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# Robotic-assisted Surgery in Partial Nephrectomy and Cystectomy: A Systematic Review

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August 2019

**Prepared for:**

Department of Veterans Affairs  
Veterans Health Administration  
Health Services Research & Development Service  
Washington, DC 20420

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## PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program is comprised of four ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program and Cochrane Collaboration. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, and interface with stakeholders. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee comprised of health system leadership and researchers. The program solicits nominations for review topics several times a year via the [program website](#).

Comments on this evidence report are welcome and can be sent to Nicole Floyd, Deputy Director, ESP Coordinating Center at [Nicole.Floyd@va.gov](mailto:Nicole.Floyd@va.gov).

**Recommended citation:** Maggard-Gibbons M, Childers CP, Girgis M, Lamaina M, Tang A, Ruan Q, Mak SS, Begashaw M, Booth MS, Shekelle PG, Robotic-Assisted Surgery in Partial Nephrectomy and Cystectomy. Los Angeles: Evidence Synthesis Program, Health Services Research and Development Service, Office of Research and Development, Department of Veterans Affairs. VA ESP Project #05-226; 2019. Available at: <https://www.hsrd.research.va.gov/publications/esp/reports.cfm>.

This report is based on research conducted by the Evidence Synthesis Program (ESP) Center located at the **West Los Angeles VA Medical Center, Los Angeles, CA**, funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

## ACKNOWLEDGMENTS

This topic was developed in response to a nomination by William Gunnar, MD, for the purpose of understanding the potential benefits and costs of robot-assisted surgery. The scope was further developed with input from the topic nominators (*ie*, Operational Partners), the ESP Coordinating Center, the review team, and the technical expert panel (TEP).

In designing the study questions and methodology at the outset of this report, the ESP consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

The authors gratefully acknowledge Roberta Shanman, Jon Bergman, and the following individuals for their contributions to this project:

### Operational Partners

Operational partners are system-level stakeholders who have requested the report to inform decision-making. They recommend Technical Expert Panel (TEP) participants; assure VA relevance; help develop and approve final project scope and timeframe for completion; provide feedback on draft report; and provide consultation on strategies for dissemination of the report to field and relevant groups.

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Department of Veterans Affairs

William Gunnar, MD  
Former National Director of Surgery (10NC2)  
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### Technical Expert Panel (TEP)

To ensure robust, scientifically relevant work, the TEP guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members are listed below:

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### **Peer Reviewers**

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center and the ESP Center work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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## EXECUTIVE SUMMARY

### INTRODUCTION

The adoption of robotic surgery continues to increase, although there remain questions concerning the utility of the robotic approach as compared to both laparoscopic and open surgery. One question that remains is whether the technical advantages of this approach translate into better clinical outcomes for patients – or at least similar. Recent studies have raised concerns that for some operations the oncologic outcomes may be worse. Further complicating the debate is the economics of the robotic platform and whether or not the benefits balance the tradeoff of increased costs.

The robotic approach is widely used across urology, with over 125,000 procedures performed in 2017.<sup>1,2</sup> In light of recent evidence questioning the utility of the robotic platform, it is important to re-visit the evidence surrounding the use of the robotic platform in urologic surgery, especially for long-term clinical and oncologic outcomes. And while the robotic approach has become the standard approach to prostatectomy, there are other urologic procedures – namely partial nephrectomy and cystectomy – where the introduction of the robotic approach is occurring, and an evidence synthesis is warranted.

To help clinicians, patients, and policymakers decide between robotic and other surgical approaches in patients undergoing partial nephrectomy and cystectomy, we were asked to conduct a systematic review of the literature.

### METHODS

This topic was developed in response to a nomination by Dr. Mark Wilson, National Director of Surgery (10NC2), and Dr. William Gunnar, former National Director of Surgery (10NC2). Key questions were then developed with input from the topic nominator, the ESP coordinating center, the review team, and the technical expert panel (TEP).

The Key Questions were:

KQ1A: What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for cystectomy?

KQ1B: What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for cystectomy?

KQ2A: What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?

KQ2B: What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?

## Data Sources and Searches

We conducted searches in PubMed from 1/1/2010-6/29/2019 and Cochrane (all databases) from 1/1/2010-6/29/2019.

## Study Selection

Studies were included if they were randomized control trials or observational studies comparing robotic surgery with either laparoscopic or open surgical approaches for either of the included surgical procedures. We also included publications of cost-effectiveness models that compared robotic surgery with laparoscopic or open surgical approaches. We included all RCTs regardless of outcomes and sample size. To be included, observational studies had to report long-term oncologic outcomes and include at least 80 robotic operations.

## Data Abstraction and Quality Assessment

We abstracted data on the following: study design, patient characteristics, sample size, tumor characteristics, intraoperative outcomes, postoperative outcomes (early), long-term functional outcomes (including kidney function) and cancer outcomes, and duration of follow-up.

Randomized controlled trials were assessed for quality (risk of bias) with the Cochrane Risk of Bias tool. We used the Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I) for observational studies.

## Data Synthesis and Analysis

Because the randomized control trials were too heterogeneous, we did not conduct a meta-analysis of trials. The observational studies were too clinically heterogeneous to support meta-analysis; hence, our synthesis is narrative. We used the criteria of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group to assess the certainty of evidence across studies.

# RESULTS

## Results of Literature Search

We identified 3,877 potentially relevant citations, of which 556 were included at the abstract screening. From these, a total of 305 abstracts were excluded. A total of 42 publications were identified at full-text review as meeting initial inclusion criteria: cost-effectiveness analyses (n=4), cost-only studies (n=4), publications describing 5 cystectomy RCTs (n=16), cystectomy observational studies (n=11), and nephrectomy observational studies (n=7). See Figure 1 for literature flow.

## Summary of Results for Key Questions

*Key Question 1A – What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for Cystectomy?*

In general, estimated blood loss was less and operating room (OR) time was longer in patients treated with robot-assisted cystectomy compared to open cystectomy. The evidence about lymph node sampling shows that in most studies, but not all, there is no difference between procedures. The few studies comparing robot-assisted cystectomy to laparoscopic cystectomy found no

difference in intraoperative outcomes. RCTs and observational studies support a conclusion that there are not significant differences between robot-assisted and open cystectomy in major complications, genitourinary complications, or length of stay (LOS). Data are too imprecise to draw any conclusions about differences or lack thereof between robot-assisted cystectomy and laparoscopic cystectomy.

***Key Question 1B – What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for Cystectomy?***

The 2 primary limitations are the underlying data behind the models and the short time horizon (which is similar to partial nephrectomy, which will be discussed to follow). The first study in cystectomy used a propensity matched internal data set and did not incorporate randomized data, despite its existence. The second does appear to have included some randomized data, but the method of pooling this data was not well-described and included both randomized and observational data. As a result, they found wide variation in their estimates on sensitivity analysis. They also did not include the latest, largest, RCT (RAZOR). While the cost analysis of one study was relatively granular and robust,<sup>3</sup> the generalizability of their operative time and LOS measures to contemporary US practice is questionable. Further, the time horizon for both studies was 90 days – which is better than for either of the partial nephrectomy studies (discussed later), but still is too short to capture any meaningful oncologic outcomes.

***Key Question 2A – What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?***

The data comparing robot-assisted partial nephrectomy to other approaches are sparse and have underlying methodologic limitations. With this caveat, there is a consistent finding of lower estimated blood loss in patients treated with robot-assisted partial nephrectomy compared to laparoscopic and open approaches. There is also a signal that length of stay is shorter and major complications are fewer with robot-assisted partial nephrectomy, but the evidence falls short of being conclusive.

***Key Question 2B – What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?***

The 2 primary limitations of these studies are (1) the data that inform their underlying model assumptions come from observational, often out-of-date, studies and (2) the very limited time horizon of their analysis (in hospital only). Without randomized data, treatment effect estimates are prone to bias from underlying patient or time differences, and these biased treatment effects are often amplified when included in a modeling study. The fact that in one of the above studies the authors assumed no difference in complications, and in the other, the authors assumed large differences, illustrates the uncertainty. For costs, one study excluded the purchase and maintenance of the robot – despite it being the primary determinant of higher costs in the other study – and both studies only looked at in-hospital costs. The time horizon for therapy dedicated to oncology treatment should at least include readmissions and subsequent care dedicated to cancer management. Small differences in readmissions, reoperations, or oncologic recurrences would like lead to large differences in the average cost of a treatment approach, none of which was considered in these studies.

## DISCUSSION

### Key Findings and Strength of Evidence

Robot-assisted surgery probably results in less blood loss than open or laparoscopic approaches, for both cystectomy and partial nephrectomy procedures. Most other differences in outcomes probably are small or nonexistent (complications, lymph node sampling, warm ischemia time, *etc*); however, the certainty of evidence is low or very low. There is a signal that length of stay may be shorter and major complications may be fewer for robot-assisted cases of partial nephrectomy, but again the certainty of evidence is low. Operating room time in cystectomy was judged to have moderate certainty that robot-assisted procedures take more time. On the crucial issues of long-term functional or oncologic outcomes, data are too sparse and imprecise to reach any conclusions. Cost effectiveness, likewise, has not been estimated with high certainty of evidence.

### Applicability

No studies were specific to VA populations. The applicability of these results to VA populations may depend on both the similarity of the patients studied to VA patients and the experience of the surgical teams using the robot to VA surgical team experience. However, the benefits for robotic approach may still be realized despite patient-level differences (VA patient population has greater burden of comorbidities than the general population), which will need to be confirmed in future studies. Urology as a surgical field has widely adopted robotic surgery, so the experience will likely translate well into the VA setting.

### Research Gaps/Future Research

Two research gaps are apparent. The first is randomized data for patients undergoing partial nephrectomy, in terms of short-term outcomes. The second is high-quality evidence with adequate long-term follow-up and sufficient statistical power to assess cancer outcomes between the operative approaches for either cystectomy or partial nephrectomy. Only 40 patients have been enrolled in RCTs with 5-year follow-up for either of these 2 procedures.

### Conclusions

Robotic-assisted surgery for cystectomy and partial nephrectomy has a few documented short-term benefits over open or laparoscopic approaches, but the cost effectiveness is unknown, and long-term oncologic outcomes are inadequately studied.

## ABBREVIATIONS TABLE

ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CCI	Charlson Comorbidity Index
CFS	Cancer-Free Survival
CKD	Chronic Kidney Disease
CSS	Cancer-Specific Survival
EBL	Estimated Blood Loss
FACT	Functional Assessment of Cancer Therapy
FDA	Food and Drug Administration
GFR	Glomerular Filtration Rate
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GU	Genitourinary
LNS	Lymph Node Sampling
LOS	Length of Stay
LPN	Laparoscopic Partial Nephrectomy
LR	Local Recurrences
LRC	Laparoscopic Radical Cystectomy
NACT	Neoadjuvant Chemotherapy
NIS	National Inpatient Samples
NMI	Non-Muscle Invasive
OR	Operating Room
OPN	Open Partial Nephrectomy
ORC	Open Radical Cystectomy
OS	Overall survival
PSM	Positive Surgical Margin
QALY	Quality-adjusted life year
QOL	Quality of Life
RAPN	Robot-Assisted Partial Nephrectomy
RARC	Robot-Assisted Radical Cystectomy
RCT	Randomized Controlled Trial
ROBINS-I	Risk of Bias in Non-Randomized Studies- of Interventions
TR	Total Recurrences
WIT	Warm Ischemia Time

# EVIDENCE REPORT

## INTRODUCTION

The robotic surgical platform was introduced in 1999, and by the end of 2017 over 3000 robotic platforms were installed throughout the United States.<sup>4</sup> Urologic surgery was one of the first surgical disciplines to adopt the robotic approach, in part because open prostatectomy was a morbid procedure and traditional minimally invasive techniques (laparoscopy) were difficult to apply to this procedure.<sup>1,2</sup> As of 2017, over 750,000 robotic procedures are performed each year in the United States including over 125,000 urologic robotic procedures.

Despite the rapid adoption of the approach, there is a growing body of literature questioning the utility of robotic surgery compared to laparoscopic and open surgery. For example, the recent ROLARR trial in rectal cancer surgery found no difference between robotic surgery and laparoscopic surgery for conversion rates, intraoperative and postoperative complications, functional outcomes, or mortality.<sup>2</sup> Further, the Laparoscopic Approach to Cervical Cancer (LACC) trial published in 2018 compared minimally invasive surgery, including laparoscopic and robotic, to open surgery in early-stage cervical cancer and found *worse* survival in the minimally invasive group.<sup>5</sup> This recently prompted the FDA to issue a warning stating that “The relative benefits and risks of surgery using robotically-assisted surgical devices compared to conventional surgical approaches in cancer treatment have not been established.” As a part of that statement, the FDA encouraged researchers to study robotic surgery, especially as it relates to long-term clinical and oncologic outcomes.

Further complicating the debate is the economics of the robotic platform. The robotic platform requires a significant upfront investment, an annual maintenance contract, and ongoing instrument purchases, not to mention staff and training costs, advertising, and infrastructure upgrade expenses. On the other hand, if the robotic platform can reduce length of stay, complications, readmissions, or improve oncologic outcomes, then these costs may be more than recuperated.

In light of recent evidence in other surgical disciplines questioning the utility of the robotic platform, it is important to re-visit the evidence surrounding the use of the robotic platform in urologic surgery, especially for long-term clinical and oncologic outcomes. And while the robotic approach has become the common approach to prostatectomy, there are other urologic procedures – namely partial nephrectomy and cystectomy – where the introduction of the robotic approach is still occurring and an evidence synthesis may be useful.

To help clinicians, patients, and policymakers make decisions about robotic and other surgical approaches in patients undergoing partial nephrectomy and cystectomy, we were asked to conduct a systematic review of benefits and cost effectiveness.

## METHODS

### TOPIC DEVELOPMENT

This topic was developed in response to a nomination by Dr. Mark Wilson, National Director of Surgery (10NC2), and Dr. William Gunnar, former National Director of Surgery (10NC2). Key questions were then developed with input from the topic nominator, the ESP coordinating center, the review team, and the technical expert panel (TEP).

The Key Questions were:

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KQ1B: What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for cystectomy?

KQ2A: What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?

KQ2B: What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?

The review was registered in PROSPERO: CRD 42019127413.

### SEARCH STRATEGY

We conducted searches in PubMed from 1/1/2010-6/29/2019 and Cochrane (all databases) from 1/1/2010-6/29/2019. The search used a broad set of terms relating to "robotic surgical procedures" or "robotic-assisted", "cystectomy" or "nephrectomy", and "cost-effectiveness". Prior to 2010, robotic procedures were not widely being performed and many surgeons were still in the so-called "learning curve". As such, our technical expert panel considered evidence from studies published prior to the year 2010 to be insufficiently relevant to modern practice. See Appendix A for complete search strategy.

### STUDY SELECTION

Four team members working in pairs independently screened the titles of retrieved citations. For titles deemed relevant by at least 1 person, abstracts were then screened independently in duplicate by 5 team members working in pairs. All disagreements were reconciled through group discussion. Full-text review was conducted in duplicate by 2 independent team members, with any disagreements resolved through discussion. Studies were included at either the abstract or the full-text level if they were randomized control trials or observational studies comparing robotic surgery with either laparoscopic or open surgical approaches for either of the included surgical procedures. We also included publications of cost-effectiveness models that compared robotic surgery with laparoscopic or open surgical approaches. We included all RCTs regardless of outcomes studied or sample size. To be included, observational studies had to report long-term

oncologic outcomes and include at least 80 operations. These thresholds were chosen such that the included studies accounted for at least 75% of the total available sample size.

## DATA ABSTRACTION

Data extraction was completed in duplicate. All discrepancies were resolved with full group discussion. We abstracted data on the following: study design, patient characteristics, sample size, tumor characteristics, intraoperative outcomes, postoperative outcomes (early), long-term functional outcomes (including kidney function) and cancer outcomes, duration of follow-up, and data needed for the Cochrane Risk of Bias tool or Cochrane Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I).

## QUALITY ASSESSMENT

Randomized controlled trials were assessed for quality (risk of bias) with the Cochrane Risk of Bias tool.<sup>6</sup> This tool requires an assessment of whether a study is at high or low (or unknown) risk of bias in 7 domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other (See Appendix C for tool; Appendix E for table). We used the Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I) for observational studies.<sup>7</sup> This tool requires an assessment of whether a study is at critical, serious, moderate, or low risk of bias (or no information) in 7 domains: confounding, selection bias, bias in measurement classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported result (see Appendix D for tool; Appendix F for table). Since observational studies are not required to have published an *a priori* protocol, we operationalized the last domain (bias in selection of the reported result) as requiring that studies report the most common variables.

## DATA SYNTHESIS

Because the randomized control trials were too heterogeneous, we did not conduct a meta-analysis of trials. The observational studies were too clinically heterogeneous to support meta-analysis; hence, our synthesis is narrative.

## RATING THE BODY OF EVIDENCE

We used the criteria of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group.<sup>8</sup> GRADE assessing the certainty of the evidence based on the assessment of the following domains: risk of bias, imprecision, inconsistency, indirectness, and publication bias. This results in categories as follows:

**High:** We are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate:** We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low:** Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.

Very low/Insufficient: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

## PEER REVIEW

A draft version of the report was reviewed by technical experts and clinical leadership. Reviewer comments and our response are documented in Appendix B.

## RESULTS

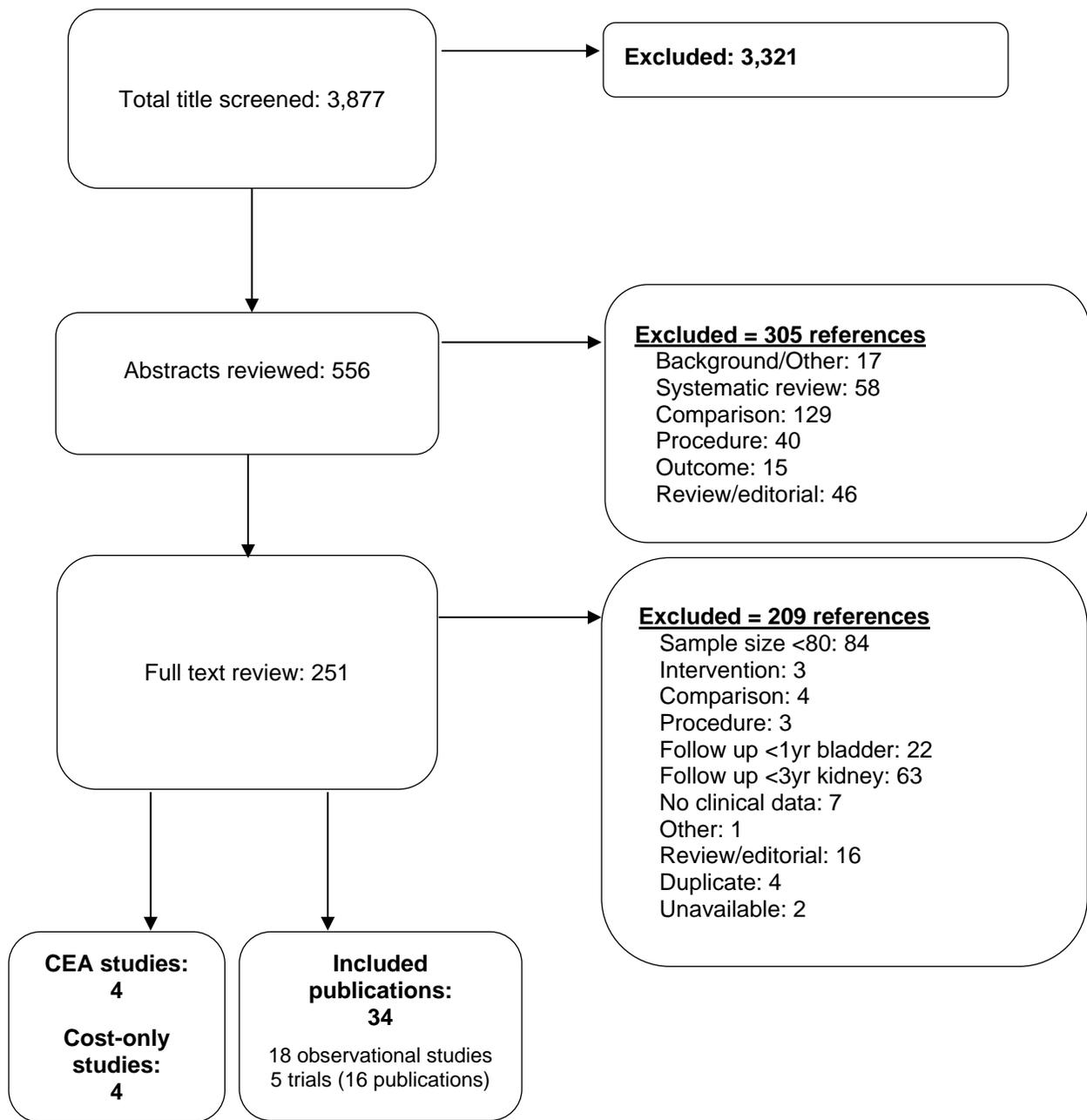
We identified 3,877 potentially relevant citations, of which 556 were included at the abstract screening. From these, a total of 305 abstracts were excluded. Excluded abstracts were categorized as background/other (n=17), systematic review (n=58), wrong comparison (n=129), wrong procedure (n=40), no long-term outcomes (n=15), and review/editorial (n=46). This left 251 publications for full-text review, of which 209 publications were excluded for the following reasons: sample size <80 (n=84), intervention (n=3), comparison, (n=4), procedure (n=3), follow-up <1 year or unclear cystectomy (n=22), follow-up < 3 year or unclear nephrectomy (n=63), no clinical data (n=7), other (n=1), review/editorial (n=16), duplicate (n=4), and full text unavailable (n=2). A full list of excluded studies from the full-text review is included in Appendix H. A total of 42 publications were identified at full-text review as meeting initial inclusion criteria: cost-effectiveness analyses (n=4), cost-only studies (n=4), publications describing 5 cystectomy RCTs (n=16), cystectomy observational studies (n=11), and nephrectomy observational studies (n=7). See Figure 1 for literature flow. Descriptions of included publications are available in the Evidence Table (Appendix G).

## DESCRIPTION OF THE EVIDENCE

For cystectomy, 5 studies were RCTs (of note, 2 publications on one study were used to abstract data for one trial, those being authored by Bochner and colleagues and published in 2014 and 2018). Of these, one was a multi-institutional study. These RCTs we judged as being low risk of bias for intraoperative, early postoperative outcomes, and long-term outcomes. The assigned risk of bias was inherent to the nature of surgical interventions (blinding of intervention and outcome reported not possible). There were 11 observational studies on cystectomy, including 3 multi-institutional studies. The quality of the observational studies was in general moderate to high risk of bias. Many used propensity modeling which helped balance the comparative arms for patient and tumor characteristics. However, the risk of bias was higher for the long-term outcomes as follow-up time was lower in the robotic study arms.

For partial nephrectomy, 7 observational studies were identified for nephrectomy and judged as having low risk of bias in measurement classification of interventions, low risk of bias due to missing data, and low risk of bias in measurement of outcomes. Bias due to deviations from intended interventions and bias in selection of the reported result were low to medium. Overall, these studies were most limited by confounding and selection bias and had high to moderate risk of bias.

**Figure 1. Literature Flow Chart**

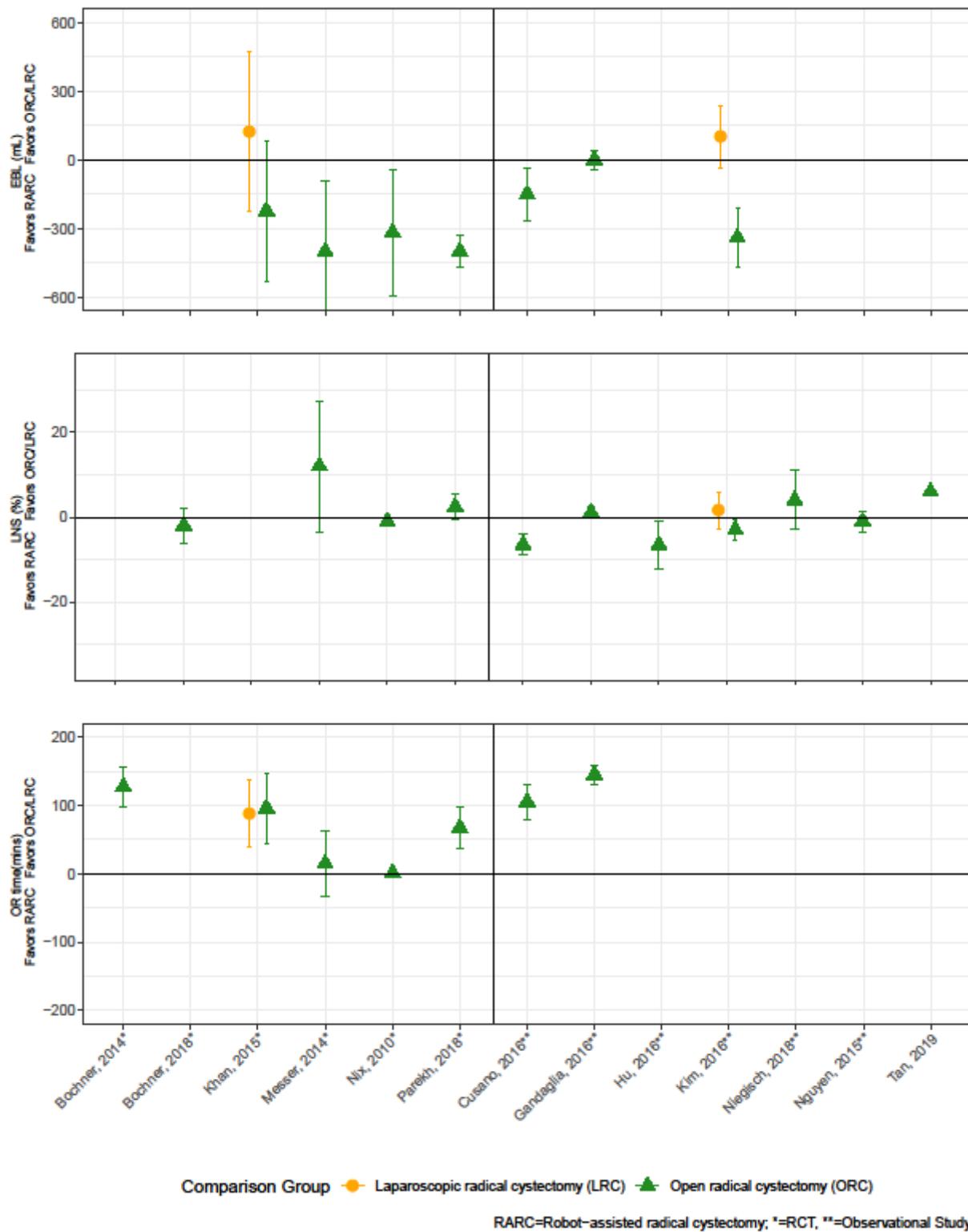


## **KEY QUESTION 1A – CYSTECTOMY: What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for cystectomy?**

We identified 16 publications that met the inclusion criteria.<sup>9-24</sup> Five studies were randomized trials<sup>9-14</sup>; of note, 2 publications were from the same study, but data were abstracted from both<sup>9,10</sup> and the remaining studies were observational. All studies compared robot-assisted cystectomy to open cystectomy, and 3 studies also compared it to laparoscopic surgery.<sup>11,18,22</sup> One of the 5 RCTs was a multi-institutional study (15 institutions) and the studies varied in size from 40 to 302 subjects. Eleven studies were observational; of these only 3 were multi-institutional. They varied in size from 148 to 9561 subjects.

Figure 2 presents graphically the results for 3 intraoperative outcomes: estimated blood loss (EBL), lymph node sampling (LNS), and operating room (OR) time. In 4 RCTs, the estimated blood loss was less in patients treated with robot-assisted cystectomy compared to open cystectomy, and in 3 of these RCTs this was a statistically significant difference. In one RCT, the estimated blood loss was slightly less in patients treated with laparoscopic cystectomy than robot-assisted cystectomy, although this difference was not statistically significant. In 2 of 3 observational studies, estimated blood loss was statistically significantly less in patients treated with robot-assisted cystectomy than open cystectomy. In one observational study, estimated blood loss was not statistically significantly less in patients treated with laparoscopic cystectomy than with robot-assisted cystectomy. For the outcome of lymph node sampling, differences between procedures were in general small and/or not statistically significant. For the outcome of OR time, 4 of 5 RCTs and both observational studies found this was greater in patients treated with robot-assisted cystectomy compared to open cystectomy, although in 1 of these studies this difference was not statistically significant. The 1 RCT that compared robot-assisted cystectomy to laparoscopic cystectomy found OR time was shorter in the latter.

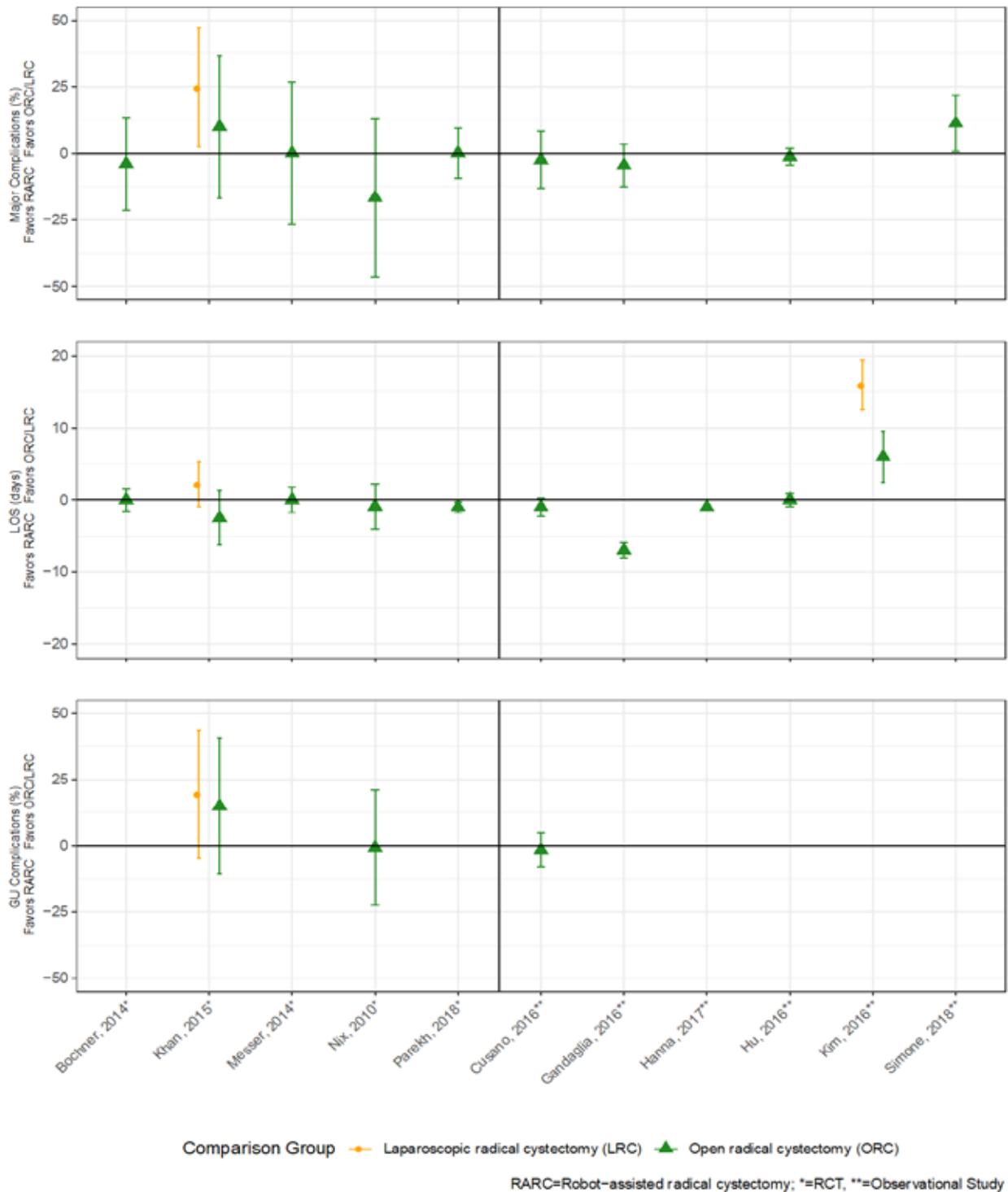
**Figure 2. Bladder Cancer: Intraoperative Outcomes**



Graphed is the point estimate and 95% confidence intervals for the difference in the indicated outcome between robot-assisted cystectomy and either open (green triangles) or laparoscopic (gold circles) approaches. Randomized trial data are on the left-hand side, observational study data are on the right-hand side.

Figure 3 presents graphically the results for 3 post-operative outcomes: major complications, genitourinary complications, and length of stay. All 5 RCTs and 3 of the 4 observational studies reported no statistically significant differences in major complications between patients treated with robot-assisted cystectomy compared to open cystectomy. Both RCTs and 1 observational study reported no statistically significant difference in genitourinary complications between patients treated with robot-assisted cystectomy and open cystectomy. All 5 RCTs and 3 of 5 observational studies reported no statistically significant differences in length of stay; in the 2 remaining studies 1 reported statistically significant longer LOS for patients treated with robot-assisted cystectomy and the other 1 reported statistically significantly shorter LOS for patients treated with open cystectomy. The 2 studies comparing robot-assisted cystectomy to laparoscopic cystectomy were inconclusive.

**Figure 3. Bladder Cancer: Postoperative Outcomes**

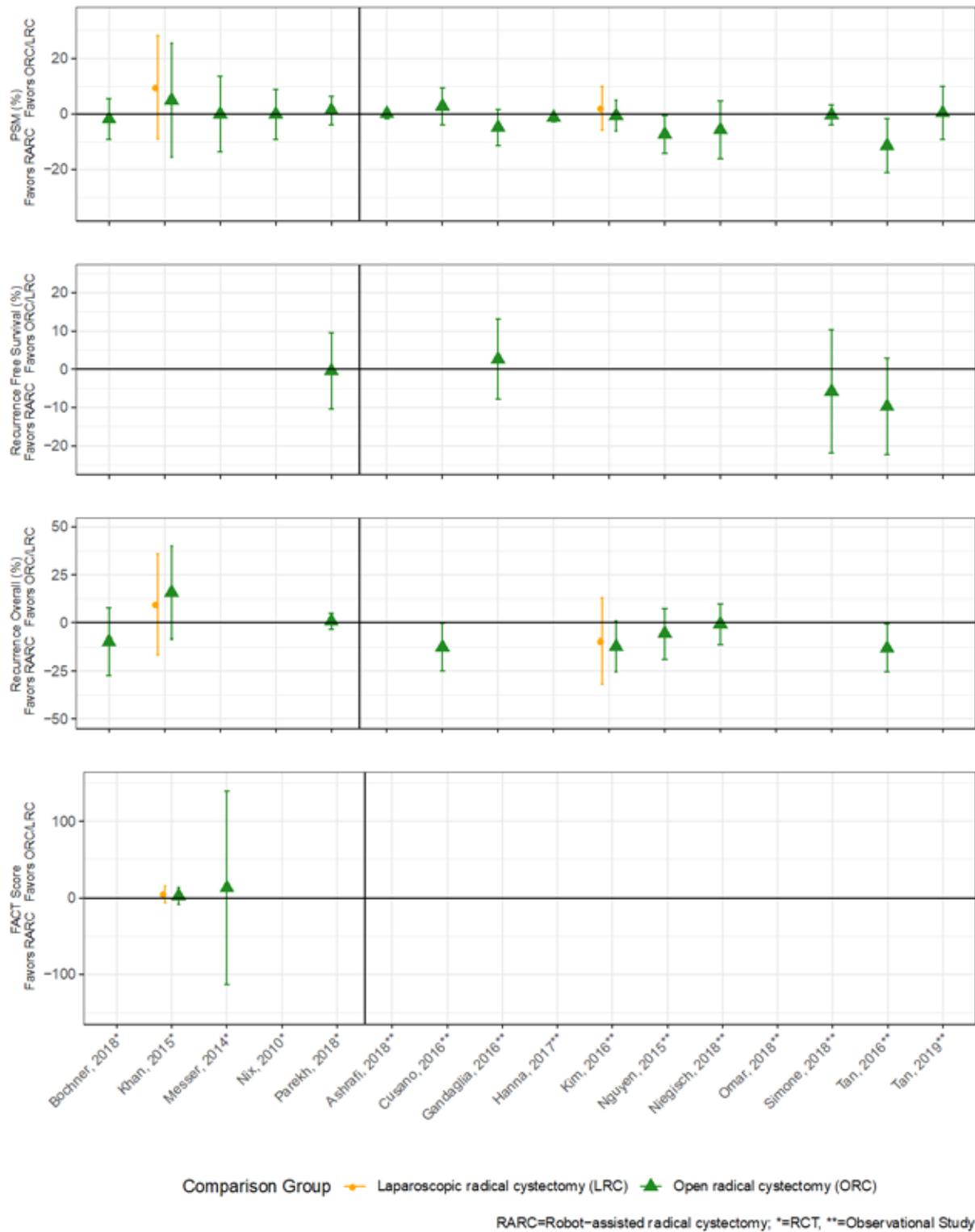


Graphed is the point estimate and 95% confidence intervals for the difference in the indicated outcome between robot-assisted cystectomy and either open (green triangles) or laparoscopic (gold circles) approaches. Randomized trial data are on the left-hand side, observational study data are on the right-hand side.

Figure 4 presents graphically the results for 4 functional or cancer-specific outcomes: Functional Assessment of Cancer Therapy (FACT), positive surgical margins, recurrence, and recurrence-free survival. With only a rare exception, no study reported statistically significant differences in any of these outcomes between patients treated with robot-assisted cystectomy and open cystectomy or laparoscopic cystectomy. However, the 95% confidence intervals of outcomes are very wide, and clinically important differences cannot be excluded.

In terms of the available data for assessing differences in long-term cancer outcomes for cystectomy studies, among the 5 RCTs there was variability in terms of lack of reporting on long-term (> 1 year) oncologic outcomes, small sample sizes, and 4 of 5 RCTs were from single institutions. Additionally, several studies commented on the fact that a significant number of patients who were approached for enrollment chose the robotic approach over entering the trial (5/55 for the Bochner et al study<sup>10</sup>; 35% for Khan et al<sup>11</sup>). For Khan and colleagues,<sup>11</sup> oncologic outcomes were reported at only 12 months and sample sizes were small (20 for the robotic-treated group, 19 laparoscopic-treated patients, and 20 open-treated patients). For Messer and colleagues,<sup>12</sup> oncologic outcomes were again reported at 12 months. For Bochner and colleagues,<sup>10</sup> the authors commented that “study was not powered to assess oncologic outcomes.” The study by Nix and colleagues<sup>13</sup> also had small sample sizes (21 in the robotic group and 20 in the open group) and oncologic outcomes were not reported. Parekh and colleagues<sup>14</sup> did report oncologic outcomes at 24 months with sample size of over 100 in both the robotic and open groups. Of note, 10% and 12% of patients assigned to each group did not go on to have the assigned surgery. In summary, the sample size and follow-up data from RCTs limit our ability to properly assess the long-term oncologic outcomes for robotic cystectomy versus the comparator procedures. Only 2 RCTs reported 5-year outcomes, and between them they only included data on 40 robot-treated cases.

**Figure 4. Bladder Cancer: Functional/Cancer Outcomes**



Graphed is the point estimate and 95% confidence intervals for the difference in the indicated outcome between robot-assisted cystectomy and either open (green triangles) or laparoscopic (gold circles) approaches. Randomized trial data are on the left-hand side, observational study data are on the right-hand side.



Of note, all urinary diversions included in the RCTs were performed extracorporeally, which was standard of care when these trials were conceived. Moreover, also most of our included observational studies exclusively analyzed RARC with an extracorporeal urinary diversion, and the remaining observational studies did not stratify their results by an extra- or intra-corporeal technique. At present, data on oncological outcomes of RARC performed with an intracorporeal urinary diversion are limited. Having said that, RARC is increasingly performed intracorporeally.

### Summary of Findings

In general, estimated blood loss was less and OR time was longer in patients treated with robot-assisted cystectomy compared to open cystectomy. The evidence about lymph node sampling shows that in most studies, but not all, there is no difference between procedures. The few studies comparing robot-assisted cystectomy to laparoscopic cystectomy found no difference in intraoperative outcomes. RCTs and observational studies support a conclusion that there are not significant differences between robot-assisted and open cystectomy in major complications, genitourinary complications, or length of stay. Data are too imprecise to draw any conclusions about differences or lack thereof between robot-assisted cystectomy and laparoscopic cystectomy.

### Certainty of Evidence for Key Question 1A

We judged the certainty of evidence for the outcomes of lower EBL for robot-assisted cystectomy compared to open cystectomy as high. Data are consistent and come from both randomized trials and observational studies. We judged the certainty of evidence that there is no difference in lymph node sampling between these two procedures as low, due to inconsistency. We judged the certainty of evidence about longer OR time for robot-assisted cystectomy compared to open cystectomy as moderate. We judged the certainty of evidence for the 3 post-operative outcomes as moderate due to some imprecision. All comparisons of robot-assisted cystectomy to laparoscopic cystectomy were judged to be very low due to sparse data.

**Table 1. Certainty of Evidence for Cystectomy Studies**

Outcome	Study Limitations	Consistency	Directness	Precision	Certainty of Evidence
Intra-operative					
Blood Loss Robot < Open	RCT: Low Observational studies: High	Consistent	Direct	Precise	High
Lymph Node Sampling Robot = Open	RCT: Low Observational studies: High	Inconsistent	Direct	Imprecise	Low
Operating Room Time Robot > Open	RCT: Low Observational studies: High	Consistent	Direct	Imprecise	Moderate
All comparisons to laparoscopic surgery	RCT: Low Observational studies: High	N/A	Direct	Imprecise	Very Low

Outcome	Study Limitations	Consistency	Directness	Precision	Certainty of Evidence
<b>Post-operative</b>					
Major complications Robot = Open	RCT: Low Observational studies: High	Consistent	Direct	Imprecise	Moderate
Genitourinary complications Robot = Open	RCT: Low Observational studies: High	Consistent	Direct	Imprecise	Moderate
Length of Stay Robot = Open	RCT: Low Observational studies: High	Consistent	Direct	Imprecise	Moderate
All comparisons to laparoscopic surgery	RCT: Low Observational studies: High	N/A	Direct	Imprecise	Very low
<b>Functional/Cancer Outcomes</b>					
All outcomes	RCTs: Low to High depending on outcome Observational studies: High	Inconsistent	Direct	Imprecise	Very low

### KEY QUESTION 1B – CYSTECTOMY: What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for cystectomy?

We identified 2 cost modeling studies for cystectomy.

The first was published in 2018.<sup>25</sup> This study evaluated robotic versus open cystectomy. The authors used their own institution data to perform a propensity matched comparison of cases to identify the treatment effects for transfusions, complications, and readmissions. They also included their own institution data related to hospital costs. Stated hospitals costs included the acquisition and maintenance of the robot as well as “variable, technical, and professional fee costs”, although no further detail (including numbers) were provided for proprietary reasons. They did a literature search to provide ranges for the clinical outcomes and for health-related quality of life. They note that for some QOL measures, cystectomy-specific values were not available, and they assumed QOL was the same across all complications. They used a 90-day time horizon. Their results report that the robot was ~\$17,000 more expensive over the 90-day time horizon but resulted in 0.32 additional QALYs over the open approach. Additional details are reportedly available in the supplement of the article, but was not available to us at the time of writing the report. An email has been sent to the authors in an attempt to obtain this data, but we did not receive a response.

The second was also published in 2018.<sup>3</sup> This study evaluated robotic versus open cystectomy. They used primarily published data in the literature to ascertain rates of minor and major complications, OR time, and LOS. Some of these data were randomized (eg, the CORAL trial) but they included data from observational studies as well. They attempted to find QOL data but found none, and so presented their results in terms of cost per complication. They used primarily internal data from 2 Dutch hospitals for cost information. Costs included purchase (\$2M,



amortized over 7 years with 200 cases per operation) and maintenance costs for the robot (\$150k/year) (total fixed costs of robot = \$2254/case), the variable cost of robot instruments (\$4,082/case), blood transfusions, OR “time” (\$11/minute), anesthesia, professional fees for the urologist, hospital stay costs (\$562/day), as well as costs of complications based on Clavien grade. They assumed an 11-day LOS for robot cases and 14 for open operations (likely much longer than contemporary US practice). They modeled 30- and 90-day time horizons. They found the extra cost of the robot to prevent one 30-day and one 90-day major complication was 62,582 euros (~\$74k) and 37,007 euros (~\$44k), respectively. Their sensitivity analyses showed very broad ranges for their estimates. For example, the risk of major complications in robot versus open surgery ranged from 29% in favor of the robot to 31% in favor of open operations. Cost information had a similarly wide confidence interval. In one analysis, they found that there were only 3 scenarios in which the robot was cost-saving – when OR time was less than 175 minutes, when LOS was less than or equal to 4 days, or if equipment costs could be reduced to 281 euros or less (their base case had OR time of 408 minutes, LOS of 11 days, and equipment costs of 3458 euros).

In addition to the above 2 studies, we identified 2 additional studies that assessed short-term costs of robot versus other approaches in cystectomy, but did not include (or make assumptions about) effectiveness, and thus were not classified as cost-effectiveness analyses. For cystectomy, the 2 published studies also reached different conclusions about short-term costs. In 1 small study (19 robotic cases and 14 open cases), differences in post-operative costs (LOS, transfusions, treatment of complications, and re-admissions) yielded a total cost of robotic procedures that was lower than open procedures (actual values not reported).<sup>26</sup> In a companion modeling study, these authors reported that robotic cystectomy cases cost 16% lower than open cystectomy cases “when robot purchase and maintenance costs are eliminated from the model.” The other study used data from 68 open cystectomy cases and 221 robotic cystectomy cases to model the short-term costs of the 2 approaches.<sup>27</sup> These authors found that robotic cases were almost 20% more expensive than open cases, and that this difference persisted (although diminished) even if the capital cost of the robot was “avoided via charitable donation”. This study concluded that “high ongoing equipment costs remain a large barrier” to the cost effectiveness of robotic procedures, but calculated that only modest improvement in quality adjusted life years (QALY) would be needed to make robotic surgery cost-effective using thresholds typical for the United Kingdom (about \$30,000 per QALY).

## Summary of Findings

The 2 primary limitations are the underlying data behind the models and the short time horizon (which is similar to partial nephrectomy, which will be discussed to follow). The first study in cystectomy used a propensity matched internal data set and did not incorporate randomized data, despite its existence. The second does appear to have included some randomized data, but the method of pooling this data was not well-described and included both randomized and observational data. As a result, they found wide variation in their estimates on sensitivity analysis. They also did not include the latest, largest, RCT (RAZOR). While the cost analysis of one study was relatively granular and robust,<sup>3</sup> the generalizability of their operative time and LOS measures to contemporary US practice is questionable. Further, the time horizon for both studies was 90 days – which is better than for either of the partial nephrectomy studies (discussed later), but still is too short to capture any meaningful oncologic outcomes.

## Certainty of Evidence for Key Question 1B

We judged the certainty of evidence for the outcome of cost effectiveness as very low, due to methods limitation, sparseness of data and inconsistent results.

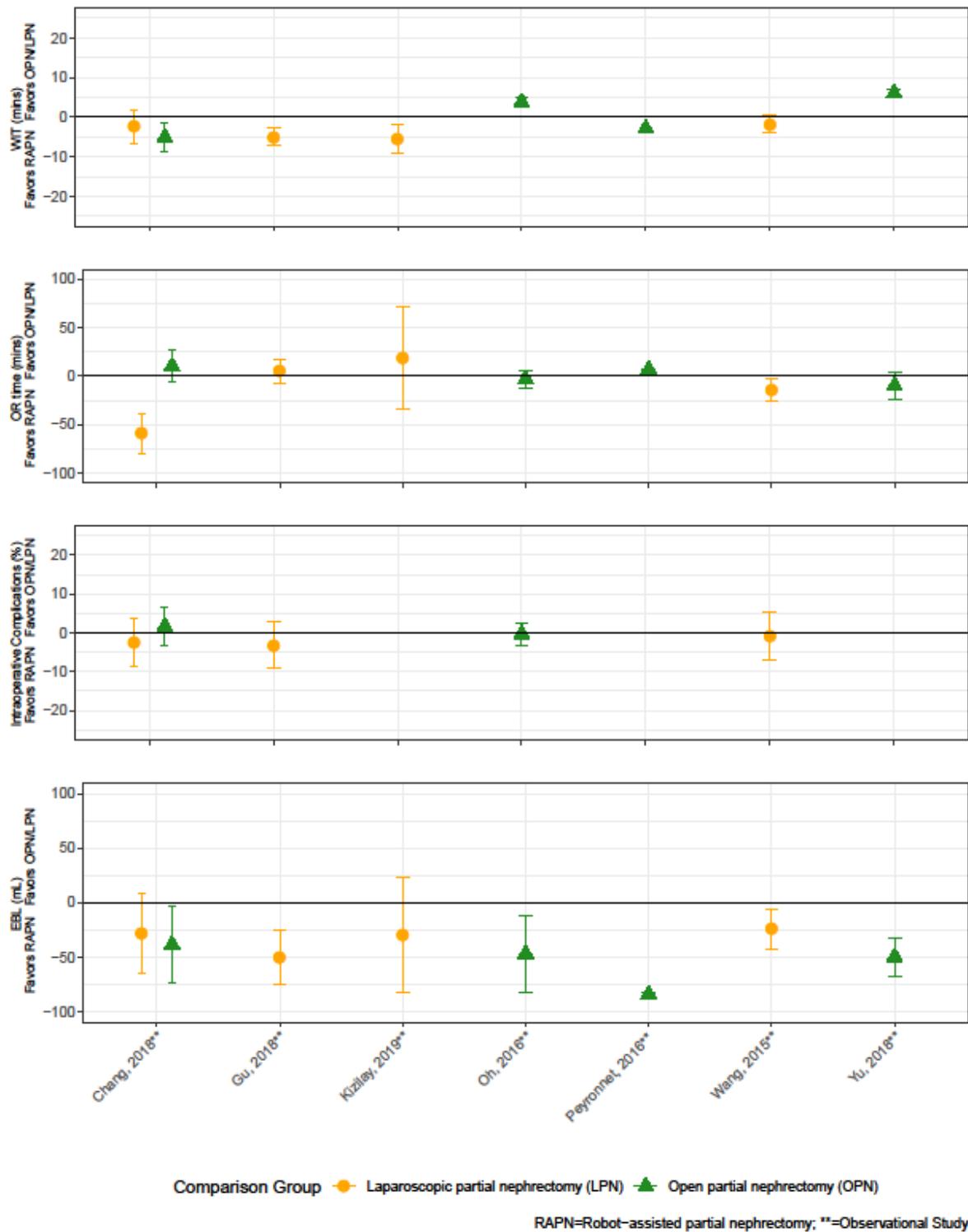
## KEY QUESTION 2A – PARTIAL NEPHRECTOMY: What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?

Compared to cystectomy, the evidence regarding robot-assisted partial nephrectomy is less in amount and of less intrinsic methodologic rigor. There are no RCTs. Correspondingly, our ability to draw conclusions, and the certainty of evidence about those conclusions, is lessened.

We identified 7 observational studies for partial nephrectomy that met the inclusion criteria.<sup>28-34</sup> One study compared robot-assisted nephrectomy to open partial nephrectomy and to laparoscopic partial nephrectomy.<sup>28</sup> Three studies compared robot-assisted nephrectomy to open partial nephrectomy,<sup>30,31,34</sup> and 3 studies<sup>29,32,33</sup> compared it to laparoscopic partial nephrectomy. There were 3 studies that were multi-institutional, varying in size from 213 to 1800 patients. In general, the quality of the studies was moderate risk of bias for intraoperative and early postoperative outcomes. Long-term outcomes were more likely to have higher risk of bias because of loss of follow-up.

Figure 5 presents the results for 4 intra-operative outcomes: EBL, intraoperative complications, OR time, and warm ischemia time (WIT). Like cystectomy, a consistent finding in these studies is lower EBL in patients treated with robot-assisted partial nephrectomy compared to either open or laparoscopic approaches. Other outcomes were either not statistically different and/or close to the null. In 1 outlier study, the authors reported longer OR time for laparoscopic versus robotic surgery (241.9 vs 182.5 min;  $p=0.001$ ).<sup>28</sup> However, the authors comment that while this was a multi-institutional study, nearly all the robotic procedures were performed at 1 of the 4 institutions, which may in part account for this difference.

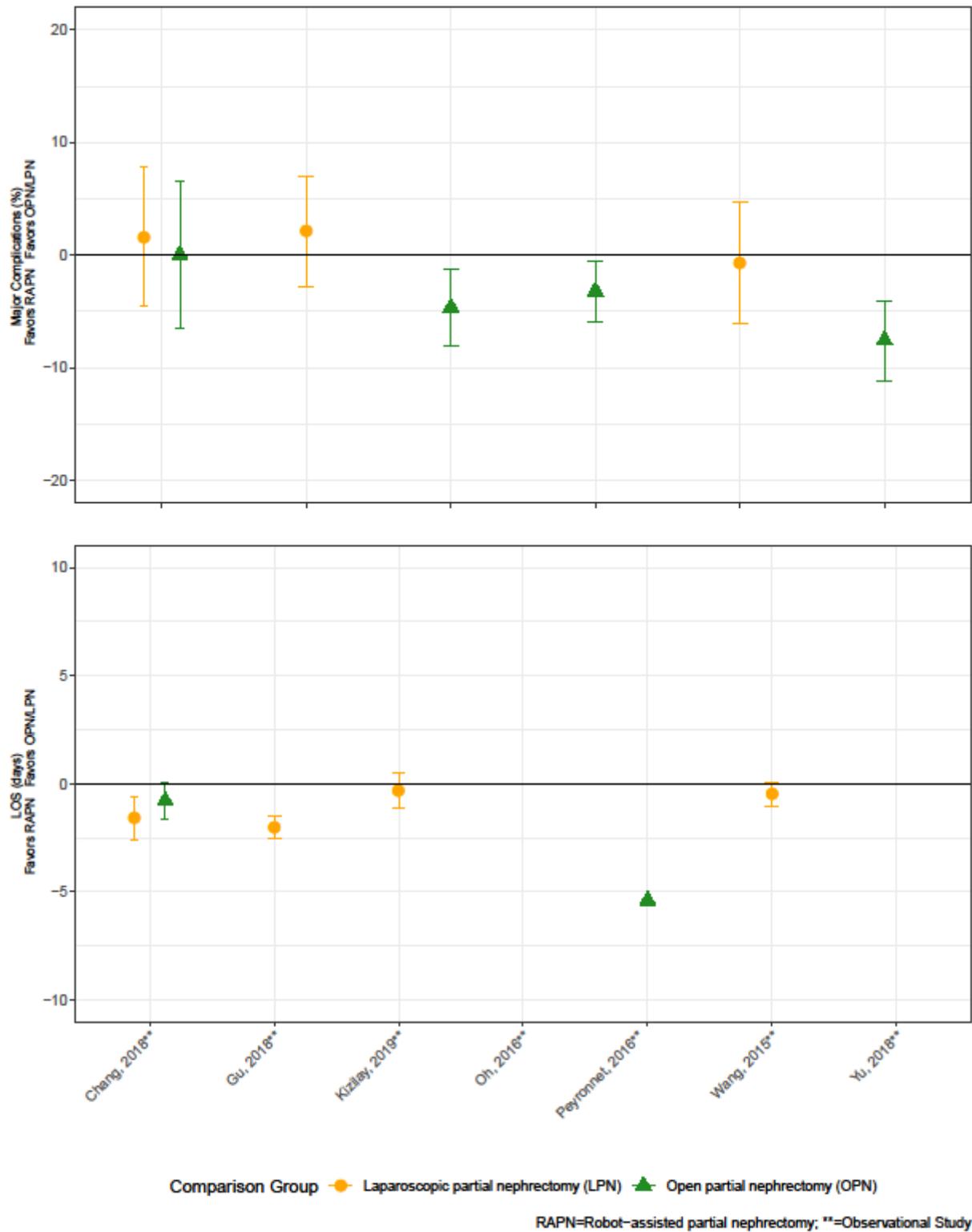
**Figure 5. Kidney Cancer: Intraoperative Outcomes**



Graphed is the point estimate and 95% confidence intervals for the difference in the indicated outcome between robot-assisted nephrectomy and either open (green triangles) or laparoscopic (gold circles) approaches. Randomized trial data are on the left hand-side, observational study data are on the right-hand side.

Figure 6 presents graphically the results for 2 post-operative outcomes: major complications and LOS. Four studies reporting LOS found this to be less for patients treated with robot-assisted partial nephrectomy compared to either open or laparoscopic approaches. In 1 study, there were no differences in LOS between robot-assisted and laparoscopic partial nephrectomy. In 3 of 4 studies, differences in the rate of major complications were lower for robot-assisted as compared to open partial nephrectomy. The remaining studies were either inconsistent and/or not statistically significantly different from the null value. The 95% confidence intervals were wide though, and a significant effect in the either direction cannot be excluded.

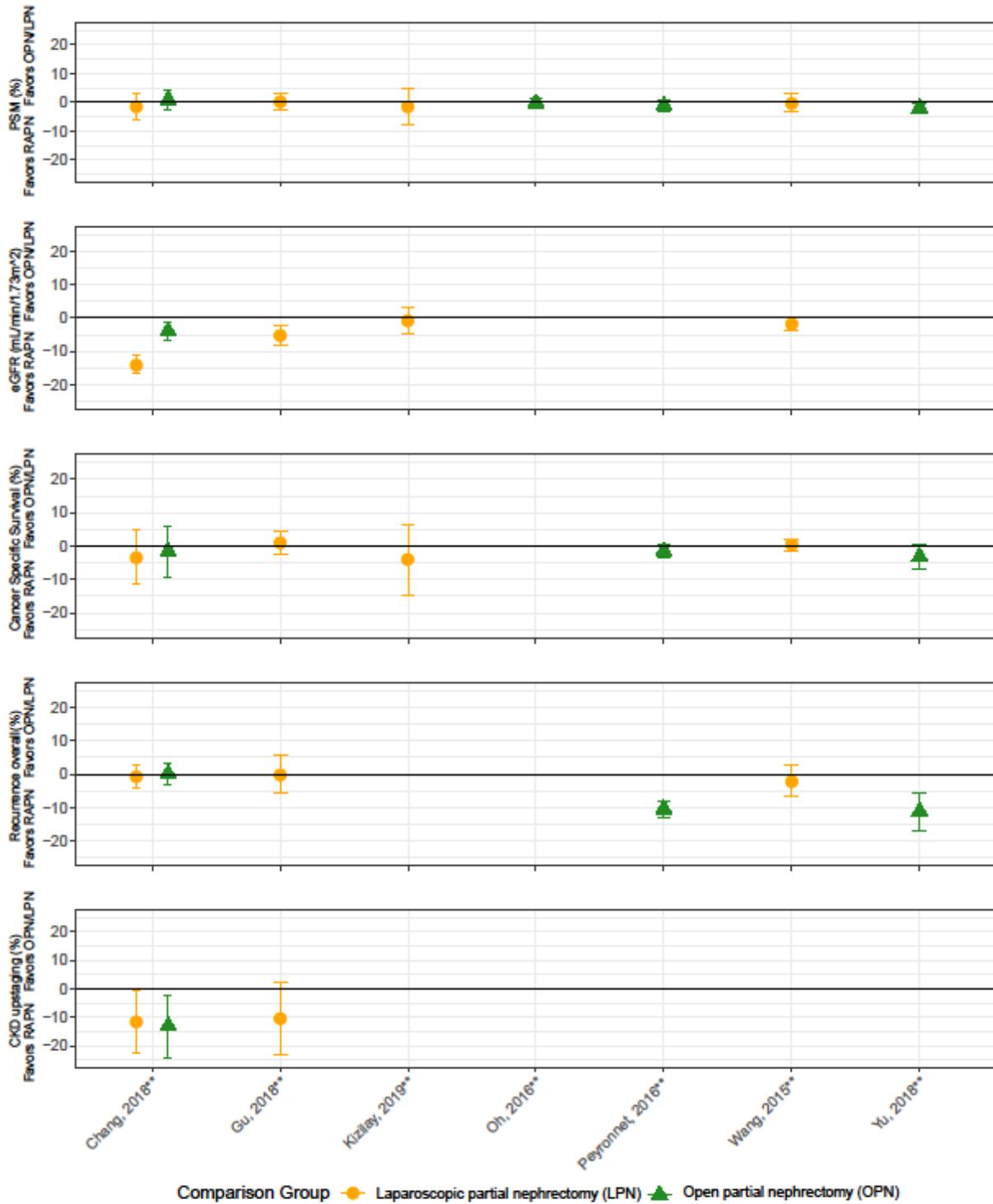
**Figure 6. Kidney Cancer: Postoperative Outcomes**



Graphed is the point estimate and 95% confidence intervals for the difference in the indicated outcome between robot-assisted nephrectomy and either open (green triangles) or laparoscopic (gold circles) approaches. Randomized trial data are on the left-hand side, observational study data are on the right-hand side.

Figure 7 presents graphically the results for 5 renal function or cancer-specific outcomes: positive surgical margins (PSM), glomerular filtration rate (GFR), cancer-specific survival, overall recurrence rate, and patients with chronic kidney disease (CKD) upstaging. With 3 exceptions, the studies reporting these outcomes found no statistically significant differences and/or results close to the null value of no difference. One exception was reported by Chang and colleagues.<sup>28</sup> They found that the incidence of chronic kidney disease (CKD) upstaging was significantly lower in the robotic approach (20.5%) as compared with to laparoscopic approach (32%,  $p = 0.035$ ) or open approach (33%,  $p = 0.038$ ). Of note, this functional kidney outcome was not reported in 3 of the other observational studies. The other 2 exceptions were studies by Peyronnet and Yu that found statistically significant differences in overall recurrence rate favoring robot-assisted surgery.

Figure 7. Kidney Cancer: Functional/Cancer Outcomes



RAPN=Robot-assisted partial nephrectomy; \*\*=Observational Study

Graphed is the point estimate and 95% confidence intervals for the difference in the indicated outcome between robot-assisted nephrectomy and either open (green triangles) or laparoscopic (gold circles) approaches. Randomized trial data are on the left-hand side, observational study data are on the right-hand side.

The data for assessing differences in long-term outcomes for partial nephrectomy studies is limited to only observational studies (7) and no RCTs. The follow-up time within studies was variable and has the potential for bias due to differences in follow-up time between groups. Chang and colleagues<sup>28</sup> did report 5-year follow-up for all 3 procedure arms, with median follow-up that was relatively similar: for robot-treated patients it was 60 (48–73) months; for laparoscopic-treated patients it was 60 (46–70) months; and for open-treated patients it was 64 (52–77) months ( $p = 0.331$  for differences between groups). However, Gu and colleagues<sup>29</sup> reported median follow-up of 20.1 months for the robotic group and 35 months for the laparoscopic group. Oh and colleagues<sup>30</sup> reported a total median follow-up of 48.3 months for the full cohort, so potential differences in follow-up time between groups is not known. Peyronnet and colleagues<sup>31</sup> reported 13-month median follow-up for robotic-treated patients as compared with 39 months for patients treated with an open approach. Wang et al,<sup>32</sup> in contrast, reported median follow-up of 31.4 months for the robotic group and 16.5 months for the laparoscopic group. Studies by Kizilay and Yu reported no differences in cancer-specific survival. Six of these 7 observational studies used propensity matching which decreased the risk of bias in terms of confounding patient-level and tumor-characteristics; however, the variable follow-up may have introduced bias into the long-term cancer and functional kidney outcomes.

It is important to note that for robotic surgery (and laparoscopic surgery) there is the inability to provide cold ischemia during partial nephrectomy as compared to open partial nephrectomy. This may favor the open procedure when looking at long-term functional outcomes, which reiterates the need for large studies with adequate long-term follow-up.

## Summary of Findings

The data comparing robot-assisted partial nephrectomy to other approaches are sparse and have underlying methodologic limitations. With this caveat, there is a consistent finding of lower estimated blood loss in patient treated with robot-assisted partial nephrectomy compared to laparoscopic and open approaches. There is also a signal that LOS is shorter and major complications are fewer with robot-assisted partial nephrectomy, but the evidence falls short of conclusive.

## Certainty of Evidence for Key Question 2A

We judged the certainty of evidence for almost all outcomes as very low, due to methodologic limitations, sparseness of data, and either imprecision or inconsistency. The exceptions were the finding that estimated blood loss is less with robot-assisted procedures, and this conclusion draws added certainty from the parallel evidence on cystectomy which is consistent and comes from RCTs. We judged the certainty of the finding that EBL is less with robot-assisted surgery as moderate. The signal regarding LOS and fewer complications were considered to be low certainty, due to the observational nature of the data.

**Table 2. Certainty of Evidence for Partial Nephrectomy Studies**

Outcome	Study Limitations	Consistency	Directness	Precision	Certainty of Evidence
<b>Intraoperative outcomes</b>					
Intraoperative complications Robot = open/lap	High	Consistent	Direct	Imprecise	Low
Operating room time Robot = open/lap	High	Inconsistent	Direct	Imprecise	Very low
Estimated blood loss Robot < open/lap	High	Consistent	Direct	Imprecise	Moderate
Warm ischemia time Robot = open/lap	High	Inconsistent	Direct	Imprecise	Very Low
<b>Post-operative outcomes</b>					
Major complications Robot < open	High	Consistent	Direct	Imprecise	Low
Major complications Robot = lap	High	Consistent	Direct	Imprecise	Low
Length of stay Robot < open/lap	High	Consistent	Direct	Imprecise	Low
<b>Functional/Cancer Outcomes</b>					
All outcomes	High	Inconsistent	Direct	Imprecise	Very low

**KEY QUESTION 2B – PARTIAL NEPHRECTOMY: What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?**

We identified 2 cost modeling studies for partial nephrectomy.

The first was published in 2011.<sup>35</sup> This study compared open, laparoscopic, and robotic partial nephrectomy. They used a healthcare sector perspective (specifically the perspective of the hospital) and looked at direct in-hospital costs. They pooled estimates from the literature to generate values for OR time and LOS and used internal cost data from a single institution related to robot, OR time (\$12.90/minute), instruments, room and board (\$508/night), lab, and pharmacy costs. Robot fixed costs included the purchase price (\$1.5M) and annual maintenance contract (\$150k). They amortized the purchase price over a 7-year time horizon and assumed 300 cases per year (average US utilization is probably closer to 200 cases/year).<sup>4</sup> They also included 5 robotic instruments at \$220/piece/case. They assumed complication rates were the same across all 3 approaches. Their results indicated that laparoscopic partial nephrectomy was the most cost-efficient with a mean direct cost of \$10,311, with a cost advantage of \$1,116 and \$1,652 over open and robotic approaches, respectively. This cost advantage was mainly driven by lower LOS for laparoscopic operations that were lost for the robot because of equipment costs. All the data they rely on is observational and, with one exception, were published prior to 2010. The assumption that complication rates are similar between the approaches is untested in randomized data and there is observational evidence (cited in the study below) that this may not be the case.



The second study was published in 2018.<sup>36</sup> This study compared open and robotic partial nephrectomy. They similarly used a healthcare sector perspective (that of the hospital) and looked at direct in-hospital costs. They relied on existing published data, specifically an analysis of the 2008-2010 National Inpatient Samples (NIS) to evaluate clinical outcomes and cost information from 2 single-site retrospective cohorts. The clinical outcomes they considered were intraoperative and postoperative complications and in-hospital death, all of which were lower in robotic surgery based on the NIS analysis. The underlying cost data excluded the purchase and maintenance of the robot, and there is a paucity of information regarding the cost accounting for the remaining cost inputs (*eg*, anesthesia, room and board).<sup>6</sup> Their results indicated that the robotic approach “dominated” the open approach because of lower in hospital costs and better clinical outcomes.

In addition to the above 2 studies, we identified 2 additional studies that assessed short-term costs of robot versus other approaches in nephrectomy, but did not include (or make assumptions about) effectiveness, and thus were not classified as cost-effectiveness analyses. Two studies assessed nephrectomy and reached differing conclusions. One concluded that robotic partial nephrectomy had lower hospital charges than laparoscopic partial nephrectomy,<sup>37</sup> while the other found that the immediate peri-operative costs of open partial nephrectomy was lower than robot partial nephrectomy.<sup>38</sup> In addition to using different comparators (the first using laparoscopic, the second using open), the 2 analyses differed in 2 other important ways: the first study used hospital charges and did not consider the capital cost of the robot, whereas the second study used hospital costs and amortized the capital cost of the robot over 60 months. This last difference was decisive, in that amortized capital costs plus operating costs of the robot added \$2,693 to the cost of each robotic partial nephrectomy for an analysis that concluded that robotic procedures were more expensive than open procedures by an overall mean cost of \$2,539.

## Summary of Findings

The 2 primary limitations of these studies are (1) the data that inform their underlying model assumptions come from observational, often out-of-date, studies and (2) the very limited time horizon of their analysis (in-hospital only). Without randomized data, treatment effect estimates are prone to bias from underlying patient or time differences, and these biased treatment effects are often amplified when included in a modeling study. The fact that in one of the above studies the authors assumed no difference in complications, and in the other, the authors assumed large differences, illustrates the uncertainty. For costs, one study excluded the purchase and maintenance of the robot – despite it being the primary determinant of higher costs in the other study – and both studies only looked at in-hospital costs. The time horizon for therapy dedicated to oncology treatment should at least include readmissions and subsequent care dedicated to cancer management. Small differences in readmissions, reoperations, or oncologic recurrences would like lead to large differences in the average cost of a treatment approach, none of which were considered in these studies.

## Certainty of Evidence for Key Question 2B

We judged the certainty of evidence for the outcome of cost effectiveness as very low, due to methods limitations, sparseness of data, and inconsistent results.

## SUMMARY AND DISCUSSION

### SUMMARY OF EVIDENCE BY KEY QUESTION

#### **Key Question 1A: What is the clinical-effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for cystectomy?**

In general, estimated blood loss was less and OR time was longer in patients treated with robot-assisted cystectomy compared to open cystectomy. The evidence about lymph node sampling shows that in most studies, but not all, there is no difference between procedures. The few studies comparing robot-assisted cystectomy to laparoscopic cystectomy found no difference in intraoperative outcomes. RCTs and observational studies support a conclusion that there are not significant differences between robot-assisted and open cystectomy in major complications, genitourinary complications, or LOS. Data are too imprecise to draw any conclusions about differences or lack thereof between robot-assisted cystectomy and laparoscopic cystectomy.

#### **Key Question 1B: What is the clinical-effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?**

The data comparing robot-assisted partial nephrectomy to other approaches are sparse and have underlying methodologic limitations. With this caveat, there is a consistent finding of lower estimated blood loss in patient treated with robot-assisted partial nephrectomy compared to laparoscopic and open approaches. There is also a signal that LOS is shorter and major complications are fewer with robot-assisted partial nephrectomy, but the evidence falls short of conclusive.

Additionally, it is important to note that for robotic partial nephrectomy cold ischemia cannot be performed. This may favor the open procedure when looking at long-term functional outcomes, but the data are sparse.

#### **Key Question 2A and 2B: What is the cost effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for cystectomy and partial nephrectomy?**

The cost effectiveness of robotic surgery for either partial nephrectomy or cystectomy is uncertain with different studies reaching different conclusions depending on how the fixed and variable costs of the robot were considered and how health outcomes (benefits or complications) were measured and valued. In any event, all cost-effectiveness data to date only consider short-term outcomes and do not include longer-term outcomes, including oncologic outcomes, that would likely significantly influence the cost/benefit ratio for any given approach.

## LIMITATIONS

### Publication Bias

We were not able to test for publication bias and can make no conclusions about its possible existence. However, we feel it is extremely unlikely that there exists a high-quality randomized trial of robotic surgery versus other surgical approaches that we did not identify, and has

similarly escaped detection by all other experts in this field. There are probably a plentitude of observational experiences about robotic therapies, from individual institutions, that have never been published, and the published literature likely represents only a small fraction of what could be known using observational studies.

### **Study Quality**

The randomized trials of cystectomy were judged to be at low risk of bias for short-term outcomes, like intraoperative and postoperative outcomes. They were judged to be at moderate risk of bias for longer-term outcomes. Likewise, the observational studies were judged to be at moderate risk of bias (due to their non-random assignment of treatments) for short-term outcomes and high risk of bias for longer-term outcomes.

### **Heterogeneity**

Some outcomes had heterogeneous results across studies (such as operating room time for patients undergoing partial nephrectomy and changes in glomerular filtration rate) while many others were more similar, such as estimated blood loss and operating time for patients undergoing cystectomy. Additionally, some findings for one procedure, like less estimated blood loss in patients getting robot-assisted cystectomy as compared to open cystectomy, were not observed for the other procedure (no such consistent differences were seen between procedures for estimate blood loss for partial nephrectomy procedures). Some of these differences may be due to inherent distinctions between the procedures themselves (meaning the option of organ preservation for kidney procedures is not relevant for cystectomy cases) but may also be due to differences in study design and execution or differences in the experience of the surgical teams involved. These cannot be disentangled without better randomized data, particularly for patients undergoing partial nephrectomy.

### **Applicability of Findings to the VA Population**

No studies were specific to VA populations. The applicability of these results to VA populations may depend on both the similarity of the patients studied to VA patients and the experience of the surgical teams using the robot to VA surgical team experience. However, the benefits for robotic approach may still be realized despite patient-level differences (VA patient population has greater burden of comorbidities than the general population), which will need to be confirmed in future studies. Urology as a surgical field has widely adopted robotic surgery, so the experience will likely translate well into the VA setting.

### **Research Gaps/Future Research**

Two research gaps are apparent. The first is randomized data for patients undergoing partial nephrectomy, in terms of short-term outcomes. The second is high-quality evidence with adequate long-term follow-up and sufficient statistical power to assess cancer outcomes between the operative approaches for either cystectomy or partial nephrectomy. RCTs for these conditions, when they have been attempted, generally do not have long-term follow-up (only 2 of 5 RCTs reported 5-year data) and then the number of enrolled subjects is too small to have sufficient statistical power to detect clinically important differences. The LACC trial for cervical cancer enrolled hundreds of patient and had 4.4 years follow-up.<sup>5</sup> In contrast, only 40 patients have been enrolled in RCTs with 5-year follow-up for either of these 2 procedures. One inherent

difference noted in the observational studies for both cystectomy and partial nephrectomy is the lower follow-up rate and shorter time interval for the robotic groups – which makes comparisons limited. This is particularly important as newer evidence for some GYN cancers suggests possible worse cancer outcomes with the robotic approach. Despite what appears to be better or equivalent technical outcomes for cystectomy and likely partial nephrectomy, acceptable cancer and functional outcomes need to be confirmed. Specifically, studies should assess the functional quality of life outcomes for the bladder cancer patients and the ongoing kidney function for the partial nephrectomy patients. Better-quality cost-effectiveness studies are warranted as well – which will add to the understanding of how to balance the clinical benefits with increased cost of the procedure and perhaps savings that better clinical outcomes afford (decreased blood loss, LOS).

## REFERENCES

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## APPENDIX A. SEARCH STRATEGIES

### DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 1/1/2010-6/29/2019

### LANGUAGE:

English

### SEARCH STRATEGY #1:

“Similar Article” searches on the following 2 articles:

Systematic review and meta-analysis of randomised trials of perioperative outcomes comparing robot-assisted versus open radical cystectomy.

Shen Z1, Sun Z2.

BMC Urol. 2016 Sep 23;16(1):59.

Robotic versus open partial nephrectomy: a systematic review and meta-analysis.

Wu Z1, Li M2, Liu B1, Cai C3, Ye H1, Lv C1, Yang Q1, Sheng J2, Song S1, Qu L1, Xiao L1, Sun Y1, Wang L1.

PLoS One. 2014 Apr 16;9(4):e94878. doi: 10.1371/journal.pone.0094878. eCollection 2014.

### SEARCH STRATEGY #2:

Robotic Surgical Procedures"[Mesh] OR robotics[mh] OR robot-assisted OR robot\*[tiab] OR robot\*[ot]

AND

nephrectom\* OR cystectom\* OR nephrectomy[mh] OR ureter OR ureteral OR ureters

NOT

editorial[pt] OR editorial[ti] OR letter[pt] OR letter[ti] OR comment[pt] OR comment[ti]

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### DATABASE SEARCHED & TIME PERIOD COVERED:

Embase – 1/1/2010-6/29/2019

### LANGUAGE:

English

### SEARCH STRATEGY:

'robot assisted surgery'/exp OR 'robot assisted surgery' OR 'robot assisted' OR robot\*

AND

'cystectomy'/exp OR 'cystectomy' OR 'nephrectomy'/exp OR 'nephrectomy' OR 'ureter'/exp OR ureter OR 'ureters'/exp OR ureters OR ureteral

AND

HUMAN

---

**DATABASE SEARCHED & TIME PERIOD COVERED:**

Cochrane – All databases – 1/1/2010-6/29/2019

**LANGUAGE:**

English

**SEARCH STRATEGY:**

MeSH descriptor: [Robotic Surgical Procedures] explode all trees OR MeSH descriptor: [Robotics] explode all trees OR (robotic-assisted OR robot\*):ti,ab,kw

AND

MeSH descriptor: [Nephrectomy] explode all trees OR MeSH descriptor: [Cystectomy] explode all trees OR MeSH descriptor: [Ureter] explode all trees OR (nephrectomy\* OR cystectomy\* OR ureter OR ureteral OR ureters):ti,ab,kw

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NOTE: FOR ALL SEARCH RESULTS, ANIMAL-ONLY STUDIES WERE DELETED MANUALLY IN ENDNOTE

NOTE: FOR ALL SEARCH RESULTS, ENDNOTE SEARCHES WERE DONE ON THE FOLLOWING TERMS IN THE RECORD TITLE OR KEYWORD:

- PEDIATRIC(S)
- PAEDIATRIC(S)
- CHILD(REN)
- INFANT(S)

RESULTS WERE REVIEWED AND ARTICLES RELATING ONLY TO NON-ADULT POPULATIONS WERE DELETED  
IN ADDITION, ARTICLES FROM JOURNALS WITH “PEDIATRIC(S)” OR “PAEDIATRIC(S)” IN THE JOURNAL NAME WERE DELETED

## APPENDIX B. PEER REVIEWER COMMENTS AND RESPONSES

Comment	Response
<p>Consider this study: J Urology 2019;201:715-720. Sathianathen et al. Robotic assisted radical cystectomy vs open radical cystectomy: Systematic Review and Meta-analysis</p>	<p>Thank you for pointing this out. This study analyzed the same 5 RCTs that have been included also in our report and, therefore, its results and conclusions are consistent with ours (with RARC presenting a decreased need for perioperative blood transfusion, but a longer operative time; there was no difference in disease progression, major complications or QOL).</p>
<p>Why did the authors choose 2010 as a start date? Understanding that the robotic platforms were introduced in 2005, and recognizing that the early literature from this period through 2010 is most likely low quality and high risk of bias, an explanation should be given for the date selection.</p>	<p>We selected 1/1/2010 search start date was chosen based on input from our TEP. After 2010 robotic-assisted procedures became more common and the studies published earlier often reflected learning curves. Thus evidence from studies published from prior to the year 2010 were determined by our TEP to be insufficiently relevant to modern practice. We have added this to the methods section.</p>
<p>The evidence likely also derives mostly from academic centers and centers of excellence and it is unclear if the mostly short-term results from these included studies would be generalizable to a broader population of urologic surgeons and VA settings.</p>	<p>The expense of the robotic platforms has limited broad uptake in community hospitals, and the bulk of the literature represents academic centers. However, as new robotic companies are emerging, community and VA hospitals may incorporate more robots. The training required to use the robot is structured and extensive, as such it is likely that non-academic surgeons will perform as a high quality level and results from our study will apply well. The contention is that centers with experience with the robotic platform can perform cystectomy and partial nephrectomy without compromising perioperative outcomes as well as oncologic outcomes. We attempted to ensure a high level of reliability between data by utilizing literature with large volume as well as recent publications such that it would not necessarily be generalizable to all urologic surgeons but potentially those who have overcome their learning curve and have adequate volume in their practice. Furthermore, a fair number of VA centers are high volume robotic centers currently. Our local VA is actually getting a second robot because of demand. We have a paragraph (page 26) that addresses the possible lack of generalizability of our findings to VA patients (page 36).</p>
<p>Line 20, this is a fragment: “over 125,000 procedures in 2017.”</p>	<p>Thank you for pointing this out, this has been corrected.</p>
<p>Line 43, “On 40 patients have been enrolled in RCTs with 5 year follow-up for either of these two procedures.” Should be “Only”.</p>	<p>Thank you for pointing this out, this has been corrected.</p>
<p>Line 48/49: “Robotic-assisted surgery for cystectomy and partial nephrectomy has a few documented short benefits” should be “short-term benefits”.</p>	<p>Thank you for pointing this out, this has been corrected.</p>

<p>Line 11 of the Evidence Report should be, “Urologic surgery was one of the first surgical disciplines to adopt robotic surgery”.</p>	<p>Thank you for pointing this out, this has been corrected.</p>
<p>Line 12 of Key Question 1a should have a semi-colon: “Five studies were randomized trials; of note, two publications were from the same study, but data were abstracted from both, and the remaining studies were observational.”</p>	<p>Thank you for pointing this out, this has been corrected.</p>
<p>Line 16 page 21 has an excess comma: “Additionally, several studies commented on the fact that a significant number of patients who were approached for enrollment, chose...” the comma before chose shouldn’t be there.</p>	<p>Thank you for pointing this out, this has been corrected.</p>
<p>This is an excellent and thorough review reviewing the literature evaluating the outcomes and cost effectiveness of minimally invasive techniques for radical cystectomy and partial nephrectomy. The authors have provided a comprehensive analysis of the published literature. The overall conclusions trending towards less blood loss for both RARC and RPN are well founded and generally accepted in the urologic literature. However, in more contemporary series, there is also a trend towards lower LOS favoring RARC. this is not reflected in the current review , largely because of the inclusion of1 observational study from Korea ( Kim et al, J Endo 2016;30:783-791) which had a very high length of stay for both ORC ( 22 days) as well as RARC (28 days) which far exceeds what most US centers experience. Most of the RCTs of robotic vs open cystectomy show avg LOS in the 7-10 day range so the Korean study does not represent current practice. Whether this is because of not using an ERAS regimen or other factors relating to hospital practices in Korea cannot be ascertained.</p>	<p>We agree with the reviewer’s assessment that the study by Kim and colleagues is an outlier. However, the remaining studies show no statistically significant differences between approaches, so that we are unable to reach a conclusion that LOS is shorter with robot-assisted surgery.</p>
<p>Figures: it would be helpful to define abbreviations shown in the graphs also in the figure legends, not just the body of the manuscript. Also, including the numbers of patients in each study should be shown to give the data better context</p>	<p>Thank you for pointing this out, this has been corrected.</p>
<p>Figure 3: Although the LOS is shown for the Kim study, the LOS data is not included in the summary for this study (Appendix G p 56)</p>	<p>Thank you for pointing this out, this has been corrected.</p>
<p>The cost effectiveness data for cystectomy from the second paper from Europe (Ref #3)</p>	<p>This is a valid consideration. However, a strength of cost-effectiveness analyses is that the relative difference</p>

<p>may not be directly comparable to costs in the US.</p>	<p>within each study is reported. As such, we believe the finding of relative differences for this study are relevant as well to non-European based work.</p>
<p>Outcomes for RARC should be stratified according to whether the urinary diversion is done intracorporeally vs extracorporeally. Most of the RCTs do not make this distinction since the data is relatively sparse, however as more surgeons are performing intracorporeal diversion, it might be expected to change postoperative outcomes (? less ileus, ) and potentially LOS and cost. The authors should include this as a possibility to consider even though the existing literature does not.</p>	<p>All urinary diversions included in the RCTs were performed extracorporeally, which was standard of care when these trials were conceived. Moreover, also most of our included observational studies exclusively analyzed RARC with an extracorporeal urinary diversion, and the remaining observational studies didn't stratify their results by an extra- or intra-corporeal technique. At present, data on oncological outcomes of RARC performed with an intracorporeal urinary diversion are limited. Having said that, RARC is increasingly performed intracorporeally, and we agree that future trials/studies should take this into consideration. We have added this comment to our limitations paragraph in the Discussion.</p>
<p>Key question 2A, p26. Last sentence comparing lap to robotic OR times for partial nephrectomy may be becoming moot since most MIS partial nephrectomies are now being done robotically.</p>	<p>Yes, we agree that the majority of partial nephrectomy cases are being performed robotically. However, our TEP believed it was still important to provide the evidence for open versus robotic and laparoscopic versus robotic, especially with the currently climate of robotic surgery oncology outcomes being questioned for other cancer types such as gynecologic surgery.</p>
<p>P 36 under "Heterogeneity". The statement regarding "clamping the arterial supply of the kidney vs inability to do so for the bladder " should be deleted or modified since it is not relevant. There is no organ preservation attempted when performing RC .</p>	<p>Thank you. This was corrected.</p>
<p>One final point that is rarely discussed by the robotic surgeons is the inability to provide cold ischemia during MIS partial nephrectomy vs open partial nephrectomy. This may favor the open procedure when looking at long term functional outcomes.</p>	<p>Thank you for your comment. This important point addressing the difference in technique has been added to the Summary.</p>

Of note, some minor improvements were made to language and presentation throughout the report. None of these changes were substantive.

As part of the revision process, we performed an update search, which resulted in 4 new included observational studies, 2 about cystectomy and 2 about partial nephrectomy. The inclusion of these new studies did not change any of the conclusions from the draft report.

## APPENDIX C. COCHRANE RISK OF BIAS TOOL

### The Cochrane Collaboration’s Tool for Assessing Risk of Bias\*

Domain	Support for judgement	Review authors’ judgement
<i>Selection bias.</i>		
<b>Random sequence generation.</b>	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.
<b>Allocation concealment.</b>	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
<i>Performance bias.</i>		
<b>Blinding of participants and personnel</b> <i>Assessments should be made for each main outcome (or class of outcomes).</i>	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
<i>Detection bias.</i>		
<b>Blinding of outcome assessment</b> <i>Assessments should be made for each main outcome (or class of outcomes).</i>	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Detection bias due to knowledge of the allocated interventions by outcome assessors.
<i>Attrition bias.</i>		
<b>Incomplete outcome data</b> <i>Assessments should be made for each main outcome (or class of outcomes).</i>	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Attrition bias due to amount, nature or handling of incomplete outcome data.
<i>Reporting bias.</i>		
<b>Selective reporting.</b>	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Reporting bias due to selective outcome reporting.
<i>Other bias.</i>		
<b>Other sources of bias.</b>	State any important concerns about bias not addressed in the other domains in the tool.  If particular questions/entries were pre-specified in the review’s protocol, responses should be provided for each question/entry.	Bias due to problems not covered elsewhere in the table.

\* <http://handbook.cochrane.org/> in Table 8.5.a

## APPENDIX D. RISK OF BIAS IN NON-RANDOMISED STUDIES – OF INTERVENTIONS (ROBINS-I)

### Bias domains included in ROBINS-I<sup>7</sup>

<i>Pre-intervention</i>	Risk of bias assessment is mainly distinct from assessments of randomised trials
<b>Bias due to confounding</b>	<p>Baseline confounding occurs when one or more prognostic variables (factors that predict the outcome of interest) also predicts the intervention received at baseline</p> <p>ROBINS-I can also address time-varying confounding, which occurs when individuals switch between the interventions being compared and when post-baseline prognostic factors affect the intervention received after baseline</p>
<b>Bias in selection of participants into the study</b>	<p>When exclusion of some eligible participants, or the initial follow-up time of some participants, or some outcome events is related to both intervention and outcome, there will be an association between interventions and outcome even if the effects of the interventions are identical</p> <p>This form of selection bias is distinct from confounding—A specific example is bias due to the inclusion of prevalent users, rather than new users, of an intervention</p>
<i>At intervention</i>	Risk of bias assessment is mainly distinct from assessments of randomised trials
<b>Bias in classification of interventions</b>	<p>Bias introduced by either differential or non-differential misclassification of intervention status</p> <p>Non-differential misclassification is unrelated to the outcome and will usually bias the estimated effect of intervention towards the null</p> <p>Differential misclassification occurs when misclassification of intervention status is related to the outcome or the risk of the outcome, and is likely to lead to bias</p>
<i>Post-intervention</i>	Risk of bias assessment has substantial overlap with assessments of randomised trials
<b>Bias due to deviations from intended interventions</b>	<p>Bias that arises when there are systematic differences between experimental intervention and comparator groups in the care provided, which represent a deviation from the intended intervention(s)</p> <p>Assessment of bias in this domain will depend on the type of effect of interest (either the effect of assignment to intervention or the effect of starting and adhering to intervention).</p>
<b>Bias due to missing data</b>	Bias that arises when later follow-up is missing for individuals initially included and followed (such as differential loss to follow-up that is affected by prognostic factors); bias due to exclusion of individuals with missing information about intervention status or other variables such as confounders
<b>Bias in measurement of outcomes</b>	Bias introduced by either differential or non-differential errors in measurement of outcome data. Such bias can arise when outcome assessors are aware of intervention status, if different methods are used to assess outcomes in different intervention groups, or if measurement errors are related to intervention status or effects
<b>Bias in selection of the reported result</b>	Selective reporting of results in a way that depends on the findings and prevents the estimate from being included in a meta-analysis (or other synthesis)

## APPENDIX E. QUALITY ASSESSMENT FOR INCLUDED RCT STUDIES

Author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Parekh, 2018 <sup>14</sup>	TM	~	~	~ *	TM	TM	TM
Bochner, 2018 <sup>10</sup>	TM	TM	~	~ *	TM	TM	TM
Khan, 2016 <sup>11</sup>	TM	TM	~	~ *	TM	TM	TM
Messer, 2014 <sup>12</sup>	TM	~	~	~ *	TM	TM	~ QOL
Nix, 2010 <sup>13</sup>	~	~	~	~ *	TM	TM	TM

TM = low risk of bias ~ = risk of bias ½ = unknown

\* low risk of bias for primary outcomes (all-cause mortality and amputation-free survival, but high risk of bias for secondary outcome

## APPENDIX F. QUALITY ASSESSMENT FOR INCLUDED OBSERVATIONAL STUDIES

### CYSTECTOMY\*

	<b>Confounding</b>	<b>Selection bias</b>	<b>Bias in measurement classification of interventions</b>	<b>Bias due to deviations from intended interventions</b>	<b>Bias due to missing data</b>	<b>Bias in measurement of outcomes</b>	<b>Bias in selection of the reported result</b>
Tan 2019 <sup>23</sup>	Moderate: propensity matched Severe: sig differences in gender, urinary diversion, disease characteristics	Low: consecutive series, all pts analyzed	Low	Low	Low	Low	Low
Ashrafi 2018 <sup>24</sup>	Severe: not propensity matched, adjusted for demographics	Low: consecutive series	Low	Low	Low	Low	Low
Niegisch 2018 <sup>39</sup>	Serious: small sample size, no propensity/multivariate Moderate: only 2 year f/u	Low Stage matching	Low	Low	Moderate: pts excluded for short f/u		Low
Simone 2018 <sup>21</sup>	Moderate: propensity matching Low: time	Low	Low	Low	Low	Low: short-term (30d) outcomes Low: long-term (4yr) outcomes Moderate: efficacy	Low
Hanna 2017 <sup>20</sup>	Severe: patients Low: time	Moderate	Moderate	Low	Moderate	Low: short-term (30d) outcomes Moderate: long-term (2yr) outcomes Low: efficacy	Moderate

	<b>Confounding</b>	<b>Selection bias</b>	<b>Bias in measurement classification of interventions</b>	<b>Bias due to deviations from intended interventions</b>	<b>Bias due to missing data</b>	<b>Bias in measurement of outcomes</b>	<b>Bias in selection of the reported result</b>
Gandaglia 2016 <sup>16</sup>	Moderate: patients (neoadj) Low: time	Moderate: difference in stage	Low	Low	Moderate	Low: short-term outcomes Low: long-term (5yr) outcomes Low: Efficacy	Low
Hu 2016 <sup>17</sup>	Serious: patients (propensity matching) Low: time	Moderate	Moderate	Low	Low: outcomes No info: efficacy	Low: short-term outcomes Low: long-term (5yr) outcomes Serious: efficacy	Moderate
Cusano 2016 <sup>15</sup>	Serious: patients Low: time	Serious	Low	Low	Low	Low: short-term outcomes Serious: long-term (<<2yr) outcomes Moderate: efficacy (only PSM)	Low
Kim 2016 <sup>18</sup>	Moderate: patients age Low: time	Low	Low	Low	Low	Low: short-term outcomes Low: long-term (4yr) outcomes Low: efficacy	Low
Tan 2016 <sup>40</sup>	Moderate: different pt populations; propensity matching Severe: time (f/u for robot short)	Moderate: learning curve; robot instituted later	Low	Low	Low	Severe: Short-term outcomes, only margins Moderate: long-term outcomes (only 2 yr) Moderate: Efficacy, margins and LNs	Low
Nguyen 2015 <sup>19</sup>	Moderate: patient age Low: time	Moderate: difference in clinical stage	Low	Low	Low	Low: short-term outcomes Moderate: long-term (2yr) outcomes Low: efficacy	Low

\*All 9 observational studies for cystectomy were most concerning for confounding due to the retrospective nature of the studies, and low in bias due to intervention deviation. Cusano et al and Nieglisch had a risk of serious confounding due to lack of propensity matching or multivariate analysis. Nieglisch also had small sample size for both arms. Hanna et al and Hu et al used large administrative datasets from NCDB (National Cancer Data Base) [Hanna] and SEER (Surveillance, Epidemiology, and End Results Program) respectively, making the studies prone to lack of standardization of surgical techniques, entering errors, misclassification, and missing observation across multiple centers. Thus both studies had seriousness for confounding bias; moderation in selection bias, bias in measurement classification, missing data bias, and reporting bias. Except for these 2 studies (due to adopting large administrative datasets and Nieglisch et al due to large amount

of excluding patients with less than 1 year follow-up), missing data bias was low among all the studies. Reporting bias was deemed to be low among all studies except Hanna et al and Hu et al as mentioned above. Cusano et al has serious selection bias due to lack of patient exclusion criteria. Gandaglia et al, Nguyen et al, and Tan et al have moderate selection bias due to prominent difference in clinical stages between arms as well as default operation of choice based on timeline of the study. Tan et al and Nieglsch et al had serious bias in short-term outcome measurement given only having PSM (positive surgical margin) results and lack of perioperative and short-term outcome results. All have moderate to serious long-term outcome bias due to short follow-up time (equal or less than 2 years), except Simone et al, Gandaglia et al, Hu et al, and Kim et al. Efficacy outcome is measured by PSM, amount of removed lymph node as well as perioperative results. The bias in efficacy outcome in Hu et al is considered to be serious as only the percentage of more than 10 lymph node removed was reported.

## PARTIAL NEPHRECTOMY

	<b>Confounding</b>	<b>Selection bias</b>	<b>Bias in measurement classification of interventions</b>	<b>Bias due to deviations from intended interventions</b>	<b>Bias due to missing data</b>	<b>Bias in measurement of outcomes</b>	<b>Bias in selection of the reported result</b>
Kizilay 2019 <sup>33</sup>	Moderate: propensity matched Severe: sig differences in tumor laterality + location (RAPN - complex tumors); intraop technique and learning curve not accounted for	Severe: not consecutive series... unclear how many pts were excluded	Low	Low	Low	Low	Low
Yu 2019 <sup>34</sup>	Moderate: propensity matched Severe: sig age, BMI, baseline eGFR, and tumor volume differences	Moderate: many pts excluded	Low	Low: conversions excluded	Moderate: missing data excluded (not clear how many)	Low	Low
Chang 2018 <sup>28</sup>	Moderate	Serious	Low	Low	Low	Low	Low
Gu 2018 <sup>29</sup>	Moderate	Serious	Low	Low	Low	Low	Low
Oh 2016 <sup>30</sup>	Moderate	Serious	Low	Moderate	Low	Low	Moderate
Peyronnet 2016 <sup>31</sup>	Serious	Low	Low	Moderate	Low	Low	Moderate
Wang 2015 <sup>32</sup>	Serious	Serious	Low	Moderate	Low	Low	Low



## APPENDIX G. EVIDENCE TABLES

### CYSTECTOMY RCT

Author Year Population  #Institutions/ Surgeons	Patient characteristics, Preop			Tumor factors			Intraoperative outcomes			Long-term outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Bochner 2018 <sup>10</sup> Bochner 2014 <sup>9</sup>  2010-2013, Memorial Sloan Kettering Cancer Center 1 institution 7 Surgeons (3 RACC & 4 ORC)		Size 60 Age 66 [60- 71] Male 85% BMI  ASA≥3 71.7%	Size 58 Age 65 [58-69] Male 72.4% BMI  ASA≥3 79.3%		NMI  CI Stage ≥ T2a 48.3%  Pa Stage ≥ T2 41.3%  NACT	NMI  CI Stage ≥ T2a 56.9%  Pa Stage ≥ T2 44.9%  NACT		OR 456 (82) EBL  Avg Lym -std 20 [13-25] Clavio-D 22% Urinary compl 10% PSM 3.6% LOS 8 (3)	OR 329 (77) EBL  Avg Lym- std 18 [13-23] Clavio-D 21% Urinary compl 9% PSM 4.8% LOS 8 (5)		LR 28.3% TR 33.3%  CSS- 5yr* 75%-80% OS- 5yr* 65-70% *Extrapol- ated from the graphs	LR 8.6% TR 43.1%  CSS- 5yr* 75%- 80% OS- 5yr* 65-70% *Extrapo lated from the graphs	No difference in recurrence or cancer specific survival or overall survival. Increase in metastatic sites for ORC. Greater local and abdominal sites in RARC.

Author Year Population  #Institutions/ Surgeons	Patient characteristics, Preop			Tumor factors			Intraoperative outcomes			Long-term outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Parekh 2018 <sup>14</sup> RAZOR  2011-2014, 15 medical centres in USA  15 institutions		Size 150 Age 70 [43- 90] Male 84% BMI 27.8 [25- 30.8] ASA ≥ 3	Size 152 Age 67 [37-85] Male 84% BMI 28.2 [24.9- 31.7] ASA ≥ 3		NMI  CI Stage ≥ T2a 13.3%  Pa Stage ≥ T2 56% NACT 27%	NMI  CI Stage ≥ T2a 13.2%  Pa Stage ≥ T2 53.9% NACT 36%		OR 428 [322- 509] EBL 300 [200- 500] Avg Lym 23.3 (12.5) Clavio-D 90d 22% 30d compl 67% Urinary compl 35% PSM 6% LOS 6 [5-10]	OR 361 [281- 450] EBL 700 [200- 1000] Avg Lym 25.7 (14.5) Clavio-D 90d 22% 30d compl 69% Urinary compl 26% PSM 5% LOS 7 [6-10]		LR 4% TR 26% CFS- 2yr 72.3%  Cancer Mortality 19% QoL (FACT- VCI + Short form 8) 126 [120.4-131.6]	LR 3% TR 27% CFS- 2yr 71.6%  Cancer Mortality 21% QoL (FACT- VCI + Short form 8) 127.5 [121.7- 133.3]	No difference in 2 year progression free survival and QoL outcomes.

Author Year Population  #Institutions/ Surgeons	Patient characteristics, Preop			Tumor factors			Intraoperative outcomes			Long-term outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Khan 2016 <sup>11</sup> Omar 2018 <sup>22</sup> CORAL  2009-2012 Guy's Hospital London UK  1 institution *90 days	Size 19 Age 68.6 (9.9) Male 79% BMI 26.2 (3.6) ASA ≥ 3 16%	Size 20 Age 68.6 (6.8) Male 85% BMI 27.5 (4.2) ASA ≥ 3 5%	Size 20 Age 66.6 (8.8) Male 90% BMI 27.4 (3.9) ASA ≥ 3 5%	NMI 26.3% CI Stage ≥ T2a 73.7% Pa Stage ≥ T2 57.9% NACT 21%	NMI 40.0% CI Stage ≥ T2a 60.0% Pa Stage ≥ T2 45.0% NACT 10%	NMI 40.0% CI Stage ≥ T2a 60.0% Pa Stage ≥ T2 30.0% NACT 15%	OR 301 (51) EBL 460 (485) Avg Lym 15.5 Clavio-D 5.3% 30d compl 26% Major compl* 11% PSM 5% LOS 9.7 (3.6)	OR 389 (98) EBL 585 (618) Avg Lym 16.3 Clavio-D 25% 30d compl 55% Major compl* 35% Urinary compl 15% PSM 15% LOS 11.9 (6.2)	OR 293 (66) EBL 808 (329) Avg Lym 18.8 Clavio-D 20% 30d compl 70% Major compl* 20% Urinary compl 15% PSM 10% LOS 14.4 (5.9)	TR-12 mo 17% CSS- 5yr 69% CFS- 5yr 71% OS- 5yr 61%  QoL (FACT BI) 127.4 (13.5)	TR-12 mo 26% CSS- 5yr 70% CFS- 5yr 60% OS- 5yr 66%  QoL (FACT BI) 122.3 (17.1)	TR- 12 mo 11% CSS- 5yr 64% CFS- 5yr 53% OS- 5yr 55%  QoL (FACT BI) 124.9 (12.7)	ORC has significant higher 30d complication rate than LRC. No difference in 90d clavien graded compilation rate. OT time is longer in RARC. No significant difference s in QoL measures.



Author Year Population  #Institutions/ Surgeons	Patient characteristics, Preop			Tumor factors			Intraoperative outcomes			Long-term outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Parekh 2013 <sup>41</sup> Messer 2014 <sup>12</sup>  2009-2011, University of Texas Health Sciences Center, San Antonio 1 institution		Size 20 Age 69.5 [62.3-74] Male 90% BMI 27.6 [24.2- 29.9] ASA≥3 85%	Size 20 Age 64.5 [59.8- 72.3] Male 80% BMI 28.3 [26.1- 32.3] ASA ≥ 3 80%		NMI  CI Stage ≥ T2a  Pa Stage ≥ T2 65% NACT 30%	NMI  CI Stage ≥ T2a  Pa Stage ≥ T2 40% NACT 35%		OR 300 [240- 366] EBL 400 [300- 762.5]  Avg Lym 11.8 [8.8- 21.5] Major compl 25% PSM 5% LOS 6 [5-9.5]	OR 285.5 [240- 321.3] EBL 800 [400- 1125] Avg Lym 23[15-28] Major compl 25% PSM 5% LOS 6 [6-9.3]		FACT-VCI* (baseline to 3mo) 119-> 116  *Functional assessment of cancer therapy – Vanderbilt cystectomy index	FACT- VCI* (baselin e to 3mo) 135->12 9	No significant difference in oncologic efficacy. RARC associated with decreased EBL and LOS. NO significant difference in Health related quality of life.

Author Year Population  #Institutions/ Surgeons	Patient characteristics, Preop			Tumor factors			Intraoperative outcomes			Long-term outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Nix 2010 <sup>13</sup> Smith 2012 <sup>42</sup> 2008-2009, University of North Carolina  1 Institution		Size 21 Age 67.4 [33- 81] Male 66.6% BMI 27.5  ASA  Avg=2.71	Size 20 Age 69.2 [51- 80] Male 85% BMI 28.4  ASA Avg=2.70		NMI  CI Stage ≥ T2a 71.4%  Pa Stage ≥ T2 81% NACT	NMI  CI Stage ≥ T2a 75%  Pa Stage ≥ T2 65% NACT		OR 4.2 EBL 258 Avg Lym 19 [12-30] Clavio-D  30d compl 33% Urinary compl 14% PSM 0% LOS 5.1	OR 3.52 EBL 575 Avg Lym 18 [8-30] Clavio-D  30d compl 50% Urinary compl 15% PSM 0% LOS 6		TR- 3yr 14% CSS- 3yr 85% OS- 3yr 81%	TR- 3yr 35% CSS- 3yr 68% OS- 3yr 65%	3 yr f/u eval shows no difference overall survival and disease specific survival, recurrence, or complications or LOS. RACC is favorable in several periop parameter (EBL, inpt narcotic requirements)



**CYSTECTOMY OBSERVATIONAL STUDIES**

Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Tan et al <sup>i</sup> 2019 <sup>23</sup>  Open vs robot  43- and 35.5- mo f/u					Pa Stage ≥ T2 (50)  NACT (38.9)	Pa Stage ≥ T2 (47.6)  NACT (14.3)		Avg Lym 28  PSM 0 (0)	Avg Lym 34  PSM 0 (0)		CFS 37.5 mo <sup>ii</sup> OS 43.0 mo <sup>iii</sup>	CFS 21.4 mo OS 35.5 mo	Nonsignificant difference in NACT (p=0.14) average lymph node yield (p=0.256), and pathological stage (p=0.856)  No significant difference in CFS (p=0.093) and OS (p=0.14)
Ashrafi, et al. 2018 <sup>24</sup>  Open vs robot  12 mo f/u		Size 238 Age 70.1 (9.9) Male 203 (85.7) BMI 27.6 (5.5) ASA≥2 189 (79.8)	Size 598 Age 69.7 (10.7) Male 475 (79.4) BMI 27.3 (4.9) ASA≥2 470 (73.6)		Pa Stage ≥ T2 146 (61.6)  NACT 56 (23.6)	Pa Stage ≥ T2 289 (48.3)  NACT 173 (28.9)		PSM 3 (1.3)	PSM 7 (1.2)		CFS No differences in Kaplan-Meier plots	CFS No differences in Kaplan- Meier plots	No significant difference recurrences (p=0.6) or cancer free survival (p=0.39)



Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Simone 2018 <sup>21</sup> Robot vs open  1 institution; 3 surgeons  yes		Size 64 Age 62.5 (7.4) Male 78.1% BMI 26.1 (3.25) ASA 12.5%	Size 299 Age 63 (8.6) Male 86.6% BMI 26.8 (3.47) ASA 20.7%		NMI 4.7%  CI Stage ≥ T2a 53.1%  Pa Stage ≥ T2 68.8%  NACT 25%	NMI 8.4%  CI Stage ≥ T2a 71.6%  Pa Stage ≥ T2 71.6%  NACT 4.7%		OR  EBL  Clavio-D 6.3% 30d compl 91.3% Major compl 6.3% PSM 0% LOS	OR  EBL  Clavio-D 0.33% 30d compl 42.2% Major compl 0.33% PSM 0.33% LOS		Local  CSS- 4yr 86.4% OS- 4yr 82.1%	Local  CSS- 4yr 85.3% OS- 4yr 79.6%	ORC higher rate perioperative complication (91.3% vs 42.2%)  Both have comparable disease- free survival, cancer- specific survival, and overall survival rates.
Hanna 2017 <sup>20</sup> Robot vs open  >1500 institutions;  yes		Size 2048 Age 69 [62- 76] Male 78.8% BMI  ASA  CCI 8.4%	Size 7513 Age 70 [62- 77] Male 74.1% BMI  ASA  CCI 7.0%		NMI 0%  CI Stage ≥ T2a 46.8%  Pa Stage ≥ T2 68.8% NACT 0%	NMI 0%  CI Stage ≥ T2a 50.1%  Pa Stage ≥ T2 46.8% NACT 0%		OR  EBL  Avg Lym 17 [10-25]  Clavio-D  30d compl  PSM 9.3% LOS 7 [6-10] Readm 10.2%	OR  EBL  Avg Lym 12 [7-20]  Clavio-D  30d compl  PSM 10.7% LOS 8 [6-11] Readm 10.2%		OS- 2yr 70.2%	OS- 2yr 62.5%	Intraop outcome wise, equivalent PSM, higher median LN count of dissection, postop wise, RARC shorter LOS, lower 30/90 day postop mortality for RARC (1.4%/ 4.8% vs 2.8%/ 6.7%. Better overall 2-yr survival in RARC



Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Cusano 2016 <sup>15</sup> Robot vs open 1 Institution 6 surgeons  No  *patients during a 10 year period with median f/u 1.38 and 1.40 yr for ORC and RARC respectively	Size 121 Age 65.9 (10.4) Male 78.5% BMI 28.2(5) ASA 3 [10- 25] 50% CCI 4 [3-5]	Size 92 Age 67.8 (10.4) Male 79.3% BMI 28.4 (5.2) ASA 3 [10- 25] 50% CCI 4 [3-5]	NMI 69.2%  CI Stage ≥ T2a 68.6%  Pa Stage ≥ T2 58.7% NACT 31.4%	NMI 72.5%  CI Stage ≥ T2a 71.7%  Pa Stage ≥ T2 68.7% NACT 22.8%	OR, time, min 508 [436- 589] EBL, mL 450 [300- 725] Avg Lym 18 [11-24]  Clavio-D  Major compl 18.2% PSM 8.3% LOS  Readm	OR 403 [359- 467] EBL 600 [450- 1100] Avg Lym 11.5 [7-19]  Clavio-D  Major compl 20.7% PSM 5.6% LOS  Readm	Local recurrences/ LR, % 22.3% Total recurrences/ TR, % CSS CFS Overall Mortality*: 24%	Local recurrences/ LR, % 34.8% Total recurrences/ TR, % CSS CFS Overall Mortality*: 37%	ORC with shorter operative time, greater blood loss and transfusion rate. No difference in LOS. Greater number of lymph removed in RARC. ORC associated with higher mortality rate. No difference in disease free survival.				



Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Gandaglia 2016 <sup>16</sup> Robot vs open  2 institution; 3 surgeons  No		Size 138 Age 70 [60.7- 77] Male 83.5% BMI 26.1 [22.9- 28.6]  ASA 39.1% CCI	Size 230 Age 70.9 [63.1- 77.5] Male 83.5% BMI 26 [23.5-29]  ASA 38.7% CCI		NMI  CI Stage ≥ T2a 64.5%  Pa Stage ≥ T2 58.7%  NACT 19.6%	NMI  CI Stage ≥ T2a 57.3%  Pa Stage ≥ T2 60.9%  NACT 0%		OR 330 [260- 370] EBL 300 [200- 430] Avg Lym 12 [8-17]  Clavio-D 15.9% 30d compl  PSM 8.7% LOS 13 [11-17] Readm 10.1%	OR 185 [165- 222] EBL 300 [200- 500] Avg Lym 13 [9-17]  Clavio-D 20.4% 30d compl  PSM 13.5% LOS 20 [16-24] Readm 15.7%		CSS- 5yr 73.5% CFS- 5yr 54.2%	CSS- 5yr 61.9% CFS- 5yr 57.1%	OR associated with shorter operative time, RARC with lower blood loss and shorter LOS. No differences in major complication and positive margin. Similar oncologic control.



Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Hu 2016 <sup>17</sup> Robot vs open  N/A Yes *Estimated based on the given range #RARC slightly better		Size 439 Age 75* Male 86.1% BMI ASA CCI	Size 7308 Age 75* Male 80.9% BMI ASA CCI		NMI 0%  CI Stage ≥ T2a  Pa Stage ≥ T2 64.0%  NACT 19.4%	NMI 0%  CI Stage ≥ T2a  Pa Stage ≥ T2 70.7%  NACT 13.0%		OR  EBL  Avg Lym ≥ 10 41.5%  Clavio-D Major compl 8.0% PSM  Readm -30d 28.2%	OR  EBL  Avg Lym ≥ 10 31.1%  Clavio-D Major compl 9.8% PSM  Readm -30d 26.1%		Hazard Ratio of 3 yr OS =0.88#  Hazard Ratio of 2 yr CSS = 0.91		RARC associated with greater lymph node yield, shorter LOC, increased home healthcare utilization. Similar overall survival, cancer specific survival.



Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Kim 2016 <sup>18</sup> Robot vs open vs lap  1 Institution  No	Size 22 Age 65 [62.8- 74] Male 90% BMI 23 [20.9- 26.1]  ASA 13.6% CCI	Size 58 Age 61.5 [54.8- 72] Male 93.1% BMI 22.8 [20.8- 25.5]  ASA 6.9% CCI	Size 150 Age 68 [60- 73] Male 82.0% BMI 23.9 [21.9- 26.3]  ASA 7.3% CCI	NMI 0  CI Stage ≥ T3a 54.5%  Pa Stage ≥ T2 100%  NACT 4.5%	NMI 0  CI Stage ≥ T3a 41.4%  Pa Stage ≥ T2 100%  NACT 1.7%	NMI 0  CI Stage ≥ T3a 52.0%  Pa Stage ≥ T2 100%  NACT 6.0%	OR 524 [490.8- 593.8] EBL 400 [300- 700] Avg Lym 19.5 [14.8- 27.3] Clavio-D  Major compl	OR 501.5 [440.8- 604.0] EBL 500 [368.8- 700] Avg Lym 18.0 [14- 25.3] Clavio-D  Major compl  PSM 3.4% LOS 28 [18-34.3] Readm	OR 508 [436- 589] EBL 840 [557.5- 1500] Avg Lym 15 [10-20] Clavio-D  Major compl  PSM 4.0% LOS 22 [17-32] Readm	Availabl e on graphs without individu al values (4 yr CFS, CSS, OS)	Available on graphs without individual values (4 yr CFS, CSS, OS)	Available on graphs without individual values (4 yr CFS, CSS, OS)	Operative time shorter for ORC, surgical blood loss and transfusion rate lower in RARC. RARC has a greater number of lymph node removed, lower disease recurrence. ORC associated with higher overall mortality. No difference in disease-free survival between groups.



Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Nguyen 2015 <sup>19</sup> Robot vs open  1 Institution  No		Size 263 Age 72 [65-79] Male 78.7% BMI 25 [23-28]  ASA 52% CCI	Size 120 Age 69 [63-75] Male 70.8% BMI 24 [24-28]  ASA 54% CCI		NMI  CI Stage ≥ T2a 64.6%  Pa Stage ≥ T2 49%  NACT 24%	NMI  CI Stage ≥ T2a 64.2%  Pa Stage ≥ T2 61% NACT 23%		OR  EBL  Avg Lym 21 [13-28]  Clavio-D  Major compl  PSM 6% LOS  Readm	OR  EBL  Avg Lym 20 [11-27]  Clavio-D  Major compl  PSM 13% LOS  Readm		LR 18%% TR 47%  Available on graphs without individual values (4 yr CFS)	LR 23% TR 59%  Available on graphs without individual values (4 yr CFS)	No significant difference in number of local or distant recurrences of 2 yr. Recurrence at extrapelvic lymph node locations and peritoneal carcinomatosis are more freq in RARC

<sup>a</sup>Median [IQR] <sup>b</sup>Mean (SD)

i Unclear what the sample size was after propensity score matching (18 and 21 before matching for iRARC and ORC respectively)

ii Recurrence free survival reported in months

iii Overall survival reported in months



**Partial Nephrectomy Observational Studies**

Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
Kizilay, et al 2019 <sup>33</sup>  Lap vs robot  1 institution  yes	Age 54.6 (12.4) Male 40 (56.4) 37 (52.2) BMI 23.8 (3.1) Preop GFR 84.9 (21.4) *Mean + SD	Age 52.9 (11.8) Male 40 (56.4) BMI 24.5 (4.2) Preop GFR 82.6 (18.1)		Tumor size 27.9 (11.8) * Mean+ SD Laterality 39 (33.9)	Tumor size 24.8 (11.2) Laterality 44 (62.0)		WIT 24.4 (12.1) OR 158 [128- 211] Median + range (not IQR)  EBL 240 [120- 330]  Transfusions 4 (5.6)  PSM 3 (4.2) LOS 3.5 [2-6] Median + range (not IQR)	WIT 18.8 (10.7) OR 176 [154- 251] EBL 210 [100- 385] Transfusions 3 (4.2) PSM 2 (2.3) LOS 3.2 [2-5]		GFR 1 yr 12.39 [3.86- 24.35]  Median + range (not IQR)  CSS 61 (85.9)  Median + range (not IQR)  OS 60 (84.8)	GFR 1 yr 11.38 [4.12-22.88]  CSS 64 (90.1) OS 59 (82.6)		No differences in 5-year OS (p=0.561) and CSS (0=0.710) rates  WIT shorter in RAPN (p=0.019)
Yu, et al. 2019 <sup>34</sup>  Open vs robot  1 institution  yes	Age 54 [45-63] *Median + IQR) Male 212 (70.0) BMI 24.7 [22.9- 26.5]	Age 56 [46- 65]  Male 204 (67.3) BMI 24.7 [22.9- 26.5]		Tumor size 27 [20-38] Clear cell 184 (60.7) Benign 37 (12.2) Stage≥T2a 2 (0.7)	Tumor size 28 [20- 40] Clear cell 186 (61.4) Benign 35 (11.6)		WIT 22 [18-27] *Median + IQR  OR 120 [100- 180] *Median + IQR	WIT 16 [13-20] OR 130 [110- 155] EBL 150 [100- 250] Transfusions 3 (1.0)		Total (5.3) *Unclear what the sample size was, only % listed  CSS (95.9)	Total (8.5) CSS (92.8)		No significant difference in 5- year recurrence (p=0.059) or CSS (p=0.135)  EBL (p<0.001), PSM (p=0.033) were



Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
		*Median + IQR Preop GFR 82.3 [71.0-92.3] Preop Renal 8 [6-9] *Median + IQR	24.4 [22.2-26.5] Preop GFR 79.2 [66.1-79.3] Preop Renal 8 [6-9]			Stage ≥ T2a 1 (0.3)		EBL 100 [50-200] *Median + IQR  Transfusions 12 (4.0)  PSM 1 (0.3)	PSM 7 (2.3)				significantly lower in RAPN
Chang, 2018 <sup>28</sup> Lap vs robot vs open  4 institutions; 6 surgeons  yes	Age 53.5 (13.3) Male 56.6% BMI 25.2 (5.7) Preop GFR 92 [83-97] Preop Renal 6.2 (1.9)	Age 53.2 (12.3) Male 50.8% BMI 24.6 (2.7) Preop GFR 94 [85-99] Preop Renal 6 (1.8)	Age 53.8 (12.9) Male 54.1% BMI 23.9 (3.1) Preop GFR 92 [84-98] Preop Renal 6.1 (1.8)	Tumor size 27 [19-43] Clear cell 66.4% Benign 11.5% Stage≥T2a 1.6% Laterality 49.2%	Tumor size 28 [22-48] Clear cell 70.5% Benign 9% Stage≥T2a 1.6% Laterality 50.2%	Tumor size 25 [20-45] Clear cell 61.5% Benign 10.7% Stage≥T2a 0.8% Laterality 51.6%	WIT 24.3 (19) OR 241.9 (90) EBL 196.1 (142)  Clavio-D 7.3% PSM 4.1% LOS 6.9 (4.3)	WIT 22 (14.6) OR 182.5 (68.6) EBL 167.7 (147)  Clavio-D 5.7% PSM 2.5% LOS 5.3 (3.4)	WIT 27.1 (13.2) OR 172.5 (64) EBL 206.4 (135)  Clavio-D 7.3% PSM 1.6% LOS 6.1 (3.2)	Local 2.5% CSS 86.9%	Local 1.5% CSS 90.2%	Local 1.6% CSS 88.5%	LPN associated with longer mean OPT (p=0.001)  RAPN had a lower mean EBL (p=0.025, LPN; p=0.040, OPN)
Gu 2018 <sup>29</sup> Lap vs robot  1 institution; 5 surgeons  yes	Age 50 [39-59] <sup>a</sup> Male 68.8% BMI 26.1 [22.2-28.4] <sup>a</sup>	Age 51 [41-60] <sup>a</sup> Male 74% BMI 26.2 [24.2-28.0] <sup>a</sup> Solitary 4.2%		Tumor size 48 [43-53] Clear cell 67.7% Benign 6.3%	Tumor size 48 [43-53] Clear cell 79.2% Benign 1.0% Stage≥T2a 1.6%		WIT 25 [19-30] <sup>a</sup> OR 128 [105-160] <sup>a</sup> EBL 150 [120-200] <sup>a</sup> Transfusion	WIT 20 [16-26] <sup>a</sup> OR 133 [110-174] <sup>a</sup> EBL 100 [50-200] <sup>a</sup> Transfusion		GFR, 6 mo 10.3 (10.9) Local  Total  CSS	GFR, 6 mo 5.1 (9.2) Local  Total  OS		LPN associated with higher EBL and LOS (p<0.001)



Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
	Solitary 4.2% Preop GFR 95.4 (16.1) <sup>b</sup> Preop Renal 8 [7-9] <sup>a</sup>	Preop GFR 93.2 (20.2) <sup>b</sup> Preop Renal 8 [7-9] <sup>a</sup>		Stage≥T2 a 1.6% Laterality 47.9%	Laterality 46.9%		8.3%  Clavio-D 2.1% GU 1% PSM 1.0% LOS 7 [5-8] <sup>a</sup>	6.3%  Clavio-D 4.2% GU 2.1% PSM 1.0% LOS 5 [5-7] <sup>a</sup>		OS			
Oh 2016 <sup>30</sup> Robot vs open  N/A  yes	Age 52.9 (12.0) Male 72.2% BMI 24.8 (3.3) Preop GFR 91.4 (56.6) <sup>b</sup>	Age 53.3 (12.9) Male 68.6% BMI 24.6 (3.0) Preop GFR 77.5 (18.6) <sup>b</sup>		Stage≥T2 a 1.6% Laterality 47.9%	Tumor size 22.0 (8.2) <sup>b</sup> Clear cell 76% Laterality 49.2%	Tumor size 22.4 (8.2) <sup>b</sup> Clear cell 75.3% Laterality 50.6%	WIT 20.8 (7.7) OR 137.5 (59.0) EBL 167.2 (236.6) Transfusion 1.6%  Clavio-D 2.2% PSM 1.33%	WIT 17.01 (7.69) OR 140.9 (46.2) EBL 214.3 (202.7) Transfusion 3.1%  Clavio-D 7.0% PSM 1.67%		GFR, 6 mo GFR, 1y Local Total CSS OS	GFR, 6 mo GFR, 1y Local Total CSS OS	OPN associated with a longer surgical margin width (p=0.016)	
Peyronnet 2016 <sup>31</sup> Robot vs open  N/A  no	Age 69.6 (3.4) Male 63.7% BMI 26.6 (0.2) Preop GFR 82.7 (1.1) <sup>b</sup>	Age 57.5 (3.6) Male 64.8% BMI 26.5 (0.2)		Stage≥T2 a 1.6% Laterality 47.9%	Tumor size 32.9 (0.6) <sup>b</sup> Clear cell 61.1% Benign 14.6%	Tumor size 39.9 (0.6) <sup>b</sup> Clear cell 74.8% Benign 4.0%	WIT 15.7 (0.3) OR 153.2 (2.0) EBL 275.1 (13) Transfusion 8.1%	WIT 18.6 (0.4) OR 146.6 (2.3) EBL 359.5 (15.2) Transfusion 12.9%		GFR, 6 mo GFR, 1y Local Total CSS	GFR, 6 mo GFR, 1y Local Total CSS	OPN had a higher complication rates (p<0.001) and greater EBL (p<0.001)  RAPN had a shorter WIT	



Author Year Population  #Institutions/ Surgeons  Propensity matching (yes/no)	Patient characteristics, Preop			Tumor factors			Intraoperative Outcomes			Long-term Outcomes			Primary Multi- variate Findings
	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	Lap	Robot	Open	
		Preop Renal 6.8 (0.1)	Preop GFR 81.2 (1.5) <sup>b</sup> Preop Renal 6.7 (0.1)					Clavio-D 7.8% GU 2.0% PSM 5.2% LOS 4.7 (0.2)	Clavio-D 11% GU 4.3% PSM 6.5% LOS 10.1 (0.2)		97.9% OS	96.3% OS	(p<0.001) and LOS (p<0.001)
Wang 2015 <sup>32</sup> Lap vs robot  N/A  no	Age 63.5 (14.8) Male 65.9% BMI 24.3 (4.2) Preop GFR 79.6 (18.3) <sup>b</sup> Preop Renal 85.8 (21.8) <sup>b</sup> Preop Renal 8.1 (1.1)	Age 61.2 (12.6) Male 67.9% BMI 25.2 (5.1) Preop GFR 79.6 (18.3) <sup>b</sup> Preop Renal 8.3 (0.9)		Tumor size 36 (17) <sup>b</sup> Clear cell 73% Benign 14.8%	Tumor size 38 (22) <sup>b</sup> Clear cell 43% Benign 11.1%		WIT 22.3 (8.4) OR 149.6 (43.5) EBL 220.8 (72.9) Transfusion 5.9%  Clavio-D 4.4% GU 3.0% PSM 1.5% LOS 8.1 (2.4)	WIT 20.5 (7.6) OR 135.6 (37.8) EBL 196.5 (63.6) Transfusion 7.6%  Clavio-D 3.7% GU 1.2% PSM 1.2% LOS 7.6 (1.8)		GFR, 6 mo 8.6 (8.1) Local  Total  CSS  OS	GFR, 6 mo 7.0 (6.4) Local  Total  CSS  OS	LPN associated with a longer OT (p=0.017)	

<sup>a</sup>Median [IQR]

<sup>b</sup>Mean (SD)



## APPENDIX H. CITATIONS FOR EXCLUDED PUBLICATIONS

### Intervention (n=3)

1. Fraisse, G., et al., *Peri-operative and local control outcomes of robot-assisted partial nephrectomy vs percutaneous cryoablation for renal masses: comparison after matching on radiological stage and renal score*. BJU Int, 2018.
2. Tanagho, Y.S., et al., *Renal cryoablation versus robot-assisted partial nephrectomy: Washington University long-term experience*. J Endourol, 2013. **27**(12): p. 1477-86.
3. Weinberg, A.C., et al., *Utilization and perioperative complications of laparoscopic cryoablation vs robotic partial nephrectomy for localized renal tumors*. Int Braz J Urol, 2015. **41**(3): p. 473-85.

### Comparison (n=4)

1. Ludwig, W.W., M.A. Gorin, and M.E. Allaf, *Reducing the cost of robotic partial nephrectomy through innovative instrument use*. European Urology, 2015. **67**(3): p. 594-595.
2. Philip, S., P. Hurley, and VSK. Mittal, *Ureteric and Bladder Injuries with Laparoscopic and Robotic Surgery: A Community Teaching Hospital Experience*. Am Surg, 2016. **82**(4): p. E76-7.
3. Pradere, B., et al., *Open partial nephrectomy vs robot-assisted partial nephrectomy for cystic renal masses: Impact of peroperative cystic spillage and oncological results*. European Urology, Supplements, 2018. **17**(2): p. e938-e940.
4. Salkini, M. and A. Lamoshi, *Recurrence patterns of renal cell carcinoma after robotic partial nephrectomy*. Journal of Endourology, 2018. **32**: p. A223.

### Procedure (n=3)

1. Gershman, B., et al., *The Association of Robot-assisted Versus Pure Laparoscopic Radical Nephrectomy with Perioperative Outcomes and Hospital Costs*. European Urology Focus, 2018.
2. Soria, F., et al., *Comparative Effectiveness in Perioperative Outcomes of Robotic versus Open Radical Cystectomy: Results from a Multicenter Contemporary Retrospective Cohort Study*. European Urology Focus, 2018.
3. Tamhankar, A.S., et al., *Robot-assisted radical nephroureterectomy with extended template lymphadenectomy for upper tract urothelial carcinoma: An outcome analysis*. Indian J Urol, 2018. **34**(3): p. 212-218.

### Follow up <1 year or unclear (cystectomy) (n=22)

1. *Multidomain Quantitative Recovery Following Radical Cystectomy for Patients Within the Robot-assisted Radical Cystectomy with Intracorporeal Urinary Diversion Versus Open Radical Cystectomy Randomised Controlled Trial: the First 30 Patients*. European urology, 2018. **74**(4): p. 531-534.
2. *Real-World Impact of Minimally Invasive Versus Open Radical Cystectomy on Perioperative Outcomes and Spending*. Urology, 2018.
3. Borza, T., et al., *No Differences in Population-based Readmissions After Open and Robotic-assisted Radical Cystectomy: Implications for Post-discharge Care*. Urology, 2017. **104**: p. 77-83.
4. Flamiatos, J.F., et al., *Open versus robot-assisted radical cystectomy: 30-day*

- perioperative comparison and predictors for cost-to-patient, complication, and readmission.* J Robot Surg, 2018.
5. Ko, O.S., et al., *Rates and Predictors of Conversion to Open Surgery During Minimally Invasive Radical Cystectomy.* J Endourol, 2018. **32**(6): p. 488-494.
  6. Koie, T., et al., *The feasibility and effectiveness of robot-assisted radical cystectomy after neoadjuvant chemotherapy in patients with muscle-invasive bladder cancer.* Jpn J Clin Oncol, 2017. **47**(3): p. 252-256.
  7. Kukreja, J.B., et al., *A comparison of pathologic and intermediate term oncologic outcomes following open and robotic radical cystectomy.* Journal of Clinical Oncology, 2019. **37**.
  8. Leow, J.J., et al., *Propensity-matched comparison of morbidity and costs of open and robot-assisted radical cystectomies: a contemporary population-based analysis in the United States.* Eur Urol, 2014. **66**(3): p. 569-76.
  9. Li, A.Y., et al., *Patient-Reported Convalescence and Quality of Life Recovery: A Comparison of Open and Robotic-Assisted Radical Cystectomy.* Surg Innov, 2016. **23**(6): p. 598-605.
  10. Mally, D., et al., *Oncological outcome of robotic-assisted radical cystectomies compared to open radical cystectomies.* Oncology Research and Treatment, 2018. **41**: p. 205.
  11. Matulewicz, R.S., et al., *National comparison of oncologic quality indicators between open and robotic-assisted radical cystectomy.* Urol Oncol, 2016. **34**(10): p. 431.e9-431.e15.
  12. Modi, P.K., et al., *Real-World Impact of Minimally Invasive Versus Open Radical Cystectomy on Perioperative Outcomes and Spending.* Urology, 2019. **125**: p. 86-91.
  13. Monn, M.F., et al., *National trends in the utilization of robotic-assisted radical cystectomy: an analysis using the Nationwide Inpatient Sample.* Urol Oncol, 2014. **32**(6): p. 785-90.
  14. Moschini, M., et al., *Propensity-score-matched comparison of soft tissue surgical margins status between open and robotic-assisted radical cystectomy.* Urologic Oncology: Seminars and Original Investigations, 2019. **37**(3): p. 179.e1-179.e7.
  15. Nazzani, S., et al., *Comparison of Perioperative Outcomes Between Open and Robotic Radical Cystectomy: A Population-Based Analysis.* J Endourol, 2018. **32**(8): p. 701-709.
  16. Necchi, A., et al., *Robot-assisted Versus Open Radical Cystectomy in Patients Receiving Perioperative Chemotherapy for Muscle-invasive Bladder Cancer: The Oncologist's Perspective from a Multicentre Study.* Eur Urol Focus, 2017.
  17. Pak, J.S., et al., *Utilization Trends and Short-term Outcomes of Robotic Versus Open Radical Cystectomy for Bladder Cancer.* Urology, 2017. **103**: p. 117-123.
  18. Sharma, P., et al., *Surgical control and margin status after robotic and open cystectomy in high-risk cases: Caution or equivalence?* World J Urol, 2017. **35**(4): p. 657-663.
  19. Soria, F., et al., *Robotic radical cystectomy is associated with shorter length of stay and less blood loss than open radical cystectomy: Results from a large multicenter retrospective cohort.* Journal of Urology, 2018. **199**(4): p. e812-e813.
  20. Tan, W.S., et al., *Intracorporeal robot-assisted radical cystectomy, together with an enhanced recovery programme, improves postoperative outcomes by aggregating marginal gains.* BJU Int, 2018. **121**(4): p. 632-639.
  21. Taylor, B., et al., *Does robotic cystectomy achieve oncologic efficacy for locally advanced bladder cancer?* Journal of Urology, 2018. **199**(4): p. e533.
  22. Yu, H.Y., 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. Eur Urol, 2012. 61(6): p. 1239-44.*

Follow up <3 years or unclear (partial nephrectomy) (n=63)

1. Alameddine, M., et al., *Trends in Utilization of Robotic and Open Partial Nephrectomy for Management of cT1 Renal Masses. Eur Urol Focus, 2018.*
2. Anderson, J.E., et al., *Hospital costs and length of stay related to robot-assisted versus open radical and partial nephrectomy for kidney cancer in the USA. J Robot Surg, 2012. 6(1): p. 19-22.*
3. Anele, U., et al., *Robotic versus laparoscopic radical nephrectomy: A matched paired multicenter analysis (rosula group). Journal of Urology, 2018. 199(4): p. e787.*
4. Arora, S., et al., *What is the hospital volume threshold to optimize inpatient complication rate after partial nephrectomy? Urol Oncol, 2018. 36(7): p. 339.e17-339.e23.*
5. Autorino, R., et al., *Incidence and risk factors for 30-day readmission in patients undergoing nephrectomy procedures: a contemporary analysis of 5276 cases from the National Surgical Quality Improvement Program database. Urology, 2015. 85(4): p. 843-9.*
6. Ayangbesan, A., et al., *Surgical approach does not impact margin status following partial nephrectomy for large renal masses. J Endourol, 2018.*
7. Banapour, P., et al., *Nephrometry score matched robotic vs laparoscopic vs open partial nephrectomy. J Robot Surg, 2018.*
8. Bertolo, R., et al., *Robot-assisted partial nephrectomy for CT2 renal tumors: Perioperative, functional and oncological outcomes from a multicenter analysis (the rosula project). Journal of Urology, 2018. 199(4): p. e540.*
9. Bertolo, R., et al., *Pure laparoscopic versus robot-assisted partial nephrectomy for ct1b renal tumors: A single tertiary center experience. Journal of Urology, 2018. 199(4): p. e544.*
10. Bertolo, R.G., et al., *Perioperative, functional and oncological outcomes of robot-assisted partial nephrectomy for cT2 renal tumors: A multicenter analysis (The ROSULA project). European Urology, Supplements, 2018. 17(2): p. e1471-e1472.*
11. Blair, B.M., et al., *Predicted versus observed 30-day perioperative outcomes using the ACS NSQIP surgical risk calculator in patients undergoing partial nephrectomy for renal cell carcinoma. Int Urol Nephrol, 2018. 50(7): p. 1249-1256.*
12. Borghesi, M., et al., *Open, laparoscopic and robot-assisted partial nephrectomy: Comparison of perioperative outcomes and trifecta rate achievement in a large, single-institution series. European Urology, Supplements, 2018. 17(2): p. e1468-e1469.*
13. Camp, C., et al., *Short-term Outcomes and Costs Following Partial Nephrectomy in England: A Population-based Study. Eur Urol Focus, 2017.*
14. Carneiro, A., et al., *Evolution from laparoscopic to robotic nephron sparing surgery: a high-volume laparoscopic center experience on achieving 'trifecta' outcomes. World J Urol, 2015. 33(12): p. 2039-44.*
15. Dagenais, J., et al., *Frozen Sections for Margins During Partial Nephrectomy Do Not Influence Recurrence Rates. J Endourol, 2018. 32(8): p. 759-764.*
16. Ellison, J.S., et al., *A matched comparison of perioperative outcomes of a single laparoscopic surgeon versus a multisurgeon robot-assisted cohort for partial nephrectomy. J Urol, 2012. 188(1): p. 45-50.*
17. Ficarra, VS, et al., *Tumor Contact Surface Area as predictor of postoperative*

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18. Ficarra, VS, et al., *A multicentre matched-pair analysis comparing robot-assisted versus open partial nephrectomy.* BJU Int, 2014. **113**(6): p. 936-41.
  19. Gadelmoula, M., et al., *Robot-assisted versus open partial nephrectomy in obese patients.* Journal of Endourology, 2018. **32**: p. A447-A448.
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40. Long, J.A., et al., *Robotic versus laparoscopic partial nephrectomy for complex tumors: comparison of perioperative outcomes*. *Eur Urol*, 2012. **61**(6): p. 1257-62.
41. Luciani, L.G., et al., *Robotic-assisted partial nephrectomy provides better operative outcomes as compared to the laparoscopic and open approaches: results from a prospective cohort study*. *J Robot Surg*, 2017. **11**(3): p. 333-339.
42. Malkoc, E., et al., *Robot-assisted approach improves surgical outcomes in obese patients undergoing partial nephrectomy*. *BJU Int*, 2017. **119**(2): p. 283-288.
43. Mari, A., et al., *Predictive factors of overall and major postoperative complications after partial nephrectomy: Results from a multicenter prospective study (The RECORD 1 project)*. *Eur J Surg Oncol*, 2017. **43**(4): p. 823-830.
44. Masson-Lecomte, A., et al., *A prospective comparison of surgical and pathological outcomes obtained after robot-assisted or pure laparoscopic partial nephrectomy in moderate to complex renal tumours: results from a French multicentre collaborative study*. *BJU Int*, 2013. **111**(2): p. 256-63.
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#### Sample Size <80 (n=84)

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