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

August 2019

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

Prepared by:
Evidence Synthesis Program (ESP) Center
West Los Angeles VA Medical Center
Los Angeles, CA
Paul G. Shekelle, MD, PhD, Director

Authors:
Principal Investigators:
Paul G. Shekelle, MD, PhD
Melinda Maggard-Gibbons, MD

Co-Investigators:
Mark Girgis, MD
Christopher P. Childers, MD, PhD
Amber Tang, BS
Qiao Ruan, BS
Margherita Lamaina, MD

Research Associates:
Selene Mak, PhD, MPH
Meron Begashaw, MPH
Marika S. Booth, MS

U.S. Department of Veterans Affairs
Veterans Health Administration
Health Services Research & Development Service

# 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.

**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 or 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.

Mark Wilson, MD
National Director of Surgery (10NC2)
Department of Veterans Affairs

William Gunnar, MD
Former National Director of Surgery (10NC2)
Department of Veterans Affairs

### 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:

John Gore, MD
Associate Professor, Adjunct Associate Professor-Surgery
University of Washington

Jim C. Hu, MD
Professor of Urology, Weill Cornell Medicine
Director, LeFrak Center for Robotic Surgery

Mark Jordan, MD
Chief of Urology
Department of Veterans Affairs, Long Beach

John Leppert, MD
Associate Professor of Urology, Stanford University
Urologist at Palo Alto VA

Joe Liao, MD
Professor of Urology, Stanford University
VA Robotic Surgeon

Matthew Rettig, MD
Medical Director, Prostate Cancer Program of the Institute of Urologic Oncology, UCLA
Professor, Division of Hematology-Oncology and Department of Urology, UCLA

Kevin Win, MD
Staff Anesthesiology, Department of Veterans Affairs

## 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.

# TABLE OF CONTENTS

**TABLES**

**FIGURES**

# 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.[4] 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.[1,2] 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.[2] 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.[5] 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:

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?

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.[6] 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.[7] 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.[8] GRADE assessing the certainty of the evidence based of 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

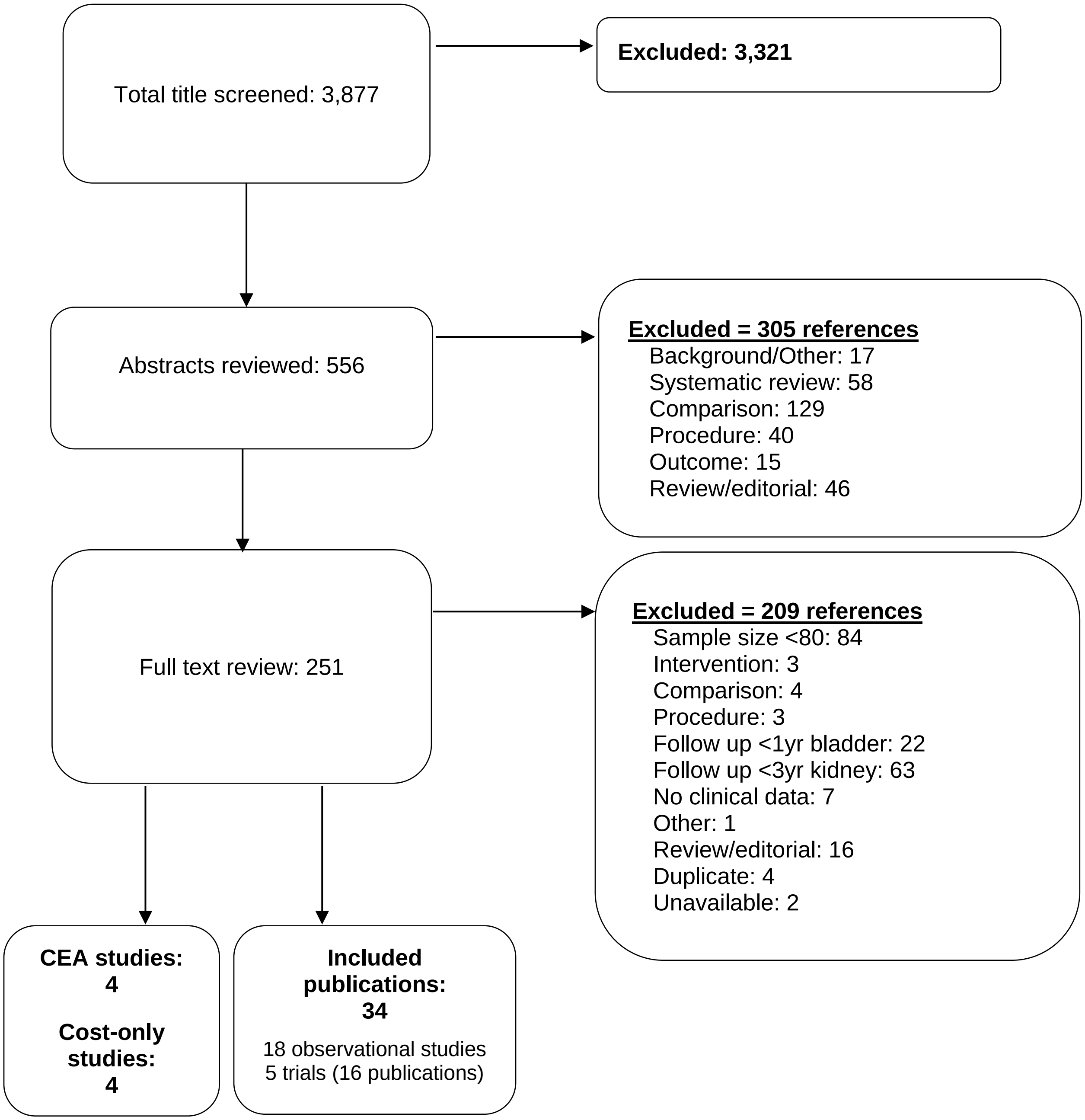
We identified 3,877 potentially relevant citations, of which 556 were included at the abstract screening. From these, a total of 305 abstracts were excluded. Excluded abstracts were categorized as background/other (n=17), systematic review (n=58), wrong comparison (n=129), wrong procedure (n=40), no 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**

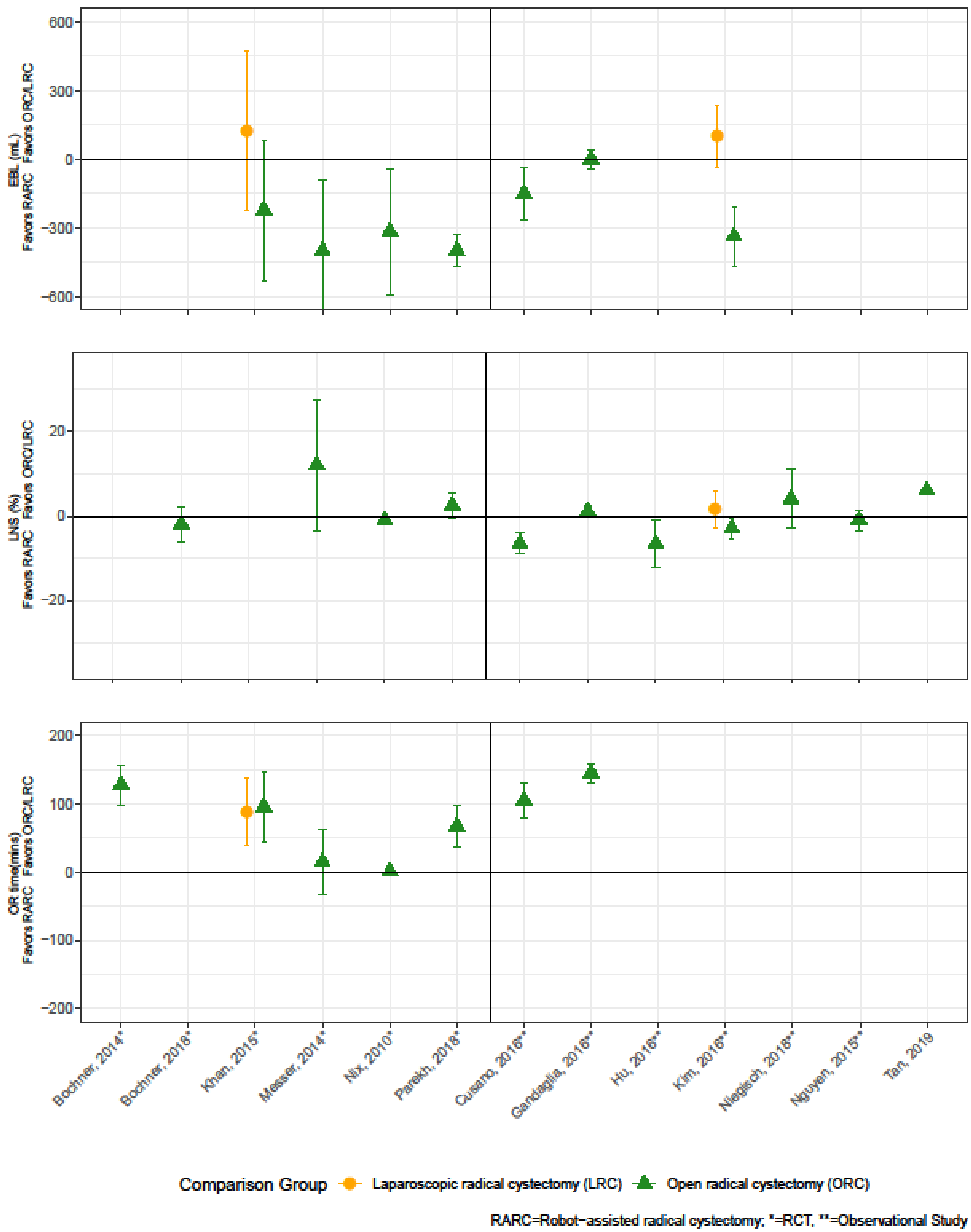


## KEY QUESTION 1A – CYSTECTOMY: What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for cystectomy?

We identified 16 publications that met the inclusion criteria.[9-24] Five studies were randomized trials[9-14]; of note, 2 publications were from the same study, but data were abstracted from both[9,10] and the remaining studies were observational. All studies compared robot-assisted cystectomy to open cystectomy, and 3 studies also compared it to laparoscopic surgery.[11,18,22] 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 that 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.

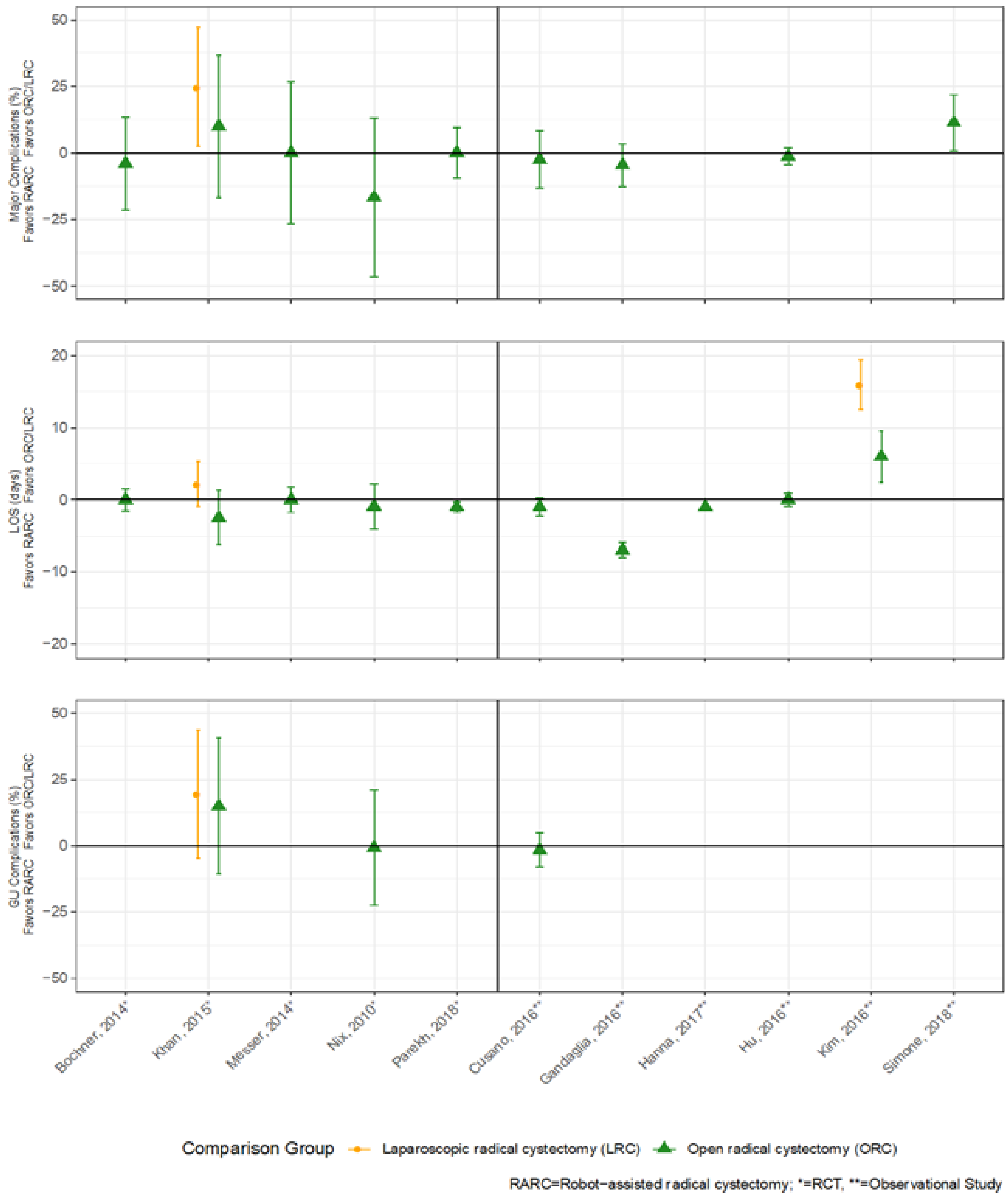
**Figure 2. Bladder Cancer: Intraoperative Outcomes**




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**

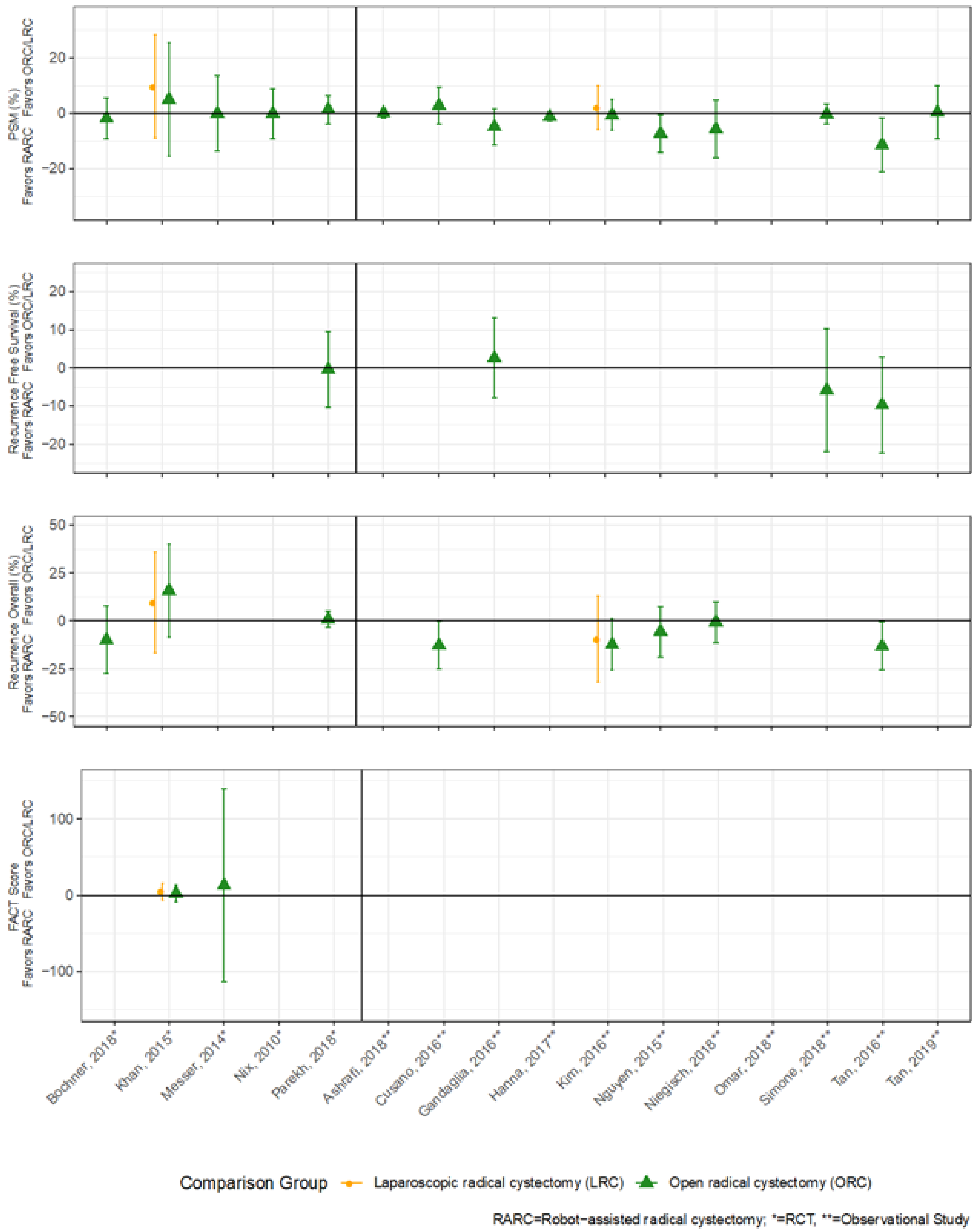



Graphed is the point estimate and 95% confidence intervals for the difference in the indicated outcome between robot-assisted cystectomy and either open (green triangles) or laparoscopic (gold circles) approaches. Randomized trial data are on the left-hand side, observational study data are on the right-hand 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[10]; 35% for Khan et al[11]). For Khan and colleagues,[11] 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,[12] oncologic outcomes were again reported at 12 months. For Bochner and colleagues,[10] the authors commented that “study was not powered to assess oncologic outcomes.” The study by Nix and colleagues[13] 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[14] 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<br>Robot < Open | RCT: Low<br>Observational studies: High | Consistent | Direct | Precise | High |
| Lymph Node Sampling<br>Robot = Open | RCT: Low<br>Observational studies: High | Inconsistent | Direct | Imprecise | Low |
| Operating Room Time<br>Robot > Open | RCT: Low<br>Observational studies: High | Consistent | Direct | Imprecise | Moderate |
| All comparisons to laparoscopic surgery | RCT: Low<br>Observational studies: High | N/A | Direct | Imprecise | Very Low |

| Outcome | Study Limitations | Consistency | Directness | Precision | Certainty of Evidence |
|---|---|---|---|---|---|
| Post-operative | | | | | |
| 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 |
| Functional/Cancer Outcomes | | | | | |
| 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.[25] 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.[3] 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).[26] 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.[27] 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,[3] 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.

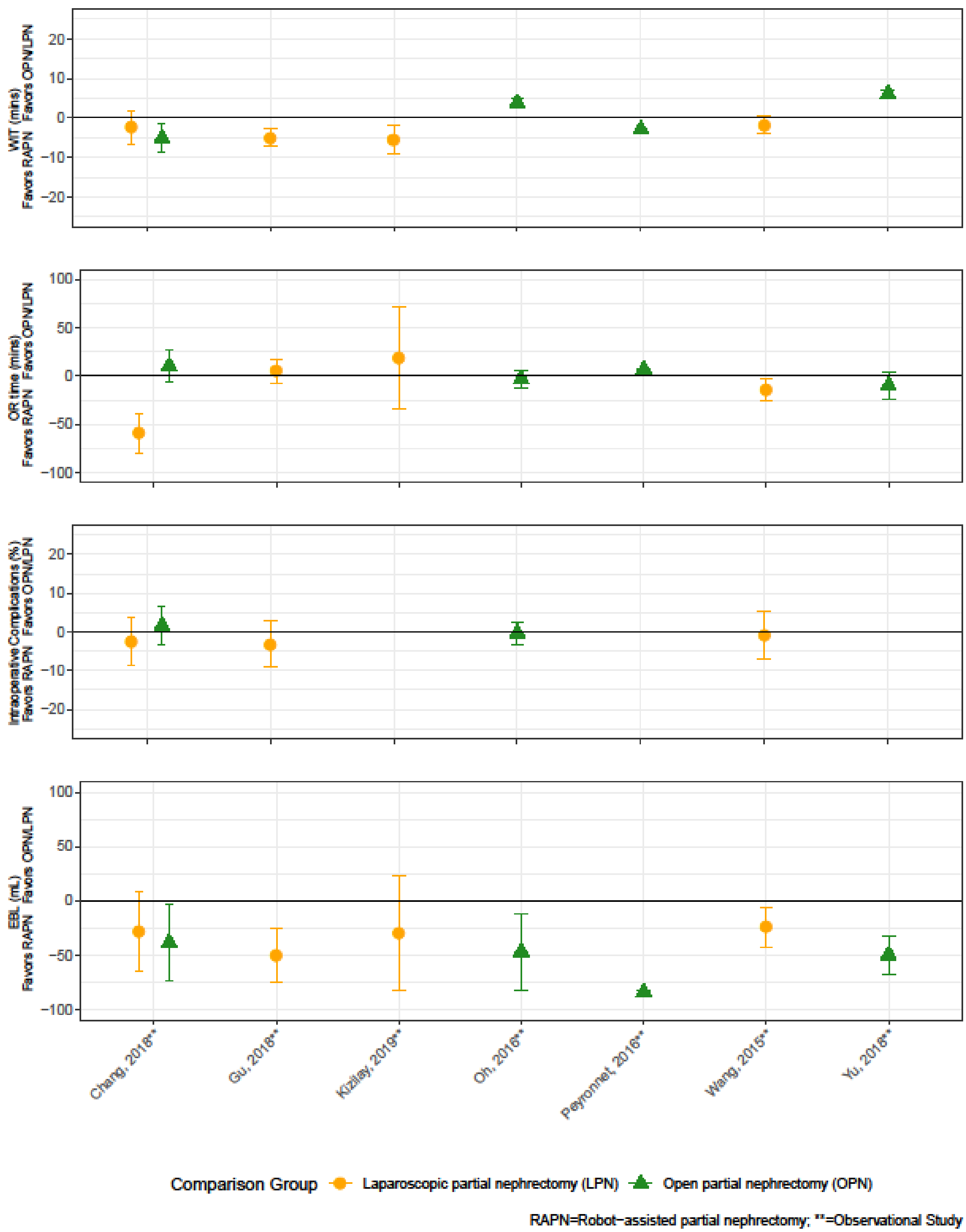
## KEY QUESTION 2A – PARTIAL NEPHRECTOMY: What is the clinical effectiveness of robotic-assisted surgery compared to open surgery or conventional laparoscopic surgery for partial nephrectomy?

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.[28-34] One study compared robot-assisted nephrectomy to open partial nephrectomy and to laparoscopic partial nephrectomy.[28] Three studies compared robot-assisted nephrectomy to open partial nephrectomy,[30,31,34] and 3 studies[29,32,33] 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).[28] 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.

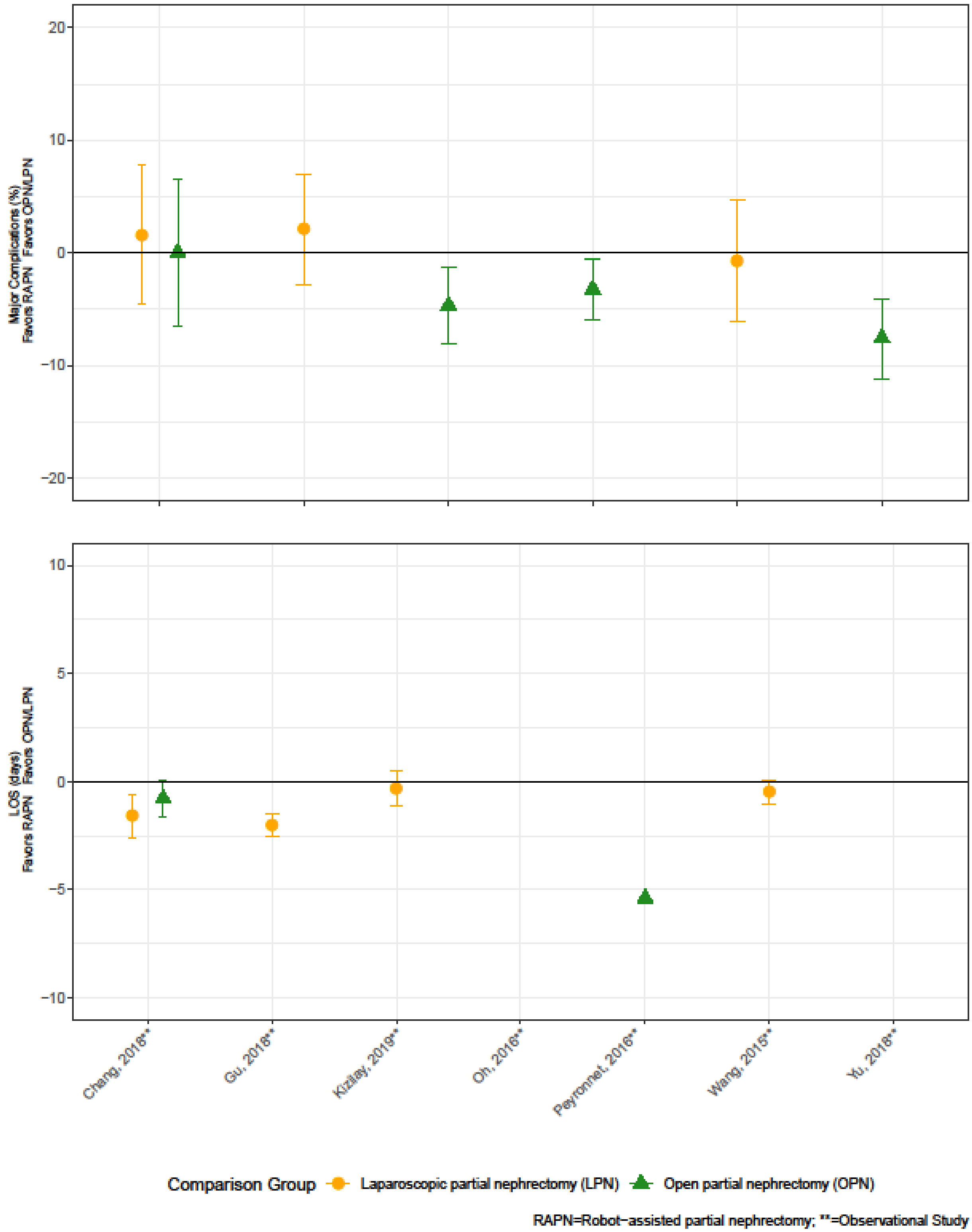
**Figure 5. Kidney Cancer: Intraoperative Outcomes**




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.

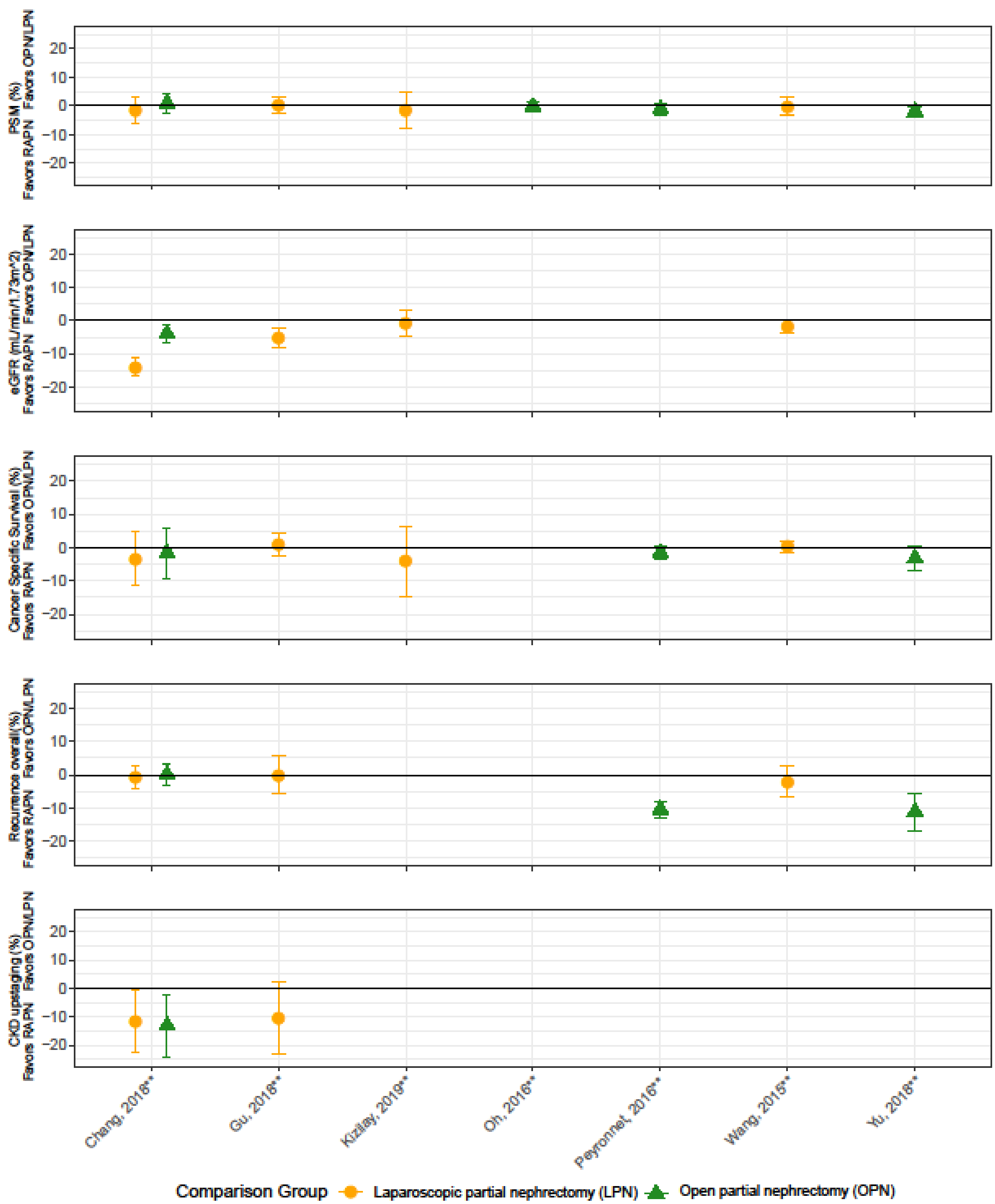
## Figure 6. Kidney Cancer: Postoperative Outcomes




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.[28] 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[28] 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[29] reported median follow-up of 20.1 months for the robotic group and 35 months for the laparoscopic group. Oh and colleagues[30] 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[31] 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,[32] 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 |
|---|---|---|---|---|---|
| Intraoperative outcomes | | | | | |
| Intraoperative complications<br>Robot = open/lap | High | Consistent | Direct | Imprecise | Low |
| Operating room time<br>Robot = open/lap | High | Inconsistent | Direct | Imprecise | Very low |
| Estimated blood loss<br>Robot < open/lap | High | Consistent | Direct | Imprecise | Moderate |
| Warm ischemia time<br>Robot = open/lap | High | Inconsistent | Direct | Imprecise | Very Low |
| Post-operative outcomes | | | | | |
| Major complications<br>Robot < open | High | Consistent | Direct | Imprecise | Low |
| Major complications<br>Robot = lap | High | Consistent | Direct | Imprecise | Low |
| Length of stay<br>Robot < open/lap | High | Consistent | Direct | Imprecise | Low |
| Functional/Cancer Outcomes | | | | | |
| 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.[35] 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).[4] 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.[36] 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).[6] 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,[37] while the other found that the immediate peri-operative costs of open partial nephrectomy was lower than robot partial nephrectomy.[38] 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.[5] 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 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


1. Hu JC, Gu X, Lipsitz SR, et al. Comparative effectiveness of minimally invasive vs open radical prostatectomy. *JAMA.* 2009;302(14):1557-1564.
2. Wright JD. Robotic-Assisted Surgery: Balancing Evidence and Implementation. *JAMA.* 2017;318(16):1545-1547.
3. Michels CTJ, Wijburg CJ, Leijte E, Witjes JA, Rovers MM, Grutters JPC. A cost-effectiveness modeling study of robot-assisted (RARC) versus open radical cystectomy (ORC) for bladder cancer to inform future research. *European urology focus.* 2018.
4. Childers CP, Maggard-Gibbons M. Estimation of the Acquisition and Operating Costs for Robotic Surgery. *JAMA.* 2018;320(8):835-836.
5. Ramirez PT, Frumovitz M, Pareja R, et al. Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer. *N Engl J Med.* 2018;379(20):1895-1904.
6. Higgins JP AD, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ.* 2011:343:d5928.
7. Sterne JA HM, Reeves BC, et al. . ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ.* 2016:355:i4919.
8. GRADE working group. 2014; http://www.gradeworkinggroup.org/. Accessed 04/26/2019.
9. Bochner BH, Sjoberg DD, Laudone VP. A randomized trial of robot-assisted laparoscopic radical cystectomy. *New England journal of medicine.* 2014;371(4):389-390.
10. Bochner BH, Dalbagni G, Marzouk KH, et al. Randomized Trial Comparing Open Radical Cystectomy and Robot-assisted Laparoscopic Radical Cystectomy: Oncologic Outcomes. *European urology.* 2018;74(4):465-471.
11. Khan MS, Gan C, Ahmed K, et al. A Single-centre Early Phase Randomised Controlled Three-arm Trial of Open, Robotic, and Laparoscopic Radical Cystectomy (CORAL). *European urology.* 2016;69(4):613-621.
12. Messer JC, Punnen S, Fitzgerald J, Svatek R, Parekh DJ. Health-related quality of life from a prospective randomised clinical trial of robot-assisted laparoscopic vs open radical cystectomy. *BJU international.* 2014;114(6):896-902.
13. Nix J, Smith A, Kurpad R, Nielsen ME, Wallen EM, Pruthi RS. Prospective randomized controlled trial of robotic versus open radical cystectomy for bladder cancer: perioperative and pathologic results. *European urology.* 2010;57(2):196-201.
14. Parekh DJ, Reis IM, Castle EP, et al. Robot-assisted radical cystectomy versus open radical cystectomy in patients with bladder cancer (RAZOR): an open-label, randomised, phase 3, non-inferiority trial. *Lancet (London, England).* 2018;391(10139):2525-2536.
15. Cusano A, Haddock P, Jr., Jackson M, Staff I, Wagner J, Meraney A. A comparison of preliminary oncologic outcome and postoperative complications between patients undergoing either open or robotic radical cystectomy. *International braz j urol : official journal of the Brazilian Society of Urology.* 2016;42(4):663-670.
16. Gandaglia G, Karl A, Novara G, et al. Perioperative and oncologic outcomes of robot-assisted vs. open radical cystectomy in bladder cancer patients: A comparison of two high-volume referral centers. *European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology.* 2016;42(11):1736-1743.

17. Hu JC, Chughtai B, O'Malley P, et al. Perioperative Outcomes, Health Care Costs, and Survival After Robotic-assisted Versus Open Radical Cystectomy: A National Comparative Effectiveness Study. *European urology.* 2016;70(1):195-202.
18. Kim TH, Sung HH, Jeon HG, et al. Oncological Outcomes in Patients Treated with Radical Cystectomy for Bladder Cancer: Comparison Between Open, Laparoscopic, and Robot-Assisted Approaches. *Journal of endourology.* 2016;30(7):783-791.
19. Nguyen DP, Al Hussein Al Awamlh B, Wu X, et al. Recurrence patterns after open and robot-assisted radical cystectomy for bladder cancer. *European urology.* 2015;68(3):399-405.
20. Hanna N, Leow JJ, Sun M, et al. Comparative effectiveness of robot-assisted vs. open radical cystectomy. *Urologic oncology.* 2018;36(3):88.e81-88.e89.
21. Simone G, Tuderti G, Misuraca L, et al. Perioperative and mid-term oncologic outcomes of robotic assisted radical cystectomy with totally intracorporeal neobladder: Results of a propensity score matched comparison with open cohort from a single-centre series. *European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology.* 2018;44(9):1432-1438.
22. Omar K, Nair R, Malde S, Thurairaja R, Dasgupta P, Khan M. Long term oncological outcomes following the randomised controlled cystectomy: open, robotic and laparoscopic (CORAL) trial. *European urology, supplements Conference: 33rd annual european association of urology congress, EAU 2018 Denmark.* 2018;17(2):e535.
23. Tan YG, Allen JCJ, Tay KJ, Lee LS. Intermediate oncological outcomes in a contemporary series of robotic and open cystectomies-a propensity score adjusted analysis. *BJU International.* 2019;123:41-42.
24. Ashrafi A, Hueber PA, Rajarubendra N, et al. Patterns of bladder cancer recurrence after open and robotic radical cystectomy. *Canadian Urological Association Journal.* 2018;12(6):S60.
25. Kukreja JB, Metcalfe MJ, Qiao W, Kamat AM, Dinney CPN, Navai N. Cost-Effectiveness of Robot-assisted Radical Cystectomy Using a Propensity-matched Cohort. *European urology focus.* 2018.
26. Martin AD, Nunez RN, Castle EP. Robot-assisted radical cystectomy versus open radical cystectomy: a complete cost analysis. *Urology.* 2011;77(3):621-625.
27. Bansal SS, Dogra T, Smith PW, et al. Cost analysis of open radical cystectomy versus robot-assisted radical cystectomy. *BJU international.* 2018;121(3):437-444.
28. Chang KD, Abdel Raheem A, Kim KH, et al. Functional and oncological outcomes of open, laparoscopic and robot-assisted partial nephrectomy: a multicentre comparative matched-pair analyses with a median of 5 years' follow-up. *BJU international.* 2018;122(4):618-626.
29. Gu L, Ma X, Wang B, et al. Laparoscopic vs robot-assisted partial nephrectomy for renal tumours of >4 cm: a propensity score-based analysis. *BJU international.* 2018;122(3):449-455.
30. Oh JJ, Lee JK, Kim K, Byun SS, Lee SE, Hong SK. Comparison of the Width of Peritumoral Surgical Margin in Open and Robotic Partial Nephrectomy: A Propensity Score Matched Analysis. *PLoS One.* 2016;11(6):e0158027.
31. Peyronnet B, Seisen T, Oger E, et al. Comparison of 1800 Robotic and Open Partial Nephrectomies for Renal Tumors. *Annals of surgical oncology.* 2016;23(13):4277-4283.

32. Wang Y, Shao J, Ma X, Du Q, Gong H, Zhang X. Robotic and open partial nephrectomy for complex renal tumors: a matched-pair comparison with a long-term follow-up. *World journal of urology*. 2017;35(1):73-80.
33. Kızılay F, Turna B, Apaydın E, Semerci B. Comparison of long-term outcomes of laparoscopic and robot-assisted laparoscopic partial nephrectomy. *The Kaohsiung journal of medical sciences.* 2019;35(4):238-243.
34. Yu YD, Nguyen NH, Ryu HY, Hong SK, Byun SS, Lee S. Predictors of renal function after open and robot-assisted partial nephrectomy: A propensity score-matched study. *International Journal of Urology*. 2019;26(3):377-384.
35. Mir SA, Cadeddu JA, Sleeper JP, Lotan Y. Cost comparison of robotic, laparoscopic, and open partial nephrectomy. *Journal of endourology.* 2011;25(3):447-453.
36. Buse S, Hach CE, Klumpen P, et al. Cost-effectiveness analysis of robot-assisted vs. open partial nephrectomy. *The international journal of medical robotics + computer assisted surgery : MRCAS.* 2018;14(4):e1920.
37. Kates M, Ball MW, Patel HD, Gorin MA, Pierorazio PM, Allaf ME. The financial impact of robotic technology for partial and radical nephrectomy. *Journal of endourology.* 2015;29(3):317-322.
38. Mano R, Schulman A, Hakimi AA, et al. Cost comparison of open and robotic partial nephrectomy using a short postoperative pathway. *Urology.* 2015;85(3):596-603.
39. Niegisch G, Nini A, Michalski R, et al. Comparison of 2-Year Oncological Outcome and Early Recurrence Patterns in Patients with Urothelial Bladder Carcinoma Treated with Open or Robot-Assisted Radical Cystectomy with an Extracorporeal Urinary Diversion. *Urologia internationalis.* 2018;101(2):224-231.
40. Tan WS, Sridhar A, Ellis G, et al. Analysis of open and intracorporeal robotic assisted radical cystectomy shows no significant difference in recurrence patterns and oncological outcomes. *Urologic oncology.* 2016;34(6):257.e251-259.
41. Parekh DJ, Messer J, Fitzgerald J, Ercole B, Svatek R. Perioperative outcomes and oncologic efficacy from a pilot prospective randomized clinical trial of open versus robotic assisted radical cystectomy. *The Journal of urology.* 2013;189(2):474-479.
42. Smith A, Nix JW, Nielsen ME, Wallen E, Pruthi R. Prospective randomized controlled trial of robotic versus open radical cystectomy for bladder cancer: median 3-year follow-up. *Journal of clinical oncology.* 2012;30(5 SUPPL. 1).