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Review – Prostate Cancer

Economic Evaluation of Robotic-assisted Radical Prostatectomy: A Systematic Review and Meta-analysis

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Abstract

Background and objective: Robotic-assisted radical prostatectomy (RARP) is a surgical option for localized prostate cancer. Cost-effectiveness analysis (CEA) findings are inconsistent when comparing it with open (ORP) and laparoscopic (LRP) radical prostatectomy approaches. We performed a systematic review and meta-analysis to pool the incremental net benefit (INB) of these approaches.

Methods: Relevant CEA studies of RARP were identified by searching the PubMed, Embase, Scopus, International Health Technology Assessment database, Tufts CEA Registry, and Centre for Reviews and Dissemination databases from January 2005 to October 2023. To be included, studies must compare costs, and quality-adjusted life years (QALYs) of RARP versus ORP or LRP, and report the incremental cost per QALY gained. Study characteristics, economic model, costs, and outcomes were extracted. INBs were calculated in 2022 US dollars adjusted for purchasing power parity. A pooled analysis was performed using a random-effect model stratified by country income level. Heterogeneity was assessed using the Q test and I² statistic.

Key findings and limitations: Thirteen studies with 17 comparisons, ten from high-income (HICs) and three from middle-income (MICs) countries, were included. Ten and five studies compared RARP with ORP and LRP, respectively. From a payer perspective, RARP was cost effective but not statistically significant compared with LRP in HICs (pooled INB: \$7507.83 [−\$1193.03 to \$16 208.69], I² = 81.15%) and not cost effective in MICs (%; −\$4499.39 [−\$16 500 to \$7526.87], I² = 17.15%). RARP showed no statistically significant cost effectiveness over ORP in both HICs (\$3322.38 [−\$1864.39 to \$8509.15], I² = 90.89%) and MICs (\$2222.60 [−\$2960.64 to \$7405.83], I² = 58.92%).

Conclusions and clinical implications: RARP is cost effective compared with LRP in HICs but lacks statistical significance. When compared with ORP, RARP is not cost effective in HICs and MICs. Our findings may support decision-making for prostate

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cancer treatment options in countries with different health care systems, especially those with limited resources.

Patient summary: Our systematic review and meta-analysis provide important information regarding robotic-assisted radical prostatectomy (RARP) compared with open (ORP) and laparoscopic (LRP) radical prostatectomy. In high-income countries, RARP is generally cost effective compared with LRP, but not with ORP, while in middle-income countries, RARP is not cost effective compared with LRP or ORP. The findings of this review can support decision-making for prostate cancer treatment options.

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1. Introduction

Prostate cancer is the second most common cancer in men worldwide [1]. Radical prostatectomy is one of the main treatments for clinically localized prostate cancer. It includes both open radical prostatectomy (ORP) and less invasive methods such as laparoscopic radical prostatectomy (LRP) and robotic-assisted radical prostatectomy (RARP) [2–4]. Owing to its high learning curve, technological complexity, and ergonomic limitations, LRP is still rarely used. In contrast, robotic-assisted surgery (RAS) with the da Vinci surgical system has become more and more popular throughout the world [5–9]. The extra wrist movements and three-dimensional imaging of the da Vinci system get around the technological difficulties with LRP [10]. Using the instrument's seven degrees of motion, accuracy, and tremor filtering, surgeons execute RARP by translating hand gestures in real time. RARP is now used more widely, having become a standard surgical technique on a global scale [3,11].

With advantages over ORP and traditional LRP, such as fewer postoperative problems, less blood loss, lower transfusion rates, shorter hospital stays, and quicker recovery, RARP's clinical efficacy is well established [12–15]. Nevertheless, with the growing demand for RARP, demonstrating only the clinical benefits is not sufficient given the limited resources for health care. Evidence on the economic value of RARP is strongly required to support policy decision-making. A recent systematic review of cost-effectiveness analyses (CEAs) of RARP has been conducted, providing evidence of economic value of RARP when comparing it with ORP and LRP [16]. However, findings from CEAs in different health care settings have come to diverse conclusions. Moreover, this systematic review provided only an overall descriptive summary of evidence from individual cost-effectiveness studies. A quantitative summary of cost effectiveness could provide robust evaluation of economic outcomes across studies. A method for a meta-analysis of cost-effectiveness findings based on all existing studies answering the same question across different assumptions has been developed [17] and applied in several areas [18,19]. The evidence generated from a meta-analysis may be useful to decision-makers, given that it provides an overall summary of economic evidence stratified quantitatively by country income level and study perspective. The findings

could facilitate decision-making in countries where context-specific cost-effectiveness studies are not available.

Medical devices used in robotic surgery, unlike pharmaceuticals, possess distinctive features necessitating consideration in economic evaluations [20].

Therefore, we conducted a systematic review and meta-analysis of CEAs by pooling the incremental net benefit (INB) to assess the cost effectiveness of using RARP for localized prostate cancer compared with ORP and LRP. The purpose of this research is to assess the economic values of using RARP for localized prostate cancer and inform policy-makers, especially in those countries where economic evidence is limited.

2. Methods

2.1. Materials and methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses protocols [21], and the protocol was registered at PROSPERO (CRD42024504163).

2.2. Data source and search strategy

We performed a comprehensive search for relevant studies in PubMed, Embase, Scopus, Cost Effectiveness Analysis Registry by Tufts Medical Centre, International Health Technology Assessment (HTA) database, and the Centre for Reviews and Dissemination (CRD) database, which includes NHS Economic Evaluation database, Database of Abstracts and Reviews of Effects, and the HTA database, from January 1, 2005 until the October 31, 2023. Databases were searched using a combination of medical subject headings and free-text terms that were grouped into the following categories: intervention (RARP) and study design (economic analyses and related terms). Details of search strategies are provided in [Supplementary Table 1](#).

2.3. Study selection

Two independent reviewers (T.B. and T.T.) screened the titles, abstracts, and full texts of studies identified in the literature search. Studies were included if these performed a CEA or cost-utility analysis reporting cost per quality-adjusted life year (QALY) comparing RARP with ORP or LRP to treat prostate cancer in any age group of male

population. Studies were excluded if these were a cost-minimization, cost-benefit, or budget impact analysis, or if these did not provide adequate data for performing a meta-analysis. Any disagreements between the two reviewers were resolved by a third independent reviewer (S.V.).

2.4. Data extraction and quality assessment

A standardized data extraction sheet was developed based on the Consolidated Health Economic Evaluation Reporting Standard (CHEERS) checklist [22]. The extracted data included the characteristics of intervention and comparator, country income level (as per the World Bank 2020 report), time horizon, study perspective, discount rate, model used, population of interest, data source, incremental cost-effectiveness ratio (ICER), incremental cost (ΔC), incremental outcomes (ΔE) and their dispersion (standard deviation, standard error [SE], or 95% confidence interval [CI]), and willingness-to-pay (WTP) threshold. The CEA plane with scatterplots representing incremental cost (ΔC) and incremental outcomes (ΔE) of the probabilistic sensitivity analysis was also retrieved and extracted using WebPlotDigitizer software version 4.6 [23].

The risk of bias (RoB) was assessed by two independent reviewers (T.B. and W.K.) using the modified Economic Evaluations Bias (ECOBias) tool consisting of 22 items [24]. Disagreements were resolved by consensus. Each item of ECOBIAS was rated yes, partly, unclear, no, or not applicable. Three items—limited sensitivity analysis bias, wrong model bias, and bias related to treatment effects—were deemed most relevant to the overall validity assessment and study context [25,26]. Studies that were assessed as “yes” for all three items were classified as having a low RoB. Studies with one or more “partly/unclear” responses were categorized as having a moderate RoB, whereas studies with at least one response as “no” were classified as having a high RoB.

2.5. Data analysis and synthesis

2.5.1. Outcome of interest

The primary outcome of interest was the INB of using RARP compared with ORP or LRP, which was calculated for each study using Equation (1) or (2) below, depending on the data reported in each of the included studies. The variance of each of the INBs was calculated using Equation (3) or (4) below [27,28].

$$\text{INB} = \Delta E (K - \text{ICER}) \quad (1)$$

$$\text{INB} = (K \times \Delta E) - \Delta C \quad (2)$$

Here, K represents the threshold of WTP, ΔE represents the incremental effectiveness, and ΔC represents the incremental cost.

$$\text{Var}(\text{INB}) = K^2 \sigma_{\Delta E}^2 + \sigma_{\text{ICER}}^2 \quad (3)$$

$$\text{Var}(\text{INB}) = K^2 \sigma_{\Delta E}^2 + \sigma_{\Delta C}^2 - 2K\rho_{\Delta C\Delta E} \quad (4)$$

Here, $\sigma_{\Delta C}^2$, $\sigma_{\Delta E}^2$, and $\sigma_{\Delta E\Delta C}$ are variances of ΔC and ΔE and their covariance, respectively, and σ_{ICER} is a variance of ICER.

2.5.2. Data preparation

Data were prepared according to five scenarios, as described in [Supplementary Table XX](#) [27]. INB and its variance were then calculated accordingly. All cost data including K , ΔC , ICER, and their variances in each currency were standardized by converting to 2022 US dollars using consumer price index [29] and purchasing power parity [30].

2.6. Statistical analysis

Each INB and its variance were calculated as per the approaches described previously [27,31,32]. Meta-analyses were performed to pool the INBs across studies stratified by country income level according to the World Bank classification (high-income [HICs] and middle-income [MICs] countries) [33] and perspectives (health care or payer perspective and societal perspective), using a random-effect model (DerSimonian and Laird [34] method). Heterogeneity between studies was assessed using the I^2 statistic. Publication bias was assessed using a funnel plot and Egger's test. Where a funnel plot was asymmetrical, a contour-enhanced funnel plot was constructed to assess whether the asymmetry was due to missing studies or heterogeneity [35]. A series of prespecified sensitivity analyses were performed by excluding studies with the following conditions: (1) imputing variance using absolute value borrowing from similar studies, (2) missing variances, and (3) a high RoB. If no meta-analysis was performed due to the insufficient number of comparisons, a narrative overview of the findings from the study was provided. All the data were prepared using Microsoft Excel version 2016 (Microsoft Corporation, Redmond, WA, USA) and analyzed by STATA version 17.0 (Stata Corporation, College Station, TX, USA), and a two-sided statistical test with a p value of ≤ 0.05 was considered statistically significant.

3. Results

3.1. Study characteristics

A total of 933 studies were identified, of which 13 studies [36–48] were found eligible to include in the meta-analysis, as detailed in [Fig. 1](#). In the analysis, 17 comparisons were drawn from 13 studies, encompassing RARP versus ORP (ten studies) [36,38–43,45–47], and RARP versus LRP (five studies) [37,38,40,43,48] from the payer's perspective. Additionally, one comparison each of RARP versus ORP [42] and that of RARP versus LRP [44] were evaluated from a societal perspective. Characteristics of these 13 studies are described in [Table 1](#).

All economic evaluation studies were performed using the payer perspective, except one study [44], which used a societal perspective, and one study in both payer and societal perspectives [42]. Ten studies were conducted in HICs (USA, UK, Denmark, Canada, The Netherlands, Ireland, and Australia) [36–38,41–47] and three from MICs (Thailand and Brazil) [39,40,48]. However, no studies were identified from low-income countries. All the comparisons used model-based economic evaluations, including Markov model ($n = 7$, 53.8%) [36,38,40,41,43,46,47], cohort-based analysis ($n = 3$, 23.1%) [39,42,45], decision tree ($n = 2$,

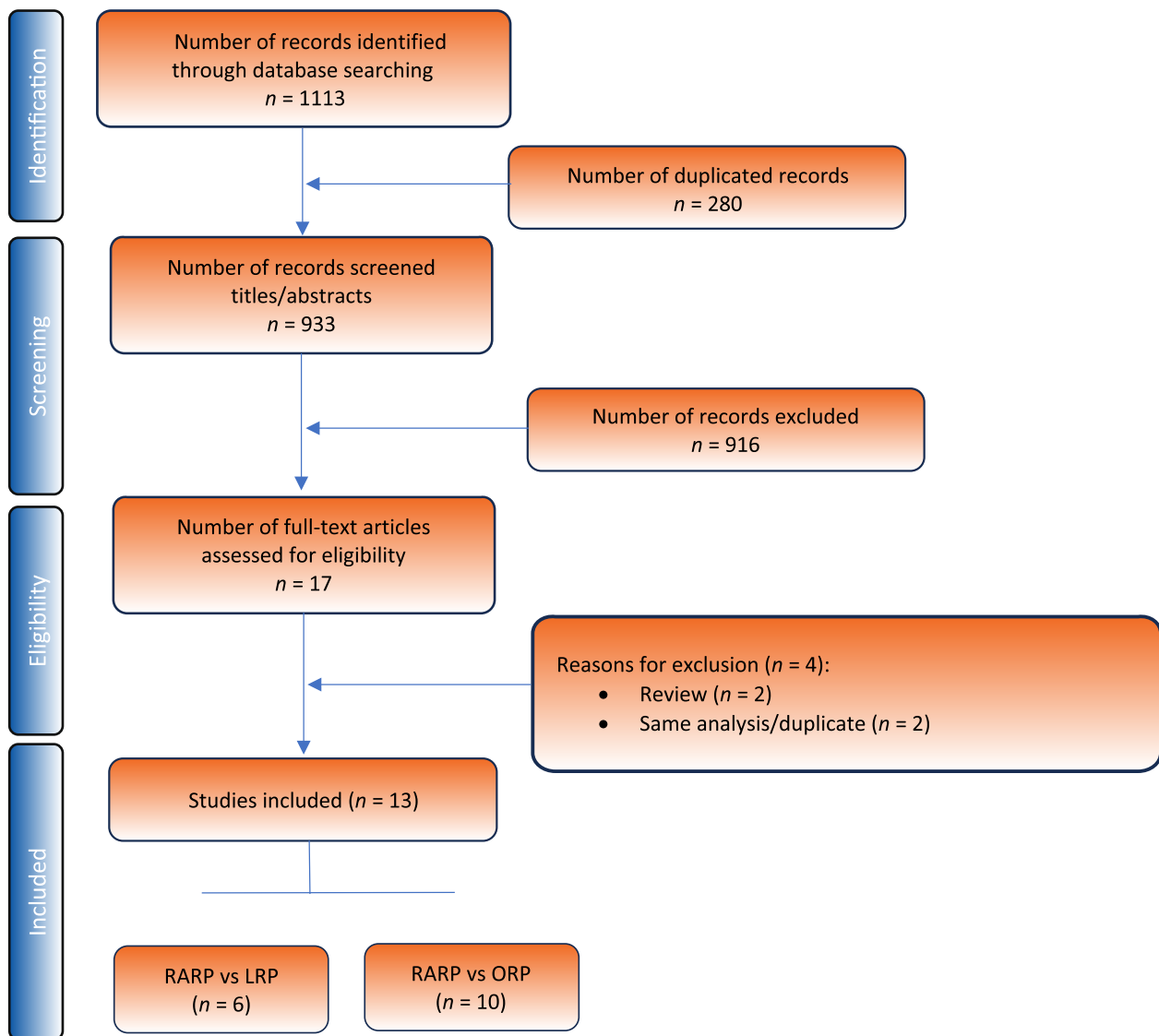


Fig. 1 – Study selection process. The last row indicates the comparison information from studies (number is >13 due to multiple comparisons; details are provided in the text). LRP = laparoscopic-assisted radical prostatectomy; ORP = open radical prostatectomy; RARP = robotic-assisted radical prostatectomy.

15.4%) [44,48], and discrete event simulation ($n = 1$, 7.7%) [37]. Clinical and utility parameters were mostly taken from published literature. Regarding the WTP threshold, eight studies [36–38,43,44,46–48] used a country-specific threshold, one study [39] used a gross domestic product-based threshold as the WTP, and four studies [40–42,45] did not report any cost-effectiveness threshold. The 10-yr time horizon was most used ($N = 4$, 30.8%) [37,43,47,48], followed by 20 yr ($N = 2$, 15.4%) [40,46], with the remaining studies varying their time horizon ($N = 5$, 38.5%) [36,39,41,42,44] from 1 to 9 yr, whereas one study [38] is lifetime and one study [45] did not report any time horizon.

3.2. RoB assessment

The RoB assessment was performed using the ECOBIAS checklist [24]; for details, see [Supplementary Table 2](#). Ten studies [36–41,43–45,47] were found to be at a moderate RoB and three studies [42,46,48] at a high RoB, with no

studies identified as being at a low RoB. Overall, most studies had a similar bias profile. Reporting and dissemination bias and bias related to consistency were unclear for most studies. Studies that did not demonstrate a bias related to lifetime horizon chosen (two studies) [42,46] and those in which results were reported according to the study protocol (one study) [48] were determined to have a high RoB.

3.3. Pooling of INBs based on payers' perspective

3.3.1. RARP versus ORP

3.3.1.1. Findings from HICs. The INBs of RARP versus ORP were estimated for eight comparisons from eight individual studies [36,38,41–43,45–47] from HICs. The pooled INB indicated that RARP is cost effective, but not statistically significant when compared with ORP from the payer perspective (INB, \$3322.38 [95% CI: −\$1864.39 to \$8509.15; $I^2 = 90.89\%$; Fig. 2). Contour-enhanced funnel plots indicated that most fell in the nonsignificant area, which indi-

Table 1 – Characteristics of the included studies

| Author (year) | Country | Country income level | Intervention | Comparisons | Perspective | Currency (year) | WTP | GDP based WTP | Modeling approach | Time horizon | Type of literature | Type of analysis | Conclusion | RoB |
|---------------------------------------|-----------------|----------------------|--------------|-------------|---------------------|-----------------|--------------------|---------------|---------------------------|--------------------|--------------------|------------------|---|----------|
| Ratchanon et al (2015) [48] | Thailand | MIC | RARP | LRP | Payer/HPC | Baht (2015) | 160K Baht per QALY | No | Decision tree | 10 yr | Journal article | CUA | RARP is not cost effective | High |
| Close et al (2013) [37] | UK | HIC | RARP | LRP | Payer/HPC | GBP (2013) | £30K per QALY | No | Discrete event simulation | 10 yr | Journal article | CUA | RARP is cost effective | Moderate |
| Cooperberg et al (2013) [38] | USA | HIC | RARP | LRP, ORP | Payer/HPC | USD (2013) | \$100K per QALY | No | Markov model | Lifetime | Journal article | CUA | No difference in effectiveness and RARP lower cost | Moderate |
| Hohwü et al (2011) [42] ^s | Denmark | HIC | RARP | ORP | Payer/HPC, societal | EUR (2011) | NR | Yes | Cohort based | 1 yr | Journal article | CEA | RARP not cost effective | High |
| Parackal et al (2020) [47] | Canada | HIC | RARP | ORP | Payer/HPC | CAD (2020) | C\$50K per QALY | No | Markov model | 10 yr | Journal article | CUA | RARP cost effective | Moderate |
| de Oliveira et al (2021) [39] | Brazil | MIC | RARP | ORP | Payer/HPC | BRL (2021) | R\$114 026.55 | Yes | Cohort based | 5 yr | Journal article | CUA | RARP cost effective | Moderate |
| Labban et al (2022) [43] ^s | UK | HIC | RARP | LRP, ORP | Payer/HPC | GBP (2022) | £30K per QALY | No | Markov model | 10 yr | Journal article | CUA | RARP cost effective | Moderate |
| Faria et al (2022) [40] | Brazil | MIC | RARP | LRP, ORP | Payer/HPC | BRL (2022) | NR | Yes | Markov model | 20 yr | Journal article | CEA | RARP cost effective | Moderate |
| Lindenberg et al (2022) [44] | The Netherlands | HIC | RARP | LRP | Societal | EUR (2022) | €80K per QALY | No | Decision tree | 7 yr | Journal article | CUA | RARP cost effective | Moderate |
| Health Quality Ontario (2017) [46] | Canada | HIC | RARP | ORP | Payer/HPC | CAD (2017) | C\$100K per QALY | No | Markov model | 20 yr | HTA report | CUA | RARP not cost effective | High |
| AHT (2017) [36] | Canada | HIC | RARP | ORP | Payer/HPC | CAD (2017) | C\$50K per QALY | No | Markov model | 9 yr | HTA report | CUA | RARP cost effective | Moderate |
| O'Malley and Jordan (2007) [45] | Australia | HIC | RARP | ORP | Payer/HPC | AUD (2007) | NR | Yes | Cohort based | Not clearly stated | Journal article | CUA | RARP cost effective | Moderate |
| HIQA (2011) [41] | Ireland | HIC | RARP | ORP | Payer/HPC | EUR (2011) | NR | Yes | Markov model | 5 yr | HTA report | CUA | RARP cost effective in high-volume health care settings | Moderate |

AUD = Australian dollar; BRL = Brazilian real; CAD = Canadian dollar; CEA = cost-effective analysis; CUA = cost-utility analysis; EUR = euro; GBP = pound Sterling; GDP = gross domestic product; HIC = high-income country; HPC = hospital cost of providing care; HTA = health technology assessment; LRP = laparoscopic-assisted radical prostatectomy; MIC = middle-income country; NR = not reported; ORP = open radical prostatectomy; QALY = quality-adjusted life year; RARP = robotic-assisted radical prostatectomy; RoB = risk of bias; USD = US dollar; WTP = willingness to pay.

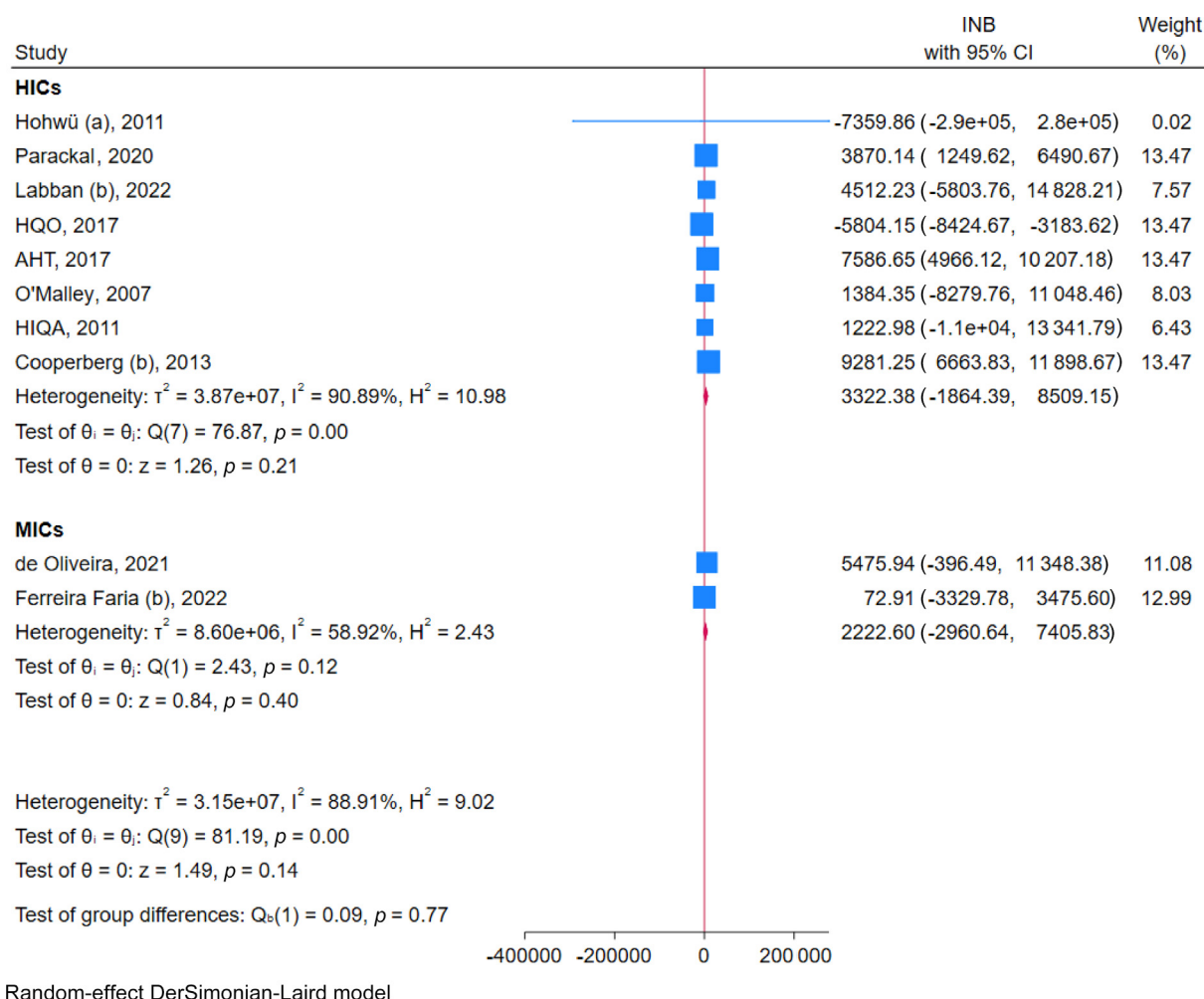


Fig. 2 – Pooling the INB of RARP versus OPR in payer perspective. CI = confidence interval; HIC = high-income country; INB = incremental net benefit; MIC = middle-income country; ORP = open radical prostatectomy; RARP = robotic-assisted radical prostatectomy.

cated that asymmetry was likely due to heterogeneity rather than a publication bias (Supplementary Fig. 1). However, Egger's test indicated no evidence of small-study effects (coefficient = -0.16 , $SE = 0.825$, $p = 0.85$). Findings from sensitivity analyses by pooling variance using absolute value borrowing from similar studies were similar to those in the primary analysis (Supplementary Fig. 5). However, the sensitivity analyses by excluding high RoB studies and excluding scenario 5 showed that the results are sensitive to the analysis approach. By excluding high RoB studies, RARP was statistically significantly cost effective compared with ORP in HICs (Supplementary Fig. 6). By excluding scenario 5 studies, RARP was statistically significantly not cost effective compared with ORP in HICs. According to the time horizon, RARP was statistically significant but not cost effective compared with ORP when using a short-term time horizon (<5 yr), while evaluating over 5 yr or lifetime, RARP was found to be more cost effective than ORP (Supplementary Fig. 7).

3.3.1.2. Findings from MICs. The INBs of RARP versus ORP were estimated for two comparisons from two MIC studies

[39,40]. The pooled INB indicated that RARP is cost effective, but not statistically significant when compared with ORP from the payer perspective (INB, \$2222.60 [95% CI: $-\$2960.64$ to $\$7405.83$; $I^2 = 59.92\%$]; Fig. 2). Contour-enhanced funnel plots indicated that most fell in the non-significant area, which indicated that asymmetry was likely due to heterogeneity rather than a publication bias (Supplementary Fig. 2). However, Egger's test indicated no evidence of small-study effects (coefficient = 4.29 , $SE = 4.49$, $p = 0.34$). Findings from the sensitivity analyses of pooling variance using absolute value borrowing from similar studies, excluding high RoB studies, and time horizon were largely consistent with those of our main analyses (Supplementary Fig. 5, 6, and 8).

3.3.2. RARP versus LPR

3.3.2.1. Findings from HICs. The INBs of RARP versus LRP were estimated for three comparisons from three HIC studies [37,38,43]. The pooled INB indicated that RARP is cost effective, but not statistically significant when compared with LRP from the payer perspective (INB, $\$7507.83$ (95% CI: $-\$1193.03$ to $\$16208.69$; $I^2 = 81.15\%$]; Fig. 3).

Contour-enhanced funnel plots showed studies in both significant and nonsignificant areas, which suggested that asymmetry was likely due to heterogeneity rather than a publication bias (Supplementary Fig. 3). However, Egger's test indicated no evidence of small-study effects (coefficient = 0.58, SE = 4.159, $p = 0.88$). Findings from sensitivity analyses were consistent with those of our primary analysis (Supplementary Fig. 9–11).

3.3.2.2. Findings from MICs. The INBs of RARP versus LRP were estimated for two comparisons from two MIC studies [40,48]. The pooled INB indicated that RARP is neither cost effective nor statistically significant when compared with LRP from the payer perspective (INB, $-\$4499.39$ (95% CI: $-\$16\,500$ to $\$7526.87$; $I^2 = 17.15\%$; Fig. 3). Contour-enhanced funnel plots indicated that most fell in the non-significant area, which indicated that asymmetry was likely due to heterogeneity rather than a publication bias (Supplementary Fig. 4). However, Egger's test indicated no evidence of small-study effects (coefficient = 91.57, SE = 125.498, $p = 0.47$). Findings from sensitivity analyses were consistent with those of our primary analysis (Supplementary Fig. 9, 10, and 12).

3.4. Pooling of INBs based on societal perspective

Only two studies have been included from the societal perspective: one comparing RARP versus ORP, and the other comparing RARP versus LRP, both conducted in HICs. There

are insufficient studies to pool INBs. Their results showed that RARP is cost effective when compared with LRP, but not cost effective when compared with ORP in HICs from societal perspectives.

3.5. Sensitivity analyses

Findings from the sensitivity analyses of RARP versus LRP in both HICs and MICs were largely consistent with those of our main analyses. Based on a sensitivity analysis pooling variance using absolute value borrowing from similar studies, RARP is cost effective but not statistically significant when compared with LRP in HICs, and RARP is neither cost effective nor statistically significant when compared with LRP in MICs (Supplementary Fig. 5). In the sensitivity analysis excluding high RoB studies, no studies were excluded in HICs and only one study was left after removing high RoB studies in MICs (Supplementary Fig. 6). In the sensitivity analysis excluding scenario 5, a meta-analysis could not be performed.

Findings from the sensitivity analyses of RARP versus ORP in HICs by pooling variance using absolute value borrowing from similar studies were similar to those in the primary analysis: RARP is cost effective but not statistically significant when compared with ORP in HICs. However, the sensitivity analyses of RARP versus ORP in HICs by excluding high RoB studies and excluding scenario 5 showed that the results are sensitive to the analysis approach. By excluding high RoB studies, RARP was

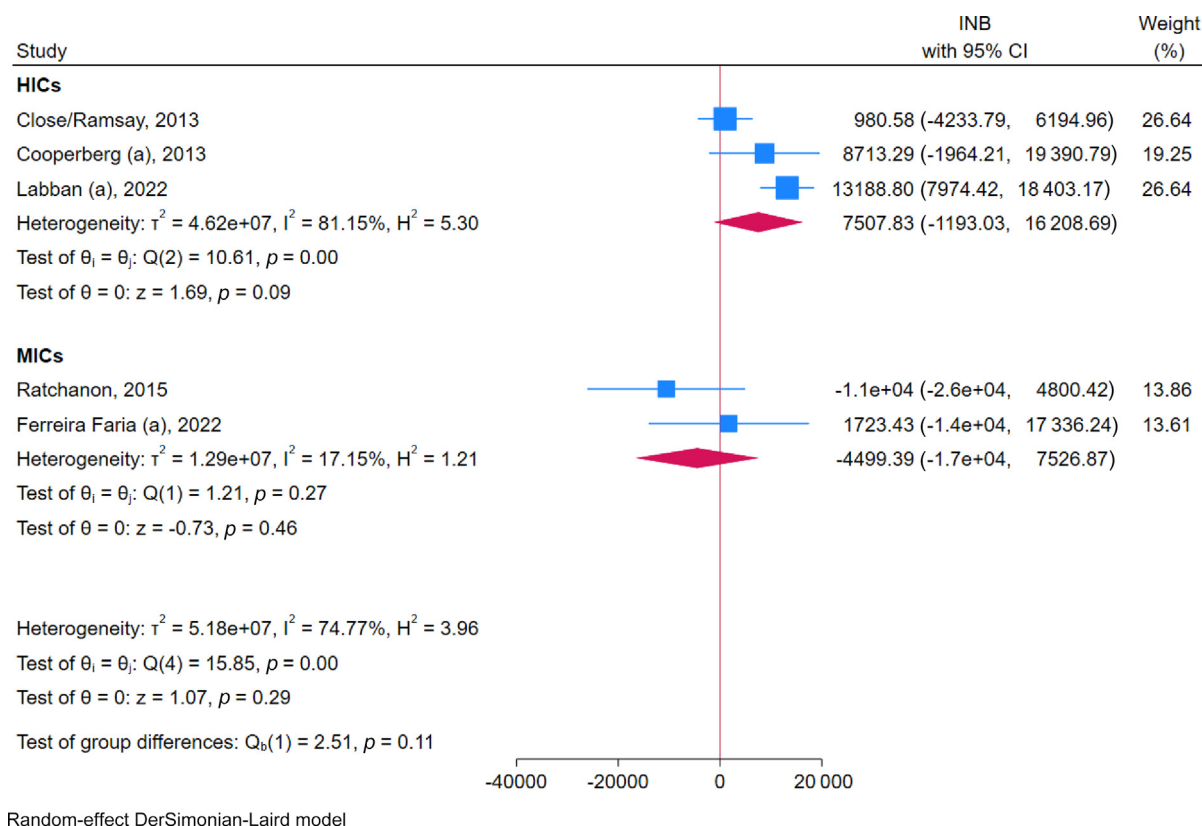


Fig. 3 – Pooling the INB of RARP versus LRP in payer perspective. CI = confidence interval; HIC = high-income country; INB = incremental net benefit; LRP = laparoscopic-assisted radical prostatectomy; MIC = middle-income country; RARP = robotic-assisted radical prostatectomy.

statistically significantly cost effective compared with ORP in HICs (see Supplementary Fig. 7). By excluding scenario 5 studies, RARP was statistically significantly not cost effective compared with ORP in HICs (see Supplementary Fig. 8).

Findings from the sensitivity analyses of RARP versus ORP in MICs, which included pooling variance using absolute value borrowing from similar studies and excluding high RoB studies, were largely consistent with those of our main analyses: RARP is cost effective but not statistically significant when compared with ORP in MICs.

4. Discussion

Our study addresses a crucial aspect of health care economics by evaluating the cost effectiveness of RARP compared with other surgical approaches from both payer and societal perspectives. The rising prevalence of prostate cancer and the continuous evolution of surgical techniques underscore the significance of understanding the economic implications associated with these interventions.

Previous systematic reviews provided an overall descriptive summary of cost-effectiveness evidence of using RARP compared with ORP and LRP [16], but a quantitative summary of the evidence was lacking. This systematic review is the first to perform meta-analyses of CEAs to assess the cost effectiveness of using RARP for localized prostate cancer patients. Our review included a total of ten and five comparisons for RARP versus ORP and RARP versus LRP, respectively, from 13 studies to perform meta-analyses stratified by country income level and perspective. Our findings suggested that RARP is cost effective compared with LRP in HICs (INB, \$3322.38 [95% CI: −\$1864.39 to \$8509.15]). When compared with ORP, RARP is not cost effective in HICs and MICs. Our findings may support decision-making for prostate cancer treatment options in countries with different health care systems, especially those with limited resources.

The comprehensive analysis of 13 selected studies, detailed in Fig. 1 and Table 1, offers a deep dive into the comparative cost effectiveness of RARP against ORP and LRP for patients with localized prostate cancer. These studies, predominantly conducted from the payer's perspective, originated from diverse income settings, encompassing both HICs and MICs. These studies employed various economic evaluation models, including Markov models, cohort-based analyses, decision trees, and discrete event simulations.

Our findings build upon existing literature investigating the economic outcomes of different surgical modalities for prostate cancer treatment. By conducting a comprehensive meta-analysis, we have synthesized evidence from multiple studies, offering a more robust understanding of the comparative cost effectiveness of RARP versus ORP and LRP.

4.1. Cost, effectiveness, and cost effectiveness of RARP

Although the higher cost and effectiveness of RARP observed in this review were consistent with those reported in the existing literature [3,11,38,47,48], the key question is whether the effectiveness gained is worth the increased

cost. While the majority of CEAs comparing RARP with ORP or LRP concluded RARP to be cost effective in this systematic literature review, a conclusive determination remains challenging due to variations in cost-effectiveness thresholds across different countries and health care environments. Studies with longer time horizons generally yielded more favorable cost-effectiveness outcomes for RARP. This correlation could be attributed to RARP incurring high upfront costs for capital, instruments, and accessories during the perioperative period, with observed improvements in patient outcomes, such as reduced rates of positive surgical margins and enhanced functional outcomes, following RARP [12,13,14,47,49], might lead to downstream health care cost savings [11] and translate into better quality of life as well.

4.2. Medical device features in RARP

Despite recommendations in multiple authoritative method publications [20,21,22,50], integration of the four recommended special characteristics of medical devices within these cost-effectiveness evaluations was limited. While the capital cost of acquiring a robotic system, representing one aspect of organizational impact, was considered in most of the studies included in this review, allocation of capital equipment costs per RARP case poses challenges due to the intricate financial arrangements in various health care systems and the shared use of robotic systems across specialties. Calculation of the capital cost of RAS should accurately reflect the actual cost allocation from the appropriate perspective and within the health care system. Only two studies included in this review [18,41] calculated the capital cost per RARP case by distributing the cost across multiple procedures across specialties to mirror the real-world practice. Moreover, if the capital cost of robotics is funded by a charitable donation, it is crucial to consider the entity that actually paid for it and align the cost calculations with the study's perspective. The learning curve, considered the most significant characteristic associated with the use of a medical device, was the second recommended feature [21].

In this systematic review and meta-analysis, although the learning curve was referenced in <50% of the studies, no measures were implemented to integrate it into the analyses. The incorporation of a robotic surgical system's learning curve could be contemplated from two perspectives. Initially, surgeons require practice to attain proficiency after adopting new technology, a process that may be expedited through rigorous training. Additionally, higher surgical volumes may not only decrease the cost per procedure (due to economies of scale), but also enhance patient outcomes and diminish operative time per procedure as surgeons refine their skills and proficiency grows [51,52].

A scenario analysis might be contemplated to deepen the comprehension of the uncertainty surrounding surgical volume, in line with the learning curve effect. Incremental innovation, the third suggested characteristic of medical devices, is prevalent in RARP. For instance, over the past two decades, four generations of da Vinci RAS systems and instruments, featuring numerous product advance-

ments, have been introduced. Nevertheless, only one study in this review addressed incremental innovation, concentrating solely on the differing costs across system generations without delving into changes in effectiveness. This limitation likely stems from a dearth of clinical studies that distinguish effectiveness among different generations of surgical systems. Postmarket observational studies for newer RAS generations or subgroup analyses for distinct system/product generations are imperative to bridge this gap. Lastly, medical device pricing exhibits more dynamism than drugs, with the launch of new technology generations often impacting the prices of the existing devices [21,22].

In this review, six studies empirically examined different equipment prices. Alongside utilizing up-to-date pricing data, researchers might also contemplate determining a threshold price at which RAS offers a minimally acceptable value. Decision-makers could then take this into account in future procurement or leasing decisions. For a health care system, the threshold price for a new technology is the point at which the system is indifferent between accepting and rejecting the technology, provided that all conditions for other options are equal [53]. This systematic review and meta-analysis did not uncover analyses that took into account threshold pricing and technological generation.

4.3. *Suggestions for future RAS cost-effectiveness studies*

This systematic literature review revealed several avenues for enhancing economic evaluations of RAS. First, the time horizon chosen should be sufficiently extensive to capture pertinent discrepancies in outcomes and costs for the diverse stakeholders. Given emerging evidence highlighting RAS' long-term clinical advantages, such as reduced positive surgical margins, this aspect warrants careful consideration [13,14,54] and better functional outcomes [7,13,14,49]; researchers ought to contemplate employing suitable timeframes that align with both the direct impacts and, where applicable, the indirect repercussions of the procedures on patient outcomes. Additionally, the proficiency of surgeons could impact both patient outcomes and procedural efficiency.

Clinical studies could enhance their assessments of surgical outcomes by including measurements and reporting on surgeons' experience and proficiency, such as the number of previously performed cases. When conducting CEAs, it would be advantageous to utilize clinical data from skilled surgeons who have surpassed the learning curve. Alternatively, researchers could consider stratified analyses based on the performance of high-volume versus low-volume centers/surgeons to more thoroughly explore the influence of surgeon proficiency. Furthermore, given the increasing availability of new robotic surgical products and manufacturers, it is crucial to differentiate between these products in economic evaluations to provide informed decision-making. As it becomes less likely that all robotic surgery platforms are equivalent, clinical studies should document outcome data across different brands and generations of devices. This documentation is essential for evaluating the incremental innovation of medical devices in CEAs.

Moreover, current research predominantly adopts societal or payer viewpoints. Future studies appraising the economic value of RAS ought to adopt a health care system outlook, as purchasing decisions are frequently made at this level. Researchers may need to choose cost and benefit elements thoughtfully to harmonize with the study's perspective within the particular country. Additionally, it is imperative to account for the infrastructure costs required to integrate the device and any potential impact on procedural expenses. This encompasses expenses such as training, potential rise in surgical volume, and transitioning procedures from inpatient to outpatient settings [55]. In light of the COVID-19 pandemic, constrained health care resources face new challenges. The relevance of considering the opportunity cost of utilizing RAS to minimize downstream health resource utilization may be heightened in this context.

The results of our meta-analysis have several important scientific implications. First, our findings suggest that RARP demonstrates favorable cost effectiveness compared with ORP and LRP, particularly in HICs. This indicates the potential economic benefits of adopting RARP as the preferred surgical approach for prostate cancer treatment. Additionally, our analysis highlights the importance of considering both payer and societal perspectives in economic evaluations to capture the full spectrum of costs and benefits associated with health care interventions.

While our study provides valuable insights into the cost effectiveness of RARP, there are several avenues for future research. Further investigation is warranted to explore the long-term economic outcomes of RARP compared with traditional surgical approaches, particularly in terms of health care resource utilization, quality of life, and patient-reported outcomes. Additionally, comparative studies conducted in low-income countries and MICs are needed to assess the generalizability of our findings across different health care settings.

Our study contributes to the growing body of literature on the economic evaluation of prostate cancer treatments, informing health care policymakers, clinicians, and patients about the comparative value of different surgical approaches. By elucidating the cost effectiveness of RARP, our findings have implications for resource allocation decisions within health care systems, potentially leading to more efficient use of health care resources and improved patient outcomes [56].

4.4. *Limitations of the systematic review*

The current review has several limitations. First, our literature search was restricted to publicly available sources, potentially overlooking CEAs in private or confidential health technology assessments. Despite our efforts to conduct a targeted search of the gray literature, these exclusions may impact the comprehensiveness of our findings. Second, the internal validity of a systematic review relies on the quality of the primary studies included. While the overall quality of the studies in our review was moderate to good, concerns arose regarding the methods used to

assess effectiveness. Furthermore, over half of the studies did not utilize local utility data specific to prostate cancer, contributing to increased uncertainty in the economic evaluations reported. Third, studies employing a cost-comparison design were excluded due to a lack of effectiveness data. Additionally, patient benefits not directly linked to clinical effectiveness measures, such as reductions in out-of-pocket expenses, were not consistently evaluated in the original studies, potentially affecting the overall assessment of value [57] and reduction in productivity loss [58]. Most of the original studies analyzed in this review did not include evaluations of these specific outcomes. By incorporating these additional patient-focused measures, we can achieve a more comprehensive assessment of the value and cost implications. Additionally, as nonsurgical treatment modalities for localized prostate cancer, such as high-intensity focused ultrasound, gain popularity [59], it is beneficial to conduct further investigations into the cost effectiveness of all available treatment options.

What is particularly intriguing is the prevalence of model-based economic evaluations across the studies, with clinical and utility parameters derived primarily from the published literature. However, the choice of WTP thresholds varied considerably, with some studies employing country-specific thresholds, others relying on gross domestic product-based thresholds, and a few not specifying any threshold at all.

Regarding the time horizon, there was a broad spectrum of durations utilized, with the 10-yr horizon being the most frequently employed one [16]. Notably, longer time horizons tended to yield more favorable cost-effectiveness outcomes for RARP, emphasizing the importance of capturing long-term clinical benefits and cost implications accurately.

The RoB assessment, conducted using the ECOBIAS checklist, revealed consistent bias profiles across most studies, albeit with some uncertainty surrounding a narrow perspective bias and reporting/dissemination bias. Additionally, concerns were raised regarding the bias related to the model structure, particularly concerning the time horizon, warranting further scrutiny in future analyses [24].

Pooling of INBs from the payer's perspective provided valuable insights into the comparative cost effectiveness of RARP versus ORP and LRP within both HICs and MICs. While RARP demonstrated no statistically significant cost effectiveness over ORP in HICs, the findings were inconclusive for MICs. Similarly, the cost effectiveness of RARP versus LRP varied depending on the income level, with RARP appearing to be cost effective but not statistically significant in HICs, while no significant cost effectiveness was observed in MICs.

A publication bias analysis indicated no evidence of asymmetry in the included studies, further validating the robustness of the findings. However, it is essential to acknowledge the limited availability of studies from a societal perspective, which hindered the pooling of INBs for a comprehensive analysis.

Our analysis underscores the sensitivity of the results to the chosen analytical approach. While the current evidence tentatively indicates that HIC RARP may present a significant cost-effective advantage over ORP, especially when

considering only high-quality studies, several important considerations warrant attention.

First, it is crucial to acknowledge the limitations inherent in the available literature. The relatively limited number of studies addressing this comparison suggests a need for caution in drawing definitive conclusions. Additionally, potential biases, such as industry funding or other conflicts of interest, may influence the outcomes and conclusions of these studies. Exploring these factors could provide valuable insights into the robustness and generalizability of the findings. Furthermore, the nuances of health care systems and resource allocation across different regions must be considered. While the observed cost effectiveness of HIC RARP compared with ORP may hold relevance in certain contexts, it is essential to recognize that health care delivery and financing mechanisms vary globally. Therefore, extrapolating these findings to settings with different socioeconomic profiles or health care infrastructures should be approached with caution. Moreover, the observed lack of statistical significance in some comparisons, particularly regarding the cost effectiveness of HIC RARP versus LRP, highlights the complexity of evaluating surgical interventions within the framework of CEA. Factors such as surgical skill, patient preferences, and long-term outcomes beyond the scope of the included studies may influence the economic value of these procedures.

In light of these considerations, our findings underscore the need for further research to elucidate the comparative cost effectiveness of different prostate cancer treatment modalities comprehensively. Future studies should aim to address existing gaps in the literature, including the incorporation of diverse patient populations, longer-term follow-up data, and rigorous assessment of potential biases.

Ultimately, decision-makers tasked with allocating health care resources should approach these findings with a critical lens, considering the broader context of available evidence, health care system characteristics, and patient-centered outcomes. By fostering a nuanced understanding of the economic implications of prostate cancer treatment options, policymakers can optimize resource allocation to maximize patient outcomes and health care system efficiency across diverse settings.

Our meta-analysis provides compelling evidence supporting the cost effectiveness of RARP compared with ORP and LRP, particularly in HICs. By integrating the findings from multiple studies and perspectives, we have advanced our understanding of the economic implications of surgical interventions for prostate cancer. Moving forward, continued research in this area is essential to inform evidence-based decision-making and optimize patient care in prostate cancer management.

5. Conclusions

To our understanding, this marks the inaugural systematic literature review and meta-analysis concerning the cost effectiveness of RAS, encompassing an assessment of recommended medical device attributes. Despite encountering diverse study methodologies leading to a lack of definitive cost-effectiveness outcomes in the literature, the prevailing

evidence suggests RARP to be both costlier and more effective than ORP and LRP across most studies, thereby establishing a foundation of support for its cost effectiveness. Notably, analyses with extended timeframes indicate a greater propensity for favorable cost-effectiveness outcomes with RARP. It is imperative that future CEAs for RARP delve deeper into the consideration of medical device features to enhance comprehension and ensure more accurate estimations of its economic value in comparison with alternative surgical and nonsurgical interventions.

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Acquisition of data: Bejrananda, Khaing, Veettil, Thongseiratch, Chaiyakunapruk.

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Data sharing: All data relevant to the study are included in the article or uploaded as online supplementary information.

Appendix A. Supplementary data

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