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Systematic literature review of cost-effectiveness analyses of robotic-assisted radical prostatectomy for localised prostate cancer

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ABSTRACT

Objectives Review and assess cost-effectiveness studies of robotic-assisted radical prostatectomy (RARP) for localised prostate cancer compared with open radical prostatectomy (ORP) and laparoscopic radical prostatectomy (LRP).

Design Systematic review.

Setting PubMed, Embase, Scopus, International HTA database, the Centre for Reviews and Dissemination database and various HTA websites were searched (January 2005 to March 2021) to identify the eligible cost-effectiveness studies.

Participants Cost-effectiveness, cost-utility, or cost-minimization analyses examining RARP versus ORP or LRP were included in this systematic review.

Interventions Different surgical approaches to treat localized prostate cancer: RARP compared with ORP and LRP.

Primary and secondary outcome measures A structured narrative synthesis was developed to summarize results of cost, effectiveness, and cost-effectiveness results (eg, incremental cost-effectiveness ratio [ICER]). Study quality was assessed using the Consensus on Health Economic Criteria Extended checklist. Application of medical device features were evaluated.

Results Twelve studies met inclusion criteria, 11 of which were cost–utility analyses. Higher quality-adjusted life-years and higher costs were observed with RARP compared with ORP or LRP in 11 studies (91%). Among four studies comparing RARP with LRP, three reported RARP was dominant or cost-effective. Among ten studies comparing RARP with ORP, RARP was more cost-effective in five, not cost-effective in two, and inconclusive in three studies. Studies with longer time horizons tended to report favorable cost-effectiveness results for RARP. Nine studies (75%) were rated of moderate or good quality. Recommended medical device features were addressed to varying degrees within the literature as follows: capital investment included in most studies, dynamic pricing considered in about half, and learning curve and incremental innovation were poorly addressed.

Conclusions Despite study heterogeneity, RARP was more costly and effective compared with ORP and LRP in most studies and likely to be more cost-effective, particularly over a multiple year or lifetime time horizon. Further cost-effectiveness analyses for RARP that more

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This review provided a comprehensive, systematic and transparent literature search strategy covering multiple databases as well as the grey literature for health technology assessment (HTA) reports. However, private or confidential HTAs containing cost-effectiveness analysis might still be missing.

⇒ The review conducted bias assessment using the Consensus on Health Economic Criteria Extended checklist, suitable for economic evaluation studies.

⇒ Four additional criteria unique to medical devices (organisational impact, learning curve, incremental innovation and dynamic pricing) were assessed for each included study.

⇒ Internal validity of the systematic review synthesis depends on the quality of the limited number of primary studies included.

thoroughly consider medical device features and use an appropriate time horizon are needed.

PROSPERO registration number CRD42021246811.

INTRODUCTION

Prostate cancer is the second most frequent malignancy (after lung cancer) in men worldwide.[1] For men diagnosed with clinically localised prostate cancer, radical prostatectomy is one of the primary treatment options. Radical prostatectomy can be performed with open radical prostatectomy (ORP) or minimally invasive techniques, including laparoscopic radical prostatectomy (LRP) and robotic-assisted radical prostatectomy (RARP). Despite being a less invasive approach, application of LRP is low,[2–4] possibly due to its technical difficulty in performing complex procedures (eg, bilateral nerve-sparing dissection and construction of watertight urethrovesical anastomosis), steep learning curve, and limitations in dexterity and ergonomics.[5–9] Robotic-assisted surgery (RAS) using the da Vinci surgical system (Intuitive Surgical Operations, Sunnyvale, California, USA) overcomes

the technical challenges encountered by LRP by allowing for additional wrist movements and three-dimensional visualisation of the operative field.[10] Surgeons perform RARP using a surgical system that translates the surgeon's hand movement from the console in real time. This is achieved through the instrument's 7 degrees of motion, with precision and tremor filtration. Globally, use of RARP has been increasing, and has become a common surgical approach in many countries.[4 11]

The clinical effectiveness of RARP has been well documented in literature. Compared with ORP, RARP has been shown to reduce postoperative complications (eg, blood loss and transfusion rate), reduce hospital length of stay and enable faster recovery.[12 13] Compared with conventional LRP, RARP offers technical advantages (eg, the fully wristed dexterity, highly magnified three-dimensional high-resolution video) to overcome challenges from the complexity of radical prostatectomy and enables more patients to benefit from minimally invasive techniques.[14 15]

Despite the increased worldwide adoption of RARP, its economic value compared with ORP and LRP remains controversial, drawing attention from policy makers, payers and health technology assessment (HTA) agencies. Multiple cost-effectiveness analyses[16–19] have been performed in different healthcare settings using different methodologies over the past decade and have come to diverse conclusions. A systematic assessment of previously conducted cost-effectiveness analyses is critical for researchers and decision-makers to understand the value of RARP and to reach consensus on the appropriate methodology to quantify its cost-effectiveness.

Moreover, medical devices, such as those used to perform robotic surgery, are characterised by distinctive features that are less frequently found in pharmaceuticals[20]; therefore, methods of conducting economic evaluations for medical devices need to consider additional attributes beyond those traditionally used in assessing drugs, such as the technology's organisational impact, learning curve, incremental innovation and dynamic pricing.[21 22] RAS is a good example to illustrate the need to evaluate medical device-specific features. First, substantial infrastructural investment in a robotic surgical systems triggers 'organisational impact'. Second, a surgeon's experience and proficiency with RAS impacts clinical outcomes and efficiency; in other words, a 'learning curve'. Third, postlaunch innovation in robotic systems and instruments routinely occur over time and may be associated with changes in clinical outcomes, efficiency and cost. For example, since the first da Vinci surgery conducted in 2000, a total of four generations of da Vinci surgical systems have been launched with numerous instrument-level upgrades. Finally, the prices of medical devices typically decrease over time due to innovation, production scale, and market competition. This 'dynamic pricing' increases the level of uncertainty when assessing RAS. To our knowledge, no study in the existing cost-effectiveness literature for RARP has investigated these medical device features.

The aim of this systematic literature review is to assess the existing cost-effectiveness studies of RARP for localised prostate cancer, evaluate how medical device features have been considered in those studies, and provide insight for future cost-effectiveness studies in the field of robotic surgery.

METHODS

The protocol for this systematic review was developed in advance and registered with PROSPERO (registration number CRD42021246811) in May 2021.

Search strategy and study selection

Multiple databases were searched to retrieve studies published from 1 January 2005 (before the earliest cost-effectiveness literature on RARP) to 1 March 2021 (search date). Specifically, the databases included PubMed, Embase, Scopus, International HTA database and the Centre for Reviews and Dissemination database, which includes the NHS Economic Evaluation database, Database of Abstracts and Reviews of Effects, and the Health Technology Assessment (HTA) database. The detailed search strategy is outlined in online supplemental appendix A.

In addition to these five databases, we also performed a targeted grey literature search of various HTA websites (eg, UK National Institute for Health and Care Excellence, US Agency for Healthcare Research and Quality Evidence-Based Reports, US Institute for Clinical and Economic Review, Canadian Agency for Drugs and Technologies in Health and Tufts Cost-Effectiveness Analysis Registry) and Google. Keywords used included robotic surgery, robot assist, da Vinci, prostatectomy and prostate cancer.

Studies were included in this review if they were cost-effectiveness analyses, cost–utility analyses (CUA) or cost–minimisation analyses, and contained da Vinci-assisted radical prostatectomy as an intervention of interest. Studies were excluded if they were not in English, did not include prostatectomy or RAS, only had cost data without cost-effectiveness outcomes, were based on duplicate patient populations, or reviews that only included primary studies already captured in our review. The inclusion and exclusion criteria specifications are detailed in online supplemental appendix B.

Two reviewers independently screened the literature and any inconsistencies in the identification of potentially relevant studies were discussed to reach a consensus. The results are reported according to Preferred Reporting Items of Systematic Reviews and Meta-Analyses guidelines.[23]

Data extraction

Data were extracted from included studies based on the study protocol. Extracted data elements included: study year, country, economic analysis type, comparator, perspective, time horizon, effectiveness measure

and outcome value, cost measure and outcome value, incremental costs and incremental effectiveness, cost-effectiveness value (eg, incremental cost-effectiveness ratio [ICER] if applicable), discount rate, sensitivity analysis parameters and authors' conclusion.

Data synthesis
The approach used for data synthesis followed steps consistent with the International Society for Pharmacoeconomics and Outcomes Research Good Practices for cost and cost-effectiveness systematic review.[24] A meta-analysis of the findings was planned if feasible and appropriate for the available data. However, if the published literature contained substantial variability in clinical outcomes, healthcare setting, methodology, effects, costs and willingness-to-pay thresholds, a structured narrative synthesis approach would be used.

Study characteristics, such as type of analysis, patient population, perspective and methodological choices, were summarised. We reported incremental costs, incremental effectiveness and ICERs. Cost-effectiveness results across studies were displayed using scatterplots by plotting incremental quality-adjusted life-years (QALYs) and incremental costs on the x-axis and y-axis, respectively. All cost data were converted and reported in 2021 US dollars using purchasing power parities along with the original cost data.

Medical device features
The application of four distinctive features recommended for economic evaluations of medical devices was evaluated in the included studies, and each one was categorised using three levels: 'adjustment made to model', 'acknowledged but no model adjustment' or 'not considered'. The study would be classified as 'adjustment made to model' if adjustments were made to the base case or sensitivity analyses. If a study only mentioned the features in its writing but no adjustment was made in modelling, it would be considered as 'acknowledged but no model adjustment'.

Critical appraisal of risk of bias
Risk of bias of economic evaluations was assessed using the Consensus on Health Economic Criteria (CHEC)-Extended checklist. The CHEC-extended checklist contains guidelines for each criterion and scoring, and can be used to evaluate model-based and trial-based economic evaluations.[25 26] A score of one point was assigned to each positive response, and zero to a negative response or for non-applicable items. The total score out of 20 items was converted to a score ranging from zero (low quality) to 100 (high quality). Included studies were categorised into four grades: low, moderate, good and excellent quality according to thresholds for the total score of ≤50, 51–75, 76–95 and >95, respectively.

Patient and public involvement
The systematic review did not involve animal or human subjects and did not use patient data. Patients and the
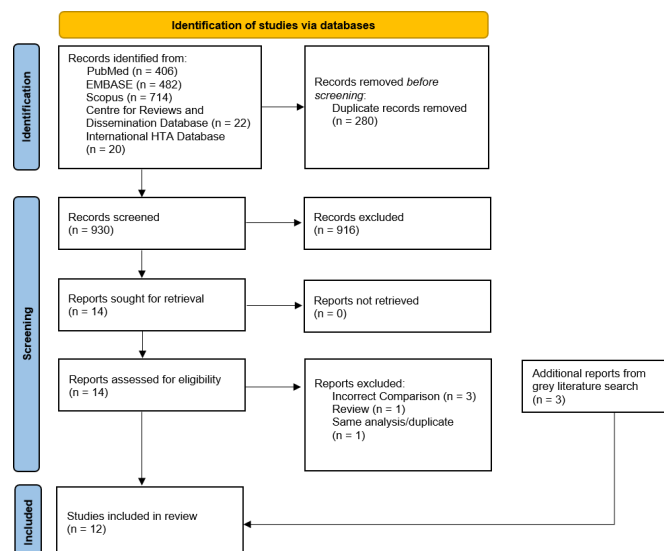

Figure 1 The PRISMA flow diagram of the literature search and selection process. PRISMA, Preferred Reporting Items of Systematic Reviews and Meta-Analyses.

public were not involved in the design and conduct of this systematic review since published studies were used to synthesise findings.

RESULTS
We identified 930 articles from the initial literature search. On reviewing, nine full-text studies from the database search and three articles from the targeted grey literature search met the inclusion criteria and were included in the final analysis (figure 1). Five studies were derived from HTA reports. Studies that were excluded tended to be costing-only studies[27 28] or had mixed RARP with other surgical modalities in an intervention group.[29 30]

Characteristics of included studies
Of the 12 studies[16–19 31–38] included in this review, 11 are CUAs. The characteristics of all studies are presented in table 1 . High variability across clinical and healthcare settings was observed. Among those studies, three[18 33 37] were conducted in Canada, two[35 36] in Australia, one[17] in USA, one[16] in UK, two[32 38] in Ireland and three[19 31 34] in other countries. Ten studies[17–19 32–38] compared RARP with ORP, 4 studies[16 17 31 32] compared RARP with LRP and 1 study[38] compared RARP versus routine care of mixed ORP and LRP. Cooperberg et al[17] and an HTA report by Alberta Health in Canada[33] additionally included other non-surgical treatments as comparators.

Most (8 out of 12) of the studies[16–19 32 33 36 37] were conducted from the payer's perspective, with 2 studies[19 35] taking a societal perspective, 1 study[31] from a healthcare system perspective and 1 study[34] from a hospital perspective. Regarding the time horizon, lifetime horizon was considered in two studies,[17 32] 5–10 years was used in seven studies,[16 31 33–35 37 38] short-term time horizon of 1 year was used in two studies[18 19] and one study[36] did not report the time horizon. Three studies[19 34 36] are observational-based

Table 1 Characteristics of included studies

Study	Country	Type of literature	Population	Intervention	Comparator	Perspective	Time horizon	Type of analysis	Methods
MSAC 2006[35]	AUS	HTA report	localised PC	RARP	ORP	Societal	10 years	CUA	Decision Tree
O'Malley 2007[36]	AUS	Journal article	PC	RARP	ORP	Payer*	*	CUA	Cohort based
Hohwü 2011[19]	DEN	Journal article	localised PC	RARP	ORP	Societal	1 year	CEA	Cohort based
HIQA 2011[38]	IRE	HTA report	PC T2-T3	RARP	Mix of ORP and LRP	Payer	5 years	CUA	Markov Model
Close 2013[16]/Ramsay 2012[40]	UK	Journal /HTA report	localised PC	RARP	LRP	Payer	10 years	CUA	Discrete event simulation
Cooperberg 2013[17]	USA	Journal article	localised PC	RARP	ORP, LRP+other†	Payer	Lifetime	CUA	Markov Model
Teljeur 2014[32]	IRE	Journal article	RP	RARP	ORP, LRP	Payer	Lifetime*	CUA	*
Ratchanon 2015[31]	THA	Journal article	localised PC	RARP	LRP	Health system	10 years	CUA	Decision Tree
AHT 2017[33]	CAN	HTA report	localised PC	RARP	ORP+others‡	Payer	9 years	CUA	Markov Model
HQO 2017[18]	CAN	HTA report	localised PC	RARP	ORP	Payer	1 year	CUA	Markov Model
Parackal 2020[37]	CAN	Journal article	localised PC	RARP	ORP	Payer	10 years	CUA	Markov Model
de Oliveira 2021[34]	BRA	Journal article	localised PC	RARP	ORP	Hospital	5 years	CUA	Cohort based

*Not clearly stated

†IMRT, BT, 3DCRT, EBRT+BT.

‡Beam radiotherapy, brachytherapy and cryoablation.

AUS, Australia; BRA, Brazil; BT, brachytherapy; CAN, Canada; CEA, cost-effectiveness analysis; CUA, cost–utility analysis; 3DCRT, three-dimensional conformal radiation therapy; DEN, Denmark; EBRT, external beam radiation therapy; IMRT, Intensity-modulated radiation therapy; IRE, Ireland; LRP, local radical prostatectomy; ORP, open radical prostatectomy; PC, prostate cancer; RARP, robotic-assisted radical prostatectomy; RP, radical prostatectomy; THA, Thailand.
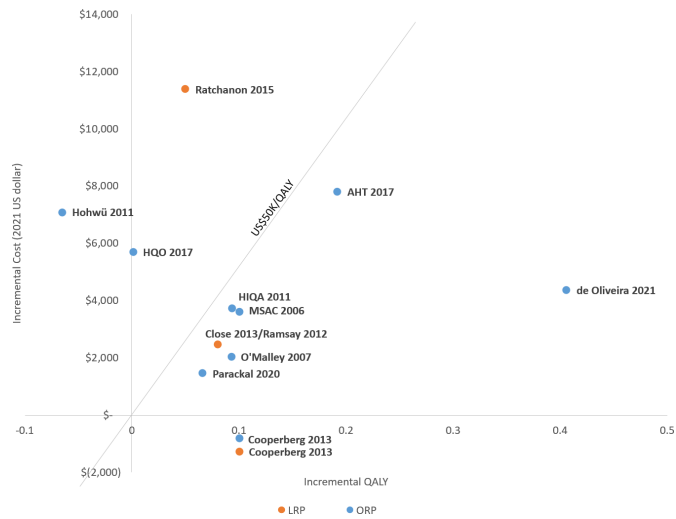
Figure 2 Incremental cost-effectiveness plane of the published study results. LRP, laparoscopic radical prostatectomy; ORP, open radical prostatectomy; QALY, quality-adjusted life-year.

modelling studies, and the rest are simulation-based analyses. Among the nine simulation-based studies, eight studies clearly reported the model methods. Among these eight studies, Markov modelling was used in five studies,[17 18 33 37 38] simple decision tree in two studies[31 35] and discrete event simulation in one study.[16]

Narrative synthesis of study results

Based on the included studies, RARP was generally associated with higher effectiveness and higher cost. All studies showed RARP had higher QALYs than ORP or LRP across various time horizons, with one exception; Hohwü *et al*[19] reported RARP had lower QALYs than ORP with a 1-year time horizon. The range of incremental QALYs gained for RARP varied from 0.05 to 0.1 when compared with LRP, and 0.001 to 0.41 when compared with ORP. In 11 of the 12 studies, RARP had higher costs relative to the comparators. The one exception was an analysis from the US payer perspective by Cooperberg *et al*,[17] which demonstrated lower cost for RARP compared with ORP and LRP; however, capital cost was not considered in the analysis. Results from the CUAs, in the form of incremental costs (standardised to 2021 USD) and incremental QALYs, were plotted and presented in figure 2. The corresponding summary is presented in table 2.

Most study results comparing RARP with ORP demonstrate RARP being cost-effective, although there is considerable heterogeneity across studies. As such, it is not appropriate to pool the cost-effectiveness results together. Five studies[17 33 34 36 37] showed RARP to be more cost-effective than ORP, while two other studies[18 19] showed RARP having higher ICERs that exceeded the willingness to pay (WTP) threshold value. Three studies[32 35 38] were inconclusive on the cost-effectiveness of RARP due to insufficient comparative effectiveness data or an unspecified WTP threshold. Interestingly, the study time horizon was observed to correlate with study conclusions

(figure 3). The only two studies[18 19] that showed RARP was not cost-effective compared with ORP used a short-term time horizon (1 year), while the other five studies[17 33 34 36 37] evaluated cost-effectiveness over 5, 9 and 10 years, or lifetime, all showed RARP to be more cost-effective than ORP.

Cost-effectiveness results for RARP compared with LRP were inconclusive given the limited number of publications (four studies),[16 17 31 32] but showed a tendency towards RARP being more cost-effective. One study[17] showed RARP as the dominant surgical option (lower cost and more effective). Two studies,[16 32] one from the UK and one from Ireland, demonstrated RARP to be cost-effective, while another study[31] conducted in Thailand found the ICER of RARP to be much higher than the stated WTP threshold.

Systematic review on inclusion of medical device features

Distinctive medical device features were considered to various extents in the included studies. Capital investment, which is one aspect of organisation impact, was widely considered. Ten[16 18 19 31–33 35–38] of 12 studies (83%) included capital investment, and one study[17] (8.5%) justified why it was not included in the analysis. Capital equipment cost and procedure volume per system were considered as sensitive parameters in seven studies (58%).[16 18 19 31 35 37 38] Dynamic pricing was reflected in five studies[16 18 35 37 38] (42%) by evaluating the uncertainty of equipment or instrument prices in the sensitivity analyses. Although none of studies quantitatively evaluated the impact of surgeon experience on outcomes and efficiency, 7 of 12 studies[16 18 33–35 37 38] (58%) mentioned 'learning curve'. In terms of incremental innovation, two studies[18 38] (17%) mentioned new generations of the surgical system and one study[16] (8.5%) included different costs for the new generation system within the analysis.

Systematic review on risk of bias

Study quality for the 12 studies was evaluated using the CHEC-Extended checklist, and results are presented in online supplemental appendix C. Among the 12 studies, 1 study[33] was classified as 'excellent', 8 studies[16–19 31 34 37 38] as 'good', 1 study[35] as 'moderate' and 2 studies[32 36] as 'low' quality. The primary reason studies were classified as low or moderate quality is that they failed to appropriately measure, value or report cost and/or effectiveness. Among the 20 items on the checklist, the majority of the studies[16–19 31 32 34–37] (10 out of 12) did not consider ethical and distributional issues, and 7 studies[16–18 34 36–38] (58%) used utility data collected from different study populations.

DISCUSSION

Our systematic literature review identified 12 studies that evaluated the cost-effectiveness of RARP for localised prostate cancer patients. Three-quarters of studies were of excellent or good quality based on the CHEC-Extended

Table 2 The summary of cost-effectiveness literature

	Study	Incremental cost (in local unit)	Incremental cost (in 2021 USD)	Incremental QALY	ICER (Original)	ICER (in 2021 USD)	Willingness to pay	Conclusion
RARP vs LRP	Ratchanon 2015[31]	120359 baht	US$11385	0.05	2407180 baht/QALY	US$227K/QALY	160K baht per QALY	RARP is not cost-effective
	Close 2013/Ramsay 2012[16 40]	GBP£1412	US$2464	0.08	GBP£18329/QALY	US$31K/QALY	£30K per QALY	RARP is cost-effective if volume >150
	Cooperberg 2013[17]	Low risk: US$-591 Intermediate risk: US$-1024 High risk: US$-104	Low risk: US$-732 Intermediate risk: US$-1268 High risk: US$-129	Low risk: 0 Intermediate risk: 0.1 High risk: 0	ICER not calculated	ICER not calculated	N/A	No difference in effectiveness And RARP lower cost
	Teljeur 2014[32]	No reported	No reported	No reported	€26643/QALY	Not reported	Not reported	Not reported
RARP vs ORP	MSAC 2006[35]	A$3742 for ED; A$4502 for UI	US$3613 for ED; US$4348 for UI	0.10 for ED; 0.01 for UI	A$37K/QALY for ED, A$450K/QALY for UI	US$36K/QALY for ED; US$435K/QALY for UI	Not reported	Lack of data
	O'Malley 2007[36]	A$2264	A$2049	0.09	A$24457/QALY	US$40K/QALY	Not reported	RARP cost-effective
	Hohwü 2011[19]	€4506	US$7093	−0.07	€64343/extra successful treatment	US$101K/extra successful treatment	N.A (main analysis CEA)	RARP not cost-effective
	HIQA 2011[38]	€2487	US$3730	0.09	€26647/QALY	US$30K/QALY	No specified threshold	No specified threshold in Ireland
	Cooperberg 2013[17]	Low risk: $−344 Intermediate risk: $−572 High risk: $−1265	Low risk: US$−425.87 Intermediate risk: US$−708 High risk: US$−1566	Low risk: 0 Intermediate risk: 0.1 High risk: 0	ICER not calculated	ICER not calculated	N/A	No difference in effectiveness, RARP has lower cost
	Teljeur 2014[32]	No reported	No reported	No reported	€26920/QALY	US$40K/QALY	Not reported	Not reported
	AHT 2017[33]	C$8541	US$7813	0.19	C$44471/QALY	US$41K/QALY	C$50K per QALY	RARP cost-effective
	HQO 2017[18]	C$6234	US$5702	0.001	C$5.2M/QALY	US$5M/QALY	C$100K per QALY	RARP not cost-effective
	Parackal 2020[37]	C$1701	US$1457	0.07	C$25704/QALY	US$22K/QALY	C$50K or 100K per QALY	RARP cost-effective
	de Oliveira 2021[34]	BRA R$9214	US$4368	0.41	R$22690.83/QALY	US$11K/QALY	R$114026.55 (3 times of GDP)	RARP cost-effective

A$, Australian Dollar; BRA, Brazil; C$, Canadian Dollar; CEA, cost-effectiveness analysis; ED, erectile dysfunction; GBP, British pound sterling; GDP, gross domestic product; ICER, incremental cost-effectiveness ratio; LRP, local radical prostatectomy; ORP, open radical prostatectomy; QALY, quality-adjusted life year; RARP, robotic-assisted radical prostatectomy; UI, urinary infection.
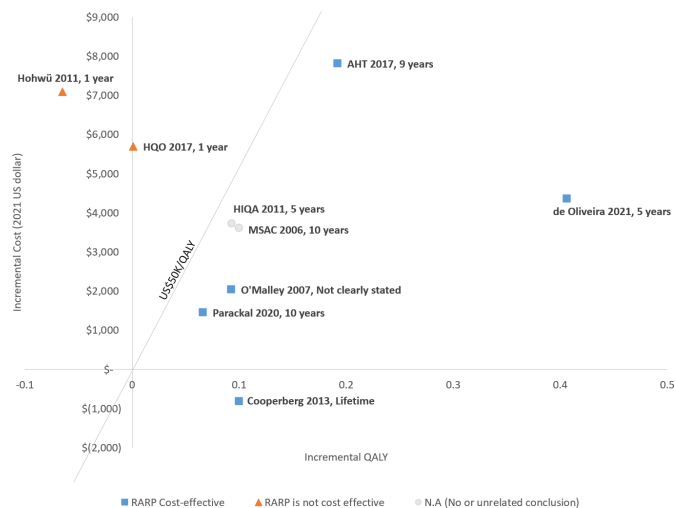
Figure 3 The cost-effectiveness and time horizon, RARP versus ORP. ORP, open radical prostatectomy; QALY, quality-adjusted life-year; RARP, robotic-assisted radical prostatectomy.

checklist. These studies vary widely in country/healthcare setting, comparators and time horizon. A majority of the studies found RARP to be more costly and more effective compared with ORP and LRP, although the cost-effectiveness conclusions (ie, the ICERs) varied and were dependent on the specific WTP thresholds used and influenced by time horizon. The four medical device features recommended to be included in economic evaluations were considered to varying degrees: capital investment in the surgical system (organisational impact) was widely considered, dynamic pricing was considered in about half of the studies, while learning curve and incremental innovation were poorly addressed in the included studies.

Cost, effectiveness and cost-effectiveness of RARP

Although the higher cost and effectiveness of RARP observed in this review were consistent with existing literature,[4 11 33 39 40] the key question is whether the effectiveness gained is worth the increased cost. Although most of the CEAs comparing RARP with ORP or with LRP concluded RARP to be cost-effective in this systematic literature review, a definitive answer remains elusive given that cost-effectiveness thresholds varied across different countries and healthcare settings. Studies with longer time horizons tended to have more favourable cost-effectiveness results for RARP. Possible explanations for this correlation is that RARP incurs a high upfront capital, instrument and accessory cost in the perioperative time period, while improved patient outcomes observed after RARP including lower rates of positive surgical margins and better functional outcomes[7 13 14 41] might lead to downstream healthcare cost savings[11] and translate into better quality of life as well.

Medical device features in RARP

Despite recommendations in multiple authoritative methods publications,[20–22 42] adoption of the four

recommended special characteristics of medical devices within these cost-effectiveness evaluations was limited. Among most of the studies included in this review, the capital cost of acquiring a robotic system, one aspect of organisational impact, was considered in the cost calculation. The allocation of capital equipment cost per RARP case is challenging, given the complex financial allocation in different healthcare systems and sharing of the use of robotic systems across specialties. The capital cost calculation of robotic assisted surgery should reflect the actual cost allocation from the appropriate perspective and healthcare system. Only two included studies[19 38] calculated the capital cost per RARP case by allocating the cost to multiple procedures across specialties to reflect real world practice. Additionally, if robotic capital cost is funded by a charitable donation, it is important to consider who actually paid for it and align cost calculations with the study perspective.

Learning curve, the second recommended medical device feature, is considered the most important characteristic associated with the use of a medical device.[21] In this systematic review, while learning curve was mentioned among 58% of the studies, no action was taken to incorporate it within the analyses. Inclusion of a robotic surgical system's learning curve could be considered on two fronts. First, surgeons need some practice to reach proficiency after adopting new technology, which could be accelerated by rigorous training. Second, higher surgical volume may not only reduce cost per procedure (economies of scale), but also improve patient outcomes and reduce the operative time per procedure as the surgeons become more skilled and their proficiency increases.[43 44] Scenario analysis could be considered to further understand the uncertainty related to surgical volume consistent with a learning curve effect.

Incremental innovation, the third recommended medical device feature, is common in RARP. For example, four generations of da Vinci RAS systems and instruments, with numerous product innovations, have been launched in the past 20 years. However, incremental innovation was considered in only one study in this review, and it focused exclusively on the differential costs by generations of systems without considering changes in effectiveness. This is likely due to lack of clinical studies that differentiate effectiveness among various generations of surgical systems. Postmarket observational studies for newer RAS generations or subgroup analysis for the different system/product generations are needed to address this gap.

Lastly, medical device pricing is considered more dynamic than drugs, and launching new generations of technology often influences the price of existing devices.[21 22] Five studies in this review empirically tested varying equipment prices. In addition to using updated pricing information, researchers could consider estimating a threshold price at which RAS provides a minimally acceptable value, which decision makers could consider in future purchasing or leasing decisions. For a healthcare system, the threshold price for a new technology is at

the point of indifference between accepting and rejecting the technology, assuming all conditions for other options are equal.[45] Analyses considering threshold price and technology generation were not found in this systematic review.

Suggestions for future RAS cost-effectiveness studies

Several opportunities to improve RAS economic evaluations were identified from this systematic literature review. First, the selection of time horizon should be long enough to capture the relevant differences in outcomes and costs to the various stakeholders. With emerging evidence demonstrating RAS' long-term clinical benefits such as less positive surgical margin[14 15 46] and better functional outcomes,[7 13 14 41] researchers should consider applying appropriate time horizons consistent with the direct and, when relevant, indirect effects of the procedures on patient outcomes. Second, surgeon proficiency may affect patient outcomes and efficiency. Clinical studies might consider measuring and reporting the experience and proficiency of surgeons (eg, number of cases performed previously) when evaluating their surgical outcomes. Cost-effectiveness analyses could use clinical data from experienced surgeons who have passed the learning curve or consider stratified analyses by the performance of high-volume versus low-volume centres/surgeons to better examine the impact of surgeon proficiency. Moreover, with increasing numbers of new robotic surgical products and manufacturers, differentiation between products is critical for economic evaluations to inform decision-making, as it will be increasingly unlikely that all robotic surgery platforms are equivalent. Clinical studies that document clinical outcomes data by different brands and generations of devices are needed to enable the evaluation of incremental innovation of medical devices in cost-effectiveness analyses. Third, existing studies are primarily conducted from societal or payer perspectives. Future studies evaluating economic value of RAS should consider a healthcare systems perspective, given the purchasing decision is often made at this level. Researchers may need to carefully select cost and benefit components to align with the perspective of the study in the specific country. Fourth, the cost of infrastructure necessary to accommodate the device and any impact of the new device on procedure costs should be considered. This may include the cost of training, increase in surgical volume and conversion of procedure from inpatient to outpatient setting.[47] Finally, the COVID-19 pandemic brings new challenges for constrained healthcare resources. The opportunity cost of using RAS to reduce downstream health resource use may be increasingly relevant in this environment.

Limitations of the systematic review

The current review is subject to several limitations. First, the literature search was limited to publicly available information. Private or confidential HTAs may contain cost-effectiveness analyses not included in this study, despite our effort to conduct a targeted grey literature search. Second, the internal validity of a systematic review synthesis depends on the quality of primary studies included. In our review, the general quality of included studies could be considered moderate to good, except for methods used to assess effectiveness. More than half of the studies did not use local utility data for prostate cancer. The lacking country-specific utility data increased the uncertainty of the published economic evaluations. Third, although studies with a cost-comparison design could provide insights on costs, they were excluded due to lack of effectiveness data. In addition, patient benefits that are not directly associated with clinical effectiveness measures, such as reduction of out-of-pocket cost[48] and reduction on productivity loss,[49] were not evaluated in most of the original studies in this review. Inclusion of these additional patient-focused outcomes may more accurately reflect value/cost. Finally, with the increasing use of non-surgical treatment for localised prostate cancer, such as high-intensity focused ultrasound,[50] it is worthwhile to further investigate the cost-effectiveness across all treatment options.

CONCLUSIONS

To our knowledge, this is the first systematic literature review on the cost-effectiveness of RAS and evaluated the application of recommended medical device features. No conclusive cost-effectiveness result was identified in the literature due to study heterogeneity; however, RARP was found to be more costly and effective compared with ORP and LRP in most studies, providing a body of evidence supporting its cost-effectiveness. Analyses with longer time horizons showed more favourable cost-effectiveness results towards RARP. Further cost-effectiveness analyses for RARP that more thoroughly consider medical device features are needed to better understand and more appropriately estimate its economic value compared with other surgical and non-surgical treatments.

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