Total costs:** Overall, in the majority of cost studies included in the analysis, total costs with VATS were lower than for corresponding open procedures, the one exception to this was studies conducted in China where inconsistency was noted
    - **United States:** Total hospital costs in US-based studies were consistently lower with VATS lung resection than with open lung resection (Figure 1-9)[52,30,37,33,36,48,56] with this difference achieving statistical significance in several studies[30,37,36,56]

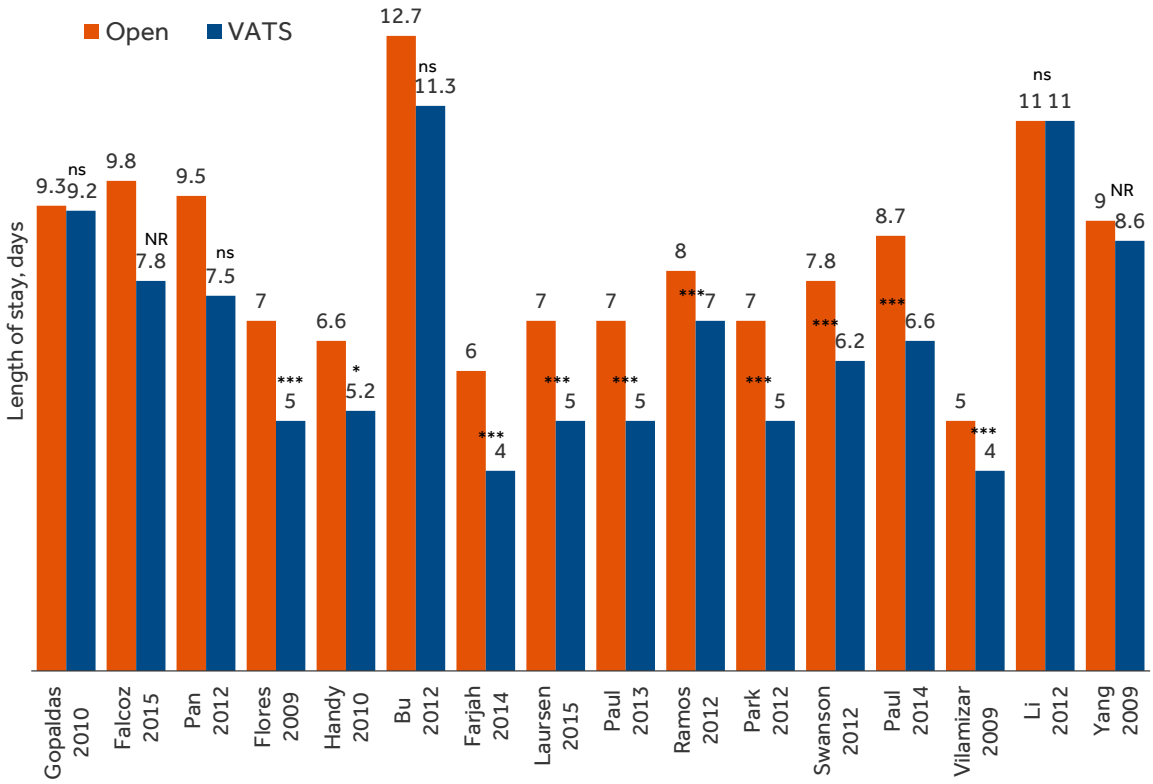
- **Europe:** In studies conducted in Europe (UK and France) total hospital costs were significantly lower with VATS lung resection than with open lung resection (Figure 1-10)[44]
- **China:** Findings of cost studies from China were inconsistent, one study reported lower costs with VATS versus open surgery[23] but a second study reported significantly higher total costs with VATS[51]

- **Savings due to clinical benefits:** Studies presenting a breakdown of total costs demonstrate that the lower post-operative ward stay costs, primarily due to a shorter LoS are a key driver of lower overall costs.[43,44,53] The lower rate of post-operative complications with VATS is also likely to translate into economic benefits

Other findings

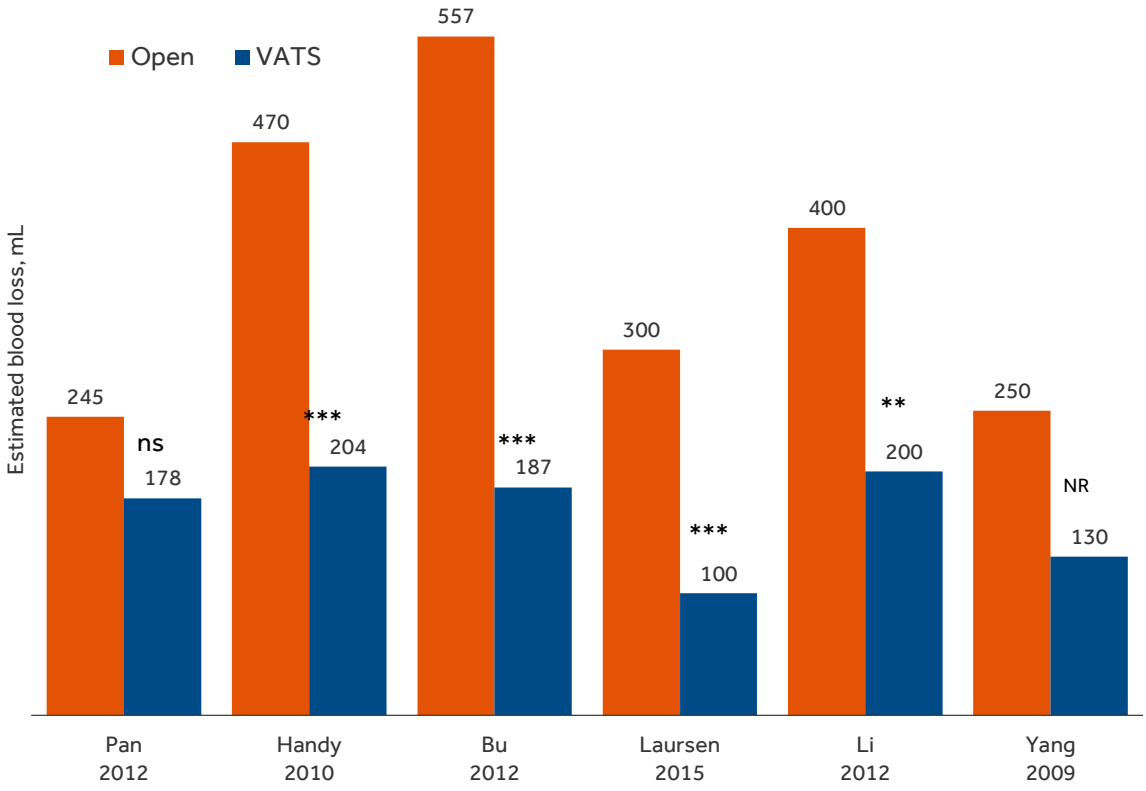
- **Learning curve:** Operating time for VATS procedures is influenced by surgeon experience and a learning curve is evidence with operating time decreasing as surgeon experience increases.[14,15,16] Higher levels of surgeon experience is also associated with reduced costs.[15]
- **Barriers to use:** A survey of surgeons showed that 92% of surgeons are willing to learn VATS lobectomy, but barriers included limited resources (50%), limited exposure/mentoring (45%) and limited clinical evidence (20%). When questioned about the advantages open thoracotomy, a high proportion of surgeons believed that VATS was associated with less post-operative pain (81%), shorter LoS (72%) and higher patient satisfaction (80%).[17]
- **Economic impact of complications:** Intra-operative and post-operative complications, which are more common with open surgery, are associated with higher overall costs. For example, in a study of VATS procedures intra-operative blood transfusion increased costs by >USD 15,000 similarly post-operative pneumonia and blood transfusion increased costs by more than USD 2,900 and USD 5,800, respectively.[18]
- **Re-admission:** Re-admission within following lung cancer resection is associated with a 6-fold increase in 90-day post-operative mortality.[19]
- **Tissue trauma:** Studies looking at inflammatory markers (e.g. tumor necrosis factor-α, interleukin-6, interleukin-8, interleukin-10 and C-reactive protein [CRP]) have shown that VATS is associated with lower levels of interleukin-6 and CRP and a quicker return of immune function compared with open lobectomy, although the significance of this remains unknown.[20]
- **Pulmonary function:** In a Japanese study of n=204 patients (n=42 with dyspnea) undergoing major lung resections (mean age 64 years) post-operative pulmonary function (including FEV_1 and FVC) shows significantly better improvement in patients undergoing VATS compared with those undergoing open thoracotomy[21]
- **High risk patients:** The benefits of VATS relative to open lobectomy in terms of reduced complications may be of particular importance in patients considered to be high risk, such as those with substantial pre-operative comorbidities.[20]
- **Quality of life:** Compared with open lobectomy VATS lobectomy has been shown to be associated with a better profile in terms of quality of life and faster return to normal activities[22]

Figure 1-4 Length of stay with VATS lobectomy versus open lobectomy



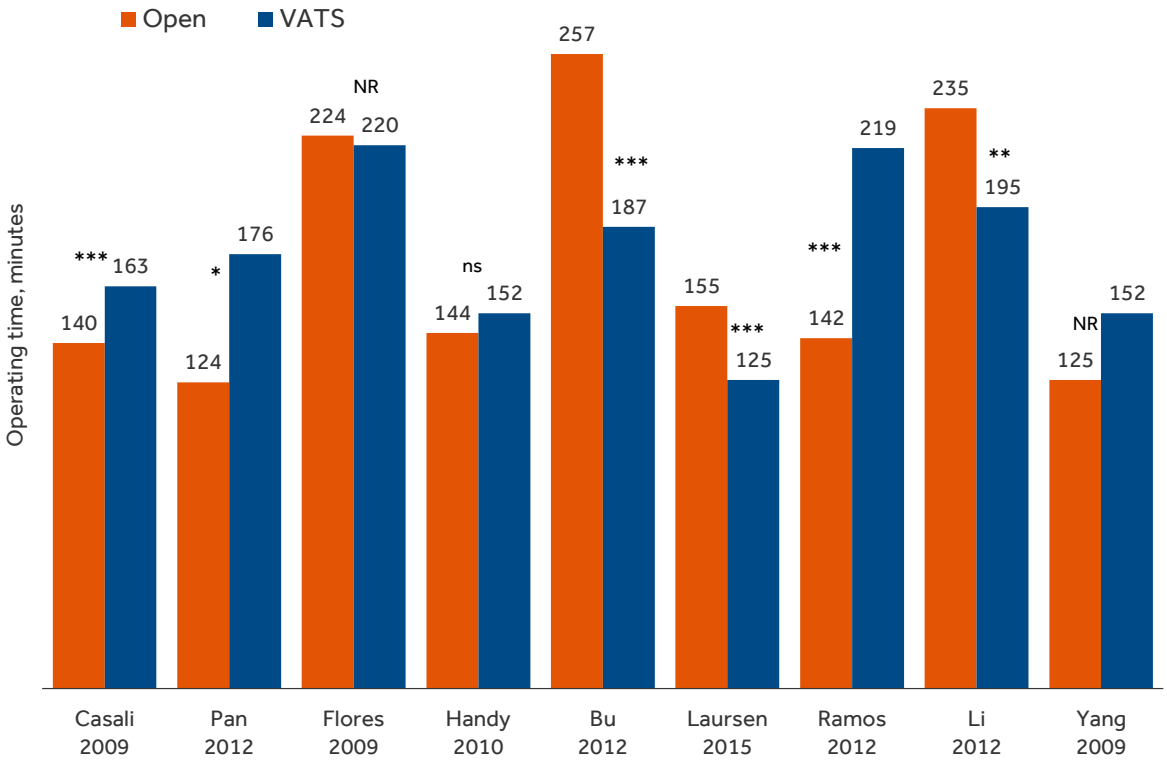
*p<0.05; **p<0.01; ***p<0.001; NR, not reported; ns, not significant

Figure 1-5 Estimated blood loss with VATS versus open lobectomy



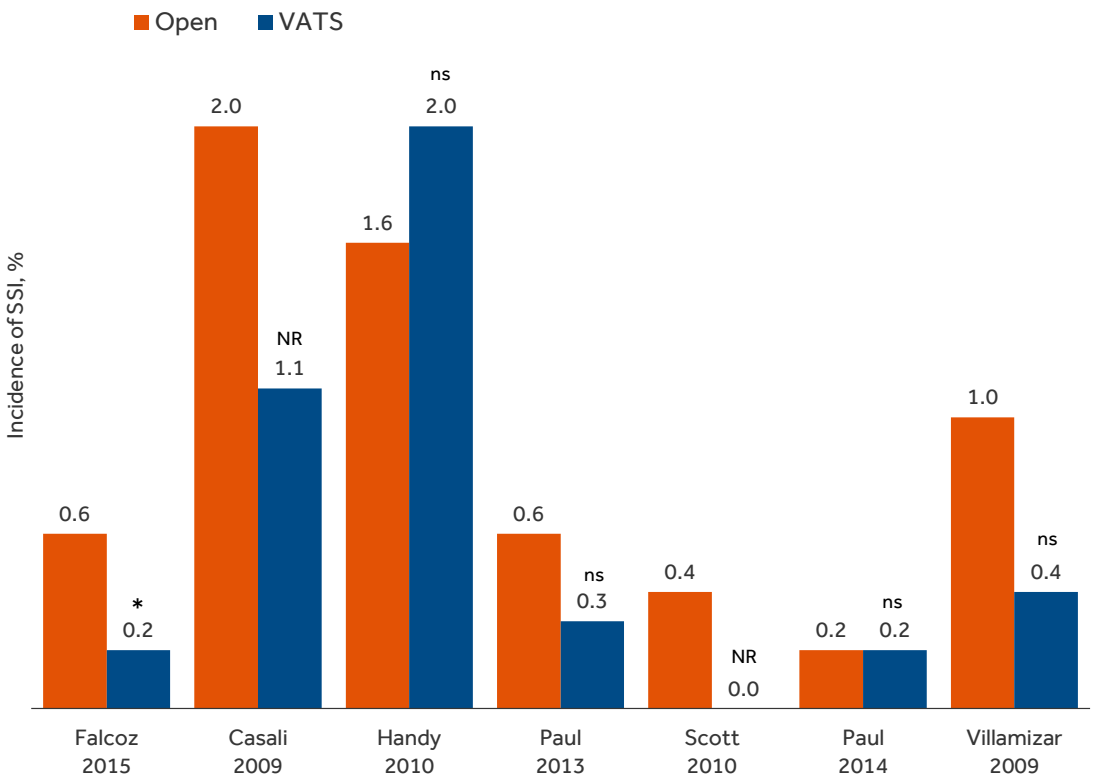
*p<0.05; **p<0.01; ***p<0.001; NR, not reported; ns, not significant

Figure 1-6 Mean (or median) operating time for VATS versus open lobectomy



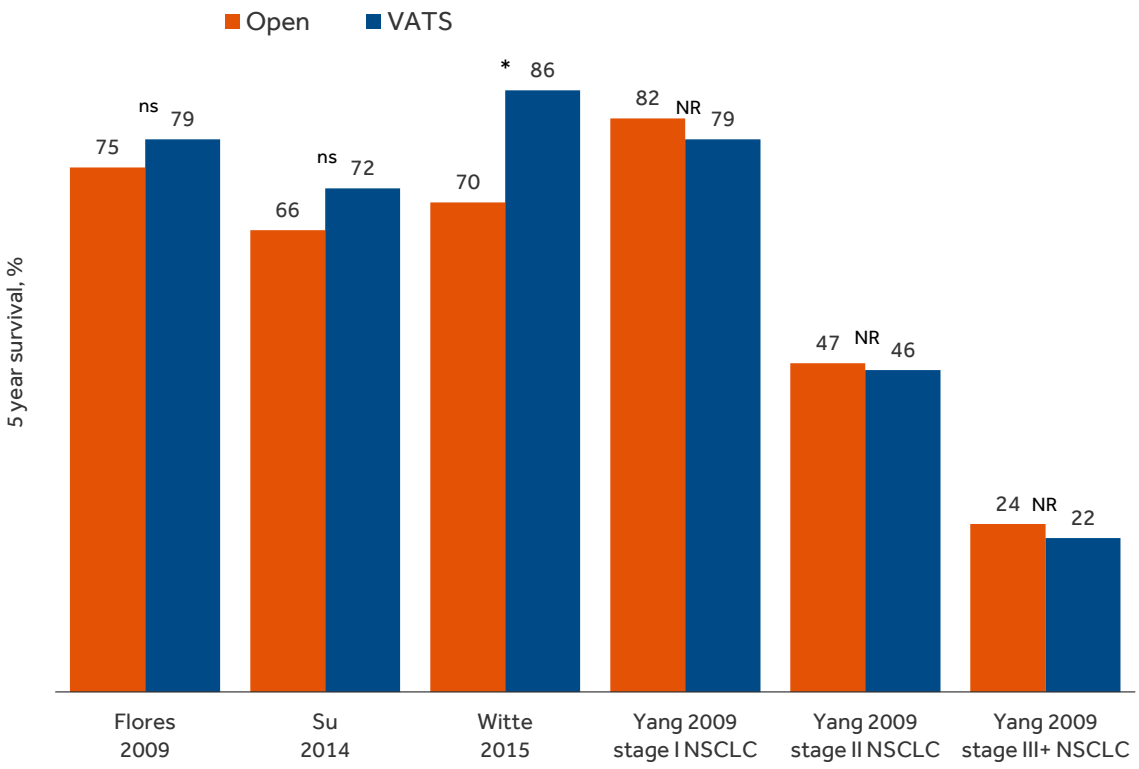
*p<0.05; **p<0.01; ***p<0.001; NR, not reported; ns, not significant

Figure 1-7 Incidence of SSI with VATS versus open lobectomy



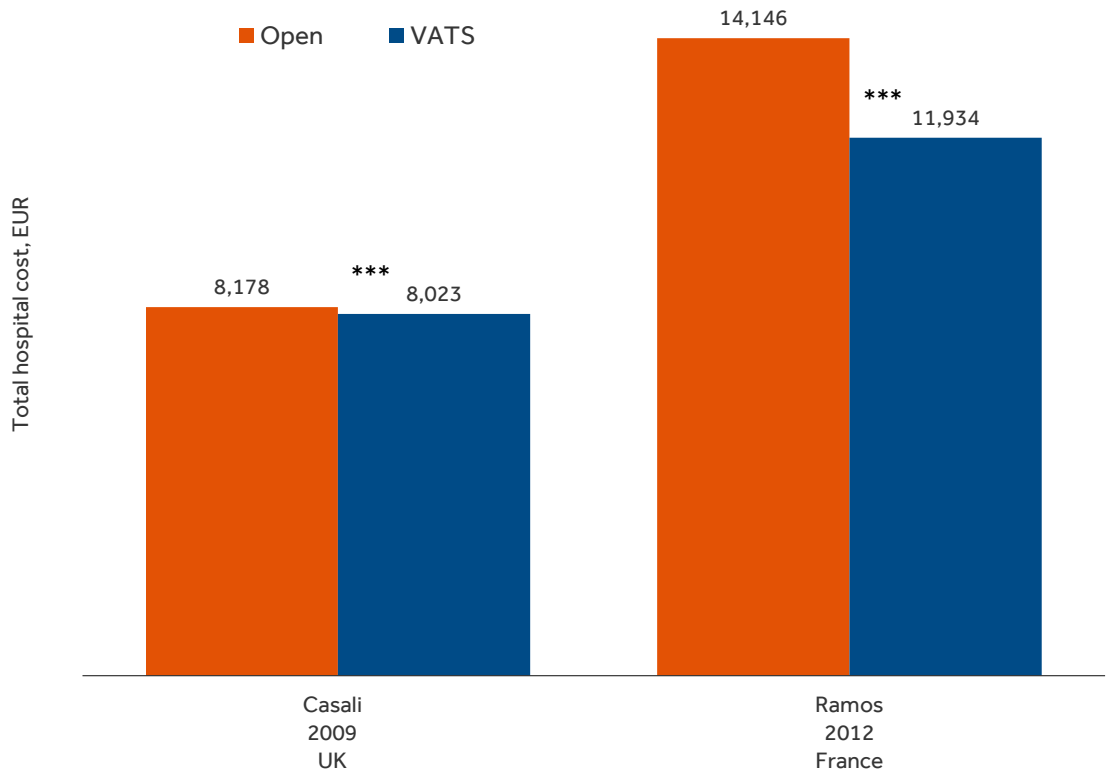
*p<0.05; **p<0.01; ***p<0.001; NR, not reported; ns, not significant

Figure 1-8 5 year survival rates in lung cancer patients undergoing VATS or open pulmonary resection



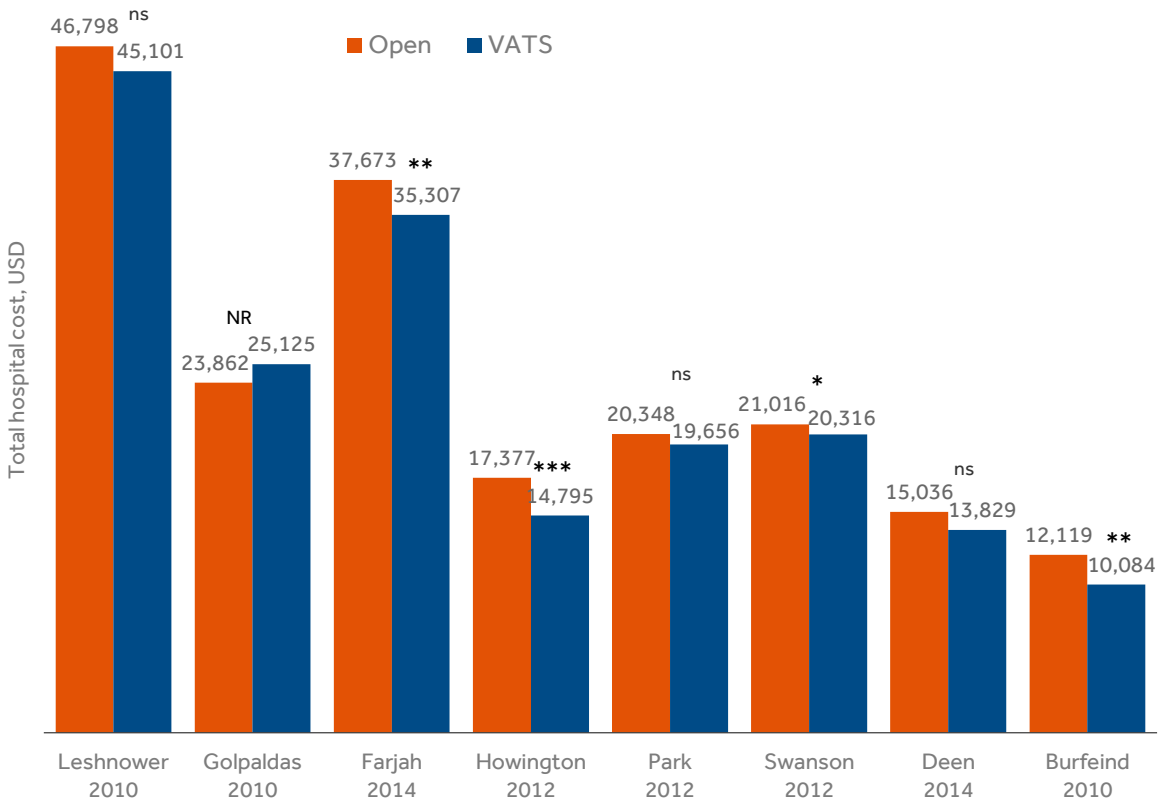
*p<0.05; **p<0.01; ***p<0.001; NR, not reported; ns, not significant

Figure 1-9 Total hospital costs of VATS versus open pulmonary resection in studies conducted in Europe



*p<0.05; **p<0.01; ***p<0.001; NR, not reported; ns, not significant

Figure 1-10 Total hospital costs of VATS versus open pulmonary resection in US-based studies



*p<0.05; **p<0.01; ***p<0.001; NR, not reported; ns, not significant

1.1.1. Clinical and economic evidence tables

A summary of clinical evidence on VATS compared with open surgery from published meta-analyses and published studies is shown in Table 1-1 and Table 1-2, respectively. A summary of economic evidence from published cost studies is shown in Table 1-3.

In the following tables outcomes where p<0.05 are underlined.

Table 1-1 Summary of meta-analyses comparing video-assisted versus open thoracic surgery

Authors	Details	Procedures	Outcome	OR (95% CI)	P value
Chen et al. 2013[23]	20 studies, n=3,457 patients	VATS versus open lobectomy for stage I non-small cell lung cancer	**Peri-operative**		
			Operating time, minutes	−14.68 (−4.68, 34.03)[a]	0.14
			Blood loss, mL	−62.49 (−79.32, −45.66)	<0.0001
			Post-operative		
			Drainage time, days	−0.39 (−0.69, −0.09)	0.01
			LoS, days	−1.74 (−2.20, −1.20)	<0.0001
			Complication incidence	0.61 (0.49, 0.76)	<0.0001
			Post-discharge		
			5 year survival	1.82 (1.43, 2.31)	<0.0001
Yan et al. 2009[24]	21 studies (2 RCTs and 19 non RCTs), n=2,641 patients	VATS versus open lobectomy for early stage NSCLC	**Post-operative**		
			Mortality	0.49 (0.06, 3.76)	0.49
			Pneumonia	0.34 (0.10, 1.16)	0.09
			Post-discharge		
			Systemic recurrence	0.57 (0.34, 0.96)	0.03
			5-year mortality	0.66 (0.45, 0.97)	0.04
Cheng et al. 2007[25]	Level A meta-analysis; 3 RCTs, n=205 patients Level B meta-analysis 33 non-RCT studies, n=3,384 patients	VATS versus open (thoracotomy) lobectomy for non-small cell lung cancer	Operating time, minutes	16.17 (2.46, 29.89)[a]	0.02
			RCT	7.62 (−24.44, 39.69)[a]	0.64
			non-RCT	17.20 (2.62, 31.79)[a]	0.02
			Blood loss, mL	−79.1 (−106.9, −52.4)[a]	<0.0001
			RCT	NA	NA
			non-RCT	−79.1 (−106.9, −52.4)[a]	<0.0001
			Chest tube drainage, days	−0.96 (−1.59, −0.34)[a]	0.002
			RCT	−1.90 (−4.05, 0.25)[a]	0.08
			non-RCT	−0.92 (−1.56, −0.28)[a]	0.005
			LoS, days	−2.60 (−1.47, −0.72)[a]	0.007
			RCT	0.10 (−1.63, 1.83)[a]	0.91
			non-RCT	−2.99 (−5.07, −0.91)[a]	0.005
			Any complication	0.48 (0.32, 0.70)	0.0002
			RCT	0.30 (0.11, 0.81)	0.02
			non-RCT	0.52 (0.34, 0.80)	0.003
			Pneumonia	0.56 (0.26, 1.21)	0.14
			RCT	0.10 (0.01, 2.17)	0.14
			non-RCT	0.68 (0.30, 1.53)	0.35

Table 1-1 Summary of meta-analyses comparing video-assisted versus open thoracic surgery					
Authors	**Details**	**Procedures**	**Outcome**	**OR (95% CI)**	**P value**
			Prolonged air leak (>7 days)	1.67 (0.92, 3.03)	0.09
			RCT	0.38 (0.09, 1.60)	0.19
			non-RCT	2.44 (1.21, 4.90)	0.01
			In-hospital mortality (non-RCT)	0.79 (0.38, 1.64)	0.53

Values below 1.00 favor VATS; values above 1.00 favor open

[a]Weighted mean difference, negative values favor VATS

Table 1-2 Summary of key clinical studies comparing video-assisted versus open thoracic surgery							
Study	**Setting**	**Study details**	**Procedure (year performed)**	**Summary of clinical findings Endpoint**	**Open**	**VATS**	**P value**
Scott et al. 2010[26] and Su et al. 2014[27]	United States	Secondary and long-term (5 year) survival analysis of the ALLIANCE trial, n=66 VATS, n=686 open (propensity matched for analysis)	VATS versus open thoracotomy (pneumonectomy, lobectomy, bilobectomy, or segmentectomy) for NSCLC	**Peri-operative**			
				Median (range) operating time, minutes	172 (40, 425)	118 (61, 450)	<0.001
				Post-operative			
				Median (range) LoS, days	7 (0, 99)	4.5 (1, 19)	<0.001
				Operative mortality	1.6%	0	1.0
				Wound infection	0.4%	0	NR
				≥1 complication	47.8%	27.3%	0.44
				Post-discharge			
				5 year overall survival (95% CI)	65.9 (62.3, 69.7)	71.6 (61.2, 83.6)	0.36
				Disease-free survival (95% CI)	69.2 (65.4, 73.3)	76.2 (63.5, 89.1)	0.55
				Local disease-free survival (95% CI)	92.6 (90.2, 95.0)	88.0 (78.6, 98.5)	0.26
Paul et al. 2013[28]	United States	Retrospective database analysis (Nationwide Inpatient Sample), n=10,554 thoracoscopy; n=57,796 thoracotomy, propensity matched	Thoracoscopy versus thoracotomy for lobectomy (2007–2008)	**Peri-operative**			
				Puncture/laceration	1.1%	0.9%	0.422
				Bleeding	1.5%	1.7%	0.474
				Post-operative			
				Mortality	2.3%	1.6%	0.0062
				Median (range) LoS, days	7 (5, 9)	5 (3, 8)	<0.001
				Any complication	50.4%	46.5%	0.003
				Pneumonia	8.2%	7.3%	0.170
				Wound infection	0.6%	0.3%	0.053
Kent et al. 2014[29]	United States	Retrospective national database analysis, n=20,238 open; n=12,427 VATS, n=430 robotic (not presented), propensity matched	Open versus VATS versus robotic lobectomy or segmentectomy (2008–2010)	**Post-operative**			
				Mortality	2.0%	1.1%	NR
				Mean LoS, days	8.2	6.3	NR
				Routine discharge	59.5%	64.5%	NR
				Prolonged LoS	9.6%	6.9%	NR
				Any complication	54.1%	45.3%	NR
				Bleeding complication	1.9%	1.3%	NR
Farjah et al. 2014[30]	United States	Retrospective study using the MarketScan database, n=6,893	VATS versus open lobectomy for lung cancer (2007–2011)	**Post-operative**			
				Median LoS, days	6	4	<0.001
				Prolonged LoS	7.2%	3.0%	<0.001
				90-day re-admission	12%	10%	0.026

Table 1-2 Summary of key clinical studies comparing video-assisted versus open thoracic surgery							
Study	**Setting**	**Study details**	**Procedure (year performed)**	**Summary of clinical findings Endpoint**	**Open**	**VATS**	**P value**
		thoracotomy, n=3,069 VATS					
Gopaldas et al. 2010[31]	United States	Retrospective national database analysis; n=12,860 thoracotomy; n=759 VATS	VATS versus open lobectomy (2004–2006)	**Post-operative**			
				LoS, days	9.3 (0.1)	9.2 (0.4)	0.696
				Mortality	3.1%	3.4%	0.676
				Total complications	43.1%	44.1%	0.592
				Wound	0.8%	1.3%	1.151
				Infection	0.6%	0.5%	0.726
				Cardiovascular	3.4%	3.9%	0.431
				Intraoperative	2.8%	4.1%	0.033
				Systemic	1.0%	1.2%	0.563
				Gastrointestinal	1.2%	1.1%	0.792
				Urinary	1.1%	0.8%	0.398
				Pulmonary	32.2%	31.2%	0.548
Paul et al. 2014[32]	United States	Retrospective national database analysis, n=5,042 thoracotomy, n=1,281 thoracoscopy, (propensity matched)	Thoracotomy versus thoracoscopy for lobectomy (2002–2007)	**Post-operative**			
				Any complication	34.7%	26.2%	<0.0001
				30-day/discharge mortality	1.01%	0.94%	1.00
				Pulmonary complication	12.2%	7.6%	0.0001
				Pneumonia	4.4%	3.0%	0.0758
				Cardiovascular complication	13.0%	8.3%	0.0002
				Bleeding requiring reoperation	0.6%	1.3%	0.0931
				Blood transfusion	4.7%	2.4%	0.0028
				Any infection	3.8%	2.0%	0.0141
Park et al. 2012[33]	United States	Retrospective database analysis, n=4,769 open, n=1,523 VATS	VATS versus open surgery for lobectomy for lung cancer (2008)	**Post-operative**			
				Total complications	43.5%	38.3%	<0.001
				Median LoS, days	7	5	<0.001
				Mortality	2.2%	1.5%	0.12
Paul et al. 2014[34]	United States	Retrospective national database, n=4,715 open, n=1,293 thoracoscopy, propensity matched	Thoracotomy versus thoracoscopic lobectomy for lung cancer (2007–2009)	**Post-operative**			
				Mean (SD) LoS, days	8.7 (6.6)	6.6 (6)	<0.0001
				Median (IQR) LoS, days	7 (5, 10)	5 (3, 8)	<0.001
				In-hospital mortality	43 (3.6)	25 (2.1)	0.0290

Table 1-2 Summary of key clinical studies comparing video-assisted versus open thoracic surgery							
Study	**Setting**	**Study details**	**Procedure (year performed)**	**Summary of clinical findings Endpoint**	**Open**	**VATS**	**P value**
Falcoz et al. 2015[35]	Multinational (Europe)	Retrospective analysis of the ESTS database, n=2,721 open; n=2,721 VATS propensity matched patients	VATS versus open lobectomy for lung cancer (2007–2013)	**Post-operative**			
				Mean (SD) LoS	9.8 (6.9)	7.8 (5.8)	NR
				Any complication	31.7%	29.1%	0.0357
				Major cardiopulmonary complication	19.6%	15.9%	0.0094
				Air leak duration <5 days	9.2%	10.1%	0.2363
				Pneumonia	6.2%	6.0%	0.7739
				Reoperation for bleeding	1.5%	1.5%	1
				Wound infection	0.6%	0.2%	0.0218
				Death	1.9%	1.0%	0.0201
Swanson et al. 2012[36]	United States	Retrospective database analysis, n=2,907 open, n=1,054 VATS	Open versus VATS lobectomy (2007–2008)	**Peri-operative**			
				Mean (SD) operation time, hours	3.75 (0.47)	4.09 (0.52)	0.000
				Post-operative			
				Mean (SD) LoS, days	7.83 (2.05)	6.15 (1.61)	0.000
Howington et al. 2012[37]	United States	Retrospective database analysis; n=999 open; n=1,052 VATS	VATS versus open wedge resection in lung cancer (2007–2008)	**Peri-operative**			
				Mean (SD) operating time, hours	3:16 (0:43)	2:82 (0:38)	0.000
				Mean (SD) LoS, days	6.34 (2.31)	4.44 (1.62)	0.000
Laursen et al. 2015[38]	Denmark	Retrospective database analysis of prospectively collected data, n=785 VATS and 594 thoracotomy	VATS versus open (thoracotomy) lobectomy for lung cancer (2005–2011)	**Peri-operative**			
				Median blood loss, mL	300	100	<0.001
				Median operating time, minutes	155	125	<0.001
				Median pleural cavity drainage, days	4.0	3.0	<0.001
				Post-operative			
				Median (range) LoS, days	7.00 (2–61)	5.00 (1–65)	<0.001
				Conversion	NA	4.5%	NA
				Re-do operation	5.2%	4.2%	0.375
				Minor complication	48.5%	36.3%	<0.001
				Major complication	35.7%	20.0%	<0.001
				Pneumonia	10.6%	7.5%	0.045
				Transfusion	23.2%	7.0%	<0.001
				ICU	4.0%	1.5%	0.004
				Infection without specification	8.4%	2.7%	<0.001

Table 1-2 Summary of key clinical studies comparing video-assisted versus open thoracic surgery							
Study	**Setting**	**Study details**	**Procedure (year performed)**	**Summary of clinical findings Endpoint**	**Open**	**VATS**	**P value**
Villamizar et al. 2009[39]	United States	Retrospective database of prospectively collected data, n=697 thoracoscopic, n=382 thoracotomy, propensity matched analysis	Thoracoscopy versus thoracotomy for lobectomy (1999–2009)	**Post-operative**			
				Median (IQR) LoS, days	5 (4, 7)	4 (3, 6)	0.0001
				Median (IQR) chest tube duration, days	4 (3, 6)	3 (2, 4)	0.0001
				Mortality	5%	3%	0.20
				No complications	51%	69%	0.0001
				Transfusion	13%	4%	0.002
				Wound infection	1%	0.4%	0.62
				Pneumonia	10%	5%	0.05
Yang et al.2009[40]	China	Retrospective analysis, n=120 VATS, n=501 open	VATS versus open lobectomy for lung cancer (1996–2003)	**Peri-operative**			
				Conversions	—	5.8%	NA
				Median operating time, minutes	125	152	NR
				Post-operative			
				Median LoS	9	8.6	NR
				Median blood loss, mL	250	130	NR
				Median drainage time, days	3.5	3.5	NR
				30 day mortality	0.9%	0%	NR
				Post-operative complications	11.2%	10.6%	NR
				Pneumonia	3.1%	3.5%	NR
				Post-discharge			
				5 year survival			
				Stage I NSCLC	81.6%	79.1%	NR
				Stage II NSCLC	47.2%	45.5%	NR
				Stage III+ NSCLC	24.1%	22.2%	NR
Flores et al. 2009[41]	United States	Retrospective database analysis of prospectively collected data n=398 VATS lobectomy, n=343 thoracotomy, propensity matched	VATS versus thoracotomy for lobectomy in stage 1A non-small cell lung cancer (2002–2007)	**Peri-operative**			
				Median operating time, hours	3:44	3:40	NR
				Conversions	—	17%	NA
				Post-operative			
				Complications (any)	30%	24%	0.05
				LoS, days	7	5	<0.0001
				5-year survival	75%	79%	0.08
Chen et al. 2014[42]	China	Retrospective chart review, n=310	VATS versus thoracotomy for pulmonary	**Peri-operative**			
				Median operating time, minutes	151	138	0.063
				Blood loss, mL	128	118	0.06

Table 1-2 Summary of key clinical studies comparing video-assisted versus open thoracic surgery							
Study	**Setting**	**Study details**	**Procedure (year performed)**	**Summary of clinical findings Endpoint**	**Open**	**VATS**	**P value**
		thoracotomy, n=76 VATS	aspergilloma (lobectomy ± segmentectomy, bilobectomy, wedge resection, pneumonectomy) (2005–2012)	**Post-operative**			
				Median LoS, days	14	10	0.016
				Post-operative pain			
				Day 0	4.2	2.6	NR
				Day 1	5.35	3.03	NR
				Day 2	4.76	2.8	NR
				Day 3	4.25	2.7	NR
				Day 7	4.18	2.4	NR
				Day 14	4.0	0.95	NR
				Day 30	3.6	0.78	NR
Casali et al. 2009[43]	United Kingdom	Retrospective single center analysis, n=93 VATS lobectomy, n=253 thoracotomy	Video-assisted thoracoscopic lobectomy versus open (thoracotomy) lobectomy for early stage lung cancer (2004–2006)	**Peri-operative**			
				Mean (SD) Time in theatre, minutes	140 (42)	163 (34)	0.00001
				Air leak	8.7%	12.9%	NR
				Surgical emphysema	0.4%	4.3%	NR
				Post-operative			
				Mean (SD) HDU length of stay, days	2.21 (0.07)	1.48 (0.2)	0.0001
				Mean (SD) ward length of stay, days	4.66 (0.17)	4.06 (0.3)	0.0001
				Mean (SD) post-operative hospital stay, days	6.87 (0.19)	5.54 (0.37)	0.001
				Wound infection	2.0%	1.1%	NR
				Pneumonia/chest infection	15.0%	11.8%	NR
Ramos et al. 2012[44]	France	Retrospective single center analysis, n=98 thoracoscopy, n=189 thoracotomy	Thoracoscopic versus open lobectomy for stage I non-small cell lung cancer (2007-2009)	**Peri-operative**			
				Median (IQR) operating time, minutes	142.0 (40.0)	219.0 (56.5)	<0.001
				Post-operative			
				Median LoS, days	8.0	7.0	<0.001
				Pneumonia	9.5%	4.1%	0.100
				Air leak	11.6%	6.1%	0.139
				Transfusion	4.2%	1.1%	0.174
				Reoperation	2.1%	1.0%	0.665

Table 1-2 Summary of key clinical studies comparing video-assisted versus open thoracic surgery							
Study	**Setting**	**Study details**	**Procedure (year performed)**	**Summary of clinical findings Endpoint**	**Open**	**VATS**	**P value**
Ilonen et al. 2011[45]	Finland	Retrospective observational study, n=116 VATS, n=116 thoracotomy, propensity matched	VATS versus open thoracotomy in stage I NSCLC lobectomy, bilobectomy or segmentectomy (2000–2010)	**Post-operative**			
				Mean (SD) LoS, days	10.8 (7.4)	2.9 (1.7)	0.001
				In hospital mortality	3.4%	2.6%	1
				Complications	26.7%	15.5%	0.026
Handy et al. 2010[46]	United States	Retrospective analysis of prospectively collected data, n=49 VATS, n=192 open	VATS versus open lobectomy for non-small cell lung cancer (1998–2007)	**Peri-operative**			
				Operation time, minutes	144	152	0.29
				Estimated blood loss, mL	470	204	0.00
				Blood transfusion	24%	4.2%	0.00
				Post-operative			
				In hospital mortality	2.6%	4.1%	0.58
				LoS, days	6.6	5.2	0.03
				Post-op ventilation >48h	4.7%	2.0%	0.40
				Pneumonia	7.9%	4.1%	0.36
				Reintubation	9.4%	4.1%	0.22
				Wound infection	1.6%	2.0%	0.82
				Pulmonary embolism	1.0%	0.0%	0.47
				Chest tube >5 days	15%	14%	0.94
				Readmission to ICU	8.9%	6.1%	0.53
				Post-discharge (6 months)			
				6-month mortality	8.3%	4.1%	0.31
				Readmission to hospital	20%	3.6%	0.03
				FEV_1 decrease, L[2]	−0.27	−0.49	0.17
				Chronic pain	29%	21%	0.43
				Requiring pain medicine	36%	7.1%	0.00
Pan et al. 2012[47]	China	Retrospective single center study, n=83 VATS, n=97 thoracotomy	VATS versus thoracotomy for lobectomy for non-small cell lung	**Peri-operative**			
				Mean (SD) blood loss, mL	245 (79)	178 (56)	0.098
				Mean (SD) operating time, minutes	124 (81)	176 (68)	0.046

[2] FEV1, forced expiratory volume in one second; a lower post-operative decrease shows less change in pulmonary function following surgery

Table 1-2 Summary of key clinical studies comparing video-assisted versus open thoracic surgery							
Study	**Setting**	**Study details**	**Procedure (year performed)**	**Summary of clinical findings Endpoint**	**Open**	**VATS**	**P value**
			cancer (2008–2010)	**Post-operative**			
				Mean (SD) pleural cavity drainage; days	4.8 (2.7)	3.6 (1.2)	0.395
				Mean (SD) LoS, days	9.5 (2.3)	7.5 (1.9)	0.043
Deen et al. 2014[48]	United States	Retrospective analysis, n=69 open, n=58 VATS and n=57 robotic (not presented in analysis)	Open versus VATS and robotic VATS (not presented) lobectomy or segmentectomy for stage I or II NSCLC, carcinoid or metastatic foci (2008–2012)	**Peri-operative**			
				Mean operating time, minutes	180	202	0.02
				Post-operative			
				Mean LoS, days	5.47	4.75	0.11
				Complication rate	30%	31%	0.942
Witte et al. 2015[49]	Germany	Prospective non-randomized comparison of registry data, n=44 open, n=56 VATS	VATS versus open thoracotomy for pulmonary segmentectomy for lung carcinoma (2002–2012)	**Peri-operative**			
				Mean operative time, minutes	195.1 (57.3)	224.8 (61.6)	0.014
				Post-operative			
				Reintervention	22.7%	23.2%	1.00
				Duration of chest tube drainage, days (IQR)	7 (5, 9)	7 (4,10)	0.807
				LoS, days (IQR)	12 (9, 16)	9 (7.75, 14)	0.034
				Post-discharge			
				5-year outcomes			
				Overall survival	69.9%	86%	0.047
				Recurrence-free survival	48.6%	58.5%	0.480
Bu et al. 2012[50]	China	Retrospective single center study, n=46 VATS and n=87 thoracotomy included in study	VATS versus thoracotomy for lobectomy for non-small cell lung cancer with tumors >5 cm (2001–2011)	**Peri-operative**			
				Mean (SD) operating time, minutes	256.7 (67.5)	186.5 (62.8)	<0.001
				Mean (SD) blood loss, mL	556.9 (187.2)	218.5 (174.6)	<0.001
				Post-operative			
				Complications	19.5%	8.7%	0.103
				Mean (SD) duration of drainage, days	7.5 (6.5)	8.0 (3.5)	0.508
				Mean (SD) LoS, days	12.7 (6.8)	11.3 (5.9)	0.241
				Post-discharge			

Table 1-2 Summary of key clinical studies comparing video-assisted versus open thoracic surgery							
Study	**Setting**	**Study details**	**Procedure (year performed)**	**Summary of clinical findings Endpoint**	**Open**	**VATS**	**P value**
				Recurrence	3.8%	2.4%	0.670
				3-year survival	64.0%	69.6%	NR
Li et al. 2012[51]	China	Retrospective analysis, n=47 thoracotomy, n=29 VATS	Thoracotomy versus VATS lobectomy for NSCLC (2000–2009)	**Peri-operative**			
				Operating time, minutes	235	195	0.003
				Blood loss, mL	400	200	0.002
				Post-operative			
				Chest drain, days	7.5 (6.6–8.7)	8.0 (6.7–10.3)	0.308
				LoS, days	11.0 (10.6–12.8)	11.0 (9.8–14.5)	0.498
Leshnower et al. 2010[52]	United States	Retrospective single center analysis, n=26 thoracotomy (open); n=15 VATS (thoracoscopic)	Video-assisted versus open segmentectomy (2002–2009)	**Peri-operative**			
				Mean (SD) operating room time, minutes	140 (38)	145 (55)	0.70
				Post-operative			
				Mean (SD) chest tube duration, days	5.2 (3.0)	2.8 (1.3)	0.001
				Mean (SD) LoS, days	8.3 (6.1)	3.5 (1.4)	0.01
				Mortality	8%	0%	0.27
				Discharge to home	85%	100%	0.63

ESTS, European Society of Thoracic Surgeons; FEV1, forced expiratory volume in 1 second; IQR, inter-quartile range; LoS, length of stay: VATS, video-assisted thoracic surgery

Table 1-3 Summary of key studies comparing economic outcomes of video assisted versus open thoracic surgery

Study	Setting	Study details	Procedures	Currency (Cost year)	Cost Outcome	Open	VATS	P value
Casali et al. 2009[43]	United Kingdom	Retrospective single center analysis, n=93 VATS lobectomy, n=253 thoracotomy	Video-assisted thoracoscopic lobectomy versus open (thoracotomy) lobectomy for early stage lung cancer (2004–2006)	EUR (year not stated)	Theater cost	1,280 (54)	2,533 (230)	0.00001
					HDU stay cost	2,571 (80)	1,713 (236)	0.00001
					Ward stay cost	4,325 (154)	3,776 (281)	0.00001
					Total cost	8,178 (167)	8,023 (565)	0.00002
Leshnower et al. 2010[52]	United States	Retrospective single center analysis, n=26 open; n=15 VATS	Video-assisted versus open segmentectomy (2002–2009)	USD (year not stated)	Total cost	46,798	45,101	0.56
Cho et al. 2011[53]	Korea	Prospective single center study, n=86 VATS, n=97 open	Video-assisted thoracic surgery (VATS) versus open lobectomy for non-small cell lung cancer (2007–2009)	USD (year not stated)	**All patients**			
					Total hospital cost	5,593	5,391	0.098
					Ward stay cost	429	268	0.000
					Anesthesia cost	474	435	0.193
					Surgical material cost	1,365	1,742	0.000
					Surgical fee	911	910	0.884
					Benefit-service cost	4,119	3,882	0.139
					Non-benefit-service cost	1,144	1,305	0.674
					Patients without complications			
					Total hospital cost	4,769	4,684	0.891
					Ward stay cost	327	234	0.000
					Anesthesia cost	478	455	0.322
					Surgical material cost	1,306	1,853	0.000
Gopaldas et al. 2010[31]	United States	Retrospective national database; n=12,860 open; n=759 VATS	VATS versus open lobectomy (2004–2006)	USD (year not stated)	Hospitalization cost	23,862 (206)	25,125 (1,093)	NR

Table 1-3 Summary of key studies comparing economic outcomes of video assisted versus open thoracic surgery								
Study	**Setting**	**Study details**	**Procedures**	**Currency (Cost year)**	**Cost Outcome**	**Open**	**VATS**	**P value**
Divisi et al. 2015[54]	Italy	Retrospective single center study, n=61 VATS, n=61 pleural drainage	VATS versus pleural drainage for primary spontaneous pneumothorax (2006–2012)	EUR (year not stated)		Chest tube	VATS	
					Total cost	4209	2319	NR
					ICER, VATS versus pleural drainage, EUR per QALY gained at			
					1 year	7,600		
					2 years	7,908		
					3 years	8,237		
					4 years	9,227		
					5 years	10,045		
Fang et al. 2014[55]	Taiwan	Retrospective database analysis, n=966 propensity matched	VATS versus open surgery for stage I NSCLC (lobectomy or sublobectomy, wedge or segmental resection) (2007–2009)	USD (2013)	Cost	21,976	22,316	NR
					Life years	0.974	0.980	
					ICER, USD per life year gained for VATS compared with open surgery	56,667		
Farjah et al. 2014[30]	United States	Retrospective cohort study using the MarketScan database, n=6,893 thoracotomy, n=3,069 VATS	VATS versus open lobectomy for lung cancer (2007–2011)	USD (year not stated)	Mean total 90 day costs	46,470	42,076	0.001
					Mean Index hospitalization costs	37,673	35,307	0.002
					Mean 90-day readmission costs	36,845	35,550	0.772
					Mean 90-day outpatient health care use costs	3,828	3,530	0.043
					Mean 90-day outpatient pharmacy costs	713	672	0.170
Howington et al. 2012[37]	United States	Retrospective database analysis; n=999 open; n=1,052 VATS	VATS versus open wedge resection in lung cancer (2007–2008)	USD (year not stated)	Hospital costs	17,377 (5,185)	14,795 (4,414)	0.000

Table 1-3 Summary of key studies comparing economic outcomes of video assisted versus open thoracic surgery								
Study	**Setting**	**Study details**	**Procedures**	**Currency (Cost year)**	**Cost Outcome**	**Open**	**VATS**	**P value**
Ramos et al. 2012[44]	France	Retrospective single center analysis, n=98 thoracoscopy, n=189 thoracotomy	Thoracoscopic versus open lobectomy for stage I non-small cell lung cancer (2007-2009)	EUR (year not stated)	Mean hospital (ward) stay (SD)	3,171 (1,566)	2,503 (873)	<0.001
					HDU and ICU	2,612 (3,495)	1,929 (3,322)	0.167
					Theatre + disposables	2,260 (399)	2,861 (458)	<0.001
					Laboratory	662 (440)	479 (336)	<0.001
					Radiology	578 (454)	452 (429)	0.014
					Total cost	14,146 (7,118)	11,934 (6,690)	<0.001
Chen et al. 2014[42]	China	Retrospective chart review, n=310 thoracotomy, n=76 VATS	VATS versus thoracotomy for pulmonary aspergilloma (lobectomy ± segmentectomy, bilobectomy, wedge resection, pneumonectomy) (2005–2012)	CNY (year not stated)	Total cost	49,000 (15,000)	43,000 (6,000)	0.016
Park et al. 2012[33]	United States	Retrospective database analysis, n=4,769 open, n=1,523 VATS	VATS versus open surgery for pulmonary lobectomy for lung cancer (2008)	USD (year not stated)	Median total cost	20,348	19,656	0.16
Swanson et al. 2012[36]	United States	Retrospective database analysis, n=2,907 open, n=1,054 VATS	Open versus VATS lobectomy (2007–2008)	USD (year not stated)	Adjusted hospital costs (SD)	21,016 (5,645)	20,316 (5,457)	0.027
Deen et al. 2014[48]	United States	Retrospective analysis, n=69 open, n=58 VATS and n=57 robotic (not presented in analysis)	Open versus VATS and robotic VATS (not presented) lobectomy or segmentectomy for stage I or II	USD (year not stated)	Procedure cost	15,036	13,663	0.169
					Operating room	4,301	4,520	0.248
					Ward	2,611	2,875	0.908
					Supplies	2,097	2,683	<0.001
					Staplers	1,537	2,033	<0.001
					ICU	2,541	1,012	0.002
					Respiratory therapy	1,084	730	0.025

Table 1-3 Summary of key studies comparing economic outcomes of video assisted versus open thoracic surgery								
Study	**Setting**	**Study details**	**Procedures**	**Currency (Cost year)**	**Cost Outcome**	**Open**	**VATS**	**P value**
			NSCLC, carcinoid or metastatic foci (2008–2012)		Laboratory Pharmacy Imaging	936 590 568	564 549 530	<0.001 0.603 0.494
Burfeind et al. 2010[56]	United States	Cost minimization analysis	Thoracoscopy versus posterolateral thoracotomy for lobectomy	USD (year not stated)	Preoperative cost Hospitalization Post-operative Professional Total costs	722 (963) 8,251 (2,958) 464 (1,313) 2,694 (1,473) 12,119 (3,476)	419 (441) 7,144 (2,148) 398 (1,402) 2,122 (1,467) 10,084 (2,820)	NR NR NR NR 0.0012
Li et al. 2012[51]	China	Retrospective analysis, n=47 thoracotomy, n=29 VATS	Thoracotomy versus VATS lobectomy for NSCLC (2000–2009)	CNY (year not stated)	Total cost	30,300 (28,600, 36,300)	48,500 (41,200, 56,700)	0.000

HDU, high dependency unit; ICER; incremental cost-effectiveness ratio; ICU, intensive care unit; NSCLC, non-small cell lung cancer; QALY, quality-adjusted life year; SD, standard deviation; VATS, video-assisted thoracic surgery

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