Robot-assisted cystectomy

QUESTIONS TO BE ADDRESSED:

1. In patients with bladder cancer, is robot-assisted cystectomy with urinary diversion (extra - or intra- corporeal) clinically effective compared to open or laparoscopic cystectomy with urinary diversion (extra - or intra- corporeal)?

2. In patients with bladder cancer, is robot-assisted cystectomy with urinary diversion (extra - or intra- corporeal) cost-effective compared to open or laparoscopic cystectomy with urinary diversion (extra - or intra- corporeal)?

3. What is the relationship between hospital surgical volume and outcomes in robot-assisted cystectomy?

4. What is the relationship between surgeon/operator experience of robot-assisted cystectomy and outcomes?

SUMMARY

Background

- Cystectomy is the removal of the bladder.

- There are three types of cystectomy:

    - Simple cystectomy is defined as the removal of the bladder only, without removal of adjacent structures or organs.
    - Radical cystectomy is the removal of the bladder, prostate and seminal vesicles in men and of the bladder, uterus, ovaries and fallopian tubes in women. It is used to treat cancer confined to the bladder.
    - Partial cystectomy is the removal of part of the bladder.

- Cystectomy can be carried out in three ways:

    - In an open cystectomy, the bladder is removed through a large incision in the front of the abdomen.
    - In a laparoscopic nephrectomy, the surgeon inserts a laparoscope and other surgical instruments through small incisions in the abdominal wall, and uses them to remove the bladder.
    - More recently, surgeons have performed robot-assisted laparoscopic cystectomy, a variant on the laparoscopic approach.

Clinical effectiveness

- We found only one randomised trial of robot-assisted assisted radical cystectomy, which was underpowered. The available unrandomised studies are potentially confounded, particularly by tumour size.

- A systematic review comparing robot-assisted and conventional laparoscopic cystectomy found no randomised trials nor any non-randomised controlled studies. Only uncontrolled studies were found. Comparison of the uncontrolled studies suggested that rates of serious complications and of positive surgical margins[1] are similar after the two procedures. Yields of pelvic lymph nodes are also similar.

- The systematic review is of only limited value, with an unclear methodology. The absence of studies directly comparing the two procedures severely restricts what can be concluded.

- We found a better quality systematic review comparing robot-assisted and open radical cystectomy which was based on a larger evidence base with one small randomised trial and seven unrandomised studies.

- Robot-assisted cystectomy emerged favourably from this review. Patients undergoing the procedure had less blood loss and a lower risk of receiving a transfusion. Complications were less common. Robot-assisted operations took longer, but those patients left hospital earlier. The yield of lymph nodes was higher, but there were no differences in the rate of positive surgical margins.

- However, there was substantial confounding and heterogeneity in this evidence, limiting its reliability.

- These findings were corroborated by two later studies.

- We found no evidence that robot-assisted cystectomy was associated with lower mortality, lower recurrence risk, longer survival or any longer-term patient advantage from the use of the robot.

Safety

- There are some indications that robot-assisted cystectomy has lower rates of some complications than open radical cystectomy.

- The absence of any studies directly comparing robot-assisted cystectomy with conventional laparoscopic cystectomy prevents any reliable conclusions about the comparative safety of these procedures.

[1] These occur when cancer is detected at the edge of a resected surgical specimen, suggesting the presence of residual tumour.

Cost effectiveness

- We found a systematic review of the costs of robot-assisted versus open radical cystectomy, which included three studies, all from the United States. The first reported higher costs with the robot-assisted procedure, but had assumptions which favoured open cystectomy. The second showed the opposite result, but contained incomplete data and was opaquely reported. The third also reported lower costs with robot-assisted cystectomy.

- We found one larger analysis with more reliable analysis, published since the systematic review, but also from the United States. This reported the robot-assisted procedure to be more expensive than the open procedure.

- We found no studies which evaluated the cost effectiveness of different forms of cystectomy.

Volume outcome relationships

- We found only very limited evidence about the relationship between hospital surgical volume and clinical outcome.

- We found three studies of the relationship between the experience and activity levels of surgeons and clinical outcomes. Taken together, they indicate that increasing surgeon experience reduces operation time and improves lymph node yield. There is no evidence of an effect on complications, positive surgical margins, blood loss, recurrence or survival.

1 Context

1.1 Introduction

Cystectomy is the removal of the bladder, usually performed to treat cancer. Robot-assisted cystectomy is a newer technique for carrying out the procedure which may have advantages for the patient.

1.2 Existing national policies and guidance

We found no national guidance on robot-assisted cystectomy.

2 Epidemiology

The most common indication for cystectomy is a malignant or, less commonly, benign tumour of the bladder. The bladder may also be removed for other reasons such as cancer in a neighbouring organ, radiation damage, trauma and intractable infection.

For people with a tumour apparently confined to the bladder, surgery is the treatment of choice and usually the only curative approach. Smaller tumours which have not penetrated the muscle of the bladder wall can be treated with endoscopic transurethral resection, which can be repeated to maintain tumour control. If the tumour invades the bladder

muscle, or is too extensive for endoscopic treatment, then the bladder can be removed. The procedure involves initial identification and ligation of the ureters, posterior dissection between the rectum and prostate, control of the lateral pedicles, anterior dissection and pelvic lymph node dissection. In women, the vagina is reconstructed with a running intracorporeal suture.

There are three types of cystectomy:

- *Simple cystectomy* is defined as the removal of the bladder only, without removal of adjacent structures or organs. It is seldom performed nowadays.

- *Radical cystectomy* is the removal of the bladder, prostate and seminal vesicles in men and of the bladder, uterus, ovaries and fallopian tubes in women. The operation also includes the removal of the perivesical tissues and pelvic lymph nodes. It is usually carried out for cancer.

- *Partial cystectomy* is the removal of part of the bladder. It is used to treat cancer that has invaded the bladder wall in a small area far enough from the openings where urine enters or leaves the bladder. We do not cover partial cystectomy in this evidence review, in line with its agreed scope.

After a complete cystectomy, surgeons reconstruct the urinary tract to provide a means by which urine can leave the body. This can be done by creating a urinary conduit using a length of small intestine from the ureters to a urostomy on the abdominal wall. Less commonly, the surgeon may create a new bladder (a neo-bladder) out of a section of the bowel, connecting the urethra to this to enable near-normal urination.

3 The intervention

Cystectomy can be carried out in three different ways:

- In an *open cystectomy*, the bladder is removed through a large incision in the front of the abdomen. Open radical cystectomy is a major operation, associated with significant perioperative complications even when performed by an experienced urologist. This is because of the long incision, prolonged abdominal wall retraction, lengthy exposure of the peritoneal surface with major fluid shifts and poor visibility, particularly in the depth of the pelvis and in the retrovesical area.

- In a *laparoscopic cystectomy*, the surgeon inserts a laparoscope and other surgical instruments through small incisions in the abdominal wall. The operation is otherwise similar to an open cystectomy. A conventional laparoscopic radical cystectomy is technically demanding, especially the intracorporeal suturing and the extensive pelvic lymph node dissection which contributes to survival. Urinary diversion or the formation of a neo-bladder can be carried out laparoscopically or, more commonly, by an open procedure.

- More recently, surgeons have performed *robot-assisted laparoscopic cystectomy*, a variant on the laparoscopic approach. Once the instruments are inserted, the surgeon sits apart from the patient, viewing the operative field in three dimensions through the laparoscope and manipulating the instruments remotely. The equipment provides three-dimensional vision and robot-assisted control of the

instruments, allowing for scaling of movement, increased precision and tremor damping. It differs from conventional laparoscopic cystectomy, which only has two-dimensional vision and offers fewer degrees of freedom for instrument movement. Differences in perspective and tactile feedback mean that robot-assisted procedures require different skills from the operator, and there is a learning curve while these are acquired.

4 Findings

4.1 Evidence of effectiveness

In June 2014, we searched for evidence about the clinical and cost effectiveness of robot-assisted cystectomy in comparison with open or conventional laparoscopic cystectomy.

We found two recent systematic reviews of controlled studies, each focussed on different questions. One compared robot-assisted and conventional laparoscopic radical cystectomy[1], and the second compared robot-assisted and open radical cystectomy[2].

Patients are often seen as more suitable for robot-assisted rather than conventional laparoscopic radical cystectomy, or for laparoscopic rather than open cystectomy, if they have less advanced disease, less comorbidity, organ-confined non-bulky tumours, and are free from obesity and coagulopathy. Bulky lymphadenopathy, locally advanced disease, marked obesity and uncorrected coagulopathy are strong contra-indications to laparoscopic radical cystectomy. This biases non-randomised comparisons of robot-assisted and conventional laparoscopic radical cystectomy in favour of the former procedure.

We also searched for relevant studies published since the search dates of these reviews. To exclude smaller studies at greater risk of bias, we included only those which were randomised and/or recruited more than one hundred participants.

Robot-assisted laparoscopic cystectomy versus conventional laparoscopic cystectomy

Challacombe et al published a systematic review of randomised controlled trials and non-randomised controlled studies comparing robot-assisted and conventional laparoscopic cystectomy, and uncontrolled studies (search date November 2010).[1] They did not meta-analyse their results. The authors note that “some of the reported series give insufficient data on the patient population undergoing [radical cystectomy], which limits the ability to compare these reports to other contemporary series.”

Challacombe et al found no randomised trials comparing robot-assisted and conventional laparoscopic cystectomy, nor any non-randomised comparative studies. They did however find six non-comparative studies of a total of 971 people having conventional laparoscopic cystectomy, and three similar studies of 153 people having robot-assisted cystectomy. Rates of serious complications were similar, ranging between 10% and 13% for laparoscopic cystectomy and 10% and 17% for robot-assisted cystectomy.

Positive surgical margins are a predictor of metastatic progression and death in bladder cancer.[3] They appear of broadly equivalent frequency in the two groups, ranging

between 0% and 9% after laparoscopic surgery and 0% and 6% after robot-assisted procedures.

Challacombe et al also reviewed rates of recurrence and mortality. Here the evidence is patchy. Only two of the five papers on robot-assisted cystectomy reported recurrence rates, and there were not enough details of how recurrence was defined and diagnosed to make it possible to compare these rates with those in people who had had other procedures. The authors report cancer-specific survival[2] figures over various periods of 85%, 94% and 95% from three of these studies, somewhat higher than those reported for laparoscopic cystectomy (80%, 82% and 92%). Overall survival figures range from 63% to 100% after laparoscopic radical cystectomy, and from 79% to 90% after the robot-assisted procedure.

The authors found no studies which compared the yield of lymph nodes after conventional laparoscopic and robot-assisted cystectomy. There were five studies of lymph node yield after laparoscopic cystectomy (732 people), and five after the robot-assisted procedure (239 people). The results were similar, with mean numbers ranging from 13 to 16 and 13 to 19 respectively.

Challacombe et al is only of limited value. The review's methodology is not clearly described. The absence of studies directly comparing the two procedures severely limits what can be concluded. The authors' decision not to meta-analyse their results was appropriate, but it leaves a set of disparate results which cannot validly be compared.

There are other drawbacks to this review and the evidence base which underlies it:

- There is only limited information on the quality of included studies. Loss to follow-up, incomplete information and biases in ascertainment may reduce their validity.
- There is insufficient information to assess the risk of bias and confounding between studies. This is an important threat to the validity of the comparisons in the review, because, as discussed above, the patients undergoing robot-assisted cystectomy may well be selected in a way which biases the studies in favour of that procedure, undermining any comparison's reliability.
- The duration of follow-up varies between studies and is not reported for two studies of robot-assisted cystectomy. This makes it impossible to interpret the recurrence and survival data.
- The duration of follow-up is generally too short for adequate information on long-term outcomes to emerge. Only one study had follow-up of more than three and a half years.

We can conclude from this review that, in selected patients, robot-assisted radical cystectomy is technically possible with apparently adequate lymph-node removal. The limited number, size and duration of the studies of the procedure, coupled with the substantial risk of confounding, mean that no further conclusions can be drawn about its performance relative to conventional laparoscopic radical cystectomy.

[2] The proportion of people diagnosed with cancer who are either still alive after a specified interval or dead from a non-cancer cause.

We found one study published too late for inclusion in Challacombe et al's review.[4] Snow-Lisy et al reported on 121 patients who underwent robot-assisted or laparoscopic radical cystectomy at a hospital in Ohio, of whom 104 had laparoscopic radical cystectomy and 17 had robot-assisted radical cystectomy.

The study was not designed to explore the relative performance of the two procedures. The authors report complication rates, which were similar (Table 1). The only other results reported by procedure were overall and cancer-specific survival, but the lack of prognostic information about participants who had each procedure and the very different durations of follow-up make this information uninterpretable.

Robot-assisted radical cystectomy versus open radical cystectomy

Tang et al published a systematic review and meta-analysis of randomised and non-randomised controlled studies comparing robot-assisted and open radical cystectomy (search date December 2012).[2] This review drew on a larger evidence base of higher quality studies than that of Challacombe et al, and its methodology was more explicitly described. Tang et al included thirteen studies reporting 1011 people who underwent robot-assisted radical cystectomy and 418 who underwent the open procedure: one RCT, seven prospective unrandomised controlled studies and five retrospective unrandomised controlled studies.

As expected, there were important differences between the two groups in the unrandomised studies. Patients undergoing the robot-assisted procedure were older, more were male and fewer had had previous abdominal surgery. Importantly, more of them had cancer confined to the bladder.

Robot-assisted cystectomy emerged favourably from Tang et al's review. Patients undergoing the procedure had less blood loss and a much lower risk of receiving a transfusion. Complications were less common. Robot-assisted operations took longer, but those patients left hospital earlier. The yield of lymph nodes was higher, suggesting more complete removal of potential metastases, though the fact that fewer had positive lymph nodes confirms that those undergoing robot-assisted surgery had less advanced cancers. There were no differences in the rate of positive surgical margins.

How reliable are Tang et al's findings? There are two major reasons for caution:

- With one exception, the studies were unrandomised. There is clear evidence of selection bias, with the smaller and less advanced cancers in the robot-assisted patients being easier to remove without complications. There was also evidence of publication bias with respect to estimated blood loss and positive surgical margins, with significant results from Egger's test.

- Consistent with this, there was widespread and marked heterogeneity in the results meta-analysed, with significant heterogeneity detected for operating time, blood loss, blood transfusions, length of hospital stay, time to normal diet and lymph node yield. This calls into question the reliability of the meta-analysis' results.

Table 1: Evidence on robot-assisted versus open and conventional laparoscopic nephrectomy

Study	Patients	Intervention	Comparator	Results	Comment
Tang et al [2]	13 studies including 957 people with bladder cancer.	Robot-assisted radical cystectomy (RRC) (418)	Open radical cystectomy (ORC) (539)	Patients undergoing RRC were older (odds ratio* (OR) 1.69, 95% confidence interval (CI), 0.50 to 2.70, P = 0.004), more were male (OR 1.45, 95% CI 1.06 to 1.97, P = 0.02), fewer had previous abdominal surgery (OR 0.68, 95% CI 0.49 to 0.96, P = 0.03) and fewer had non-organ-confined cancer (OR 0.57, 95% CI 0.33 to 0.97, P = 0.04). Duration of operation: weighted mean difference (WMD) 70.7 min, 95% CI 46.40 to 94.98 min, P < 0.001. Blood loss WMD -599 ml, 95% CI, -881ml to -317ml, P < 0.001. Blood transfusions: OR 0.13, 95% CI 0.03 to 0.46, P = 0.002. Length of hospital stay: WMD -4.6 days, 95% CI -6.7 to -2.46 days, P < 0.001. Time to normal diet: WMD -1.57 days, 95% CI -2.57 to -0.58 days, p = 0.002. No significant difference between in rates of positive surgical margins. Lymph node yield: WMD 2.18 nodes, 95% CI 0.89 to 3.47, p = 0.001. Positive lymph nodes: OR 0.64, 95% CI 0.42 to 0.96, P = 0.03. Complication rate: OR 0.54, 95% CI 0.40 to 0.72, P = 0.001.	Well-conducted and reported systematic review and meta-analysis. Substantial risk of bias and confounding and widespread heterogeneity.
Parekh et al [6]	People with biopsy-proven	Robot-assisted	Open radical cystectomy	Operation time: RRC 300 mins, ORC 286 mins, P = 0.329. Estimated blood loss:	Well designed but severely

San Antonio, USA Randomisation July 2009 to June 2011	bladder cancer of clinical stage T1 to T3, N0, M0 and candidates for an open or robotic approach. Exclusion criteria included multiple prior abdominal and pelvic open surgical procedures, morbid obesity and clinical lymph node positive bladder cancer with grossly enlarged pelvic or retroperitoneal lymph nodes.	radical cystectomy (RRC) (20)	(ORC) (19)	RRC 400 ml, ORC 800ml, P = 0.003. Blood units transfused: RRC 0, ORC 2, P = 0.410. Inpatient stay: RRC 6 days, ORC 6 days, P = 0.288. Days to normal diet: RRC 4, ORC 6, P = 0.50. Complications: RRC 25%, ORC 25%, P = 0.50. Positive surgical margins: RRC 5%, ORC 5%, P = 0.50. Yield of lymph nodes; RRC 11, ORC 23, P = 0.135. Positive lymph nodes: RRC 20%, 20%, P = 0.50.	underpowered trial with balanced randomisation.
Kader et al [7] Winston Salem, USA	Consecutive patients undergoing radical cystectomy with curative intent for bladder cancer	Robot-assisted radical cystectomy (RRC) (100), two surgeons	Open radical cystectomy (ORC) (100), four surgeons	Duration of operation: ORC 393 min, RRC 451 min, P < 0.01. Ileal conduit urinary diversion RRC 97%, ORC 83%, P = 0.032. Estimated blood loss: RRC 423ml, ORC 986ml, P < 0.001. Transfusion rates: RRC 15%, ORC 47%, P < 0.001. No patient required conversion from RRC to ORC.	There were no significant differences in sex, age, body mass index, ASA classification, number of previous

				90-day complication rate: RRC 35%, ORC 57%, P = 0.001. Major complication rate: RRC 10%, ORC 22%, P = 0.019. Positive lymph nodes: RRC 30%, ORC 24%, P = 0.31. Lymph node yield: RRC 17.7, ORC 15.7, P = 0.551. Positive surgical margins: RRC 12%, ORC 11%, P = 0.864.	abdominal surgeries, and exposure to pelvic radiation or neoadjuvant chemotherapy.
Snow-Lisy et al [4] Cleveland, USA 1999 to 2008	People with recurrent or high-grade superficial or muscle-invasive bladder cancer but no extra-vesical spread or metastases.	Robot-assisted radical cystectomy (RRC) (17)	Laparoscopic radical cystectomy (LRC) (104, 87 with extracorporeal urinary diversion and 17 with neobladder formation)	Complications: RRC 53%, LRC 41%, χ^2 = 0.802, P = 0.37**	No information on participants analysed by procedure performed, nor on method of assignment. Oncological outcomes uninterpretable because of variation in duration of follow-up.

* Higher value of odds ratio means more common in robot-assisted group.

** Calculated by SPH.

The one randomised trial included by Tang et al was small and underpowered for most outcomes, with only 41 participants.[5] It reported significant advantages from robot-assisted cystectomy for operating time, estimated blood loss and time to normal diet, so these findings from the wider systematic review can be regarded as more reliable.

We found three studies published too recently for inclusion in Tang et al's review.

Parekh et al published a pilot randomised controlled trial of open versus robot-assisted radical cystectomy.[6] The authors recruited 40 participants at a hospital in Texas, suitable for both procedures; data were available on 39 of these. The trial was underpowered for definitive comparisons, but did report lower estimated blood loss after the robot-assisted procedure.

Kader et al reported a study comparing two cohorts of one hundred consecutive patients treated with open or robot-assisted radical cystectomy at a hospital in North Carolina.[7] The cohorts were comparable. Kader et al report that robot-assisted operations took longer but incurred less blood loss with lower rates of blood transfusion and complications. There were no differences in rates of positive surgical margins and lymph node retrieval.

Aboumohamed et al published a comparison of health-related quality of life after robot-assisted and open radical cystectomy.[8] Using the Bladder Cancer Index and the European Organization for Research and Treatment of Cancer Body Image scale, they compared 82 people who underwent robot-assisted radical cystectomy with 100 who underwent open radical cystectomy, with participants completing the two surveys preoperatively and twice thereafter. Baseline urinary, bowel, sexual function, and body image were not different between both the groups, but postoperative analysis showed better sexual function in open cystectomy group (P = 0.047), with no significant differences between both the groups in the other three domains (P = 0.11, 0.58, and 0.93 respectively). The choice of diversion technique made no significant difference.

Trials in progress

We searched clinicaltrials.gov and found no trial results relevant to this review. The Wales Cancer Trials Unit notified a pilot randomised trial of open radical cystectectomy versus laparoscopic or robot-assisted radical cystectectomy in people with bladder cancer (clinicaltrials.gov identifier NCT01196403). The trial opened in 2009 and was due to complete in December 2010, but no results are available.

4.2 Safety

Differences in rates of complications were reported in some of the studies described above. There are some indications that robot-assisted cystectomy has lower rates of some complications than open radical cystectomy.

4.3 Evidence of cost effectiveness

We found a systematic review of the cost effectiveness of robot-assisted versus open radical cystectomy (search date not stated, but the paper was published in 2011).[9] Lee et al included three previous comparisons, all from the United States.

The first was based on a comparison of twenty robot-assisted and twenty open radical cystectomies carried out at a university hospital in North Carolina.[10] Both categories of patient followed the same clinical pathway, so lengths of inpatient stay were identical; complication rates were assumed to be identical, though patients having an open cystectomy had higher transfusion costs. Costs were 11% higher with robot-assisted surgery (US$16,248, £9,600) than with open surgery ($14,608, £8,600). This was because of the longer duration of the robot-assisted procedure and the purchase, maintenance and disposable equipment costs of the robot. This study is clearly reported, though the assumptions both favour open cystectomy.

The second study was from the Mayo Clinic in Phoenix, Arizona.[11] Martin et al reported a cost comparison based on 19 consecutive patients undergoing robot-assisted radical cystectomy and 14 undergoing the open alternative. This showed a 38% "total" cost advantage with robot-assisted surgery, which rose to 60% when hospital stay, drugs, transfusions, treatment of complications and related readmissions were taken into account. It is not clear what "total" means in this context, what the absolute costs were – they could not be published for "proprietary reasons" – and how the costs of the robot were taken into account.

These authors also developed a model to illustrate the effect of changing parameters on the cost differences between the two procedures. The most influential parameters were operative time, followed by length of stay, the cost of robot supplies and the number of cases treated annually.

Martin et al is opaquely reported. The absence of information on the absolute level of cost inputs and differences make the study hard to interpret.

Lee et al's review also included a paper with Lee as the first author, from New York Presbyterian Hospital.[12] It described a larger series of 83 patients undergoing robot-assisted radical cystectomy and 103 patients undergoing the open alternative. Lengths of stay were shorter and complications less frequent after robot-assisted procedures, offsetting the higher costs of purchasing and maintaining the robot. The costs for patients having an ileal conduit were $25,505 (£15,000) for open surgery and $20,659 (£12,200) for robot-assisted procedures. This was based on $1.65m (£970,000) to purchase a robot depreciated over seven years, an annual maintenance contract of $125,000 (£73,500) and 361 procedures a year.

We found one study published too recently for inclusion on Lee et al's review.[13] Yu et al analysed all patients undergoing open and robot-assisted radical cystectomy in 2009 recorded in the US Nationwide Inpatient Sample[3]. There were 1444 open radical cystectomies for bladder cancer, and 224 robot-assisted radical cystectomies, performed at 234 hospitals. There were only 55 conventional laparoscopic radical cystectomies, and they were excluded "because of inability to power adjusted analysis". Results were adjusted using propensity scores for confounders.

Yu et al found complications to be less common after robot-assisted cystectomy (49% versus 64%, P = 0.035). Rates of blood transfusion, routine discharge, length of stay and pelvic lymph node dissection were similar. Based on billing data, rather than underlying

[3] This is a 20% stratified probability sample of eight million acute hospital stays in the United States. It is the largest all-payer inpatient care observational cohort in the US.

costs, the robot-assisted procedure was significantly more expensive (median $28,100 (£16,500) versus $24,303 (£14,300), P = 0.023).

Yu et al's study is the most reliable that we found. It is based on a much larger sample from a more broadly representative set of hospitals, so the results are likely to be more widely generalisable, at least within the United States. The adjustment for confounders also improves the reliability of the reported comparison. However, the results are based on the prices paid for the procedure rather than the costs of providing it, so the impact of buying and maintaining the robot is not explicit.

In considering these studies, the following factors are relevant:

- The study reflects costs at hospitals in the United States. Costs in the NHS will be different from those reported.
- Sample sizes were small in two studies.
- The surgeons whose results Lee et al include may achieve better results than average. If the duration of robot-assisted operations and inpatient stays is longer for less experienced and accomplished surgeons, that approach will be more expensive.
- There may be selection bias between the patients receiving the different procedures.
- Achieving high numbers of robot-assisted procedures per year may be ambitious.

It is hard to draw clear conclusions from this set of studies. Smith et al's assumptions probably bias their analysis against robot-assisted cystectomy, by ignoring its beneficial effect on complications and inpatient stay. Martin et al's lack of inclusion of cost data makes their study hard to interpret. Lee et al and Yu et al reach opposite conclusions; Yu et al is probably more reliable because of its much larger and more diverse sample.

In any case, these cost studies are sensitive to factors such as the cost of the robot and other inpatient costs which vary between the United States and the NHS. Only studies based on NHS costs and outcomes can be regarded as reliable and relevant to NHS decision-makers.

Importantly, we found no cost comparisons of robot-assisted and conventional laparoscopic radical cystectomy.

4.4 Hospital surgical volume and outcomes in robot-assisted cystectomy

We found no studies on this question, though Hellenthal et al reported an association between hospital volume and lymph node yield (see below).[14]

4.5 Surgeon/operator experience and outcomes in robot-assisted nephrectomy

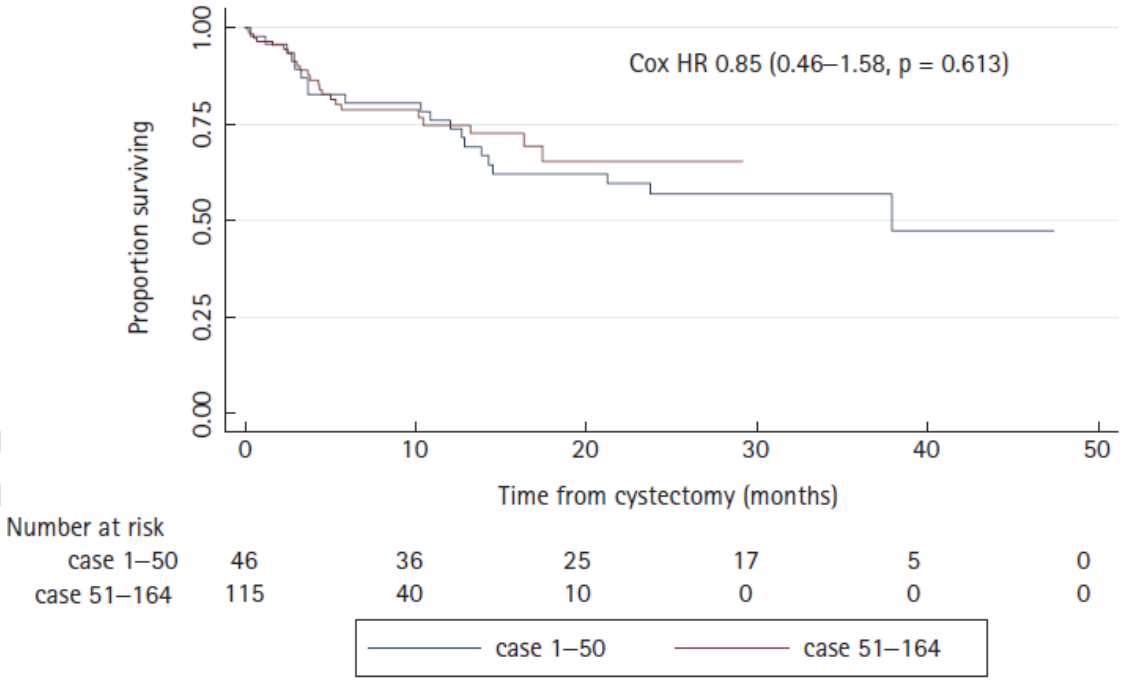
We found three studies of the relationship between the experience and activity levels of surgeons and clinical outcomes.

Hayn et al reported a single surgeon's experience of 164 robot-assisted radical cystectomies at a hospital in New York state.[15] Patients were divided into three groups (patients 1 to 50, 51 to 100 and 101 to 164) and stratified by age group, gender, pathological tumour stage, lymph node status, surgical margin status and sequential case number.

Median follow-up was eight months, with a range from 0 to 47 months. There was no change in complication rates (P = 0.78) nor in hospital readmission rates (P = 0.588) as the surgeon's experience increased. There was also no improvement in mean estimated intraoperative blood loss (P = 0.548) or positive surgical margins (P = 0.545). Case number was, however, significantly associated with shorter operative time (P < 0.001) and the mean number of lymph nodes retrieved (P < 0.001). Mean cystectomy operative time decreased from 180 min in the initial cases to 136 min in the last cohort, and lymph node yield increased from an average of 16 nodes in the first 50 cases to 26 nodes in the latest patients.

To evaluate the association of sequential case number to overall survival, patients were divided into an initial group of 50 patients and a subsequent group of 114 patients so that follow-up would be roughly equivalent. Overall survival in these two groups was similar (P = 0.613) (Figure 1).

Figure 1: Overall survival by accumulated surgeon experience

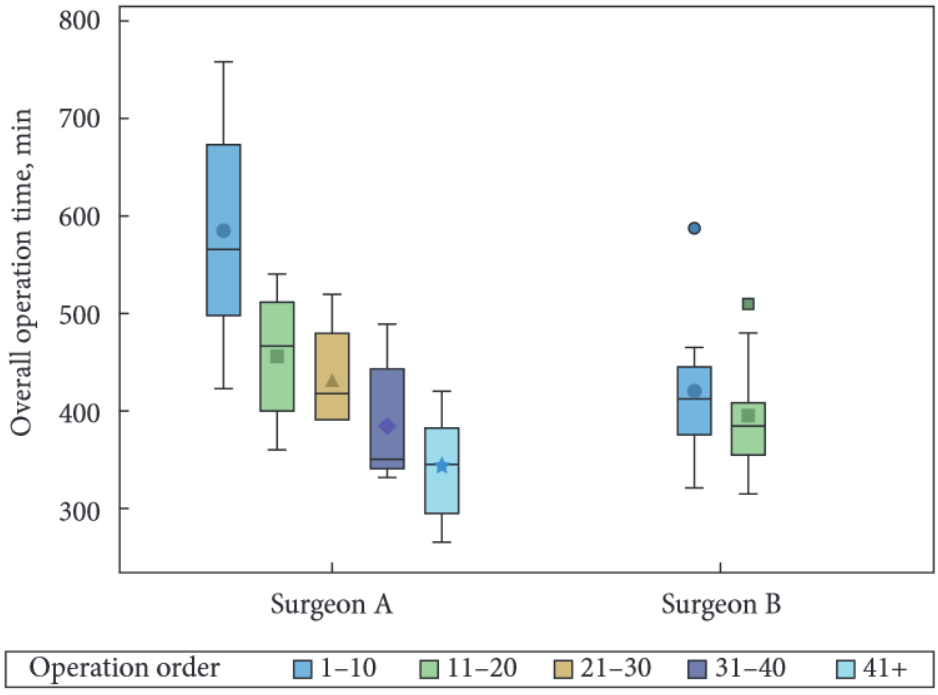


Source: Hayn et al []

We found a second study, of the learning curve of two surgeons performing robot-assisted radical cystectomy with the formation of a neo-bladder.[16] Two surgeons at a hospital in Stockholm prospectively recorded the results of the first 47 (surgeon A) and 20 (surgeon B) patients respectively on whom they carried that procedure.

Each surgeon's patients were divided into groups of 10 and the results for each group compared. The duration of operations fell significantly with increasing experience for surgeon A ($P < 0.001$) but not surgeon B ($P = 0.10$) (Figures 2 and 3). Surgeon A also showed a reduction in the risk of conversion to open surgery from 30% in the first group to 0% in latter groups ($P < 0.01$); Surgeon B had only one conversion in the second group of 10 (not significant).

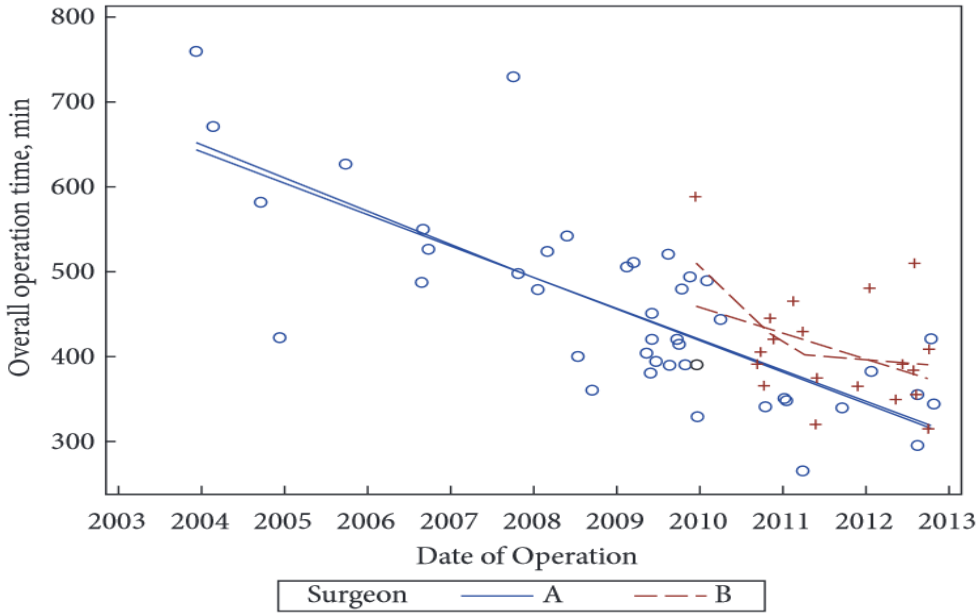
Figure 2: Operation times for Surgeons A and B



Note false zero to vertical axis

Source: Collins et al [16]

Figure 3: Scatter plot of Surgeon A's and Surgeon B's operating times



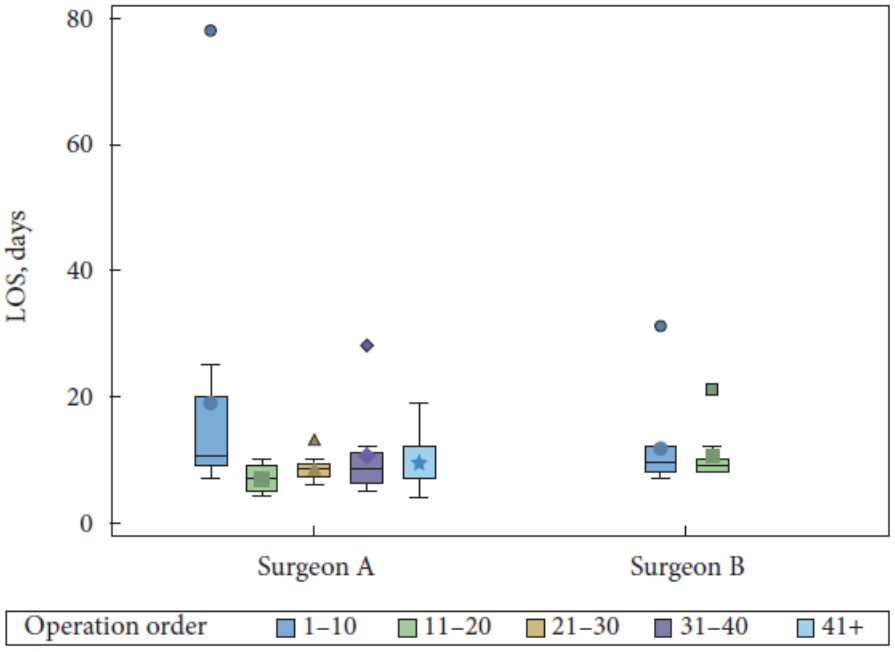
Note false zero to vertical axis.

The two regression lines for each surgeon apparently represent the whole series and the first ten and then the remaining cases respectively, though this is not made clear in the paper.

Source: Collins et al [16]

For Surgeon A, there was a decrease in mean length of inpatient stay from nineteen days in the first group to nine days in the later groups, although this may have been driven by an outlier operation. There was no change in the median length of stay with increasing experience for either surgeon (P = 0.166) (Figure 4).

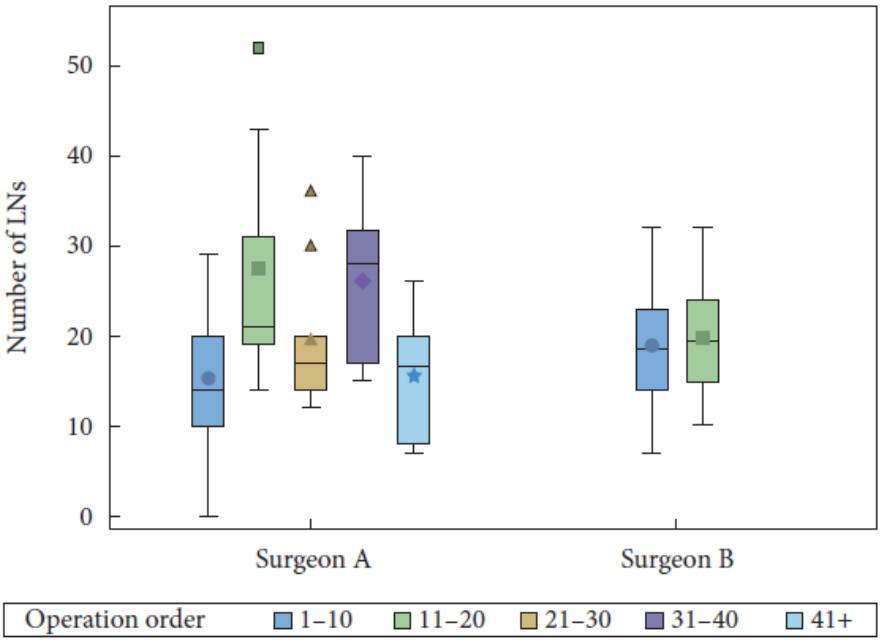
Figure 4: Length of stay for Surgeons A and B



Source: Collins et al [16]

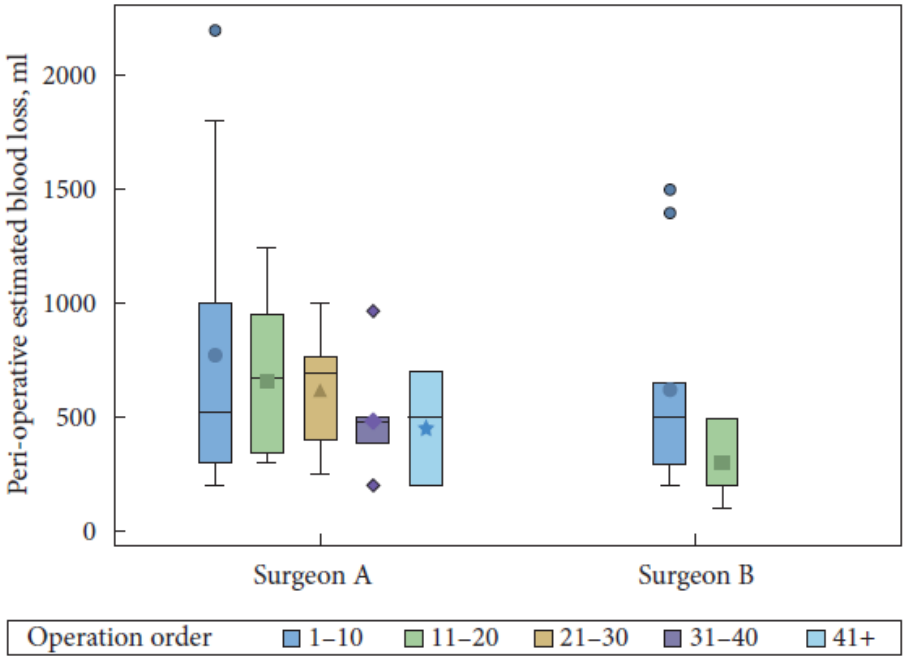
The mean total yield of lymph nodes and mean estimated blood loss did not change with experience in either surgeon's series (Figures 5 and 6). In Surgeon A's series, rates of early complications decreased from 70% in the first group to 30% in later groups ($P < 0.05$). Late major complications also decreased from 50% in the first group to zero in later groups ($P = 0.011$).

Figure 5: Lymph node yields for Surgeons A and B



Source: Collins et al [16]

Figure 6: Estimated blood loss for Surgeons A and B



Source: Collins et al [16]

In the third study, Hellenthal et al used an international database to investigate the relationship between surgical experience and lymph node yield.[14] They analysed data on 527 patients who underwent robot-assisted radical cystectomy for bladder cancer by 22 surgeons at the 15 participating institutions, mostly in the United States. Fourteen surgeons in the consortium had performed up to 20 cases and eight had performed more than 20 cases.

Overall, 437 of 527 patients (83%) had at least 10 nodes sampled, and 225 patients (43%) had 20 or more nodes removed. By the 20th case, patients were about five times more likely to undergo lymphadenectomy than those in the first 10 cases (95% CI 2.41 to 10.07, P < 0.001). Robot-assisted procedures done at institutions with more than 50 cases were 2.1 times more likely to be accompanied by lymphadenectomy than lower-volume institutions (95% CI = 1.32 to 3.38, P= 0.002). Similarly, robot-assisted operations done by surgeons who had performed more than 20 cases were 3.85 times more likely to be accompanied by lymphadenectomy than those done by low-volume surgeons (95% CI = 2.38 to 6.23, P < 0.001).

After multivariate adjustment for stage and institutional volume, surgeon volume remained significantly associated with undergoing lymphadenectomy, with surgeons with more than 20 cases being 2.37 times more likely to perform lymphadenectomy than lower-volume surgeons (95% CIs 1.39 to 4.05, P= 0.002). Patients at institutions which had carried out more than 50 robot-assisted radical cystectomies were twice as likely to have a lymphadenectomy as those at the lower volume institutions.

Taken together, this evidence indicates that increasing surgeon experience reduces operation time and improves lymph node yield. There is no evidence of an effect on complications, positive surgical margins, blood loss, recurrence or survival.

4.6 Summary of section 4

The evidence about robot-assisted cystectomy is inadequate. The only randomised trial is small and under-powered, and the unrandomised and uncontrolled studies are subject to important confounding. Also, many of the available studies may have been carried out by particularly expert surgeons whose results may not be achievable in less skilled hands.

The comparison of the procedure with conventional laparoscopic cystectomy is severely hampered by the absence of studies reporting results from both operations. Little can be securely concluded from the existing evidence.

There is more evidence comparing the procedure with the open alternative. It indicates that robot-assisted radical cystectomy takes longer to carry out, but is associated with less blood loss, fewer complications and shorter inpatient stays. Longer-term cancer-related outcomes appear similar, and no evidence of other durable advantages for patients has emerged.

Evidence about costs is entirely from the United States and contradictory. The studies reporting higher costs with robot-assisted procedures are somewhat more robust, but their generalisability to the NHS may be limited.

Perhaps unsurprisingly, as surgeons gain experience of robot-assisted cystectomy, they can perform the operation faster. They also appear to resect more pelvic lymph nodes. However, there are no reported improvements in complication rates, operative blood loss, positive surgical margins, recurrence or patient survival.

5 Cost and Activity

No information was available on this.

6 Equity issues

No ethical issues were identified.

7 Discussion and conclusions

1. *In patients with bladder cancer, is robot-assisted cystectomy with urinary diversion (extra - or intra- corporeal) clinically effective compared to open or laparoscopic cystectomy with urinary diversion (extra - or intra- corporeal)?*

   Yes, at least in comparison with the open procedure. In the short-term, robot-assisted radical cystectomy appears at least as clinically effective as the open alternative, and offers advantages in terms of lower rates of blood loss and complications, and shorter

admissions. However, it takes longer to perform and there is no evidence of longer term advantages for patients.

We found little reliable evidence comparing robot-assisted and conventional laparoscopic radical cystectomy.

2. *In patients with bladder cancer, is robot-assisted cystectomy with urinary diversion (extra - or intra- corporeal) cost-effective compared to open or laparoscopic cystectomy with urinary diversion (extra - or intra- corporeal)?*

   We do not know. The available evidence is from the United States and gives contradictory results, partly because of costing offsets between the robot's high cost and the savings from earlier discharge. We do not believe that this evidence can be securely extrapolated to the NHS.

3. *What is the relationship between hospital surgical volume and outcomes in robot-assisted cystectomy?*

   We do not know. We found only very limited evidence on this question.

4. *What is the relationship between surgeon/operator experience of robot-assisted cystectomy and outcomes?*

   More experienced surgeons carry out robot-assisted radical cystectomy faster than less experienced ones and resect more lymph nodes. There is no evidence of an effect on complications, positive surgical margins, blood loss, recurrence or survival. There is no apparent threshold, with results improving from as soon as the first ten procedures completed.

8 References

1. Challacombe BJ, Bochner BH, Dasgupta P, et al. The role of laparoscopic and robotic cystectomy in the management of muscle-invasive bladder cancer with special emphasis on cancer control and complications. *Euro Urol* 2011; 60: 767-775.
2. Tang K, Xia D, Li H et al. Robotic vs. open radical cystectomy in bladder cancer: a systematic review and meta-analysis. *Eur J Surg Oncol* 2014; http://dx.doi.org/10.1016/j.ejso.2014.03.008.
3. Dotan ZA, Kavanagh K, Yossepowitch O, et al, Positive surgical margins in soft tissue following radical cystectomy for bladder cancer and cancer-specific survival. *J Urol* 2007; 178: 2308-2312.
4. Snow-Lisy, DC, Campbell SC, Gill IS et al. Robotic and laparoscopic radical cystectomy for bladder cancer: Long-term oncologic outcomes. *Euro Urol* 2014; 65: 193-200.
5. Nix J, Smith A, Kurpad R, et al. Prospective randomized controlled trial of robotic versus open radical cystectomy for bladder cancer: perioperative and pathologic results. *Eur Urol* 2010; 57: 196-201.
6. Parekh, DJ, Messer J, Fitzgerald J, et al. Perioperative outcomes and oncologic efficacy from a pilot prospective randomized clinical trial of open versus robotic assisted radical cystectomy. *J Urology* 2013; 189: 474-479.
7. Kader, AK, Richards KA, Krane KS, et al. Robot-assisted laparoscopic vs open radical cystectomy: comparison of complications and perioperative oncological outcomes in 200 patients. *BJU Int* 2013; 112: E290-E294.
8. Aboumohamed AA, Raza SJ, Al-Daghmin A, et al. Health-related quality of life outcomes after robot-assisted and open radical cystectomy using a validated bladder-specific instrument: a multi-institutional study. *Urology* 2014; 83: 1300-8.
9. Lee R, Chughtai B, Herman M, et al. Cost-analysis comparison of robot-assisted laparoscopic radical cystectomy (RC) vs open RC. *BJU Int* 2011; 108: 976-983.
10. Smith A, Kurpad R, Lal A, et al. Cost analysis of robotic versus open radical cystectomy for bladder cancer. *J Urol* 2010; 183: 505-509.
11. Martin AD, Nunez RN, Castle EP. Robot-assisted radical cystectomy versus open radical cystectomy: a complete cost analysis. *Urology* 2011; 77: 621-625.
12. Lee R, Ng CK, Shariat SF, et al. The economics of robotic cystectomy: cost comparison of open versus robotic cystectomy. *BJU Int* 2011; 108: 1886-1892.
13. Yu HY, Hevelone ND, Lipsitz SR, et al. Comparative analysis of outcomes and costs following open radical cystectomy versus robot-assisted laparoscopic radical cystectomy: results from the US Nationwide Inpatient Sample. *Euro Urol* 2012; 61: 1239-1244.
14. Hellenthal NJ, Hussain A, Andrews PE, et al. Lymphadenectomy at the time of robot-assisted radical cystectomy: results from the International Robotic Cystectomy Consortium. *BJU Int* 2011; 107: 642-6.
15. Hayn MH, Hellenthal NJ, Seixas-Mikelus SA, et al. Is patient outcome compromised during the initial experience with robot-assisted radical cystectomy? Results of 164 consecutive cases. *BJU Int* 2011; 108: 882–7.
16. Collins JW, Tyritzis S, Nyberg T, et al. Robot-assisted radical cystectomy (RARC) with intracorporeal neobladder - what is the effect of the learning curve on outcomes? *BJU Int* 2104; 113: 100-107.

9 Search Strategy

Search date June 2014.

Inclusion criteria for identification of relevant studies

Patients/Population	Intervention	Comparator	Outcomes	Study types
Adults (18 years or over) with bladder cancer	Robot-assisted cystectomy with or without extra/intra corporeal urinary diversion (including search terms 'robotics' and 'da Vinci;)	Open cystectomy with or without extra/intra corporeal urinary diversion Laparoscopic cystectomy with or without extra/intra corporeal urinary diversion	Clinical effectiveness Adverse events/complications Mortality Quality of life (including patient self-reported outcome measures) Occupational-related outcomes Length of stay Re-admissions Cost/cost-effectiveness Any	Meta-analyses Systematic reviews Randomised controlled trials Prospective non-randomised clinical study Other clinical study Health economics studies

Search strategy

1. robotics/
2. robot*.ti.
3. (robot* adj5 assist*).ti,ab.
4. (robot* adj5 (surg* or procedure* or operat*)).ti,ab.
5. da vinci.ti,ab.
6. 1 or 2 or 3 or 4 or 5
7. Urinary Bladder Neoplasms/su [Surgery]
8. Urinary Bladder/su [Surgery]
9. cystectomy/
10. (bladder* adj5 (surg* or procedure* or operat*)).ti,ab.
11. ((bladder* adj5 (cancer* or neoplas* or metasta* or malignan* or tumo?r* or carcinoma*)) and (surg* or procedure* or operat*)).ti,ab.
12. (cystectom* or urin* diversion*).ti,ab.
13. bladder*.ti.
14. 7 or 8 or 9 or 10 or 11 or 12 or 13
15. 6 and 14
16. (robot* adj5 (cystectom* or urin* diversion*)).ti,ab.
17. 15 or 16

18. limit 17 to english language
19. limit 18 to "reviews (maximizes specificity)"
20. limit 18 to "therapy (best balance of sensitivity and specificity)"
21. limit 18 to ("economics (best balance of sensitivity and specificity)" or "costs (best balance of sensitivity and specificity)")
22. (outcome* adj3 volume).ti,ab.
23. (surgeon* adj3 volume).ti,ab.
24. ((hospital or institution* or centre* or center*) adj5 volume).ti,ab.
25. (outcome and volume).ti.
26. ((high* or low* or medium*) adj3 volume).ti,ab.
27. (caseload* or case load*).ti,ab.
28. 22 or 23 or 24 or 25 or 26 or 27
29. 18 and 28

1. robotics/
2. robot*.ti.
3. (robot* adj5 assist*).ti,ab.
4. (robot* adj5 (surg* or procedure* or operat*)).ti,ab.
5. da vinci.ti,ab.
6. 1 or 2 or 3 or 4 or 5
7. urologic surgical procedures/ or urologic surgical procedures, male/
8. Urinary Tract/su [Surgery]
9. ((urin* or urolog* or urogenital) adj5 (surg* or procedure* or operat*)).ti,ab.
10. 7 or 8 or 9
11. 6 and 10
12. (robot* adj5 (urin* or urolog* or urogenital)).ti,ab.
13. 11 or 12
14. limit 13 to english language
15. limit 14 to "reviews (maximizes specificity)"
16. limit 14 to "therapy (best balance of sensitivity and specificity)"
17. limit 14 to ("economics (best balance of sensitivity and specificity)" or "costs (best balance of sensitivity and specificity)")
18. (outcome* adj3 volume).ti,ab.
19. (surgeon* adj3 volume).ti,ab.
20. ((hospital or institution* or centre* or center*) adj5 volume).ti,ab.
21. (outcome and volume).ti.
22. ((high* or low* or medium*) adj3 volume).ti,ab.
23. (caseload* or case load*).ti,ab.
24. 18 or 19 or 20 or 21 or 22 or 23
25. 14 and 24