

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Robot-assisted surgery in a broader health care perspective: A difference-in-difference-based cost analysis of a national prostatectomy cohort
AUTHORS	Hyldgård, Vibe; Laursen, Karin; Poulsen, Johan; Søgaard, Rikke

VERSION 1 - REVIEW

REVIEWER	Humphreys, Mitchell Mayo Clinic USA
REVIEW RETURNED	04-Feb-2017

GENERAL COMMENTS	<p>This article aims to compare the difference in cost between robot assisted prostatectomy, laparoscopic prostatectomy and open prostatectomy while attempting to include cost of health care provided 12 months prior to surgery and 12 months after surgery using a national registry. Several studies have already demonstrated from a financial perspective that robot assisted prostatectomies have a higher cost than open prostatectomy when accounting for surgical procedure as well as hospitalization. A major flaw of this study lies in the design and the assumption that health care received 12 months before and 12 month after is related to prostate cancer. Furthermore, studies that compare the outcomes between robot assisted prostatectomies and open prostatectomies have demonstrated that robot assisted prostatectomies have equal if not better outcomes. The registry that the authors use to assess health care usage before and prior to surgery unfortunately do not detail the main indication for the visit. Furthermore, often times patients who just recently have surgery typically will follow-up with the surgeon/specialist, which was not accounted for as well as any referral and visits with oncologists. Thus, the paper does not add to our current understanding and body of literature.</p>
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REVIEWER	Charlotte Camp HCD Economics, United Kingdom
REVIEW RETURNED	08-Feb-2017

GENERAL COMMENTS	<p>There is an ongoing need for research regarding the economic value story for RARP. The cost effectiveness literature for RARP continues to be lacking in the absence of an RCT, but a thorough evaluation has been conducted in the UK (Ramsay et al., 2012) and in Denmark (Løvschall et al., 2015), among others. The question to which this paper should seek to contribute an answer is the extent to which RARP represents a cost-saving (or cost-effective) option in Denmark. This paper goes some way to evaluating the comparative</p>
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	<p>costs of patients at intervention and in the follow-up periods. In terms of the methodology, the analysis is presented clearly and the technique is robust. I am unsure, however, of the value of exploring the differential costs 12 months before and 12 months after intervention. I understand that this is to obtain average costs between the three patient cohorts prior to intervention, but the value of this method lies more in exploring cost trajectories for chronic conditions, where an intervention seeks to alleviate long-term symptoms – as opposed to a presumed ‘curative’ treatment such as RP. Analysing average costs before and after (as in Tables 2 and 3) are potentially interesting, but not overly useful or meaningful. No meaning can be drawn from their absolute values. Adjusting for the characteristics observed in the 12-month pre period within the regression would be equivalent.</p> <p>The paper is suitable for publication with some revisions:</p> <ul style="list-style-type: none"> • Please elaborate further on the Danish context. To what extent do the DRG tariffs represent the cost of treatment in Denmark? Does the differential cost of RARP presented in this paper represent a higher tariff or higher rates of complications? If it is the procedure itself, is there a dedicated tariff for RARP that incorporates the cost of surgical peripherals? Given that the cost of the intervention is the primary driver of higher costs in the full 12-month period, it would be useful to understand this cost further. • What can the authors say about complication rates at intervention - is there reason to suggest that costs may be recouped via reduced complications? This would impact upon QALY outcomes and hence cost-effectiveness. • What were the mean costs at intervention – in Tables 2 and 3, is the intervention resource use/cost incorporated into the ‘after’ period? It is difficult to tell. Can the ‘intervention’ period be split out? What proportion of the cost difference seen between RALP, OP, and LP is due to differences in costs incurred at the intervention versus later in the period? • Could we know the trend in procedure volume across the observation period? How many procedures are recorded in e.g. 2006? • In what way does this paper relate to the HTA conducted by the lead author (with others)? What does the author consider that this paper adds, that is not already covered within the HTA? • Please also discuss the ethics/consent process for accessing the relevant datasets <p>Further questions (that do not necessarily require consideration in the manuscript, but further information would be valuable):</p> <ul style="list-style-type: none"> • The differential costs shift around a lot in each of the years (Table 3) - is this due to changes in the tariff? • The authors have described that correction of the regression for centre volume proxies had no discernible effect. Given the level of discrepancy in costs across the years observed, might it be useful to conduct a sub-analysis of e.g. 2012-2014? • It would interesting to explore the reasons why LRP is cheaper than both ORP and RARP in the ‘After’ period – it would be expected that the intervention costs of LRP would sit midway between ORP
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REVIEWER	Lukas Hefermehl Kantonsspital Baden, Switzerland
REVIEW RETURNED	10-Apr-2017

GENERAL COMMENTS

The author present a cost analysis study, which is part of a prostatectomy company cohort in Denmark. It is based on the question whether or not health care costs are higher or lower for higher for robotic assisted radical prostatectomy (RALP) compared to open or lap. Prostatectomy.

The study covers an interesting topic in urology an public health. One of the interesting aspects of the study is that it's focus does not only covers the operation but the health care costs of 12 months prior an 12 months after surgery. They show that RALP is more expensive during the OR but no difference before and after.

However some parts of the manuscript require clarification.

Title: consider writing "prostatectomy cohort"
Abstract : results: definition of significant, give numbers .
Conclusion: to investigate on the "argument " was not mentioned in the objectives. Consider conclusion related to objective.
The conclusion is true for Denmark, maybe not applicable worldwide. Needs to be stated.

Limitations: another limitation is the lack of data on real cost for the hospital (operating time, disposables, nurse support postop, need for blood transfusions) on one hand and socioeconomic costs (duration of absence of work, pads etc).

It needs to be mentioned that DRG not represent real cost or real income of a hospital. Furthermore DRGs for the three mentioned types of surgery are different in Denmark but are equal in other countries using a DRG system.

Interesting finding in "supplementary material": the difference in DRGs between RALP an open RP has almost doubled between 2006 and 2013. This is very interesting and might be specific for Denmark. It needs clarification. Does it mean that the system strongly motivates hospitals to use robots?
It needs to be mentioned that DRG and "cost" are not the same, depending of n the perspective- DRG is a calculated artificial number. If the authors are looking at "a broad healthcare perspective ", the might consider a discussion of why DRG should be lowered (or augmented) compared to open RP (why is the DRG of open RP almost half of the DRG of RALP (2013: 8'000€ vs 14'000!) when hospitalisation is longer a the same time.

Page 15;12 abbreviation LRP is LP

Table 2 and 3. Define before and after
Why do the authors calculate "difference" instead of total .

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: M. Humphreys

Institution and Country: Mayo Clinic, USA

Competing Interests: None declared

This article aims to compare the difference in cost between robot assisted prostatectomy, laparoscopic prostatectomy and open prostatectomy while attempting to include cost of health care provided 12 months prior to surgery and 12 months after surgery using a national registry. Several studies have already demonstrated from a financial perspective that robot assisted prostatectomies have a higher cost than open prostatectomy when accounting for surgical procedure as well as hospitalization. A major flaw of this study lies in the design and the assumption that health care received 12 months before and 12 month after is related to prostate cancer. Furthermore, studies that compare the outcomes between robot assisted prostatectomies and open prostatectomies have demonstrated that robot assisted prostatectomies have equal if not better outcomes. The registry that the authors use to assess health care usage before and prior to surgery unfortunately do not detail the main indication for the visit. Furthermore, often times patients who just recently have surgery typically will follow-up with the surgeon/specialist, which was not accounted for as well as any referral and visits with oncologists. Thus, the paper does not add to our current understanding and body of literature.

“We agree that several studies on the financial perspective of the index admission have been published and generally show that robot-assisted surgery is more expensive than non-robot-assisted surgery. However, the motivation of the present study is to include also the costs of activity after this index admission (follow up with e.g. surgeon/specialist and oncologists, readmission, reoperation etc.), which could potentially alter the conclusion. If robot-assisted surgery leads to fewer/more of these events this will increase/decrease the total cost, which is the relevant cost measure for system- or hospital-level decision-making. This is actually the case as is now reported in a new sensitivity analysis in the Results section page 14 where we report that looking at the follow up period in isolation reflects a reduced service use of € 2032 compared with OP.

This also means that we do include the follow up with e.g. surgeon/specialist and oncologist in the analysis, which is thus – along with any related events occurring during the first 12 months post surgery – the contribution of this study to the literature.

The concern about inclusion of activity not related to prostate cancer might be related to unclear definition of the advantages of the difference-in-difference (DiD) design in the manuscript. The quasi-experimental DiD design is one of the strongest designs for isolating a causal effect (or cost) when patients haven't been randomised (see e.g. Dimik and Ryan 2014 [1]). In this context, it means that costs related to e.g. general comorbidity cancel out when we report the DiD estimate; the first difference compares with that of a before-after study and removes individual-person-level service use that is constant over time (e.g. chronic comorbidity) whereas the difference between groups removes secular trends (e.g. trends in handling prostate cancer or comorbidity). An additional precaution against selection bias we combine the DiD design with regression-based adjustment for a number of pretreatment characteristics such that e.g. comorbidity becomes balanced between the groups. This relaxes the main assumption of the DiD approach of parallel trends (that the groups would have shown the same trends if assigned to the same surgical technique) (Abadie 2005 [2]).

We have critically revised the text on page 3, 5, and 17 to clarify the implications of the analytical design.

We might add that an alternative to the chosen design could have been to restrict the analysis to activity in the national health care use registries based on e.g. ICD-diagnoses for cancer. We initially considered this alternative approach but realized that the results would then become sensitive to coding practice (it appeared that e.g. complications after prostatectomy were not always coded under a cancer diagnosis). Furthermore we would not be able to take full advantage of the DiD design, and we thus concluded that 'non-manipulated' inclusion of all activity would be the most transparent and robust methodological choice."

Reviewer: 2

Reviewer Name: Charlotte Camp

Institution and Country: HCD Economics, United Kingdom

Competing Interests: None declared

There is an ongoing need for research regarding the economic value story for RARP. The cost effectiveness literature for RARP continues to be lacking in the absence of an RCT, but a thorough evaluation has been conducted in the UK (Ramsay et al., 2012) and in Denmark (Løvschall et al., 2015), among others. The question to which this paper should seek to contribute an answer is the extent to which RARP represents a cost-saving (or cost-effective) option in Denmark. This paper goes some way to evaluating the comparative costs of patients at intervention and in the follow-up periods. In terms of the methodology, the analysis is presented clearly and the technique is robust. I am unsure, however, of the value of exploring the differential costs 12 months before and 12 months after intervention. I understand that this is to obtain average costs between the three patient cohorts prior to intervention, but the value of this method lies more in exploring cost trajectories for chronic conditions, where an intervention seeks to alleviate long-term symptoms – as opposed to a presumed 'curative' treatment such as RP. Analysing average costs before and after (as in Tables 2 and 3) are potentially interesting, but not overly useful or meaningful. No meaning can be drawn from their absolute values. Adjusting for the characteristics observed in the 12-month pre period within the regression would be equivalent.

The paper is suitable for publication with some revisions:

- Please elaborate further on the Danish context. To what extent do the DRG tariffs represent the cost of treatment in Denmark? Does the differential cost of RARP presented in this paper represent a higher tariff or higher rates of complications? If it is the procedure itself, is there a dedicated tariff for RARP that incorporates the cost of surgical peripherals? Given that the cost of the intervention is the primary driver of higher costs in the full 12-month period, it would be useful to understand this cost further.

"Thank you for the suggestion, we have inserted the following text in the methods section page 6.

The DRG tariffs for prostatectomy cover the activity from the day of admission to the day of discharge (preparation, surgery, remobilisation and discharge) whereas follow-up visits and other events after discharge, e.g. caused by complications, are therefore separately reimbursed. The specific tariffs for prostatectomy are shown in supplementary material Table S1. The higher tariff of the robot-assisted surgery (on average € 4525) thus refers to the rather expensive instrument kit required for each surgery, robot maintenance costs and longer operating time. The theoretical interpretation of the DRG tariff is an average long-term cost."

- What can the authors say about complication rates at intervention - is there reason to suggest that costs may be recouped via reduced complications? This would impact upon QALY outcomes and hence cost-effectiveness.

“We know from international clinical series (Løvschall et al. 2015 [3]) that robot-assisted surgery is associated with less blood loss, shorter admissions and fewer complications. This might lead to lower costs and, as the reviewer note, better quality of life. But as these events in many cases represent quite limited impact time the impact on QALY might be limited. This was also the conclusion of Løvschall et al. 2015 – as well as our rationale behind focusing then on the cost side, which appeared to be least informed part of the case. Indeed, the cost saving argument has been used by e.g. Danish decision-makers for investing in robots despite the lack of evidence.”

- What were the mean costs at intervention – in Tables 2 and 3, is the intervention resource use/cost incorporated into the ‘after’ period? It is difficult to tell. Can the ‘intervention’ period be split out? What proportion of the cost difference seen between RALP, OP, and LP is due to differences in costs incurred at the intervention versus later in the period?

“We have inserted an extra line in table S1 reporting an average difference of € 4525 for the index admission. We also report a new sensitivity analysis where the main model is rerun while excluding the tariff of the index admission. The sensitivity analysis shows that the overall RALP-attributable costs of 2459 for OP and 3860 for LP cover a reduced service use in the after period of € 2032 (95% CI 1287 – 2777) for OP and € 716 (95% CI -2879 – 4311) for LP, respectively. New text is inserted in the Results section page 14.

We understand the reviewer’s wish for splitting up in detailed periods representing e.g. diagnostics, admission, early follow up and longer-term follow up, which we have indeed tried. Unfortunately the patient pathways are structurally quite different and we run into the issue of judging whether differences are due to coding practice (diagnosis, timing and provider) or a real difference attributable to the technology. The non-split period of 12 months before/after provides a safety margin such that we avoid these issues.”

- Could we know the trend in procedure volume across the observation period? How many procedures are recorded in e.g. 2006?

“We have provided an additional table in the supplemental material (Table S2), which shows the annual volume for the comparators.”

- In what way does this paper relate to the HTA conducted by the lead author (with others)? What does the author consider that this paper adds, that is not already covered within the HTA?

“The present analysis uses the same material (all Danish patients over an 8-year period) but is restricted to departments where all surgical techniques and thus focused on the direct comparison between techniques. Furthermore this analysis extends from a description of the material and the total costs to apply a deeper and more sophisticated econometric design in order to estimate the attributable cost. It should also be noted that the HTA has not been internationally published (only a Danish report is available – with a 1.5 page length English summary).”

- Please also discuss the ethics/consent process for accessing the relevant datasets

“We have extended the text in the Ethics section such that it states that consent is not required for register-based studies according the Danish Ethical Committee system (page 8).”

Further questions (that do not necessarily require consideration in the manuscript, but further information would be valuable):

- The differential costs shift around a lot in each of the years (Table 3) - is this due to changes in the

tariff?

“The tariffs explain only a minor proportion of the variation over years (Table 4 versus Table S1). The large variation at the end of the period could also be related to dissemination of the technology to more inexperienced centers or to changes in thresholds for clinical indication but that remains speculation only, as evidence would have to be based on more details on the patients from e.g. a clinical database (which is not available for the Danish context).”

- The authors have described that correction of the regression for centre volume proxies had no discernible effect. Given the level of discrepancy in costs across the years observed, might it be useful to conduct a sub-analysis of e.g. 2012-2014?

“Thank you for this suggestion. We have conducted the requested analysis and reported it in the manuscript as a sensitivity analysis, which does not significantly alter the findings (the average attributable costs increases from €2459 to €3889 compared with OP and reduces from €3860 to €3359 compared with LP) (page 14).”

- It would be interesting to explore the reasons why LRP is cheaper than both ORP and RARP in the 'After' period – it would be expected that the intervention costs of LRP would sit midway between ORP

“We have now reported an additional sensitivity analysis where we have excluded the tariffs for the index admissions. This analysis confirms the mechanism implied by the reviewer's interest namely that LP sits midway between OP and RALP. We interpret this as comparable after-periods for LP and RALP whereas the after-period for OP is characterised by significantly more activity (€ 2332 (95% CI 1287 – 2777)) (page 14).”

Reviewer: 3

Reviewer Name: Lukas Hefermehl

Institution and Country: Kantonsspital Baden, Switzerland

Competing Interests: None

The author presents a cost analysis study, which is part of a prostatectomy cohort in Denmark. It is based on the question whether or not health care costs are higher or lower for higher or lower for robotic assisted radical prostatectomy (RALP) compared to open or lap. Prostatectomy.

The study covers an interesting topic in urology and public health. One of the interesting aspects of the study is that its focus does not only cover the operation but the health care costs of 12 months prior and 12 months after surgery.

They show that RALP is more expensive during the OR but no difference before and after.

However some parts of the manuscript require clarification.

Title: consider writing "prostatectomy cohort"

“Thank you. We have used your suggestion.”

Abstract : results: definition of significant, give numbers .

“We have inserted p-values in the results section.”

Conclusion: to investigate on the "argument " was not mentioned in the objectives. Consider conclusion related to objective.

The conclusion is true for Denmark, maybe not applicable worldwide. Needs to be stated.

"We have rephrased the first sentence of the conclusion: In this study from the Danish context, the use of RALP generates a factor 1.3 additional cost when compared with OP and a factor 1.6 additional cost when compared with LP, on average, based on 12 months follow-up."

Limitations: another limitation is the lack of data on real cost for the hospital (operating time, disposables, nurse support postop, need for blood transfusions) on one hand and socioeconomic costs (duration of absence of work, pads etc).

It needs to be mentioned that DRG not represent real cost or real income of a hospital. Furthermore DRGs for the three mentioned types of surgery are different in Denmark but are equal in other countries using a DRG system.

"We have clarified in the text what is included in the Danish DRG tariffs for prostatectomy on page 6. These are based on microcosting studies that are in principle repeated every second year and as such relatively valid in terms of reflecting a national average real cost. We acknowledge that the societal cost perspective is important but as we are to the best of our knowledge the first to even include the broader health care sector, we believe the societal perspective is a natural next step."

Interesting finding in "supplementary material": the difference in DRGs between RALP an open RP has almost doubled between 2006 and 2013. This is very interesting and might be specific for Denmark. It needs clarification. Does it mean that the system strongly motivates hospitals to use robots?

"The Danish Ministry for Health, who is responsible for the DRG tariffs, has traditionally been very cautious about tariffs not incentivizing the use of particular techniques, which is also why the tariffs are negotiated quite frequently. We believe that the tariffs reflect the true national average costs at the time they are agreed upon and we know that tariffs increase as new and inexperienced departments take up the technology (and e.g. require more man hours per procedure than experienced departments). We have extended Table S1 with an average tariff and a note explaining the variation over years."

It needs to be mentioned that DRG and "cost" are not the same, depending of n the perspective- DRG is a calculated artificial number. If the authors are looking at "a broad healthcare perspective ", the might consider a discussion of why DRG should be lowered (or augmented) compared to open RP (why is the DRG of open RP almost half of the DRG of RALP (2013: 8'000€ vs 14'000!) when hospitalisation is longer a the same time.

"This is due to the rather expensive instrument kit required for each surgery undertaken by robot-assistance, robot maintenance costs and longer operating time as explained in the new text on the DRG tariff page 6 E.g. the instrument kit alone corresponds to the cost of about 3 bed days, whereas the annual cost of maintenance costs for one robot corresponds to around 400 bed days."

Page 15;12 abbreviation LRP is LP

"Thank you. This has been corrected."

Table 2 and 3. Define before and after
Why do the authors calculate "difference" instead of total.

“Before and after has now been defined as table notes. In table 2 and 3 we do report the total cost for the before and the after period along with the difference between them. In table 4 (main results) we report the estimate that reply to our aim, namely the attributable cost.”

References

1. Dimick JB, Ryan AM. Methods for evaluating changes in health care policy: the difference-in-differences approach. JAMA. 2014;312:2401–2.
2. Abadie A. Semiparametric Difference-in-Differences Estimators. Rev. Econ. Stud. 2005;72:1–19.
3. CFK · Folkesundhed & Kvalitetsudvikling Region Midtjylland. Medicinsk teknologivurdering af robotassisteret kirurgi (HTA of robot-assisted surgery). Aarhus; 2015.

VERSION 2 – REVIEW

REVIEWER	Lukas Hefermehl Kantonsspital Baden, Switzerland
REVIEW RETURNED	01-Jun-2017

GENERAL COMMENTS	The authors have put a good effort in the revision of the new manuscript . They have correctly answered all questions an concerns.
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