Canadian Agency for Drugs and Technologies in Health

RAPID RESPONSE REPORT: SUMMARY WITH CRITICAL APPRAISAL

TITLE: Robot-assisted Surgery for Partial Nephrectomy and Cardiac Surgery: A Review of the Clinical and Cost-Effectiveness – An Update

DATE: 15 November 2012

CONTEXT AND POLICY ISSUES

Robotic surgery for prostatectomy, hysterectomy, nephrectomy, and cardiac surgery are four procedures of interest to Canadian jurisdictions, based on clinical importance and the current and predicted use of robotic surgery. The da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA) is the most widely marketed and studied surgical robot, comprising a telemanipulation system in which the operating surgeon directs three or four surgical arms from a computer video console using master handles, while seated in close proximity to the patient.[1]. The da Vinci Surgical Robotic System was first licensed for laparoscopic and thoracoscopic procedures by Health Canada in March 2001, with various components of the surgical system being thereafter approved from June 2005 to September 2006.[2] Eleven tertiary care centres in six Canadian cities have purchased 11 da Vinci surgical robots (as of January 1, 2011).[3]

Robot-assisted surgery may offer benefits to patients through the use of minimally invasive techniques. Surgeons may also benefit from this technology through improved ergonomics (e.g., three-dimensional visualization and freedom, and intuitiveness of movement-enabled eye-hand coordination that may be lost in laparoscopic surgery), potentially resulting in better surgical performance. Robot-assisted surgery is, however, associated with significant capital and operating costs. The cost estimate, obtained in 2010, of the da Vinci robot was C$2.7 million, with annual maintenance costs of approximately C$186,000. In addition, the average instrument cost per procedure was reported to be approximately C$2,600.[3]

In 2011, CADTH conducted a health technology assessment report with meta-analyses to compare clinical efficacy between robot-assisted, open, and laparoscopic surgeries, and a systematic review of the economic literature to assess the economic evidence on robotic surgery.[3] Based on primary meta-analyses of the included studies, robotic partial nephrectomy had statistically significant shorter length of hospital stay as compared to laparoscopic partial nephrectomy. Findings on robot-assisted cardiac surgery were scarce, but seemed to favour robot-assisted surgery for length of hospital stay. The population impact analysis suggests that up to 31 Canadian centres could adopt the robotic technology. Hospital budget impact of robotic surgery program showed that, among robotic surgery for prostatectomy, hysterectomy, nephrectomy, and cardiac surgery, the latter procedure was the least costly indication-specific program, with net program costs of $0.9 million and $2.2 million for partial nephrectomy over seven years.

This report aims to update the CADTH health technology assessment report regarding the clinical effectiveness and cost-effectiveness of robot-assisted surgery for partial nephrectomy and cardiac surgery, as compared to laparoscopic and open surgical approaches.

RESEARCH QUESTIONS

1. What is the updated evidence on the clinical effectiveness of robot-assisted surgery for partial nephrectomy?

2. What is the updated evidence on the clinical effectiveness of robot-assisted surgery for cardiac surgery?

3. What is the updated evidence on the cost-effectiveness of robot-assisted surgery for partial nephrectomy?

4. What is the updated evidence on the cost-effectiveness of robot-assisted surgery for cardiac surgery?

KEY MESSAGE

Partial nephrectomy
Findings from systematic reviews showed that robot-assisted partial nephrectomy (RAPN) appears to be an effective and safe approach, providing similar clinical and oncologic outcomes compared with laparoscopic partial nephrectomy (LPN) and open partial nephrectomy (OPN), while providing the shortest length of hospital stay. Cost-analysis studies found that RAPN required the highest cost of equipment and maintenance; significant reduction in robotics cost was required before RAPN could be cost-effective.

Cardiac surgery
Findings from individual studies showed that robot-assisted cardiac procedures were a safe alternative compared to conventional surgery and mini-thoracotomy. Despite longer operative time, the robotic approach provided similar clinical outcomes after mitral valve repair. Shorter length of intensive care unit and hospital ward stay was also found with robot-assisted mitral valve repair (RAMVR). Cost-analysis showed that operative cost of RAMVR was higher than the open procedure due to robot instrument cost, but this was compensated by a decrease in costs due to shorter hospital stay with RAMVR.

Larger trials with subanalyses based on surgeon's learning experience, kidney mass characteristics, and mitral valve disease etiologies are needed to provide insights on the impact of the learning curve and health status of patients on the clinical effectiveness of robot-assisted surgeries. Trials with longer follow-up time are also needed to better determine the impact of robot-assisted surgery on long term outcomes such as mortality, and its cost-effectiveness.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including Medline and Embase (via OVID), PubMed, The Cochrane Library (2012, Issue 9), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology assessment agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and non-randomized studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2010 and September 28, 2012.

Literature Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and examined the full-text publications for the final article selection. Selection criteria are outlined in Table 1.

Table 1: Selection Criteria	
Population	Patients undergoing robotic surgery for partial nephrectomy or cardiac surgery
Intervention	da Vinci Surgical System
Comparator	Open or laparoscopic surgery
Outcomes	• disease-specific survival rate, biochemical failure rate, positive margin rate, operative time, length of hospital stay, reduction of blood loss/transfusion • reduction of pain (measured by pain scales), health-related quality of life (e.g., QoL scales, functional measures), need for secondary treatments (e.g., adjuvant or salvage radiation), time to mobilization, time to return to work • adverse events (typical post-operative complications)
Study design	Health technology assessment, systematic review, meta-analyses. If no systematic reviews are identified, randomized controlled trials (RCTs). non-RCTs and individual economic evaluations will be selected.

Literature Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1, if they were published prior to January 2010, if they were duplicate publications of the same study, or if they were referenced in a selected systematic review.

Critical Appraisal of Individual Studies

The quality of the included systematic reviews, clinical, and economic evaluation studies was assessed using the AMSTAR,[4] Downs and Black,[5] and Drummond[6] checklists, respectively. Numerical scores were not calculated. Instead, the strengths and limitations of individual studies were summarized and presented.

SUMMARY OF EVIDENCE

Quantity of Available Evidence

The literature search yielded 589 citations. No additional studies were identified by searching the grey literature. After screening of abstracts, 29 potentially relevant studies were selected for full-text review, and eight studies were included in the review.

The PRISMA flowchart in Appendix 1 details the process of the study selection.

Summary of Study Characteristics

Study design

This report included two systematic reviews[7,8] regarding the clinical effectiveness of robot-assisted surgery for nephrectomy; one was produced in the UK,[7] and one in the US[8]. The systematic review(SR) by Mir et al.[8] also provided information regarding the cost-effectiveness of robot-assisted surgery for nephrectomy. One SR[7] included cohort observational studies with no randomization; the other SR[8] included case series.

Six observational studies[9-14] informed this report on the clinical effectiveness of robot-assisted surgery for cardiac indications. One of these studies[14] was also included for the cost-effectiveness of robot-assisted surgery for cardiac indications. One study[9] was a prospective post-operative patient questionnaire, while the remainder were retrospective observational studies.

Population

The two SRs included patients requiring partial nephrectomy. One SR[7] reviewed seven studies, with a total of 717 patients. The other SR, that was also included for the cost-effectiveness question,[8] reviewed 33 studies, with a total of 5,442 patients.

The studies included for cardiac surgery ranged from 57 patients[11] to 1,305 patients.[10] All studies were conducted in the US except the one which was also included for the cost-effectiveness question,[14] and it was conducted in Australia. Five studies[9,10,12-14] were on patients requiring mitral valve repair, and one study[11] focused on patients undergoing cardiac myxoma resection.

Interventions and comparators

One SR[7] compared robot-assisted nephrectomy with laparoscopic partial nephrectomy; the other SR[8] compared robot-assisted nephrectomy with both open and laparoscopic procedures. All of the observational studies[9-14] compared robot-assisted cardiac surgery with conventional sternotomy. Two of these studies[10,13] also compared robot-assisted surgery against mini-thoracotomy.

Outcomes

One SR[7] reported outcomes of warm ischemic time (the time an organ remains at body temperature after its blood supply has been reduced or cut off), operative time, blood loss, conversion rate, length of hospital stay, complications, and positive margin rate (the rate of the presence of cancer cells at the edge of tissue that has been removed). The other SR[8] reported operative times, length of hospital stay, and direct costs. The main outcomes reported by most of the studies on cardiac surgery were operating time, length of hospital stay, mortality, adverse events, and transfusion rate. One study[9] focused entirely on post-operative quality of life measures.

A detailed summary of the included studies is provided in Appendix 2.

Summary of Critical Appraisal

Regarding evidence on partial nephrectomy, the systematic reviews were generally well conducted. A comprehensive literature search was performed following the establishment of a research question and inclusion criteria. The meta-analyses performed in the included systematic reviews included studies with small patient cohorts which may have reported early experience in robotic surgery; the pooled mean estimate could therefore be skewed towards the early learning curve results. Since the included trials on robotic partial nephrectomy were not randomized, patient demographics and tumour characteristics could be different between patient groups undergoing laparoscopic/robot-assisted surgeries compared to open surgery, with the latter having more comorbidities and harder-to-resect tumours. Therefore, the comparison in clinical and oncologic outcomes can be disadvantageous for the open approach. The economic evaluation study did not report incremental analysis, and the cost data were from one institution, thus limiting the generalizability of the findings.

Regarding evidence on cardiac surgery, all included studies were observational. Observational studies are not randomized, and therefore have the potential for allocation bias. As well, none of the studies indicated that those measuring the main outcomes were blinded, increasing the potential for outcome reporting bias. The studies all used valid main outcome measures and accounted for most potential confounders. The study by Suri et al.[9] was a prospective, quality of life questionnaire of patients, following discharge from hospital. The study did not consider patients lost to follow-up, and quality of life was assessed only at one point, and not on a prospective basis.

A summary of the critical appraisal conducted for selected studies can be found in Appendix 3.

Summary of Findings

Main findings of included studies are summarized in detail in Appendix 4.

1. <u>What is the updated evidence on the clinical effectiveness of robot-assisted surgery for partial nephrectomy?</u>

Overall, two systematic reviews performed meta-analysis on the comparative clinical effectiveness of robot-assisted partial nephrectomy (RAPN) to laparoscopic partial nephrectomy (LPN) or open partial nephrectomy (OPN).[7,8] RAPN appears to be a safe approach which provided similar clinical and oncologic outcomes and a shorter length of hospital stay.

A systematic review/meta-analysis included seven observational studies that compared clinical perioperative outcomes and oncological outcomes after RAPN and LPN.[7] Findings showed that most clinical outcomes (such as operative time, blood loss, conversion to open surgery rate, length of hospital stay, post-operative complications) and oncologic outcomes (such as positive margin rate) are similar between robotic and laparoscopic approaches. Warm ischemic time was however statistically significantly in favour of the robotic approach.

A systematic review and meta-analysis that included 33 case series, compared operative time, length of hospital stay and costs between RAPN, LPN and OPN.[8] Findings showed that the open approach resulted the longest mean length of stay (5.9 days), while the laparoscopic approach gave 3.2 days and the robotic approach, 2.6 days. The three surgical approaches were found to have similar operative times (193, 200 and 188 minutes for OPN, LPN and RAPN respectively). The study did not report the statistical significance of the differences.

2. What is the updated evidence on the clinical effectiveness of robot-assisted surgery for cardiac surgery?

Overall, six observational studies compared the clinical effectiveness of robot-assisted cardiac surgery to non-robot-assisted cardiac procedures.[9-14] Findings showed that the robot-assisted procedure was a safe alternative compared to the other two approaches.

Five included studies comparing robot-assisted mitral valve repair (RAMVR) to open (sternotomy) mitral valve repair (OMVR), including two also comparing to mini thoracotomy (MVR), found that the RAMVR can be performed with similar success rates compared to the other two procedures.[9,10,12-14] RAMVR gave similar clinical outcomes such as 30-day mortality,[10] post-operative complications and blood transfusion rates.[12,13] Operative time was found to be 39 to 42 minutes longer with RAMVR than sternotomy, and 11 minutes longer than mini thoracotomy, while length of hospital stay was 1 to 1.6 days shorter than sternotomy, and 0.9 days shorter than mini thoracotomy.[13] Functional quality of life outcomes within the first two years were similar between RAMVR and OMVR, with an earlier median time to return to work in favour of the robotic approach.[9] Robotic excision of atrial myxoma took less time than the open procedure, and gave similar outcomes on length of intensive care unit and hospital ward stay, neurological events, atrial fibrillation rate and blood transfusion compared to open excision of the mass.[11]

3. What is the updated evidence on the cost-effectiveness of robot-assisted surgery for partial nephrectomy?

One systematic review performed a cost analysis of RAPN, LPN and OPN using hospital cost data and utilized operative time and length of hospital stay from 33 case series as cost determinants.[8] Findings showed that given similar operative times between the three surgical approaches, the main determinants of costs were length of hospital stay and surgical equipment costs. RAPN had the highest cost of maintenance and equipment per case (US$1,820) compared to LPN (US$825) and OPN US($285). OPN has the highest room and board cost (US$3,022) compared to RAPN (US$1,334) and LPN (US$1,650). Operating room cost, surgeon and anesthesia professional fees were similar between the three approaches. The authors concluded that LPN was the most cost-effective approach between the three approaches due to lower instrumental cost than RAPN and shorter length of stay than OPN. Sensitivity analyses found that in order for RAPN to be cost-effective, significant reductions in robotic costs were required.

4. What is the updated evidence on the cost-effectiveness of robot-assisted surgery for cardiac surgery?

A cost-analysis study was performed in Australia on 107 robotic and 40 open mitral valve repairs.[14] Findings showed that operative costs per case of robot-assisted mitral valve repair (RAMVR) was AUD$2,573 more than open mitral valve repair (OMVR), mostly attributable to the robot instrument costs. Mean total post-operative costs for the robotic approach was AUD$1,949 less than the open approach, mainly due to decreases in costs associated with shorter intensive care unit stay and hospital ward stay. Mean hospital costs, excluding capital costs, were not significantly increased by the use of robot compared to conventional approach (AUD$18,503 versus AUD$17,880)

Limitations

Most studies were observational in design. Few studies had follow-up duration longer than five years; this is also a limitation of the 2011 CADTH HTA report that found a lack of long term data. The included meta-analyses included studies with small patient cohorts which may have reported early experience in robotic surgery, the pooled mean can be therefore skewed towards the early learning curve results. Large multicenter trials reporting data beyond the initial learning curve with subanalyses based on surgeon's experience are required in order to determine the effect of fully operational surgical robotic programs. Since the included trials on robotic partial nephrectomy were not randomized, patient demographics and tumour characteristics may not be balanced between patient groups undergoing laparoscopic/robot-assisted surgeries compared to open surgery, with the latter having more comorbidities and harder-to-resect tumours. Therefore, the comparison in clinical and oncologic outcomes can be disadvantageous for the open approach. Included trials on robotic cardiac surgery also included patients with diverse mitral valve disorder etiologies, and patients who underwent open surgery tend to be older and have more serious mitral valve diseases which potentially worsen the outcomes. The evidence on cost-effectiveness from the included economic systematic review on partial nephrectomy was weak due a lack of studies describing incremental cost-effectiveness ratio or cost per adjusted quality of life-year. Costs analyses conducted in other countries may limit the generalizability of the findings to a Canadian context. Prospective comparative studies with longer follow-up time are needed to better determine the impact of robot-assisted surgery on long term outcomes such as mortality, and its cost-effectiveness.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Findings from systematic reviews showed that RAPN appears to be an effective and safe approach which provided similar clinical and oncologic outcomes compared to LPN and OPN, while providing the shortest length of hospital stay. RAPN required the highest cost of equipment and maintenance; significant reduction in robotics cost was required before the robotic approach could be cost-effective.

Findings from individual studies showed that robot-assisted cardiac procedure was a safe alternative compared to conventional surgery and mini-thoracotomy. Despite longer operative time, the robotic approach provided similar clinical outcomes after mitral valve repair with shorter length of hospital stay. Since the higher operative cost of robotic mitral valve repair was offset by a decrease in costs due to shorter hospital stay, there was no significant difference in costs between robotic and conventional approaches.

Findings from this updated Rapid Response review reconfirmed the conclusions of the CADTH health technology assessment in 2010, which identified similar short-term clinical outcomes and shorter length of hospital stay for patients undergoing robot-assisted partial nephrectomy and cardiac surgery compared to non-robotic approaches, despite the uncertainty about the clinical relevance of the size of these differences. Stratification by study design did not appear to reveal any patterns in the data. There was insufficient information on surgeons' experience to perform a sensitivity analysis exploring the impact of the learning curve on clinical outcomes after robotic partial nephrectomy and cardiac surgery.

Cost-analysis studies on robot-assisted surgery reported conflicting results, due to the heterogeneity of the economic studies, with regional differences in administration and infrastructural costs, size of the hospitals, and procedural costs and charges. Cost-minimization analysis from the 2010 CADTH health technology assessment showed that by increasing the annual caseload, the incremental costs per patient for robotic surgery can be lowered, "*The investment made in acquiring this technology is large, and institutions that choose to adopt this technology need to monitor their costs and outcomes so that they can maximize its cost-effective use in their centre. To decrease costs, centres could maximize caseloads, consider keeping the robot operational for longer, if possible, and use the technology for multiple indications, particularly those with greater potential impact on patient outcomes and institutional cost savings".*[3]

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca

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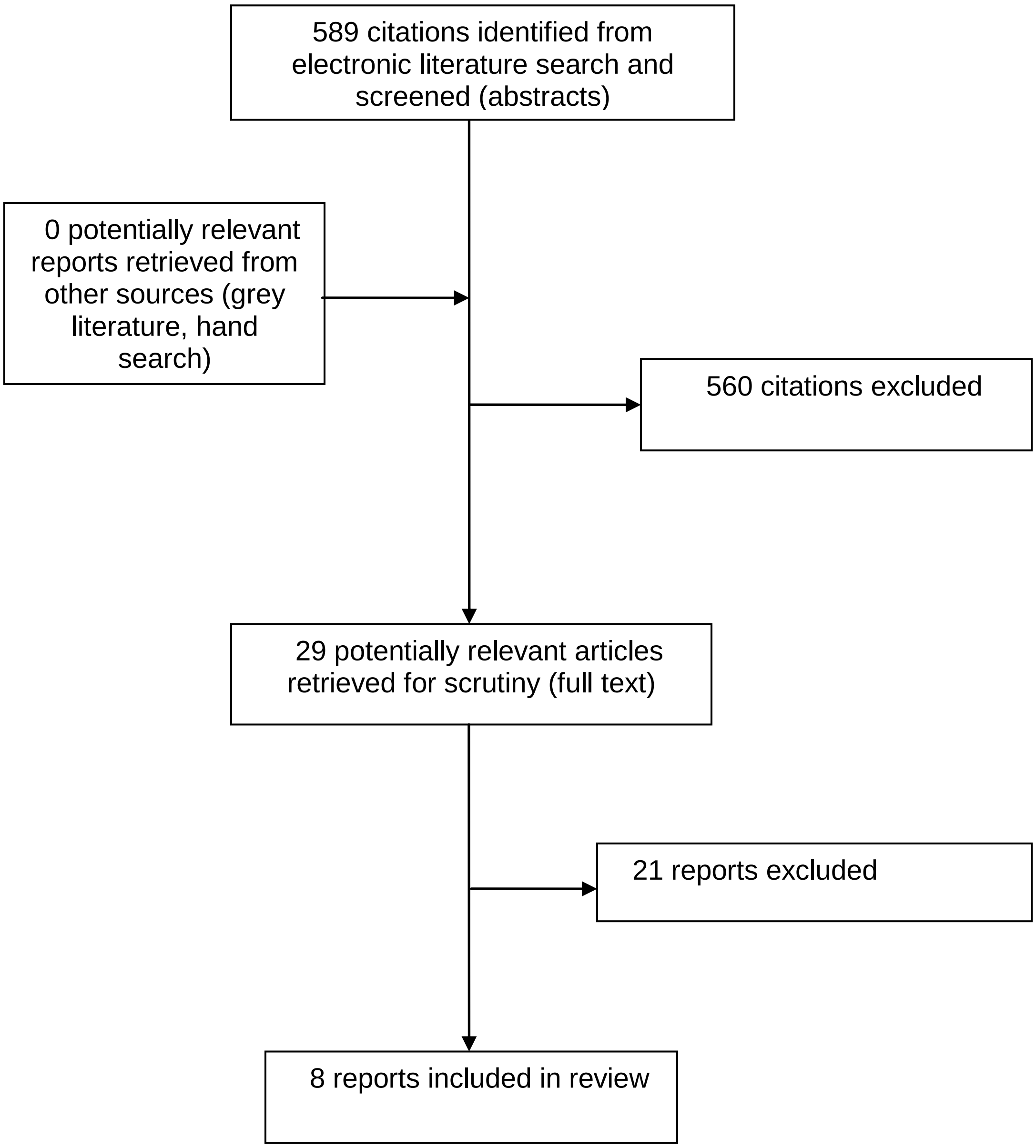
Appendix 1: Selection of Publications



Appendix 2: Characteristics of Included Studies

Table A1: Characteristics of Included Clinical Studies

First Author, Year, Country, Length of Study	Study objectives	Comparator(s)	Included patients and study types	Main comparative clinical outcomes reported
Systematic Reviews/Meta-Analyses – Partial Nephrectomy				
Aboumarzouk, 2012[7] UK 12 years; searched from 2000-2012	*"To review published literature comparing robotic partial nephrectomy (RPN) with laparoscopic partial nephrectomy (LPN)."* (p. 1 of e-publication)	Laparoscopic partial nephrectomy	Patients with small renal masses Total: 7 studies; 717 patients Study types included in SR: cohort observational studies with no randomization	Warm ischemic time; operative time; blood loss; conversion rate; length of hospital stay; complications; positive margin rate
Mir, 2011[8] US 11 years; searched from 2000-2011	"*To compare direct costs associated with open partial nephrectomy (OPN), laparoscopic partial nephrectomy (LPN), and robot-assisted LPN (RALPN)."* (p. 447)	Open and laparoscopic partial nephrectomy	Patients with small renal masses Total: 33 studies; 5,442 patients Study types included in MA: Case series	Operative time; length of hospital stay; direct costs
Observational Studies – Cardiac Surgery				
Suri, 2012[9] US 23 months	*"To understand the early post-operative functional effect of surgical MV repair for degenerative leaflet prolapse in minimally symptomatic patients using standard validated QOL assessment tools."* (p. 761)	Conventional trans-sternotomy	Patients who had undergone mitral valve repair, with or without patent foramen ovale closure or left atrial cryoablation for atrial fibrillation Total: 141 patients Study type: Pilot study, post-operative patient questionnaire	Quality of life measures (physical and mental function; chest pain; fatigue; return to work)
Stevens, 2012[10] US 17 years	*"…investigated whether the timing of mitral valve (MV) repair or surgical approach affects outcomes in patients with MV regurgitation."* (p. 1462)	Sternotomy and video-assisted right mini-thoracotomy	Patients with isolated MV regurgitation and with or without concomitant ablations for atrial fibrillation Total: 1,305 patients Study type: Retrospective observational	30-day mortality; adjusted survival; neurological events
Schilling, 2012[11] US	*"We report our retrospective data comparing robotically assisted myxoma excision with standard median*	Median sternotomy excision	Patients who underwent cardiac myxoma resection Total: 57 patients	Operating time; mortality; neurological events; atrial fibrillation rate; blood transfusion

Table A1: Characteristics of Included Clinical Studies

First Author, Year, Country, Length of Study	Study objectives	Comparator(s)	Included patients and study types	Main comparative clinical outcomes reported
10 years	*sternotomy excision."* (p. 423)		Study type: Retrospective observational cohort	
Suri, 2011[12] US 2.5 years	*"We therefore compared early outcomes of robotic versus open mitral valve repair for patients with mitral valve prolapse."* (p. 970)	Trans-sternal (open) valvuloplasty	Patients who underwent MV repair Total: 301 patients Study type: Retrospective observational	Postoperative ventilation time; in-hospital death; early post-operative surgical outcomes (e.g., myocardial infarction, major adverse events, atrial fibrillation, or blood transfusion); length of hospital stay; length of ICU stay
Mihaljevic, 2011[13] US 3 years	*"The purpose of this study was to provide a contemporary comparison of the safety and efficacy of robotic MV repair with those of complete sternotomy, partial sternotomy, and mini-anterolateral thoracotomy in concurrently treated patient with myxomatous MV disease limited to posterior leaflet repair."* (p. 72)	Complete sternotomy, partial sternotomy, and mini-anterolateral thoracotomy	Patients undergoing isolated posterior leaflet repair for myxomatous MV disease Total: 759 patients Study type: Retrospective observational	Cardiopulmonary bypass time; length of hospital stay; in-hospital death; neurologic, pulmonary, and renal complications
Kam, 2010[14] Australia 3 years	*"The aim of this study was to perform a cost-analysis of robotic MVR with direct comparison to conventional MVR surgery."* (p. 413)	Median sternotomy	Patients undergoing isolated MVR for degenerative mitral valve disease Total: 147 patients Study type: Retrospective observational	Operating time; length of hospital stay; length of ICU stay

ICU = intensive care unit; MV = mitral valve; MVR = mitral valve repair; QOL = quality of life

Appendix 3: Summary of Critical Appraisal of Included Studies

Table A2: Critical Appraisal of Included Studies		
First author, year	**Strengths**	**Limitations**
Systematic reviews - Nephrectomy		
Aboumarzouk, 2012[7]	• a priori design was provided • independent data extractors • comprehensive literature search • status of publication was used as an inclusion criterion • list of included and excluded studies provided • characteristics of included studies provided • quality of the included studies documented • methods to combine findings were appropriate • conflict of interest was stated	• comparative analyses were not adjusted for the baseline differences in patient characteristics • likelihood of publication bias was not assessed
Mir, 2011[8]	• research question was stated • economic importance of the research question was stated and justified • rationale for choosing alternative programs or interventions compared was stated • choice of form of economic evaluation was justified • sources of effectiveness estimates used were stated • details of the design and results of effectiveness study were given • details of the methods of synthesis or meta-analysis of estimates were given primary outcome measures were clearly stated • approach to sensitivity analysis was given • methods for the estimation of quantities and unit costs were described • currency and price data were recorded • answer to the study question was given • conclusions follow from the data was reported	• details of model use were not given • incremental analysis was not reported • time horizon of costs and benefits was not stated • data used for cost model from 1 institution • did not include additional costs of complications
Observational studies – Cardiac surgery		
Suri, 2012[9]	• objective and main outcomes to be measured clearly described • patient characteristics clearly described • main outcome measures used accurate • estimates of random variability and actual *P* values reported for main outcomes • potential confounders taken into consideration	• no randomization or blinding • patients lost to follow-up not considered • QoL was assessed only at one point, and not on a prospective basis • results may not be generalizable (single institution) • very limited reporting of adverse events
Stevens, 2012[10]	• objective clearly described • interventions and patient characteristics clearly described • main outcome measures used accurate • major adverse events reported • estimates of random variability and actual *P* values reported for main outcomes • some potential confounders taken into consideration	• retrospective cohort study • results may not be generalizable (single institution) • no randomization or blinding • additional potential confounders (e.g., patients lost to follow-up)
Schilling,	• objective clearly described	• retrospective cohort study

Table A2: Critical Appraisal of Included Studies		
First author, year	**Strengths**	**Limitations**
2012[11]	• patient characteristics clearly described • major adverse events reported • estimates of random variability and actual *P* values reported for main outcomes • some potential confounders taken into consideration	• main outcomes to be measured not described • no randomization or blinding • results may not be generalizable (single surgeon) • lack of long-term follow-up
Suri, 2011[12]	• objective and main outcomes to be measured clearly described • interventions clearly described • patient characteristics clearly described • major adverse events reported • main outcome measures used accurate • estimates of random variability and actual *P* values reported for main outcomes • some potential confounders taken into consideration	• retrospective cohort study • no randomization or blinding
Mihaljevic, 2011[13]	• objective and main outcomes to be measured clearly described • interventions clearly described • patient characteristics clearly described • major adverse events reported • main outcomes used accurate • actual *P* values reported for main outcomes • potential confounders taken into consideration	• retrospective cohort study • no randomization or blinding • estimates of random variability not reported for main outcomes
Kam, 2010[14]	• objective and main outcomes to be measured clearly described • interventions clearly described • patient characteristics clearly described • major adverse events reported • main outcomes used accurate • actual *P* values reported for main outcomes • potential confounders taken into consideration • learning curve taken into consideration	• retrospective cohort study • no randomization or blinding • initial capital costs of establishing a program with robotic surgery not taken into account

Appendix 4: Main Study Findings and Authors' Conclusions

Table A3: Main Study Findings and Authors' Conclusions		
First Author, Publication Year	**Main Study Findings**	**Authors' Conclusions**
Research question 1 (evidence on the clinical effectiveness of robot-assisted surgery for partial nephrectomy)		
Systematic Review		
Aboumarzouk, 2012[7]	Warm ischemic time: RPN shorter than LPN (MD -2.83; 95% CI: -4.53 to -1.13; *P* = 0.001) There was no statistically significant differences regarding operative time (*P* = 0.57), blood loss (*P* = 0.76), conversion rate (*P* = 0.84), length of hospital stay (*P* = 0.37), complications (*P* = 0.86) or positive margin rate (*P* = 0.93)	"*In early experience, RPN appears to be a feasible and safe alternative to its laparoscopic counterpart with decreased warm ischemia times noted*" (p 1)
Mir, 2011[8]	OR time: RAPN: 188min LPN: 200min OPN: 193 min (*P* values not reported) LOS: RAPN: 2.6 days LPN: 3.2 days OPN: 5.9 days (*P* values not reported)	"*Despite similar OR times, LPN is more cost effective than OPN because of shorter LOS. Because of lower instrumental costs, LPN is the most cost effective despite a longer LOS than RALPN*" (p 447)
Research question 2 (evidence on the clinical effectiveness of robot-assisted surgery for cardiac surgery)		
Observational studies		
Stevens, 2012[10]	**MVR** 30-day mortality: similar for RAMVR, OMVR, and video-assisted minithoracotomy (*P* = 0.409) Adjusted survival: similar for RAMVR, OMVR, and video-assisted minithoracotomy (*P* = 0.357) Neurological events: fewer in RAMVR and videoscopic groups compared to OMVR (*P* = 0.013)	"*Minimally invasive MV repair techniques render similar outcomes as the sternotomy approach*" (p 1462)
Schilling, 2012[11]	**Excision of atrial myxoma** Operating time: RA excision of atrial myxoma: 2.7 hrs Open excision of atrial myxoma: 3.5 hrs (*P* = 0.02) LOS, ICU LOS, mortality, neurological events, atrial fibrillation rate, blood transfusion: not statistically significant difference	"*Robotic excision of atrial myxomas is safe and may be an alternative to traditional open surgery in selected patients*" (p 423)
Suri, 2012[9]	**MVR** QOL measures 12-24 months after surgery No statistically significant differences regarding DASI, SF-12, LASA (chest pain and fatigue) between RAMVR and OMVR LASA (QOL): RAMVR: 9.3 ± 0.2 OMVR: 8.6 ± 0.2 (*P* = 0.034) Median time to return to work: RAMVR: 33 days OMVR: 54 days (*P* < 0.001)	"*Functional QOL outcomes within the first 2 years after early MV repair are excellent using open and robotic programs. A robotic approach may be associated with slighted improved early QOL and return to employment-based activities*"(p 761)
Suri, 2011[12]	**MVR** LOS, ICU LOS, postoperative ventilation time: shorter with RAMVR compared to OMVR (*P* < 0.001)	"*Robotic repair effectively corrects mitral regurgitation, offers excellent freedom from adverse events, and facilitates rapid weaning from*

Table A3: Main Study Findings and Authors' Conclusions		
First Author, Publication Year	**Main Study Findings**	**Authors' Conclusions**
	There was no in-hospital death. No statistically significant differences regarding early post-operative surgical outcomes such as myocardial infarction, major adverse events, complication, atrial fibrillation, blood transfusion between RAMVR and OMVR	*ventilation, translating into earlier hospital dismissal*" (p 970)
Mlhaljevic, 2011[13]	**MVR** Cardiopulmonary bypass time: 42 min longer for RAMVR than complete sternotomy, 39 min longer than partial sternotomy, and 11 min longer than right mini-anterolateral thoracotomy (*P* < 0.0001) LOS: 1.0day shorter with RAMVR than complete sternotomy, 1.6 days shorter than partial sternotomy, and 0.9 day shorter than right mini-anterolateral thoracotomy (*P* < 0.001) There was no in-hospital death. No statistically significant differences regarding neurologic, pulmonary and renal complication between the approaches.	"*Robotic repair of posterior mitral valve leaflet prolapse is as safe and effective as conventional approaches. Technical complexity and longer operative times for robotic repair are compensated by lesser invasiveness and shorter hospital stay*" (p 141)
Kam, 2010[14]	**MVR** Operating time: 18% longer with RAMVR compared to OMVR (239 min vs 202 min; *P* < 0.001; 95% CI: 11 – 27%) LOS: reduced by 26% with RAMVR (6.47 days vs 8.76 days; *P* < 0.001) ICU LOS: reduced by 19% (37 hrs vs 45 hrs; *P* = 0.002)	" *Robotic mitral repair can be performed with similar repair success rates as conventional surgery with a shorter recovery time, but a slighter longer operative time*" (p 413)
Research question 3 (evidence on the cost-effectiveness of robot-assisted surgery for partial nephrectomy)		
Systematic review		
Mir, 2011 [8]	Direct cost: RAPN: $11,962 (10,238 – 13,504) LPN: $10,311 (8,543 – 12,348) OPN: $11,427 (10,521 – 13,457) Surgical equipment cost: RAPN: $1,820 LPN: $825 OPN: $285 Operating room cost: RAPN: $2,423 (1,068 – 2,657) LPN: $2,576 (1,290 – 4,180) OPN: $2,494 (1,664 – 3,431) Amortized robot cost (case): $1,214 Surgeon professional fees: RAPN: $1,563 LPN: $1,563 OPN: $1,387 Anesthesia professional fees: RAPN: $2,148 LPN: $2,237 OPN: $2,185 Room and board cost:	"*Despite similar OR times, LPN is more cost effective than OPN because of shorter LOS. Because of lower instrumental costs, LPN is the most cost effective despite a longer LOS than RALPN. RALPN has high cost of maintenance and instrumentation, which is partially compensated by the shorter LOS*" (p 447)

Table A3: Main Study Findings and Authors' Conclusions		
First Author, Publication Year	**Main Study Findings**	**Authors' Conclusions**
	RAPN: $1,334 (965 – 2642) LPN: $1,650 (1,168 – 2,083) OPN: $3,022 (2,946 – 4,115)	
Research question 4 (evidence on the cost-effectiveness of robot-assisted surgery for cardiac surgery)		
Cost analysis study		
Kam, 2010[14]	Operative procedure cost: RAMVR: AUD$12,328 OMVR: AUD$ 9,755 (*P* value not reported) Post-operative costs: RAMVR: AUD$6,174 OMVR: AUD$ 8,124 ($P < 0.001$) Direct cost RAMVR: AUD$18,503 OMVR: AUD$ 17,880 ($P = 0.176$)	"*There is no significant increase in cost over conventional surgery*" (p 413)

DASI = Duke Activity Status Index; ICU = intensive care unit; LASA = Linear Analogue Self-Assessment; LOS = length of hospital stay; LPN = laparoscopic partial nephrectomy; MVR = mitral valve repair; OMVR = open mitral valve repair; OPN = open partial nephrectomy; OR = operating room; QOL = quality of life; RALPN = robot-assisted laparoscopic partial nephrectomy (robot-assisted partial nephrectomy); RAMVR = robot-assisted mitral valve repair; RAPN = robot-assisted partial nephrectomy; SF-12 = Short Form 12-Item Health Survey.